



**The University of  
Nottingham**

Using primary care data to assess population-level estimates of maternal smoking and nicotine replacement therapy during pregnancy

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## **ABSTRACT**

**Background:** Smoking in pregnancy is the most significant preventable cause of poor health outcomes for women and their babies and, therefore, is a major public health concern. In the UK there is a wide range of interventions and support for pregnant women who want to quit. One of these is nicotine replacement therapy (NRT) which has been widely available for retail purchase and prescribing to pregnant women since 2005. However, measures of NRT prescribing in pregnant women are scarce. These measures are vital to assess its usefulness in smoking cessation during pregnancy at a population level. Furthermore, evidence of NRT safety in pregnancy for the mother and child's health so far is nebulous, with existing studies being small or using retrospectively reported exposures.

**Aims and Objectives:** The main aim of this work was to assess population-level estimates of maternal smoking and NRT prescribing in pregnancy and the safety of NRT for both the mother and the child in the UK. Currently, the only population-level data on UK maternal smoking are from repeated cross-sectional surveys or routinely collected maternity data during pregnancy or at delivery. These obtain information at one point in time, and there are no population-level data on NRT use available. As a novel approach, therefore, this thesis used the routinely collected primary care data that are currently available for approximately 6% of the UK population and provide longitudinal/prospectively recorded information throughout pregnancy. The specific objectives for this thesis were:

- To assess the quality of smoking data recorded during pregnancy in primary care
- To quantify annual NRT prescribing trends in and around pregnancy and describe the characteristics of mothers prescribed NRT

- To assess the association between NRT and smoking exposure during pregnancy and major congenital anomalies (MCAs), stillbirth, low birth weight and mode of delivery

**Methods:** All women aged 15-49 years, with pregnancies ending in live or stillbirth, were identified from The Health Improvement Network (THIN) primary care database (2000-2009). Medical Read codes related to smoking status and Multilex smoking cessation drug prescription codes were used to extract data on women's smoking status and NRT prescriptions. The proportion of pregnancies with a smoking status record was calculated and logistic regression was used to assess how this varied by women's characteristics. Women were categorised as being smokers or non-smokers during pregnancy based on the recorded Read codes. Where smoking data were missing during pregnancy, smoking status recorded before pregnancy (up to 27 months before pregnancy, ever before pregnancy) was used as a proxy for smoking status during pregnancy. Annual smoking measures from THIN were then compared to other national datasets. Pregnancies ending in early fetal losses were not included for calculating smoking prevalence, as these outcomes can go unrecognised or can be the first recognised sign of pregnancy, making early ascertainment of all pregnancies uncomprehensive; this was also broadly in line with pregnancy ascertainment in the other national datasets. Prescribing prevalence of NRT and patterns of prescribing in terms of frequency, timing and different form of NRT were assessed. Logistic regression was used to assess women's likelihood of receiving NRT prescriptions by maternal characteristics. Absolute and relative risks (99% Confidence Interval (CI)) for four birth outcomes (MCAs, stillbirth, low birth weight and mode of delivery) were calculated for women prescribed NRT (defined as the NRT group) and women who continued to smoke during pregnancy (defined as smokers) compared to women who did not smoke during pregnancy (defined as non-smokers) with appropriate adjustments for potential

confounders. To assess MCAs and birth weight in relation to NRT and smoking a restricted cohort of children was used who had maternal-child linked records in THIN.

**Results:** There were 277,552 pregnancies in 215,703 women, of which 28% had a gestational smoking status record. In 2000, smoking status was recorded in 9% of pregnancies; 43% in 2009. Smoking estimates from THIN data did not completely agree with estimates from other sources. For example, in 2009 smoking prevalence was 12.9% in THIN, compared to 19.5% in Child Health Systems Programme (CHSP) data. However, the use of smoking data recorded up to 27 months before conception increased the THIN prevalence to 22.9%, which was slightly higher, but compared better with the CHSP estimates.

NRT was prescribed in 4,826 pregnancies for an average duration of 2 weeks (Interquartile range 1-2 weeks), which represented 2% of all pregnancies (11% in smokers). NRT prescribing prevalence before and after pregnancy was half the prevalence during pregnancy. NRT prescribing increased with socioeconomic deprivation (Odds Ratio (OR) =1.33, 95% CI 1.14-1.52) for the most compared to the least deprived group). Prescribing was higher in pregnant smokers with asthma (OR=1.34, 95% CI 1.21-1.50) and mental illness (OR=1.29, 95% CI 1.18-1.43) compared to smokers without these diagnoses.

The absolute risk of MCA was 279/10,000 live births. Compared with non-smokers the adjusted OR for MCA in the NRT group was 1.34 (99% CI 0.94-1.91). No statistically significant increase in the risk of MCA for the NRT group was found when the reference group was changed to smokers (OR=1.35, 99% CI 0.94-1.93). The absolute risk of stillbirth was 4/1000 live and stillbirths. Compared with non-smokers the adjusted OR for stillbirth in the NRT group was 1.19 (99% CI 0.47-3.01). In smokers, the risk of stillbirth increased by 27% compared to non-smokers (OR 1.27, 99% CI 1.01-1.60). The mean birth weight



was 3.41kg (standard deviation 0.59) and the absolute risk of low birth weight was 6.4%. Compared to non-smokers, the risk of women having low birth weight babies was 93% higher in the NRT group (OR 1.93, 99% CI 1.48-2.53). However, there was no statistically significant increase in the risk of low birth weight in the NRT group compared with smokers. There was no increased risk of assisted delivery or caesarean section in the NRT group compared to smokers. However the risk of assisted delivery decreased by 25% in the NRT group (Relative Risk Ratio 0.75, 99% CI 0.60-0.93) compared to non-smokers.

**Conclusion:** The completeness of smoking status recording during pregnancy in primary care data is improving; however, under-recording of smoking status during pregnancy still results in unreliable estimates of the prevalence of smoking in pregnancy and needs improvement. Pre-conception smoking records are reasonably complete and it is possible that low recording in pregnancy is because a woman's smoking status has not changed or that increased interaction with other health services, such as midwifery, during pregnancy means women are less likely to be asked about their smoking by their primary physician and information on their smoking does not get relayed back to their primary care record. Nevertheless records should be updated in pregnancy to ensure comprehensive health care. NRT was most commonly prescribed in pregnancy for about two weeks, which may not be adequate time for effective smoking cessation. Nevertheless, prescribing was higher during pregnancy compared to the nine months before and after pregnancy, which makes establishing its safety during pregnancy even more crucial. The safety studies in this thesis did not find NRT to be any more harmful than smoking during pregnancy if not beneficial. Considering that smoking in pregnancy remains one of the largest public health problems in the UK, improvements of antenatal and postnatal smoking in primary care may not only help identify women for

preventive measures earlier but would be invaluable for safety studies considering the outcomes are rare yet severe.

## **PUBLICATIONS AND CONFERENCE PRESENTATIONS**

### **PUBLICATIONS FROM THESIS WORK**

Dhalwani NN, Tata LJ, Coleman T, Fleming KM, Szatkowski L. Completeness of maternal smoking status recording during pregnancy in United Kingdom primary care data. *PLoS ONE*. 2013; 8(9):e72218.

Dhalwani NN, Szatkowski L, Coleman T, Fiaschi L, Tata LJ. Prescribing of nicotine replacement therapy in and around pregnancy: a population-based study using primary care data. *British Journal of General Practice*. 2014; 64(626): e554-e560

Dhalwani NN, Tata LJ, Coleman T, Fiaschi L, Szatkowski L. A comparison of United Kingdom primary care data with other national data sources for monitoring the prevalence of smoking during pregnancy. *Journal of Public Health*. 2014; doi: 10.1093/pubmed/fdu060

Dhalwani NN, Szatkowski L, Coleman T, Fiaschi L, Tata LJ. Nicotine replacement therapy in pregnancy and major congenital anomalies in offspring. *Pediatrics* Revision in process

### **OTHER RELATED PUBLICATIONS**

Hardy B, Szatkowski L, Tata LJ, Coleman T, Dhalwani NN. Smoking cessation advice recorded during pregnancy in United Kingdom primary care. *BMC Family Practice*. 2014; 15(1), 21.

## **CONFERENCE PRESENTATIONS**

Dhalwani NN, Szatkowski L, Coleman T, Fiaschi L, Tata LJ. Maternal smoking, nicotine replacement therapy in pregnancy and stillbirth: A population-based study using the United Kingdom primary care data. 20<sup>th</sup> IEA World Congress of Epidemiology, Alaska, USA, 17<sup>th</sup>-21<sup>st</sup> August (Oral presentation)

Dhalwani NN, Szatkowski L, Coleman T, Fiaschi L, Tata LJ. Maternal smoking, nicotine replacement therapy in pregnancy and congenital malformations in offspring: A population-based study using the United Kingdom primary care data. 20<sup>th</sup> IEA World Congress of Epidemiology, Alaska, USA, 17<sup>th</sup>-21<sup>st</sup> August (Oral presentation)

Dhalwani NN, Szatkowski L, Coleman T, Fiaschi L, Tata LJ. Nicotine replacement therapy in pregnancy and stillbirth: A population-based study using the United Kingdom primary care data. 38<sup>th</sup> Annual Meeting of the MacDonald Obstetric Medicine Society, Nottingham, UK, 25<sup>th</sup> April 2014 (Oral presentation)

Dhalwani NN, Tata LJ, Coleman T, Szatkowski, L. Prescribing of NRT in and around pregnancy- A Population based study using primary care data. Annual Scientific Meeting of the Society for Academic Primary Care, Nottingham, UK, 3<sup>rd</sup>- 5<sup>th</sup> July 2013 (Oral presentation)

Dhalwani NN, Tata LJ, Coleman T, Szatkowski, L. Prescribing of NRT in and around pregnancy- A Population based study using primary care data. Annual Scientific Meeting of the Society of Social Medicine, Brighton, UK, 11<sup>th</sup> -13<sup>th</sup> September 2013 (Oral presentation)

Dhalwani NN, Tata LJ, Coleman T, Fiaschi L, Szatkowski L. Can primary care data be used to monitor the prevalence of current smoking during pregnancy? A

comparison with other national datasources. European Congress of Epidemiology 2013, Aarhus, Denmark 11<sup>th</sup>-14<sup>th</sup> August 2013 (Poster presentation)

Dhalwani NN, Tata LJ, Coleman T, Szatkowski, L. Prescribing of NRT in and around pregnancy- A Population based study using primary care data. European Congress of Epidemiology 2013, Aarhus, Denmark 11<sup>th</sup>-14<sup>th</sup> August 2013 (Poster presentation)

Dhalwani NN, Tata LJ, Coleman T, Szatkowski, L. Prescribing of NRT in and around pregnancy- A Population based study using primary care data. Annual Scientific Meeting of the Society for Academic Primary Care, Nottingham, UK, 3<sup>rd</sup>- 5<sup>th</sup> July 2013 (Oral presentation)

Dhalwani NN, Tata LJ, Coleman T, Szatkowski L. Prescribing of NRT in and around pregnancy – A population based study using primary care data. Tackling Smoking in 21<sup>st</sup> Century Britain, York, UK, 7<sup>th</sup> November – 9<sup>th</sup> November 2012 (Poster presentation)

Dhalwani NN, Tata LJ, Coleman T, Szatkowski L. Prescribing of NRT in and around pregnancy – A population based study using primary care data. 14<sup>th</sup> Annual Meeting of the Society for Research on Nicotine and Tobacco, Helsinki, Finland, 30<sup>th</sup> August-2<sup>nd</sup> September 2012 (Poster-oral presentation)

Dhalwani NN. Using primary care data to explore women's smoking behaviour and their use of smoking cessation therapies in and around pregnancy.

Undertaking a PhD in substance misuse: a one-day national symposium – Society for Study of Addiction, Oxford, UK, 9<sup>th</sup> July 2012 (Oral presentation)

Dhalwani NN. Use of Nicotine Replacement Therapy in pregnancy women and the association between maternal NRT use and adverse foetal outcomes. UK Centre for Tobacco Control Research Postgraduate Conference, Bath, UK 21<sup>st</sup> - 22<sup>nd</sup> November 2011 (Oral presentation)

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## **LIST OF ABBREVIATIONS**

AHD	Additional Health Data
AIS	Additional Information Services
BMI	Body Mass Index
BNF	British National Formulary
BP	Blood Pressure
CAs	Congenital Anomalies
CBT	Cognitive Behavioural Therapy
CDC	Center for Disease Control
CHSP-PS/CHSP	Child Health Systems Programme (Pre-school component)
CI	Confidence Interval
CNS	Central Nervous System
CO	Carbon monoxide
COPD	Chronic Obstructive Pulmonary Disease
CPRD	Clinical Practice Research Data link
CSD	Cegedim Strategic Data
DNBC	Danish National Birth Cohort
e-PACT	Electronic Prescribing Analysis and Cost Tool
EPIC	Epidemiology and Pharmacology Information Core
ePROs	electronic Patient-Reported Outcomes
EUROCAT	European Surveillance of Congenital Anomaly
FDC	Full Data Collection
GLF	General Lifestyle Survey
GP	General practitioner
GPRD	General Practice Research Database
HEA	Health Education Authority
HES	Hospital Episodes Statistics



HR	Hazard Ratio
HSE	Health Survey for England
ICD	International Classification of Diseases
IFS	Infant Feeding Survey
IHS	Integrated Household Survey
InPS	InPractice Systems
LRT	Likelihood Ratio Test
MHRA	Medicines and Healthcare products Regulatory Authority
MREC	Multi-centre Research Ethics Committee
MRI	Magnetic Resonance Imaging
NBDPS	National Birth Defects Prevention Study
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NICU	Neonatal Intensive Care Unit
NRT	Nicotine Replacement Therapy
ONS	Office for National Statistics
OR	Odds Ratio
OTC	Over the counter
PAH-SYMPACT	Pulmonary Artery Hypertension Symptoms and Impact
PASS	Power Analysis & Sample Size Software
PHR	Public Health Research Consortium
PPROM	Pre-term premature rupture of membranes
PRAMS	Pregnancy Risk Assessment Monitoring System
QOF	Quality and Outcomes Framework
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RR	Relative Risk/Risk Ratio
RRR	Relative Risk Ratio

SATOD	Smoking at the Time of Delivery
sd	Standard Deviation
SHS	Second hand smoke
SIDS	Sudden Infant Death Syndrome
SMR	Scottish Morbidity Record
SNAP	Smoking Nicotine and Pregnancy Trial
SSS	Stop Smoking Services
SSSP	Stop Smoking Services for Pregnant women
STS	Smoking Toolkit Study
THIN	The Health Improvement Network
TIA	Transient Ischaemic Attack
UK	United Kingdom
USA	United States of America
VAMP	Value Added Medical Products
WHO	World Health Organisation

# **1 INTRODUCTION**

## **1.1 HEALTH EFFECTS**

Smoking in pregnancy is the most significant preventable cause of poor health outcomes for women and their babies.<sup>1,2</sup> Approximately one-third of all perinatal deaths in the United Kingdom (UK) are attributable to smoking.<sup>3</sup> In the United States of America (USA) maternal smoking in pregnancy increases infant mortality by 40% and approximately 5% of infant deaths in the USA have been attributable to maternal smoking.<sup>4</sup> It not only affects perinatal outcomes adversely but has also been related to problems in later childhood as discussed below.

### **1.1.1 Obstetric and perinatal complications**

Maternal smoking during pregnancy causes a myriad of obstetric and perinatal complications. Some of the most important complications are discussed below.

#### *1.1.1.1 Placental complications*

Smoking during pregnancy reduces blood flow to the uteroplacental fetal unit and results in higher frequency of placental abruption.<sup>5</sup> Additionally, it has been linked to placental enlargements and increased placental weight consequently increasing the risk of placenta previa.<sup>6</sup> A meta-analysis of 13 published studies presented a pooled odds ratio (OR) of 1.90 (95% Confidence Interval (CI) 1.8-2.0) for placental abruption associated with maternal smoking.<sup>7</sup> Furthermore, data from the Swedish Medical Birth Registry including about 2 million births reported 53% greater risk of placenta previa in smokers compared to non-smokers in a dose-dependent manner.<sup>8</sup> Cigarette smoking during pregnancy is

also an independent risk factor for pre-term premature rupture of membranes (PPROM)<sup>9</sup> with a 70% increase in the risk (OR 1.70, 95% CI 1.18-2.25).<sup>10</sup>

#### *1.1.1.2 Low birth weight*

In developed countries, maternal smoking is one of the major risk factors for low birth weight (a birth weight of less than 2500g<sup>11</sup>).<sup>12</sup> A proposed mechanism behind this is the reduced uterine blood flow and fetal hypoxia caused by smoking.<sup>13,14</sup> A study including 5,166 live births occurring in Pelotas, Brazil found an increased risk of low birth weight associated with maternal smoking during pregnancy (OR 1.45, 95% CI 1.30-1.95).<sup>15</sup> A case-control study from Boston based on 207 cases of low birth weight and 534 controls found the risk of having low birth weight babies to be twice as high in smokers compared to non-smokers (OR 2.1, 95% CI 1.2-3.7).<sup>16</sup> Similar effect estimates were found in another study based on 6,284 singleton live births in Switzerland.<sup>17</sup> Another cohort study from the UK using the Millenium Cohort data found similar risk of low birth weight associated with maternal smoking during pregnancy (OR 1.92, 95% CI 1.60-2.29)<sup>18</sup> More recent data from Johannesburg and Soweto report that the birth weight of infants with smoking mothers was 165g less than of infants with non-smoking mothers.<sup>19</sup> Even more recent data from Sweden suggest a dose response relationship between maternal smoking and low birth weight such that for light smokers (1-9 cigarettes per day) the birth weight of infants reduced by 162g and for heavy smokers (> 9 cigarettes per day) birth weight reduced by 226g compared to non-smokers.<sup>20</sup>

#### *1.1.1.3 Preterm birth*

In the 2010 report on global, regional and national causes of child mortality 35% of neonatal deaths were attributable to preterm birth,<sup>21</sup> making it one of the most important contributors to infant deaths worldwide.<sup>22</sup> Cigarette smoking during pregnancy is one of the few modifiable risk factors for preterm birth.<sup>23</sup> A

systematic review of 20 prospective studies on maternal cigarette smoking and preterm birth reported 27% increased risk of preterm birth associated with gestational cigarette smoking.<sup>24</sup> A more recent case-control study from Italy based on 299 cases of preterm birth found that the adjusted ORs were 1.54 and 1.69 for preterm babies and 1.90 and 2.46 for early preterm babies for 1–10 and more than 10 cigarettes/day respectively.<sup>25</sup> Another case-control study from 10 European countries found that the odds of preterm birth increased by 40% in smoking mothers (OR 1.39, 95% CI 1.20-1.60).<sup>26</sup>

#### *1.1.1.4 Ectopic pregnancy*

Ectopic pregnancy results when the fertilised egg is implanted outside the uterus.<sup>10</sup> A meta-analysis of nine studies assessing adverse pregnancy outcomes in relation to maternal smoking reported a pooled OR of 1.77 (95% CI 1.31-1.22) for ectopic pregnancy among smokers.<sup>10</sup> A more recent case-control study from France including 803 cases of ectopic pregnancy and 1,633 deliveries found a dose response relationship with quadrupling risk in women smoking  $\geq 20$  cigarettes per day compared to non-smokers.<sup>27</sup>

#### *1.1.1.5 Birth defects/ congenital anomalies*

Literature suggests an association between maternal smoking in pregnancy and several major congenital anomalies (MCAs). A systematic review based on 173,687 congenital anomaly cases and 11.7 million controls demonstrated an increased risk of heart defects (OR 1.09, 95% CI 1.02-1.17), musculoskeletal defects (OR 1.16, 95% CI 1.05-1.27), limb defects (OR 1.26, 95% CI 1.03-1.73), orofacial clefts (OR 1.28, 95% CI 1.20-1.36), gastrointestinal defects (OR 1.27, 95% CI 1.18-1.36) and other defects associated with maternal smoking but no increase in the risk of all major anomalies combined (OR 1.01, 95% CI 0.96-1.07).<sup>28</sup>

#### *1.1.1.6 Stillbirth and miscarriage*

Cigarette smoking during pregnancy is known to cause fetal growth restriction leading to stillbirth. A recent meta-analysis of four studies found a 36% increased risk of stillbirth (OR 1.36, 95% CI 1.27-1.46).<sup>29</sup> Another meta-analysis of 25 observational studies reported the risk of miscarriage to be 32% higher in women who smoke during pregnancy compared to non-smokers (pooled O 1.32, 95% CI 1.21-1.44).<sup>30</sup>

#### *1.1.1.7 Caesarean section*

Evidence of the relationship between maternal smoking and mode of delivery is inconclusive to date. A cross-sectional analysis of 170,254 pregnancies delivered in Schleswig-Holstein, Germany between 1991 and 1997 reported no statistically significant difference in caesarean delivery between non-smokers and smokers.<sup>31</sup> However, a recent study conducted in Israel, including approximately 6000 pregnancies reported the risk of any operative or instrumental intervention to be higher in smokers compared to non-smokers OR 1.24 (95% CI 1.01–1.52).<sup>32</sup>

#### *1.1.1.8 Sudden infant death syndrome (SIDS)*

Published data support a dose-response relationship between maternal smoking during pregnancy and SIDS. A systematic review of 31 studies on maternal smoking and SIDS reported a twofold increase in the risk of SIDS associated with maternal smoking (OR 2.06, 95% CI 1.83-2.38).<sup>33</sup> Additionally, smoking in the postpartum period was also found to double the risk of SIDS (pooled OR 1.94, 95% CI 1.55-2.34). More recent data from another meta-analysis of 35 case-control studies reported similar risks for smoking during pregnancy (OR 2.25, 95% CI 2.03-2.50) and in the postpartum period (OR 1.97, 95% CI 1.77-2.19).<sup>34</sup> The effects of cigarette smoking on cardiovascular and respiratory systems are said to play a key role in predisposition to SIDS in infants.<sup>13</sup>

### **1.1.2 Problems in early childhood and adolescence**

Maternal smoking in pregnancy has also been linked to several problems for a child's health in early childhood and adolescence. These problems are further aggravated by second hand smoke (SHS) exposure if the mothers continue to smoke or relapse after delivery. Some of these problems are discussed below.

#### *1.1.2.1 Respiratory problems*

Smoking during pregnancy has been shown to reduce lung function in children. A cohort study including 58,841 births in Finland reported 35% greater risk of asthma in children under the age of seven whose mothers smoked more than 10 cigarettes per day during pregnancy (OR 1.35, 95% CI 1.13-1.62) and 23% increased risk in children whose mothers smoked less than 10 cigarettes per day (OR 1.23, 95% CI 1.07-1.42) compared to children of non-smoking mothers.<sup>35</sup> A meta-analysis of 79 observational studies assessing the association between prenatal and passive smoke exposure on asthma and wheezing found that maternal smoking during pregnancy increased the risk of asthma by 85% (pooled OR 1.85, 95% CI 1.35-2.53) and the risk of wheezing by 41% (OR 1.41, 95% CI 1.19-1.67) in children  $\leq 2$  years. Exposure to postnatal maternal smoking was also associated with a 70% increased risk of wheezing in children  $\leq 2$  years (OR 1.70, 95% CI 1.24-2.35) and a 21% increase in the risk of asthma (Hazard Ratio (HR) 1.21, 95% CI 1.01-1.45).<sup>36</sup>

#### *1.1.2.2 Cancer (Leukaemia, Central nervous system tumours, lymphomas)*

Leukaemia, central nervous system (CNS) tumours and lymphomas account for more than two-thirds of all cancers diagnosed in children.<sup>37</sup> A meta-analysis of 30 studies on the association between maternal tobacco use during pregnancy and childhood cancer suggested a 10% increase (OR 1.10, 95% CI 1.03-1.19) in all cancers however no significant associations were found for leukaemia and CNS tumours.<sup>38</sup> A more recent meta-analysis including a total of 6,566 patients

from 12 observational studies also did not show a clear association between maternal smoking during pregnancy and development of brain tumours in children (Risk Ratio (RR) 1.05, 95% CI 0.90-1.21).<sup>39</sup> However, another meta-analysis exploring the association between childhood lymphoma and smoking during pregnancy found a 22% increase in the risk of non-Hodgkin lymphoma associated with maternal smoking during pregnancy (OR 1.22, 95% CI 1.03-1.45, n=7 studies).<sup>40</sup>

#### *1.1.2.3 Obesity/ Overweight*

Childhood obesity has become a health concern in many countries including the UK and the US.<sup>41</sup> Women who smoke during pregnancy are more likely to have babies with low birth weight. These infants often show greater 'catch-up' growth resulting in childhood obesity.<sup>42</sup> A meta-analysis of 17 observational studies found that babies of mothers who smoked during pregnancy were 64% more likely to develop childhood obesity compared to babies of non-smokers.<sup>43</sup>

#### *1.1.2.4 Ear infections*

A prospective study including 8,556 pregnant women and their babies found the prevalence of otitis media to be higher in children of mothers who smoked during pregnancy such that children of mothers who smoked 1-9 cigarettes during pregnancy were 60% more likely to develop acute ear infection in the first five years of life compared to children of non-smoking mothers. In comparison, odds ratio for developing acute ear infection is reported to be 2.6 (95% CI 1.6-4.2) and 3.3 (95% CI 1.9-5.9) in children of mothers who smoked 10-19 and more than 20 cigarettes during pregnancy respectively.<sup>44</sup> Maternal smoking after pregnancy has also been shown to increase the risk of middle ear infections in children by 62% (OR 1.62, 95% CI 1.33-1.97) in a meta-analysis of 20 studies.<sup>45</sup>



#### *1.1.2.5 Cognitive and behavioural problems*

Prenatal smoking exposure in children has been associated with reduced cognitive abilities and academic achievements.<sup>46</sup> A Swedish study on over 375,000 adolescents found that children whose mothers smoked during pregnancy had an increased risk of poor school performance after controlling for maternal and birth characteristics (1-9 cigarettes per day OR 1.59, 95% CI 1.55-1.63,  $\geq 10$  cigarettes per day OR 1.92, 95% 1.86-1.98).<sup>47</sup> A systematic review of studies conducted over a 30 year period between 1973 and 2002 demonstrated a link between smoking during pregnancy and attention deficit hyperactivity disorder (ADHD) in children.<sup>48</sup> The odds of developing antisocial behaviour in children with prenatal smoking exposure are shown to be 1.5-4 times greater than unexposed children.<sup>49</sup> Furthermore, children with prenatal tobacco exposure have also shown to have 30-40% higher risk of psychiatric hospitalisations for substance abuse.<sup>50</sup>

#### *1.1.2.6 Diabetes*

The British National Child Development Study examined the association between maternal smoking during pregnancy and the risk of diabetes in children and found that the risk of type 2 diabetes in children increased by 11% (OR 1.11, 95% CI 0.31-4.04) for light smokers and quadrupled for heavy smokers (OR 4.55, 95% CI 1.82-11.36).<sup>51</sup>

### **1.2 ECONOMIC BURDEN**

Smoking during pregnancy also imposes a substantial economic burden on society. A report by the Public Health Research Consortium (PHR) in 2010 suggested that costs to the UK National Health Services (NHS) related to maternal outcomes associated with smoking are estimated to be between £8 million and £64 million per year based on different costing methodologies.<sup>52</sup>

Furthermore, costs related to infants' increased risk of preterm delivery, low birth weight, SIDS, perinatal mortality, asthma, otitis media, and upper and lower respiratory infections are estimated to be between £12 million and £23.5 million per year.<sup>52</sup> A study conducted by Petrou and colleagues (2005) in the UK looking at the association between maternal smoking and hospital inpatient costs in childhood found that after adjusting for clinical and socio-demographic factors, the mean cost difference when comparing infants born to women who smoked at least 20 cigarettes per day to infants of non-smoking mothers was £462, over the first five years of life. When infants born to women smoking 10-19 cigarettes per day were compared to infants of non-smoking mothers this difference was £307.<sup>53</sup>

### **1.3 SMOKING IN PREGNANCY – CURRENT PREVALENCE**

#### **1.3.1 International picture**

Smoking in pregnancy has become a global public health issue, especially in developed countries. Despite the harms associated with maternal smoking during pregnancy the prevalence of smoking during pregnancy across developed countries still remains high with the prevalence ranging between 10-15% in USA, Canada, Australia and Japan.<sup>54-57</sup> Within Europe, the prevalence figures vary from low figures of <5% in Lithuania and Sweden to as high as 17% in France.<sup>58</sup>

#### **1.3.2 National prevalence and trends over time in the UK**

##### *1.3.2.1 Trends over time*

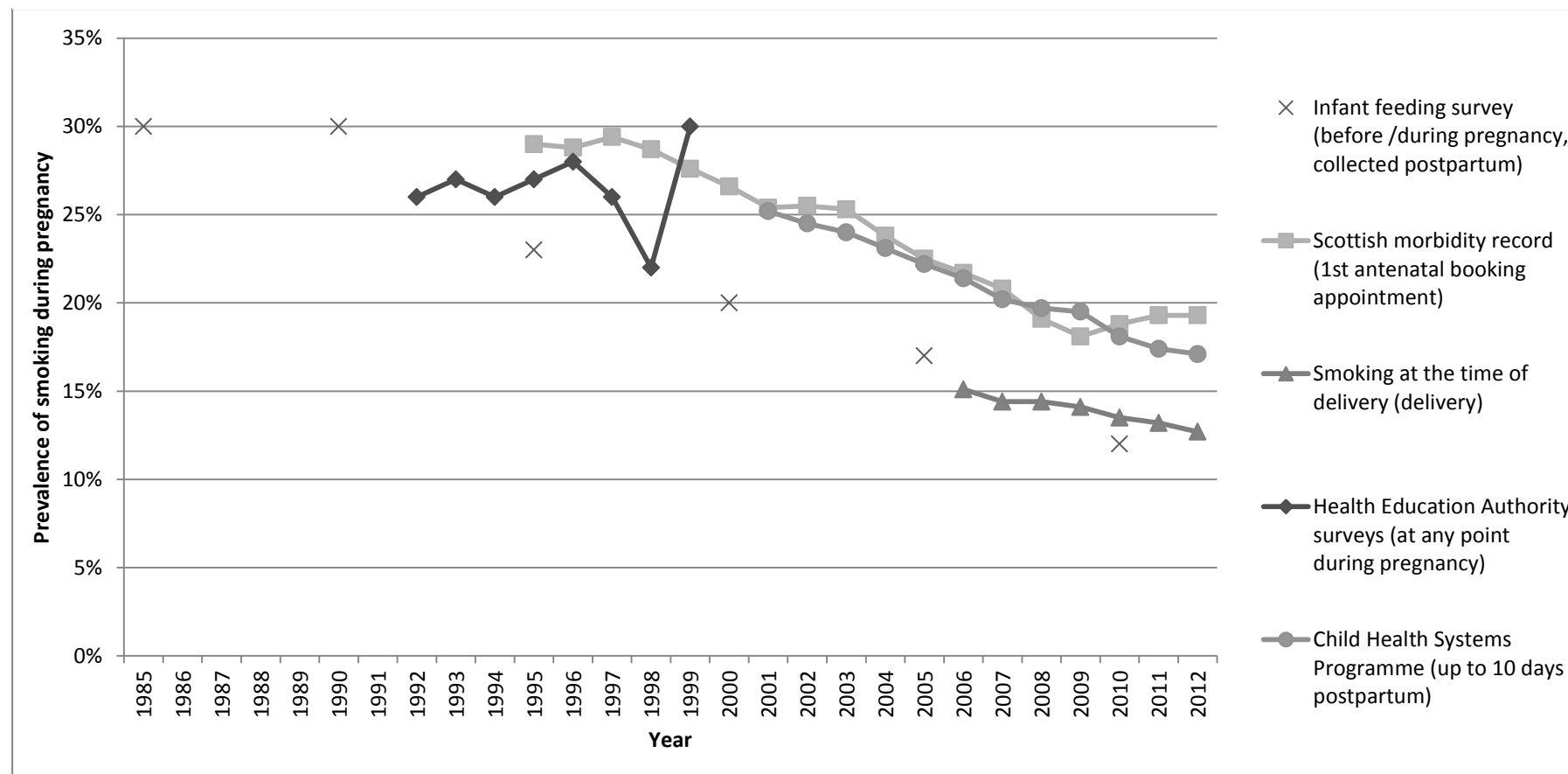
There are four sources in the UK which collect data on smoking in pregnancy. Some of these cover all pregnancies whilst others collect data on a sample of women to capture self-reported smoking status at one or more time points during pregnancy. The Infant Feeding Survey (IFS) 2010, which randomly samples births in the UK every 5 years and measures smoking at delivery

retrospectively at six to eight weeks postpartum in the UK showed that 26% of women smoked before or during pregnancy and 12% smoked throughout pregnancy.<sup>59</sup> The Smoking at the Time of Delivery (SATOD) data, is collected in maternity wards by midwives and measure smoking behaviour at the time of delivery in England, reported 12.6% women to be smoking at the time of delivery in England in 2012.<sup>60</sup> Data from the Scottish Morbidity Records (SMR) collected in antenatal clinics, which measure smoking at the time of first antenatal appointment report slightly higher prevalence compared to the other two data sources (19.3%).<sup>61</sup> The Child Health System Programme Pre-School component (CHSP-PS) data collected by health visitors approximately 10 days postpartum from Scotland report similar prevalence of maternal smoking during pregnancy (17.1%) in 2012.<sup>61</sup>

Figure 1-1 summarises the trends in smoking prevalence during pregnancy in the UK from 1985 to 2012 from the available data sources and the time at which smoking status was assessed in each of these data. Overall there has been a reduction in smoking prevalence during pregnancy in the past two decades and all the data sources reflect a downward trend in maternal smoking during pregnancy. The earliest measures of smoking during pregnancy are obtained from the IFS. According to the IFS, 39% of women smoked before pregnancy and 30% smoked during pregnancy in 1985<sup>62</sup> which has now reduced by over 50% with about 12% women smoking throughout pregnancy.<sup>59</sup> In addition to these routinely collected data and the IFS, the Health Education Authority (HEA), now part of the National Institute for Health and Clinical Excellence (NICE), also conducted a series of small surveys between 1992 and 1999 and found that the prevalence of smoking in pregnancy reduced from 26% in 1992 to 22% in 1998 but then peaked at 30% in 1999 with small fluctuations in the prevalence during the entire seven year period. A potential explanation for this paradoxically high prevalence in 1999 and fluctuations in the prevalence could be the sampling

method for the survey. Women were selected using quota sampling as opposed to probability sampling and also the sample sizes for each of these surveys only ranged from 625-1100 pregnant women,<sup>63,64</sup> which makes the findings less generalisable.

**Figure 1-1- Trends in maternal smoking during pregnancy from available data**



#### *1.3.2.2 Smoking and socio-demographic characteristics*

Maternal smoking prevalence during pregnancy varies by age. According to the IFS 2010 35% of pregnant women in the younger age group (< 20 years) smoked throughout pregnancy compared to 9% of pregnant women in the older age group (> 35 years). Results from SMR data also indicate a similar trend where the prevalence of current smoking in pregnant women younger than 20 years was 38.2% compared to 12.8% in pregnant women over 40 years in 2010.

There is also a marked social gradient in the prevalence of smoking during pregnancy. Data from IFS 2010 showed that 4% of pregnant women in the managerial/ professional group smoked throughout pregnancy in comparison to 20% of pregnant women in the routine/manual group.<sup>59</sup>

### **1.4 SMOKING CESSATION DURING PREGNANCY**

#### **1.4.1 Benefits of smoking cessation during pregnancy**

McBride and colleagues suggest that pregnancy may be a teachable moment for smoking cessation where there is an increased perception of risk which prompts strong emotional responses and triggers cessation.<sup>65</sup> Therefore, a higher proportion of women stop smoking during pregnancy than at other times in their lives.<sup>65</sup> Smoking cessation during pregnancy is associated with reductions in various maternal and fetal complications in addition to the general health benefits. A prospective cohort study conducted in New Zealand and Australia on 2,504 pregnant women suggested that women who stopped smoking before 15 weeks of gestation had similar rates of spontaneous preterm birth and small for gestational age infants as those in non-smokers, indicating that these adverse outcomes can be reduced by quitting early in pregnancy.<sup>66</sup> Another study from Sweden using the Swedish Birth Register concluded that stopping smoking

between the first prenatal care visit and the 32<sup>nd</sup> week of gestation prevented smoking-associated deficits in birth weight, head circumference and brain-to-body weight ratio.<sup>67</sup> These findings are supported by another study from Taiwan using the Pregnancy Risk Assessment Monitoring System (PRAMS) data which found that the babies of mothers who quit smoking during the first trimester weighed 168 g more than the babies born to smokers and there was no difference in birth weight between babies born to women who quit and never smokers (p-value 0.63).<sup>68</sup> A Cochrane review has shown that smoking cessation interventions reduce low birth weight by 17% (RR 0.83, 95% CI 0.73-0.95, n=16 studies) and preterm birth by 14% (RR 0.86, 95% CI 0.74-0.98, n=14 studies).<sup>69</sup> A study based on a USA 1995 birth cohort reported that using smoking cessation interventions to reduce maternal smoking during pregnancy would prevent 108 cases of SIDS annually, which equated to 3.5% of overall SIDS deaths in the USA.<sup>70</sup>

Apart from these health benefits smoking cessation during pregnancy may also generate financial benefits for the NHS. It is estimated that spending between £13.60 and £37 on smoking cessation interventions per pregnant smoker would yield positive cost savings for the NHS.<sup>52</sup> A study conducted in the USA on 227 pregnant smokers found that for every \$1 spent on smoking cessation for pregnant women, as estimated \$3 in neonatal intensive care costs can be saved.<sup>71</sup> Another American based study found that an annual drop of a single percentage point in maternal smoking prevalence during pregnancy would prevent 1300 low birth weight live births and save \$21 million in direct medical costs.<sup>72</sup>

#### **1.4.2 Smoking cessation interventions for pregnant women**

Given the harms of maternal smoking during pregnancy and benefits of cessation, the World Health Organization (WHO) recently produced guidelines for

the prevention and management of tobacco use and second-hand smoke exposure during pregnancy. These guidelines recommend all healthcare providers to ask pregnant women about their tobacco use as early as possible in the pregnancy and at every antenatal care visit and to offer advice and psychosocial interventions for tobacco cessation to all pregnant women who are smokers or recent quitters.<sup>73</sup> No recommendations were made on the use of nicotine replacement therapy (NRT) during pregnancy due to the lack of evidence of the safety, efficacy and adherence to the treatments (see Section 1.5 for further details). Other drugs that are licensed as smoking cessation aids for the general population (bupropion and varenicline) are not currently recommended for use during pregnancy. Table 1-1 summarises the different psychosocial interventions currently used/evaluated for smoking cessation in pregnant women and the evidence for effectiveness of each intervention. Currently financial incentivisation, counselling and self-help are shown to be effective for smoking cessation during pregnancy. There is mixed evidence on the effectiveness of other psychological interventions in pregnancy such as feedback and social support.



**Table 1-1 – Psychosocial interventions for smoking cessation in pregnant women and evidence for effectiveness**

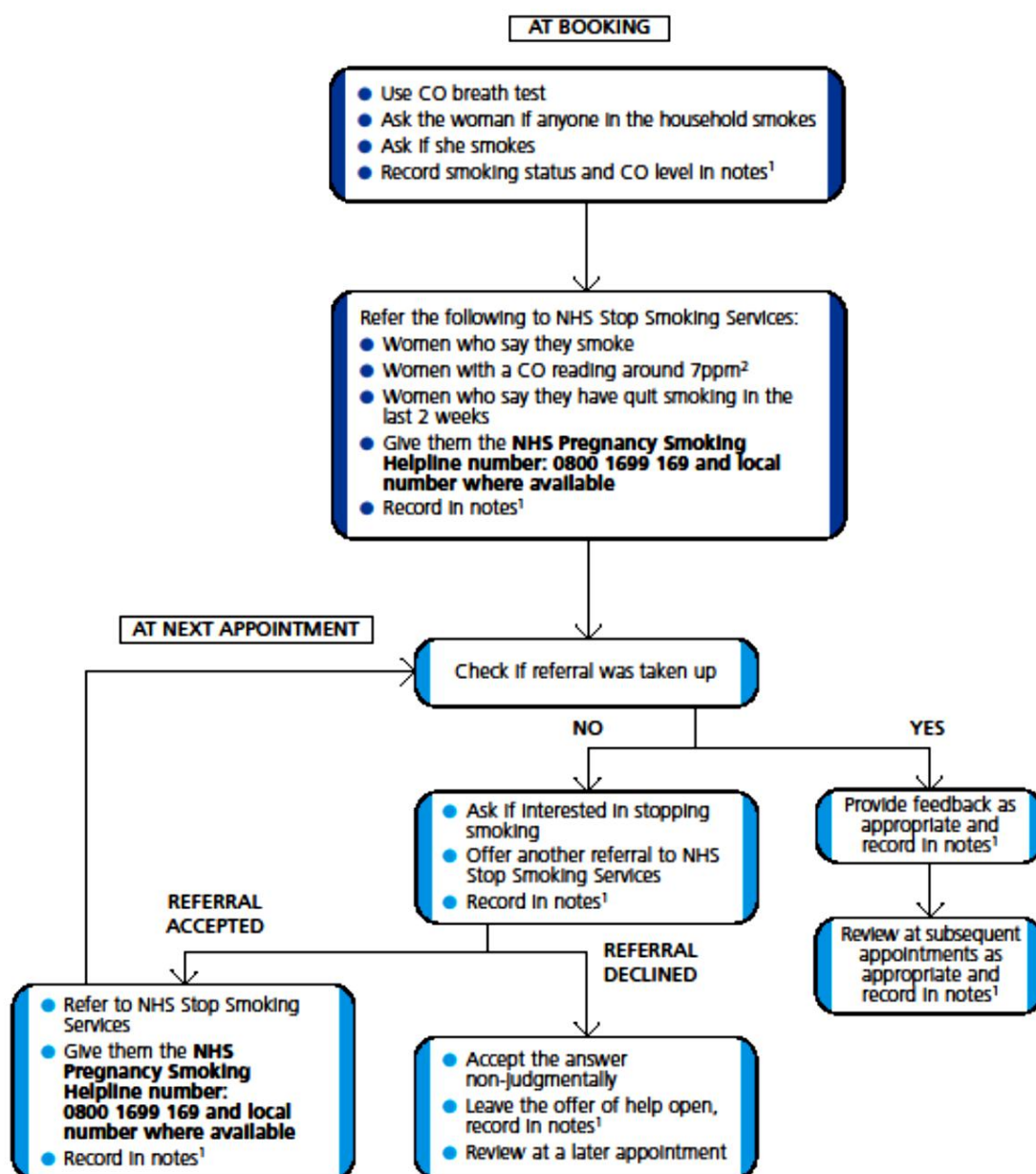
Interventions	Description	Evidence
Cognitive behavioural therapy	<ul style="list-style-type: none"><li>Scheduled face-to-face meetings between pregnant smokers and specialist adviser which may take place individually or in groups typically over a period of at least 4 weeks after the quit date.<sup>74</sup></li></ul>	A systematic review of 86 trials assessing psychosocial interventions for smoking cessation reported that pregnant women provided behavioural counselling such as CBT or MI were 44% more likely to be abstinent in late pregnancy compared to pregnant women given usual care (RR 1.44, 95% CI 1.19-1.75) and women receiving less intensive interventions (RR 1.35, 95% CI 1.00-1.82). <sup>75</sup>
Motivational interviewing	<ul style="list-style-type: none"><li>Directive, client-centred counselling style for eliciting behaviour change, with a focus to help in exploration and resolution of ambivalence regarding smoking cessation.<sup>76</sup></li><li>Aims to increase the likelihood of making an attempt to change a person's harmful behaviour</li><li>ranges from brief 20 minutes face to face sessions to telephone and group consultations etc.<sup>77</sup></li></ul>	
Self-help materials	<ul style="list-style-type: none"><li>Written materials such as booklets but also includes videos or audiotapes<sup>78</sup></li><li>Offered to pregnant women who are referred to Stop Smoking Services (SSS)</li><li>Women who opt-out of SSS are also offered these self-help materials<sup>79</sup></li><li>May also be supplemented by telephone counselling or quit lines<sup>74</sup></li><li>Wide-reaching as they can be easily disseminated</li><li>Low-cost</li></ul>	A meta-analysis of 12 trials assessing self-help interventions for smoking cessation in pregnant women reported that pregnant women who were given self-help material were 83% more likely to quit compared to women given usual care including brief intervention (pooled OR 1.83, 95% CI 1.23-1.73) <sup>80</sup>
Interventions based on stages of change theory – 'transtheoretical model'	<ul style="list-style-type: none"><li>The core of the transtheoretical model of behaviour change and acts as a basis for behavioural counselling for smoking cessation<sup>81</sup></li><li>Five stages of change i.e. pre-contemplation, contemplation, preparation, action and maintenance.<sup>82</sup></li><li>Tool to develop individually tailored communications for smoking cessation in form of counselling and self-help materials etc.</li></ul>	Mixed evidence regarding the success of interventions based on 'stages of change' theory <sup>79</sup> Lumley and colleagues reported a pooled RR of 0.99 (95%CI 0.97-1.00) for smoking cessation in late pregnancy for interventions based on 'stages of change' theory <sup>69</sup> Less emphasis was placed on 'stages of change' in the updated review and the interventions were broadly categorised as counselling interventions in the new review. <sup>75</sup>
Financial incentivisation	<ul style="list-style-type: none"><li>Thought to influence individual's motivation and self-regulation and also increase health professionals' engagement with patients<sup>83</sup>. These include incentives such as gift and other vouchers</li></ul>	Women who were offered incentives used the services more than women not incentivised. Furthermore, women from the incentivised group reported the experience motivating for their smoking cessation <sup>83</sup>

Interventions	Description	Evidence
	or payments <sup>75</sup>	<p>The four trials with financial incentives as the main intervention compared to usual care showed a three-fold increase in the abstinence in late pregnancy (RR 2.95, 95% CI 1.55-5.63), however the trials included are from the USA<sup>75</sup></p> <p>A Randomised Controlled Trial (RCT) is in progress in the UK to evaluate the effectiveness of this intervention in the UK<sup>84</sup></p>
Feedback	<ul style="list-style-type: none"> <li>Giving feedback to pregnant women on the effects of smoking on the child and their own health. This includes interventions such as ultrasound monitoring, carbon monoxide or urine cotinine measurements etc.<sup>75</sup></li> </ul>	<p>Chamberlain and colleagues reported a significant effect of feedback on abstinence only when compared with usual care and provided in conjunction with other interventions (RR4.39, 95% CI 1.89-10.21) however no significant effect was found when compared to less intensive interventions (approximate of usual care) (RR 1.19, 95% CI 0.97-2.31).<sup>75</sup></p>
Social Support	<ul style="list-style-type: none"> <li>Including peer/partner support, or support from a healthcare professional<sup>75</sup></li> </ul>	<p>In a recent meta-analysis, social support by peers was reported to increase the abstinence in late pregnancy by 49% (Pooled RR 1.49, 95% CI 1.01-2.19) however social support by partner was not reported to have a significant effect of self-reported abstinence (RR 1.02, 95% CI 0.70-1.50).<sup>75</sup></p>

Reducing maternal smoking during pregnancy has been an NHS priority since the beginning of the last decade. In March 2011 the government published a white paper titled "*Healthy lives healthy people: A tobacco control plan for England*" which set out how tobacco control would be delivered in the context of new public health systems. One of the aims of this plan is to reduce the rates of smoking throughout pregnancy from 14% to 11% or less by 2015.<sup>2</sup> Currently in the UK there are interventions and support available for pregnant women who want to quit including self-help interventions, pharmacotherapy, specialist support and intensive interventions offered by the NHS Stop Smoking Services (SSS).<sup>85</sup> These services came into place in 2000 following the 1998 tobacco control strategy<sup>86</sup> and since 2001 provide individualised support to pregnant women in clinic settings, home settings and on the phone.<sup>85</sup> Data from the NHS-SSS suggest that about half (46%) of pregnant smokers who use these services quit at the 4 week follow-up.<sup>87</sup> However, less than 14% of pregnant smokers access these services.<sup>88</sup> Therefore, to improve the uptake of these smoking cessation services NICE formulated guidelines on stopping smoking during pregnancy and childbirth in 2010.<sup>79</sup> These guidelines recommend all midwives to assess pregnant women's smoking status at booking, do a carbon monoxide (CO) breath test and refer them to the NHS-SSS. Other healthcare professionals such as general practitioners (GPs), practice nurses, family nurses, obstetricians, paediatricians, sonographers and others are recommended to use any appointment as an opportunity to assess smoking status and offer smoking cessation advice and an NHS-SSS referral to those who want to stop.<sup>79</sup> Similar to the WHO guidelines, bupropion and varenicline are contraindicated for use during pregnancy in the UK. In light of the insufficient data on the safety and effectiveness of NRT, NICE recommends a discussion of the risks and benefits of NRT before prescribing and to only prescribe NRT if cessation without NRT fails.<sup>79</sup>

NICE has also recommended an 'opt out' referral pathway through which the details of all identified pregnant smokers should be passed on to the local smoking cessation service without the need for direct consent.<sup>85</sup> Figure 1-2 explains the detailed pathway for referrals from maternity services to NHS Stop Smoking Services.

**Figure 1-2 - Pathway for referrals from maternity to NHS Stop Smoking Services**



<sup>1</sup> Preferably the patient handheld record.

<sup>2</sup> Lower level (e.g. 3 ppm) may apply for light/inrequent smokers. Note: higher level might apply if prior exposure to other sources of pollution, e.g. traffic fumes, leaky gas appliances.

Adopted with permission from: National Institute for Health and Clinical Excellence (2010) Quitting smoking in pregnancy and following childbirth PH26. London: National Institute for Health and Clinical Excellence

## **1.5 NICOTINE REPLACEMENT THERAPY**

Nicotine replacement therapy (NRT) contains low doses of nicotine in different medicinal forms. Its use is indicated outside of pregnancy for abrupt cessation of smoking, or to reduce the amount of cigarettes smoked before completely quitting.<sup>89</sup> It can also be used to minimise passive smoking, to treat cravings and reduce compensatory smoking after enforced abstinence in smoke-free environments.<sup>89</sup> The main mode of action of NRT is the stimulation of nicotine receptors in the ventral tegmental area of the brain and the consequent release of dopamine in the nucleus accumbens. This combined with other peripheral actions of nicotine leads to a reduction in nicotine withdrawal symptoms in regular smokers who abstain from smoking.<sup>90</sup> Use for smoking cessation during pregnancy serves two important purposes: firstly, it delivers nicotine without delivering other harmful chemicals and teratogenic products from tobacco smoke to pregnant women and secondly it reduces withdrawal symptoms including cravings.<sup>91</sup>

The use of NRT for smoking cessation during pregnancy is now supported by many countries in the world. The guidelines for smoking cessation in the USA, Australia, and New Zealand recommend that NRT can be used by pregnant women.<sup>92-94</sup> The Ontario Provincial Medical Association in Canada also recommends that NRT should be made available to pregnant women who are unable to quit using non-pharmacological methods.<sup>95</sup> Similar policies are in place for NRT use during pregnancy in European countries like France and Germany.<sup>95</sup>

In the UK, NRT was made available on NHS prescription in 2001; however, its use was contraindicated in pregnancy due to safety fears; for example, concerns about its potential vaso-constrictive properties and potential placental transfer. In 2003 guidance for NRT prescribing was revised such that NRT use in pregnancy was cautioned rather than contra-indicated.<sup>96</sup> In November 2005 the

Medicines and Healthcare products Regulatory Authority (MHRA) conducted a comprehensive review on the safety of NRT during pregnancy and despite a lack of conclusive evidence for efficacy, indicated that NRT use was likely to be less harmful than smoking,<sup>97</sup> consequently broadening the UK licensing arrangements for NRT to include pregnant women in December 2005.<sup>98</sup> As a result NRT can now be prescribed in specialist settings such as the Stop Smoking Services for Pregnant women (SSSPs) as well as in primary care settings. NICE recommends initially prescribing 2 weeks of NRT for use to pregnant women from the day they agree to stop and providing further prescriptions based on re-assessment.<sup>79</sup> NRT is available both on NHS prescription and over-the-counter (OTC) in many different forms and strengths. Table 1-2 presents a detailed description of currently available NRT formulations in the UK which are also available to pregnant women in the UK.

**Table 1-2- Nicotine Replacement Therapy formulations currently available in the UK<sup>89,90</sup>**

<b>Formulation</b>	<b>Available Strength</b>	<b>Specific side-effects</b>	<b>Maximum recommended daily dose</b>	<b>Additional information</b>
Nicotine chewing gum	2mg, 4mg	Increased salivation, irritation of the throat	60 mg	Treatment to continue for 3 months for smoking cessation
Nicotine inhalation cartridge	10mg, 15mg	Irritation of the throat, reversible atrial fibrillation	12 cartridges of 10mg/ 6 cartridges of 15mg	Single 10mg cartridge lasts for 20 minutes and 15 mg cartridge lasts for 40 minutes
Nicotine lozenge	1 mg, 1.5mg, 2mg, 4mg,	Increased salivation, diarrhoea, constipation, dysphagia, oesophagitis, gastritis, mouth ulcers, bloating, flatulence, taste disturbance, thirst, gingival bleeding, halitosis, chest pain, rash, hot flushes	15 lozenges	Treatment to continue for 6-12 weeks for smoking cessation
Nicotine sublingual tablets	2mg	Dry mouth	40 tablets	Treatment to continue for 3 months for smoking cessation
Nicotine oral spray	1mg/spray	Arrhythmia, hot flushes, sweating, myalgia, chest pain, abdominal pain, flatulence, taste disturbance, dry mouth, paraesthesia, watery eyes, blurred vision	2 sprays per craving episode, 4 sprays every hour and 64 sprays daily	-
Nicotine nasal spray	500 mcg/spray	Coughing, nasal irritation, epistaxis, sneezing, watery eyes	64 sprays daily, twice every hour for 16 hours	Treatment to continue for 8 weeks for smoking cessation



Nicotine transdermal patches	5mg/16 hrs, 10mg/16 hrs, 25mg/16hrs, 7mg/24hrs, 14mg/24hrs, 21mg/24hrs	Abnormal dreams, sweating, myalgia, arthralgia, arrhythmia, chest pain, dry mouth, minor skin irritation,	25mg/16hrs	>10 cigarettes daily - high-strength patch daily for 6–8 weeks, followed by the medium-strength patch for 2 weeks, and then the low-strength patch for the final 2 weeks <10 cigarettes medium-strength patch for 6–8 weeks, followed by the low-strength patch for 2–4 weeks
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### **1.5.1 Effectiveness of NRT for smoking cessation in pregnant women**

In non-pregnant smokers NRT is shown to increase quit rates by 1.5-2.0 times the rate of those trying to quit without NRT<sup>99</sup> however, the evidence of effectiveness of NRT during pregnancy is inconclusive. A recent multicentre, double blinded, randomised, placebo-controlled trial on Smoking, Nicotine and Pregnancy (SNAP) enrolled 1050 pregnant women across England to evaluate the effectiveness of NRT patches for prolonged abstinence and found no significant difference in the rate of abstinence from quit date until delivery between the NRT and placebo group (OR 1.26, 95% CI 0.82-1.96).<sup>100</sup>

Furthermore, a systematic review including this trial and five other randomised controlled trials on NRT and smoking cessation in pregnant women, including 1745 women in total, found similar results with no difference for smoking cessation in later pregnancy for NRT in comparison to the placebo group (RR 1.33, 95% CI 0.93-1.91).<sup>101</sup> A potential explanation for reduced effectiveness of NRT during pregnancy is the increased metabolism of nicotine during pregnancy. Several studies have reported higher metabolism of nicotine and cotinine (the primary metabolite of nicotine) in pregnant women compared to non-pregnant population<sup>102,103</sup> such that the half-life of cotinine is reduced to nine hours in pregnancy compared to 17 hours in non-pregnant women.<sup>104</sup> Dempsey and colleagues studied metabolism of nicotine and cotinine in 10 healthy pregnant smokers after intravenous administrations of nicotine and found that both nicotine and cotinine are metabolised more rapidly during pregnancy than in the postpartum period with nicotine clearance being 60% higher during pregnancy compared to outside pregnancy and cotinine clearance being 140% higher. The half-life of cotinine was also significantly higher during pregnancy compared to outside pregnancy (8 hours vs. 16 hours).<sup>104</sup> Another study compared nicotine metabolism using segmental hair analysis during each trimester of pregnancy in a large cohort of pregnant women and observed a significant decrease in hair

nicotine concentrations from the first to third trimester among steady smokers, accompanied by a significant increase in hair cotinine concentrations as nicotine clearance increases during later pregnancy.<sup>105</sup>

Another factor related to the low effectiveness of NRT during pregnancy may be low adherence to the prescribed doses of NRT with a median duration of NRT use to be about two weeks.<sup>100,106-109</sup> In the general population NRT use is recommended for 8-12 weeks for optimal effectiveness therefore two weeks of NRT may be very short to show any effectiveness.<sup>107,110</sup>

### **1.5.2 Safety of NRT for pregnant women**

There is very limited evidence of the safety of NRT during pregnancy and to date the evidence remains inconclusive. A recent systematic review of randomised controlled trials found no differences in the risk of preterm birth (RR=0.85, 95% CI 0.57-1.26), neonatal intensive care unit (NICU) admissions (RR= 0.94, 95% CI 0.64-1.38), miscarriage (RR 1.24, 95% CI 0.37-4.17), and neonatal death (RR 0.28, 95% CI 0.06-1.41) between NRT and placebo groups.<sup>101</sup> Additionally, no increased risk of low birth weight (OR=1.66, 95% CI 0.64-4.27) and stillbirth (RR 1.98, 95% CI 0.55-7.07) was found in the NRT group compared to the placebo group.<sup>101</sup> In contrast, observational data from the PRAMS, USA found that the risk of low birth weight to be twice in mothers who use NRT during pregnancy (OR 1.95, 95% CI 1.10-3.46) compared to non-smokers.<sup>111</sup> Studies using the Danish National Birth Cohort have found no significant association between NRT use and changes in birth weight ( $\beta$  co-efficient=0.25g per week of NRT use) (95% CI -2.31,2.81)<sup>112</sup> or stillbirth (HR) 0.83, 95% CI 0.34-2.00).<sup>113</sup> Evidence of the association between NRT use and congenital anomalies is also inconclusive. The SNAP trial found no increase in the risk of congenital anomalies associated with NRT use in pregnant women (OR 0.70, 95% CI 0.30-1.66).<sup>100</sup> The Danish National Cohort Data however suggest an increased relative risk for congenital malformations associated with NRT use (RR 1.61, 95% CI 1.01-

2.58).<sup>114</sup> The rate of caesarean section deliveries associated with NRT use has only been assessed in the SNAP trial which found it to be 20.7% which was approximately 45% higher in the NRT group as compared to placebo group (OR 1.45, 95% CI 1.05-2.01).<sup>100</sup>

These studies will be discussed in detail in Chapter 6 and Chapter 7.

### **1.5.3 Views and attitudes of pregnant women regarding NRT use in pregnancy**

The licensing arrangements for NRT have now been broadened to allow use as a smoking cessation medication during pregnancy in the UK. However, as highlighted above, the evidence around its safety and effectiveness is inconclusive. The attitudes and views of pregnant women and care providers vary with some favouring the use of NRT during pregnancy and some being sceptical about it. These views play a key role in the uptake of NRT during pregnancy as the use and uptake of NRT may depend on women's perceptions on the usefulness and safety of the drug. In a small survey of 150 pregnant smokers, identified through antenatal clinics in South West London, approximately half of the pregnant smokers (45%) expressed interest in using NRT. Women who smoked >10 cigarettes per day showed more interest in using NRT than women who smoked <10 cigarettes per day (55.9% vs. 37.4%,  $p=0.03$ ).<sup>115</sup> Another survey was conducted in the UK after NICE guidelines for smoking cessation supported the use of NRT during pregnancy to aid quit attempts. This survey was based on 145 pregnant women in their third trimester, identified through obstetric case notes. Approximately 70% of these pregnant women expressed interest in using NRT during pregnancy for smoking cessation.<sup>116</sup> Similar figures are reported in an Australian study of 256 pregnant women in an antenatal clinic where 63% of pregnant smokers expressed interest in using NRT if it were provided free of charge.<sup>117</sup> In a qualitative study to investigate the potential barriers to smoking cessation using NRT via focus

groups, the use of patches was considered to be acceptable to most of the women. Some patients with medical problems or history of obstetric complications expressed doubts about using NRT and some were even sceptical of the effectiveness of NRT.<sup>118</sup> However, this study was conducted on a selective sample of women in Australia therefore the results may not be applicable to other countries like the UK. Additionally, this study was conducted before the guidelines on NRT use in pregnancy were formulated and the licensing arrangements for NRT were broadened, which may have caused a shift in women's perceptions about NRT use during pregnancy. In a more recent qualitative study on 10 pregnant women in a semi-rural area of England, patches were the preferred form of NRT.<sup>119</sup> However, the biggest concern highlighted by these women was that nicotine would harm the baby. Some other concerns related to NRT patch use were the dislike of marks left by the patch and finding a safe unobtrusive place to wear them on the body. Nevertheless, some found the patch to be very discreet with the advantage that once it was worn they forgot about it.<sup>119</sup>

#### **1.5.4 Views and attitudes of health care professionals regarding NRT use in pregnancy**

Another important factor in general population prescribing of NRT is the perceptions of health care providers regarding NRT use in pregnancy which may influence their practices and attitudes towards NRT prescribing. In a small survey based on 61 obstetric and paediatric nurses, practitioners and physicians in six community health centres in Boston, USA in 2000, 92% of obstetric providers stated that they would prescribe NRT to pregnant women if safety data were available. However, only 44% of the total sample was prescribing NRT at the time of the study.<sup>120</sup> A more recent study based on 154 obstetricians/gynaecologists in Ohio, USA reported that only 25% of these specialists prescribed NRT to pregnant women, 32% perceived it as being safe in pregnancy

and only 14% considered it to be effective. Obstetricians/ gynaecologists who perceived NRT to be safe, effective, had confidence in their ability to effectively prescribe NRT and had their colleagues prescribing NRT were more likely to prescribe NRT (OR 20.0, 4.7, 3.9, and 6.7 respectively).<sup>121</sup> In a similar study by the same authors assessing perception of nurses and midwives 74% of the them believed that NRT would reduce the number of pregnant smokers however only 26% were confident in their ability to prescribe/ recommend NRT to pregnant women.<sup>122</sup> A postal survey of 780 health professionals including general practitioners (GPs) and midwives from New Zealand in providing maternity care reported that only 24% of these GPs and midwives perceived NRT to be appropriate to be prescribed to pregnant women.<sup>123</sup> Nevertheless, since NRT is more widely available now and its use is supported by several international guidelines<sup>124-126</sup> this proportion may have increased as a result. In a UK survey of 368 GPs working in four districts of Nottingham, 62% of GPs considered NRT to be effective in pregnancy and 70% considered it to be safer than smoking however only 45% believed NRT to be safe in pregnancy.<sup>127</sup> Even after relaxation of licensing arrangements of NRT in the UK, allowing health professionals to prescribe NRT to pregnant women, NRT in pregnancy was identified as a controversial issue in a qualitative study of midwives and health visitors and midwives expressed concerns in suggesting NRT use to pregnant women.<sup>128</sup> Some of these concerns were related to time-constraints, lack of training and definitive knowledge about the effectiveness of NRT and poor of compliance to NRT during pregnancy.<sup>128</sup>

#### **1.5.5 NRT prescribing and use in pregnant women**

Although NRT has been available in different forms for over a decade and pregnant women have been encouraged to use NRT for smoking cessation if smoking cessation without NRT fails, the literature describing trends in NRT prescribing and use by this group is very limited. Studies using the Danish

National Birth Cohort to investigate associations between NRT use and adverse pregnancy outcomes presented self-reported NRT use in pregnant women to be 0.3% in the first 12 weeks of gestation and between 2 to 2.5% when NRT use was assessed until 17-27 weeks of gestation.<sup>112-114,129</sup> A similar study from the USA, using the 2004 PRAMS data reported NRT use to be 4% among pregnant women.<sup>111</sup> A more recent study from the USA based on 296 pregnant smokers enrolled in an RCT reported that 7.4% of these pregnant smokers used NRT during pregnancy.<sup>130</sup> A small study based on 145 pregnant smokers in an antenatal clinic in the UK, before the changes in licensing arrangements took place, found that none of the women in this study were prescribed or counselled about NRT.<sup>116</sup> Another study linking Scottish maternity records with dispensed prescribing data in Tayside, Scotland in 2007 found that 2.4% of the pregnant women were prescribed NRT during pregnancy.<sup>131</sup> In contrast, a recent study conducted in 44 NHS Stop Smoking Services (SSS) across England reported NRT use to be as high as 85% in pregnant smokers attending these services.<sup>132</sup> However, women attending the SSS are more motivated to give up smoking than the general population and therefore these rates may not be true for the whole population.

## **1.6 SUMMARY AND THESIS OBJECTIVES**

Smoking during pregnancy causes significant health and economic burden. Therefore, up-to-date estimates of smoking in pregnancy are not only important for monitoring trends but also important to assess the effectiveness of current interventions and policies to tackle this problem.

Most drugs are contraindicated during pregnancy however NRT is licensed for use in pregnancy in many other countries. In the UK, it is widely available for prescribing for smoking cessation in pregnant women since 2005. However, estimates of the use and prescribing of NRT in pregnant women are scarce.

These measures are vital to assess the utilisation and uptake of NRT which is available on the NHS. Furthermore, evidence of NRT safety in pregnancy is inconclusive with most RCTs being too small to detect an effect and most observational studies using retrospective reporting of exposures making them prone to recall bias.

Therefore, the main aim of the work presented in this thesis was to assess the overall prescribing and safety of NRT in pregnancy. In order to meet this aim, the following objectives were addressed:

1. To assess the completeness of smoking status recording and cessation advice during pregnancy in THIN data
2. To compare the prevalence of maternal smoking in pregnancy from THIN data with other available data sources in the UK
3. To quantify annual trends of NRT prescribing in and around pregnancy in the UK
4. To assess whether NRT prescribing during pregnancy varies with maternal characteristics
5. To investigate the relationship between antenatal exposure to NRT, maternal smoking and major congenital anomalies among children
6. To investigate the relationship between antenatal exposure to NRT, maternal smoking and other birth outcomes (stillbirth, low birth weight and mode of delivery)

## **1.7 OUTLINE OF THESIS CHAPTERS**

**Chapter 2** briefly reviews potential data sources to assess the objectives of this thesis and describes in detail the main data source chosen for the studies in this thesis (The Health Improvement Network data).



**Chapter 3** assesses the completeness of smoking status recording during pregnancy in primary care data (Objective 1)

**Chapter 4** assesses the potential utility of these data to produce population-level estimates of smoking in pregnancy (Objective 2)

**Chapter 5** quantifies the prescribing of NRT in and around pregnancy and describes trends and patterns using descriptive statistics as well as poisson models (Objective 3 and 4)

**Chapter 6** investigates the association between maternal NRT or smoking exposure and major congenital anomalies in the offspring (Objective 5)

**Chapter 7** assess the relationship between maternal NRT or smoking exposure and stillbirth, low birth weight and mode of delivery (Objective 6)

**Chapter 8** summarises the main findings of the work presented in this thesis, discusses the public health implications and suggests avenues for future research.

## 2 POTENTIAL DATA SOURCES AND DESCRIPTION OF THE DATA USED

This chapter briefly presents potential data sources that measure smoking, NRT and other covariates required for the studies in this thesis and then describes in detail the main data source used i.e. The Health Improvement Network primary care data.

In the UK, there are a number of routinely collected data or annual/quarterly/quinquennial surveys which assess different parameters of smoking and NRT use. Table 2-1 compares these data sources on some of the attributes that were essential for the studies in this thesis.

**Table 2-1 - Potential data sources in the UK to measure smoking and NRT trends and safety**

<b>Data source</b>	<b>Smoking outside pregnancy</b>	<b>Smoking in pregnancy</b>	<b>NRT data</b>	<b>Sociodemographic factors</b>	<b>Birth outcomes*</b>
General Lifestyle Survey (GLF) <sup>133</sup> /Integrated Household Survey (IHS) <sup>134</sup>	Yes	No	No	Yes	No
Health Survey for England (HSE) <sup>135</sup>	Yes	No	No	Yes	No
Office for National Statistics (ONS) Opinions Survey <sup>136</sup>	Yes	No	No	Yes	No
Smoking Toolkit Study (STS) <sup>137</sup>	Yes	No	Yes	Yes	No
Infant Feeding Survey (IFS) <sup>59,138,139</sup>	No	Yes	No	Yes	No
Smoking at Time of Delivery (SATOD) <sup>60</sup>	No	Yes	No	No	No
Child Health Systems Programme (CHSP) <sup>61</sup>	No	Yes	No	Yes	No
Scottish Morbidity Record (SMR) – smoking at booking <sup>61</sup>	No	Yes	No	Yes	No
Commercial over-the-counter NRT data <sup>140</sup>	No	No	Yes	No	No
Electronic Prescribing Analysis and Cost Tool (e-PACT) <sup>141</sup>	No	No	Yes	No	No
Data from the Stop Smoking Services <sup>142</sup>	No	No	Yes	Yes	No
Primary Care Data <sup>143-145</sup>	Yes	Yes	Yes	Yes	Yes

\*congenital anomalies, birth weight, stillbirth, mode of delivery

Out of the 12 data sources listed in Table 2-1 only five sources assess smoking status specifically in relation to pregnancy and four sources assess NRT use/prescribing. However, the table above clearly highlights that compared to all the other potential data sources a large dataset of primary care data could potentially provide information on all the attributes required for this thesis including information on smoking status during and outside pregnancy, prescribing of NRT, sociodemographic factors and birth outcomes. In addition, it has other health information on women such as comorbidities. Therefore, these data have the potential to provide detailed information on smoking and NRT use in and around pregnancy, offering a large amount of data for a period of about 20 years, without the costs and time involved in using some other bespoke studies. The Health Improvement Network (THIN) primary care database was chosen as the dataset to be used for this thesis over the Clinical Practice Research Datalink and QRESEARCH it had an established pregnancy cohort with mother-child linkages at the time of the study which is essential for assessing the effects of pregnancy exposures (e.g. smoking, NRT) on birth outcomes (stillbirth, congenital anomalies). Additionally, about half of the general practices that contribute to THIN also contribute to CPRD.<sup>143</sup>

## **2.1 INTRODUCTION TO THE HEALTH IMPROVEMENT NETWORK DATA**

THIN is an electronic primary care database of anonymised patient records from general practices across the UK. It contains medical, prescription, lifestyle and socio-demographic information routinely collected by GPs. THIN was set up in November 2002 following collaboration between the Cegedim Strategic Data (CSD) Medical Research UK, formerly known as the Epidemiology and Pharmacology Information Core (EPIC), part of the group who developed the Clinical Practice Research Database (CPRD) formerly called the General Practice Research Database (GPRD)<sup>146</sup> and InPractice Systems (InPS) who developed the

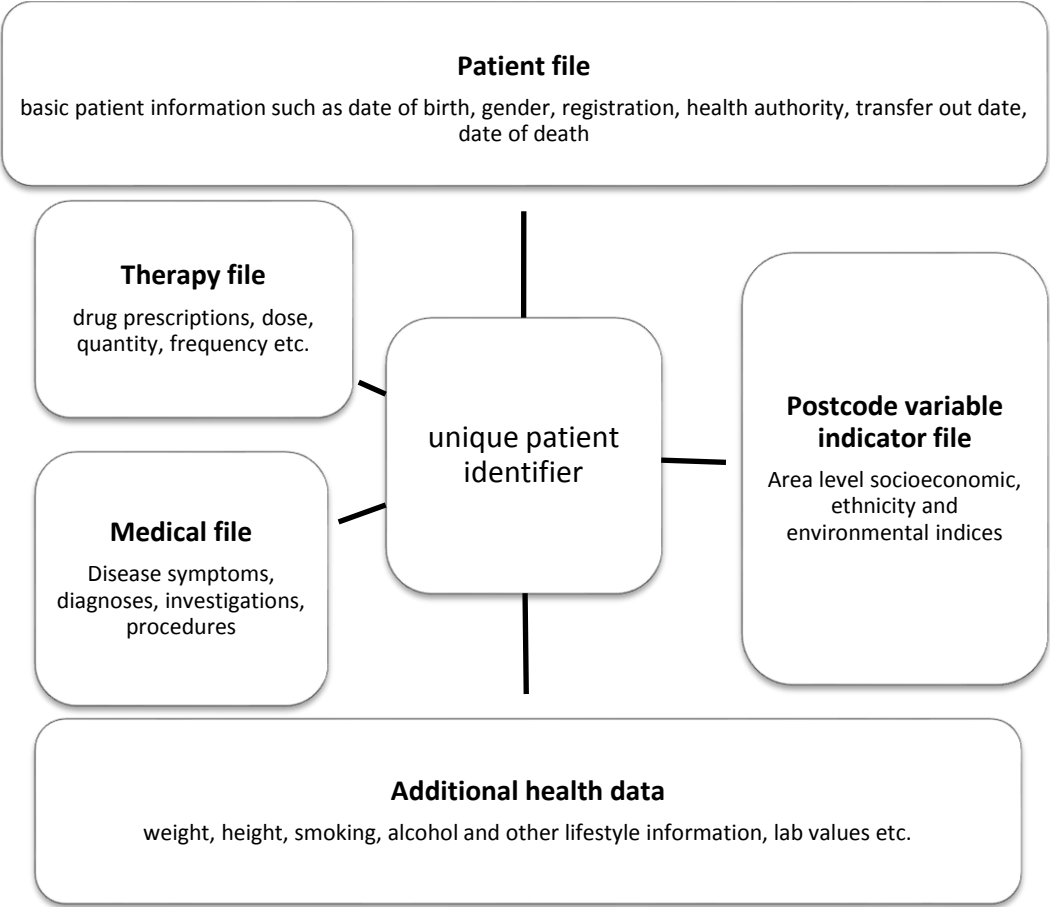
Vision software<sup>143,147</sup> Data are collected prospectively for all the registered patients who are alive. Additionally, historical information is available for patients who have died or transferred out of the practices. All practices participating in THIN use Vision software for their prospective data recording. On joining THIN an initial Full Data Collection (FDC) is conducted where all the retrospective data are collected.<sup>143</sup> Retrospective medical data are also available in each patient's records although general practices may have previously used a number of different software systems to record their data, mostly using the Value Added Medical Products (VAMP) system to enter patient data,<sup>148</sup> which was used in the Clinical Practice Research Data link (CPRD) formerly known as the GPRD.

THIN adds to existing data every quarter to update the dataset with a lag of three to eight months between data being entered and being available for research.<sup>149</sup> With each new release of the dataset the number of practices contributing data to THIN increases as a result of recruitment of new practices, though a small number of practices also leave the scheme.

## **2.2 DATA FORMAT OF THIN**

Information for each patient is split into four main files, which are linked together by a unique patient identification number. Figure 2-1 describes the structure and information contained in each of these files. In addition to these files, there is a Postcode Variable Indicators (PVI) file containing postcode linked area-level socioeconomic, ethnicity and environmental indices however ethnicity information was only available for <15% of the women for the version of data used for this thesis (85% missing, 11% European, 0.6% Asian, 0.6% Black, 1.2% Other White, 1.1% Mixed race) and therefore ethnicity was not included as a covariate in the studies conducted in this thesis<sup>150</sup>

**Figure 2-1 - Structure of THIN data**



Clinical information in the Medical and Additional Health Data (AHD) file is coded using medical Read codes, a coded thesaurus of clinical terms including signs, symptoms, diagnoses, investigations and procedures etc.<sup>151</sup> The medical Read codes in the file are also complemented by the AHD codes in the AHD file which describe details of lab values and other anthropometric measurements. More detailed clinical information and comments are entered as free text; these data were not available for this work.<sup>150</sup> Prescriptions are entered using multilex drug codes which are linked to the British National Formulary (BNF).

### **2.3 VERSION USED FOR THIS PHD – THIN 1009**

The version of THIN used for the studies conducted as part of this thesis contains anonymised data from 495 practices across England, Scotland, Wales and Northern Ireland with a total of 9.5 million patients and covers approximately 5.7% of the UK population. Of these over 3.46 million patients are currently registered with active practices and can be prospectively followed. Data are available from January 1990 to September 2010.<sup>143</sup> However, data for 2010 were only available for the first nine months of the year and, therefore, all the studies discussed in this thesis have only used data until December 2009.

### **2.4 STRENGTHS AND LIMITATIONS OF DATASET IN RELATION TO THE PHD WORK**

Electronic primary care data such as THIN are a good resource for descriptive epidemiology. However, there are limitations to its use which are important to consider. The relative strengths and limitations of THIN, particularly with reference to studying smoking and NRT prescribing in pregnancy are discussed below.

#### **2.4.1 Nature of data recording**

THIN has information on smoking status, prescriptions, cessation advice and counselling recorded prospectively compared to retrospective data collection in other data sources such as IFS and SATOD, which minimises the potential for misclassification due to recall or reporting errors. In addition to the smoking information, it also contains other clinical information recorded prospectively which may affect the smoking behaviour and other outcomes under study. Furthermore, THIN is based on routinely-collected data and reflects real life situation rather than experimental settings. It is therefore also useful to study the effect of certain policy and guideline changes on patient behaviour in the general population. These data however present a picture of routine UK clinical practice and inevitably lack information on people who did not consult their GPs for medical problems, which needs to be kept in mind while interpreting the findings from any study using primary care data. Additionally, the recording of different covariates will vary in the population as these data are not collected at regular intervals.

#### **2.4.2 Size, representativeness and generalisability**

Small sample sizes are one of the biggest drawbacks of many research studies in pregnancy as they result in reduced statistical power and are much less likely to represent the target population. THIN is a large database with information on over nine million patients and approximately two million women in their childbearing years from approximately 500 practices around the UK. Utilising THIN to estimate the prevalence of smoking and NRT prescribing in pregnancy could potentially produce precise estimates based on routine data with no added costs to conduct any surveys.

Most people in the UK are registered with a GP. General practices voluntarily contribute data to THIN and therefore may have a slight under-representation of

the most deprived socioeconomic group compared with the UK as a whole. Nevertheless, electronic primary care data have been shown to be generally representative of the UK population in terms of demographics, prevalence of major conditions and mortality rates.<sup>152</sup> Therefore, estimates of the clinical burden of disease, drug prescribing and the utilisation of primary care resources can be reasonably generalised to the population of the UK.

### **2.4.3 Validity and data quality of exposures/ outcomes of interest**

Independent studies have shown high validity for both common and rare outcomes in THIN, including fertility rates.<sup>152-154</sup> THIN has also been previously validated for recording of smoking status at a national and regional level in the general population<sup>149,155</sup> and prescriptions for smoking cessation medications.<sup>156</sup> Additionally, the prevalence of congenital anomalies in THIN is shown to be consistent with European Surveillance of Congenital Anomalies (EUROCAT) data<sup>157</sup> and has been validated against written GP records.<sup>158</sup> Other pregnancy outcomes, however, have not been validated but show similar estimates to national figures (e.g. stillbirth).<sup>159</sup>

As these data are primarily not collected for research purposes, information on certain exposures and outcomes may be more complete in certain groups compared with the general population. For example, a GP is more likely to ask and update smoking status in smokers as smoking is an important risk factor for many other medical conditions. Additionally, GPs address an average of two to three different medical problems during a single consultation<sup>160,161</sup> however, only the dominant topics of the visit may be coded.<sup>141, 142</sup> Therefore the information contained in these data heavily relies on the GPs' assessment of the extent and importance of the problem. Behavioural factors such as smoking, alcohol, exercise and diet etc. may therefore not always be recorded. Initial inspection of THIN data demonstrated poor recording of smoking status before 2000.



Therefore, for the purposes of this thesis analysis was limited to data from 2000 onwards.

Additionally, some drugs such as NRT are available from multiple sources in the UK for example GPs, SSS and OTC. Therefore, THIN may only be able to give population-based estimates of prescribing in primary care and not from other sources. NRT only became available on NHS prescription in 2001.<sup>162</sup> Therefore, the studies in this thesis assessing NRT prescribing and safety only analyse data from 2001 onwards.

#### **2.4.4 Duration of follow-up**

The average follow-up time for each woman in the data is approximately 4.5 years. This may be useful when assessing prevalence of smoking at a population level and comparing trends in smoking prevalence and NRT prescribing over time. Whilst this is a relatively short time in the context of a lifetime, it surpasses other available data where cross-sectional sectional surveys are used.

#### **2.4.5 Contemporaneous**

The version of THIN used for this thesis has data up to September 2010. However, THIN data are updated routinely and have a lag of only three to eight months before the data become available for research. Therefore, methods used in this thesis could be utilised to provide contemporaneous and timely estimates of smoking in future.

### **2.5 MOTHER-CHILD LINK**

To assess the health effects of maternal exposures on children, the anonymised primary care records of mothers and their children in THIN version 1009 were linked to form a pregnancy cohort with maternal-child linked records. This was done by Dr Linda Fiaschi and Dr Laila J. Tata using unique household

identification numbers to find mothers and children within the same household and then matching them using the delivery details in the mothers' primary care records and birth details in the children's primary care records. Approximately 87% of the children registered within three months of birth are matched to their mothers' records. This dataset was created independent of the work in this thesis and serves as a resource for several studies within the Division of Epidemiology and Public Health. This mother-child linked data was used for Objectives 5 and 6 (safety of NRT).

## **2.6 ETHICAL APPROVAL**

All data are anonymised before leaving the practice such that individual patient identifiers such as the name, address, date of birth, hospital number and specific location of general practices cannot be identified by researchers. THIN data collection was approved by the NHS South-East Multi-centre Research Ethics Committee (MREC) in 2003.<sup>163</sup> Ethical approval for the use of THIN data for studies on smoking and NRT prescribing prevalence was obtained from THIN Scientific Review Committee (Ref.No 11-047). Ethical approval for the studies on NRT safety in pregnancy was obtained from the Medical Research Ethics Committee, administered and approved by the NHS MREC (REC Ref. 04/MRE01/9).

### **3 COMPLETENESS OF SMOKING STATUS**

#### **RECORDING DURING PREGNANCY IN THIN**

##### **3.1 INTRODUCTION**

Current recommendations in the UK emphasise that all healthcare workers involved in a pregnant woman's care (e.g. midwives, GPs, practice nurses and obstetricians) should assess the woman's smoking status at the earliest possible stage of pregnancy and offer cessation advice and a referral to specialist stop smoking advisers for women who smoke.<sup>74,79,164-166</sup> Documentation of a woman's smoking status in her medical records is recommended to enable her healthcare team to offer appropriate support throughout the pregnancy.<sup>165</sup> Midwives record these data on the handheld maternity records and GPs record this information in the electronic primary care data. In the UK women must be registered with a GP in order to receive antenatal care provided by the NHS and, although most antenatal contacts are with midwives, an estimated 77% of women see their GPs first for confirmation of pregnancy before attending an antenatal booking appointment with a midwife.<sup>167</sup> This visit is therefore an ideal opportunity for the GPs to assess smoking status, communicate it to the healthcare team and provide advice on quitting, given the benefits of quitting early in pregnancy.<sup>66-68</sup> Primary care is the central hub in the current UK health care system and the assessment and complete documentation of smoking status, amongst other health indicators, in primary care is important to increase opportunities for providing smoking cessation advice and interventions during pregnancy. However, the extent to which smoking status is assessed and recorded during pregnancy in primary care is currently unknown. Additionally, there are no measures on whether GPs provide smoking cessation advice to pregnant women and how well it is recorded. These are important questions not only to identify missed opportunities for smoking cessation in primary care but

also to assess the potential utility of these data to generate smoking estimates during pregnancy at a population-level.

This chapter is aimed at addressing the very important questions highlighted above. It begins with a brief overview of the Quality and Outcomes Framework (QOF), a national scheme introduced to increase the recording of medical conditions and lifestyle factors, including smoking, in primary care data. This is followed by an investigation of the completeness of maternal smoking status recording during pregnancy in THIN data, assessing the annual proportion of pregnant women who have a record of their smoking status during pregnancy in their primary care data and how this varies with sociodemographic factors and maternal morbidities. This study was published in *PLOS One* in September 2013 and is attached as Appendix 10.1.

Appendix 10.2 presents the results of a study which assessed the completeness of recording of smoking cessation advice during pregnancy in primary care and variations in completeness with maternal factors. This study was conducted as a BMedSci project undertaken by Bethany Hardy and jointly supervised by myself and Dr Lisa Szatkowski. This paper was published in *BMC Family Practice* in February 2014 and it attached as Appendix 10.2.

### **3.2 QUALITY AND OUTCOMES FRAMEWORK**

In April 2004, a new contract for GPs was implemented which introduced a number of pay-for-performance targets as part of the QOF.<sup>168</sup> A set of indicators was developed under four main domains (clinical, organisational, patient experience and additional service) to measure the performance of GP practices using points. Approximately 7.5-8% of the QOF points (worth around £10,000) per year per practice are related to the recording of smoking status and delivery of smoking cessation advice.<sup>169-171</sup> At the time of its introduction, the QOF required GPs to document the smoking status of patients with hypertension, diabetes, asthma and certain other smoking-related morbidities every 15 months and have at least one record of smoking status in the absence of these morbidities. In 2006, this was slightly changed to require all GPs to document smoking status of all patients at least once every 27 months. The target was then changed in 2013 to every 24 months for the general population and every 12 months for patients with chronic conditions.<sup>171</sup> No rules however have been developed for the recording of smoking status or smoking cessation advice specifically during pregnancy. A detailed explanation of the QOF rules for smoking status recording in the general population from 2004 to date is given in Table 3-1.

**Table 3-1 - QOF requirements for recording of smoking status<sup>172,173</sup>**

		2004-2005	2005-2006	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014
Recording of smoking status in those with specific conditions	Hypertension	The notes of patients with any one or combination of these conditions should contain a record of smoking status in the previous 15 months, except those who have never smoked where the smoking status need only be recorded once since diagnosis.									The notes of patients with any one or combination of these conditions should contain a record of smoking status in the previous 12 months, except those who have never smoked where the smoking status need only be recorded once since diagnosis.
	Coronary heart disease										
	Diabetes mellitus										
	COPD*										
	TIA** or stroke										
	Asthma										
	Chronic kidney disease										
	Schizophrenia, bipolar disorder or other psychoses										
	Peripheral Artery Disease										

		<b>2004-2005</b>	<b>2005-2006</b>	<b>2006-2007</b>	<b>2007-2008</b>	<b>2008-2009</b>	<b>2009-2010</b>	<b>2010-2011</b>	<b>2011-2012</b>	<b>2012-2013</b>	<b>2013-2014</b>
Recording of smoking status in all registered patients in the general population		The notes of patients aged 15-75 should contain at least one record of smoking status.		The smoking status of patients aged 15+ should be recorded in every 27 months, except those who have never smoked where smoking status need be recorded only once.		The smoking status of patients aged 15+ should be recorded every 27 months, except those who have never smoked where smoking status is to be checked annually until age 25. Ex-smokers are to be asked about smoking status on an annual basis until they have been a non-smoker for 3 years.					The smoking status of patients aged 15+ should be recorded every 24 months, except those who have never smoked where smoking status is to be checked annually until age 25. Ex-smokers are to be asked about smoking status on an annual basis until they have been a non-smoker for 3 years.

Table adapted with permission, and updated from Szatkowski L (2011) PhD Thesis: Can primary care data be used to evaluate the effectiveness of tobacco control policies? Data quality, method developments and assessment of the impact of smokefree legislation using data from The Health Improvement Network. Nottingham: University of Nottingham.

\*COPD – Chronic Obstructive Pulmonary Disease, TIA – Transient Ischaemic Attack

Shaded areas represent the time when there are no QOF recording rules in place for specific conditions

The introduction of the QOF led to an improvement in the recording of clinical information in primary care medical records including the data on smoking status and smoking cessation advice. A study examining the impact of the QOF rules on the recording of smoking targets in primary care using THIN found that with the introduction of the QOF in 2004, the recording of smoking status in the general population improved such that the overall proportion of patients with a smoking status record within the last 27 months increased from 30% in 2003 to over 40% in 2004 and increased steadily over time such that in 2008 the proportion of patients with a smoking status record within the last 27 months in THIN was approximately 65%.<sup>174</sup> Similar increases were seen for recording of smoking status in patients with chronic conditions where this proportion increased from 50% in 2003 to over 75% in 2004 and then plateaued.<sup>174</sup> A similar study using the QRESEARCH primary care database, including 525 general practices across the UK, reported similar results with a 33% increase in the recording of smoking status between 2001/2002 and 2006/2007 with large increases in the collection of smoking data after the implementation of the QOF.<sup>175</sup>

### **3.3 JUSTIFICATION FOR THE STUDY**

In the general practice population as a whole the recording of patients' smoking status is more complete after the introduction of the QOF.<sup>149,155</sup> However, as discussed above the QOF set no specific incentives for the recording of smoking status in pregnant women. Having smoking status recorded in a pregnant women's medical records is not only useful for clinical management, but also increases opportunities for health professionals to provide smoking cessation interventions throughout pregnancy and afterwards. Additionally, a cohort of pregnant smokers was required as a denominator to calculate NRT prescribing prevalence and also as a comparison group to compare the safety of NRT in this thesis. Therefore, the primary aim of this study was to assess the completeness



of recording of smoking status during pregnancy in primary care medical records over time and investigate whether completeness varied with women's sociodemographic and health-related characteristics. Additionally, the secondary aim of this work was to investigate whether, despite having no specific targets for pregnancy, there was an increase in the completeness of smoking status recording during pregnancy in UK primary care after the introduction of the QOF.

### **3.4 METHODS**

#### **3.4.1 Study population**

For this particular study the population included all pregnancies recorded in THIN between 2000 and 2009 in women of reproductive age (15-49 years), as defined by the WHO,<sup>176</sup> which resulted in either a live birth or a stillbirth. Pregnancies ending in spontaneous abortions and terminations were not included in the study population as these do not have comprehensive information on pregnancy-related exposures and outcomes.

#### **3.4.2 Smoking status records**

Records of maternal smoking status during pregnancy were identified using Read codes.<sup>151</sup> These included codes for current, never, and ex-smoking, codes indicating the type or number of cigarettes smoked, and codes indicating smoking cessation interventions delivered to patients. Code lists are attached as Appendix 10.5. Women were also considered to be smokers if they had a prescription for a smoking cessation drug (nicotine replacement therapy, bupropion or varenicline) in their medical records during pregnancy. Code lists are attached as Appendix 10.6. Further information was extracted using the smoking AHD codes in Appendix 10.7. This method of classifying smoking status in electronic primary care data to calculate smoking prevalence has been previously validated in general population.<sup>149</sup>

### **3.4.3 Maternal characteristics**

To investigate the factors that may be associated with the recording of maternal smoking status during pregnancy, data were extracted on the following maternal characteristics. Code lists for the morbidities discussed below are attached as Appendix 10.8.

#### *3.4.3.1 Age and socioeconomic status*

Age was considered as a categorical variable with five-year age bands progressing from 15 years through to 49 years with seven categories in total.

Socio-economic status was assessed using quintiles of the Townsend index of material deprivation.<sup>177</sup> The Townsend deprivation index measures area level deprivation based on four indicators: unemployment, house ownership, car ownership and overcrowding. This was derived using the 2001 Census data, converted into five equal quintiles and then matched to UK postcodes to give deprivation quintiles for each postcode, quintile 1 being the least deprived group and quintile 5 being the most deprived group.

#### *3.4.3.2 Diabetes*

For each pregnancy, women were said to have diabetes if there was a medical Read code for diabetes or a prescription of insulin or an oral hypoglycaemic agent documented in the therapy file or a diabetes record in the AHD file within 27 months before conception until delivery. Although the QOF required the smoking status of patients to be recorded every 15 months in patients with diabetes and other comorbidities until 2013, for the general population smoking status needed to be recorded every 27 months.<sup>173</sup> Since this thesis is focused around smoking in pregnant women (who represent a fairly healthy group from the general population) the period of 27 months was set as a cut-off point for extraction of diabetes and all other morbidities for consistency purposes.

#### *3.4.3.3 Hypertension*

For each pregnancy, a woman was said to have hypertension if there was a Read code for hypertension recorded in the medical file or three or more readings of high blood pressure (BP) (systolic > 140mmHg with/ or diastolic >90mmHg) documented in the AHD file between 27 months before conception until delivery.

#### *3.4.3.4 Asthma*

Women were defined as having asthma if they had a medical code for asthma within 27 months before conception until delivery or if they had a medical code for asthma any time in their general practice record before delivery and a drug prescription for asthma within 27 months before conception until delivery to identify if women had active asthma in and around the time of pregnancy

#### *3.4.3.5 Mental illness*

This variable included five psychiatric conditions: depression, anxiety, bipolar disorder, schizophrenia and other psychoses. A woman was said to have a mental illness if there was a definitive diagnosis (based on International Classification of Diseases (ICD)-10 codes) of any of the above mental illnesses in a woman's primary care record between 27 months before conception until delivery.

#### *3.4.3.6 Pre-conception body mass index*

Body Mass Index (BMI) was extracted from the medical file using Read codes. Information on BMI was also extracted from the AHD file using the AHD information on weight. The most recent recording of BMI within 27 months before conception was considered to keep it consistent with the method of determining all other comorbidities.

BMI was then divided into four categories according to the WHO classification<sup>178</sup>: normal (18.5-24.9 kg/m<sup>2</sup>), underweight (<18.5 kg/m<sup>2</sup>), overweight (25-29.9 kg/m<sup>2</sup>), obese (≥30 kg/m<sup>2</sup>). A separate category was created for missing BMI information.

#### **3.4.4 Statistical analysis**

The prevalence of smoking status recording during pregnancy was calculated for each year from 2000 to 2009 as the number of pregnancies with at least one recording of smoking status during the gestational period divided by the total number of pregnancies delivered in that year. These data were plotted graphically.

For women who only had records of being a never smoker up to the age of 25 and who did not have a record of smoking during a subsequent pregnancy, a never smoking record was imputed during gestation. Similarly, for women who had no smoking status records during gestation but who were recorded as ex-smokers for three consecutive years before the conception an ex-smoking record was imputed during gestation. The annual proportion of pregnancies with a recording of smoking status during the gestational period was then recalculated. These imputations were based on the QOF rules discussed in Section 3.2. Since April 2006 the QOF has not required GPs to record smoking status of patients after the age of 25 years if they have been a never smoker until that age.<sup>179</sup> After 2008, if a patient who once smoked has been recorded as an ex-smoker for three years, GPs need no longer check and update the patient's smoking status records.

Logistic regression was used to calculate ORs for associations between women's characteristics and the recording of smoking status during pregnancy. All covariates that reached statistical significance ( $p < 0.05$ ) in the univariable analysis were initially included in the multivariable analyses and each covariate

was tested sequentially in the multivariable model. Covariates that reached statistical significance ( $p < 0.05$ ) in the multivariable analysis were retained in the final model. As some women had more than one pregnancy during the study period that contributed to the analyses, this potential clustering of pregnancies within women was accounted for by calculating robust CIs around the odds ratios using the clustered sandwich estimator. The clustered sandwich estimator allows for intragroup correlation (i.e. more than one pregnancy for each woman).<sup>180,181</sup>

Logistic regression was carried out for two separate time periods: before the implementation of the QOF (January 2000-April 2004) and after the implementation of the QOF (April 2004-December 2009). The introduction of the QOF incentivised the recording of smoking status in patients with smoking-related chronic conditions therefore it was expected to be an effect modifier of the association between recording of smoking status during pregnancy and these morbidities.

Visual comparisons of the magnitude, precision and statistical significance of the odds ratios for each maternal factor in the pre and post-QOF periods were made in order to assess whether the association between maternal factors and the recording of smoking status during pregnancy changed after the QOF was introduced.

## **3.5 RESULTS**

### **3.5.1 Baseline characteristics**

A total of 215,703 women with pregnancies resulting in live births or stillbirths were identified between January 2000 and December 2009. Of these, 162,295 (75.0%) had only one pregnancy, 46,062 (21.5%) had two pregnancies and 7,346 (3.5%) had three or more pregnancies, giving a total of 277,552 pregnancies. The mean age at conception was 29.5 years (standard deviation

(sd) 5.9) and the average length of pregnancy was 39.4 weeks (sd 2.2). Table 3-2 describes the baseline characteristics of the study population in the pre-QOF and post-QOF time periods. The overall prevalence of diagnosed asthma, diabetes, hypertension and mental illness within the study population was approximately 8%, 2%, 2.5% and 9% respectively. Information on socioeconomic status (Townsend index) was missing for 6% of the total pregnancies and information on BMI was missing for 42% of pregnancies.

**Table 3-2 - Baseline characteristics of the study population**

	Pre-QOF(January 2000- March 2004)			Post-QOF (April 2004- December 2009)		
	Total pregnancies (n=98,373)	Pregnancies with a gestational smoking record (n=12,381)**		Total pregnancies (n=179,179)	Pregnancies with a gestational smoking record (n=64,188)	
	n	n	%*	n	n	%*
<b>Age at Conception</b>						
15-19 years	5,529	953	(17.2%)	9,854	4,856	(49.3%)
20-24 years	14,809	2,202	(14.9%)	29,323	12,607	(43.0%)
25-29 years	25,732	3,175	(12.3%)	45,416	16,758	(36.9%)
30-34 years	32,621	3,750	(11.5%)	54,574	17,437	(32.0%)
35-39 years	16,614	1,944	(11.7%)	32,778	10,296	(31.4%)
40-44 years	2,907	338	(11.6%)	6,868	2,123	(30.9%)
45-49 years	161	19	(11.8%)	366	111	(30.3%)
<b>Townsend Score in quintiles</b>						
Quintile 1 – least deprived	24,760	2,850	(11.5%)	38,815	11,733	(30.2%)
Quintile 2	19,288	2,277	(11.8%)	32,962	11,025	(33.4%)
Quintile 3	18,592	2,317	(12.5%)	35,209	12,542	(35.6%)
Quintile 4	17,128	2,279	(13.3%)	33,982	13,114	(38.6%)
Quintile 5 - most deprived	13,252	1,964	(14.8%)	25,742	10,915	(42.4%)
Missing	5,353	694	(13.0%)	12,469	4,859	(39.0%)
<b>Pre-conception Body Mass Index (kg/m<sup>2</sup>)</b>						
Normal(18.0-24.9)	26,663	3,948	(14.8%)	59,267	21,209	(35.8%)
Underweight(<18.0)	1,968	293	(14.9%)	4,355	1,714	(39.4%)
Overweight(25-29.9)	11,923	1,867	(15.7%)	29,476	10,957	(37.2%)
Obese(>=30)	7,125	1,240	(17.4%)	20,993	8,406	(40.0%)
Missing	50,694	5,033	(9.9%)	65,088	21,902	(33.6%)
<b>Asthma</b>	6,537	1,297	(19.8%)	16,807	8,911	(53.0%)
<b>Hypertension</b>	2,372	377	(15.9%)	4,962	1,959	(39.5%)
<b>Diabetes</b>	1,345	194	(14.4%)	4,864	1,857	(38.2%)
<b>Mental illness</b>	8,717	1,439	(16.5%)	17,294	7,373	(42.6%)

\*pregnancies with a gestational smoking record in each sub-category divided by the total number of pregnancies in the respective sub-category

\*\* women had information on whether they were an ex/never/current smokers or had a smoking cessation prescription

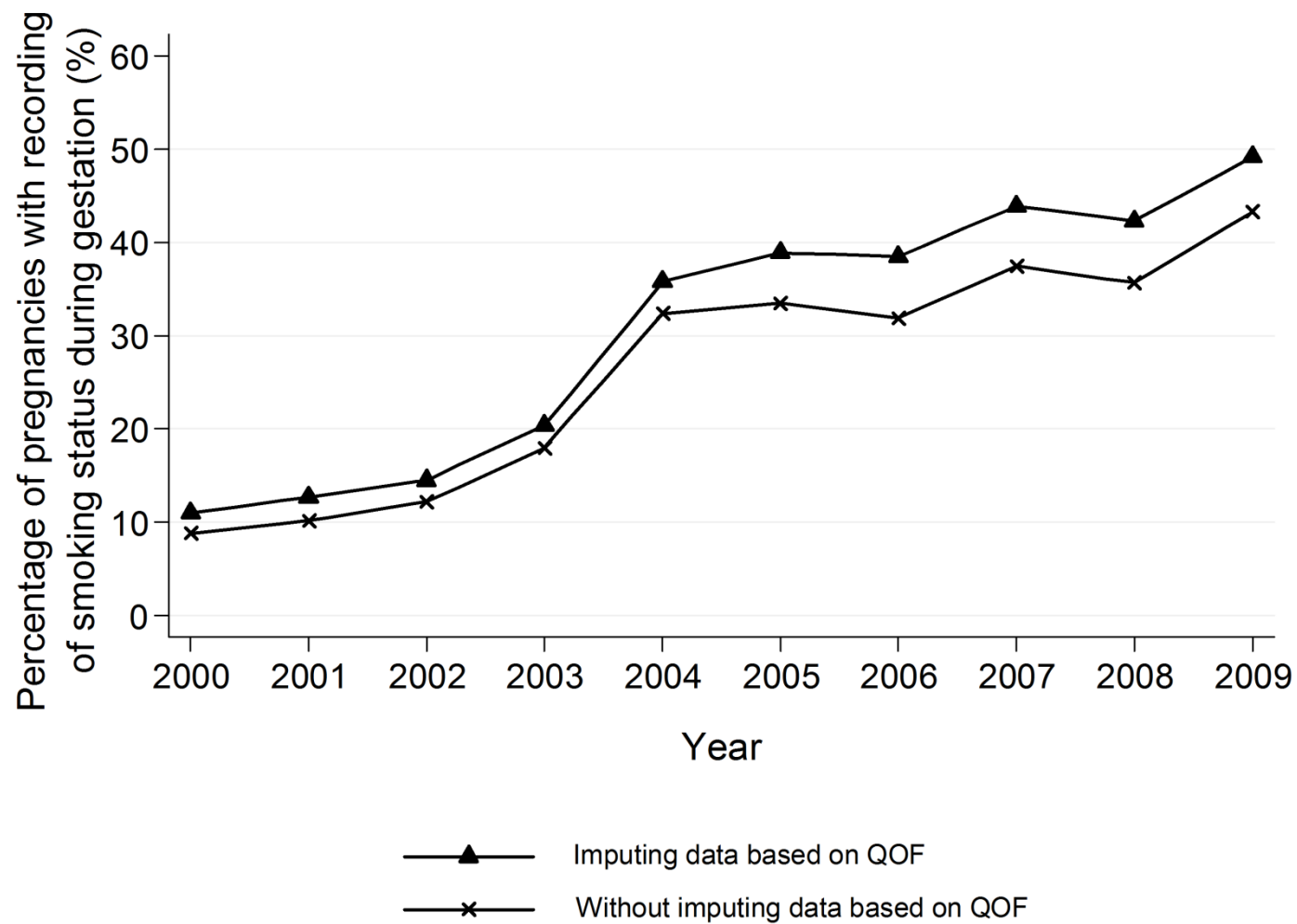
### **3.5.2 Completeness of maternal smoking records**

A record of smoking status at any point during gestation was present in 76,569 (28%) of the 277,552 pregnancies. Of the 76,569 pregnancies in which there was smoking status information, 913 (1.2%) only had a recording for smoking cessation drug prescription with no accompanying Read codes indicating smoking status. In 56,605 (73.9%) pregnancies, women had their smoking status recorded only once during the gestational period, whereas in 19,964 (26.1%) pregnancies, smoking status was recorded more than once. Figure 3-1 shows the proportion of pregnancies with smoking status recorded during gestation from 2000 to 2009. In 2000, smoking status was recorded during the gestational period for only 1,943 (8.8%) of the total 22,111 pregnancies. This proportion increased steadily to 18% in 2003, with the proportion rising to 32.3% in 2004. After 2004 it increased steadily on an annual basis such that the proportion of pregnancies with smoking status recorded during gestation in 2009 was 43.3% (13,360 out of 30,880 pregnancies).

When data for never smoking and ex-smoking were imputed based on the QOF rules, the overall proportion of pregnancies with a record of smoking status during gestation increased to 32.1%. In 2000, smoking status was recorded during gestation for only 11.0% of pregnancies which increased to 35.8% in 2004 and 49.2% in 2009.



**Figure 3-1 - Annual proportions of pregnancies in THIN with smoking status recorded during gestation (2000-2009)**



### **3.5.3 Factors associated with recording of maternal smoking status during pregnancy**

Table 3-3 shows variations in the recording of smoking status during pregnancy by women's sociodemographic characteristics and morbidities in the pre-QOF and post-QOF time periods. Overall, the magnitude of effect of the associations between most maternal characteristics and recording of smoking status during gestation was higher in the post-QOF period compared to the pre-QOF period. The recording of smoking status during pregnancy varied with socioeconomic status such that pregnant women from the most deprived group (quintile 5) were 17% more likely to have their smoking status recorded during pregnancy than pregnant women from the least deprived group (quintile 1) before the implementation of the QOF (OR 1.17, 95% CI 1.10-1.25) and 42% more likely afterwards (OR 1.42, 95% CI 1.37-1.47). Similarly, pre-QOF pregnant women with a diagnosis of asthma were 63% more likely to have their smoking status recorded during pregnancy than pregnant women without asthma (OR 1.63, 95% CI 1.53-1.74) and post-QOF pregnant women with asthma were over twice as likely to have their smoking status recorded during pregnancy (OR 2.08, 95% CI 2.02-2.15). Having a diagnosis of diabetes was not associated with the recording of gestational smoking status pre-QOF (unadjusted OR 1.17, 95% CI 1.00-1.36), ( $p=0.290$ ). However, post-QOF it was associated with a 12% increase in the odds of recording of gestational smoking status (OR 1.12, 95% CI 1.05-1.19). Recording of smoking status during pregnancy was also related to hypertension and mental illness. In both time periods the odds of a woman having her smoking status recorded during pregnancy were greater at younger ages compared with older ages and also greater in overweight and obese women. However, the magnitude of effects and corresponding CIs in the pre-QOF and post-QOF periods overlapped.

**Table 3-3 - Odds of having smoking status recorded during gestation by women's characteristics pre-QOF and post-QOF**

	Pre-QOF(January 2000- March 2004)				Post-QOF(April 2004-December 2009)			
	UOR (95% CI)	p-val	AOR (95% CI)	p-val	UOR (95% CI)	p-val	AOR (95% CI)	p-val
<b>Age at conception</b>								
15-19 years	1.48 (1.37 - 1.60)		1.56 (1.44 - 1.70)		1.66 (1.59-1.74)		1.62 (1.54 - 1.69)	
20-24 years	1.24 (1.17 - 1.32)		1.22 (1.15 - 1.30)		1.29 (1.25-1.32)		1.24 (1.20 - 1.28)	
25-29 years	1	<0.001	1	<0.001	1	<0.001	1	<0.001
30-34 years	0.92 (0.87 - 0.97)		0.95 (0.91 - 1.00)		0.80 (0.78-0.82)		0.84 (0.82 - 0.86)	
35-39 years	0.94 (0.88 - 0.99)		0.99 (0.93 - 1.05)		0.78 (0.75-0.80)		0.83 (0.80 - 0.85)	
40-44 years	0.93 (0.83 - 1.05)		0.99 (0.88 - 1.12)		0.76 (0.72-0.81)		0.80 (0.76 - 0.85)	
45-49 years	0.95 (0.59 - 1.53)		0.99 (0.61 - 1.60)		0.74 (0.59-0.93)		0.77 (0.61 - 0.97)	
<b>Townsend Score</b>								
Quintile 1 (least deprived)	1		1		1		1	
Quintile 2	1.03 (0.78 - 1.09)		1.01 (0.95 - 1.07)		1.16 (1.12-1.19)		1.12 (1.09 - 1.16)	
Quintile 3	1.09 (1.03 - 1.16)	<0.001	1.03 (0.97 - 1.10)	<0.001	1.28 (1.24-1.32)	<0.001	1.18 (1.14 - 1.21)	<0.001
Quintile 4	1.18 (1.11 - 1.25)		1.07 (1.00 - 1.13)		1.45 (1.40-1.49)		1.26 (1.22 - 1.30)	
Quintile 5 (most deprived)	1.34 (1.25 - 1.42)		1.17 (1.10 - 1.25)		1.69 (1.64-1.75)		1.42 (1.37 - 1.47)	
Missing	1.14 (1.04 - 1.25)		1.06 (0.97 - 1.16)		1.47 (1.41-1.54)		1.34 (1.29 - 1.40)	
<b>Body Mass Index (kg/m<sup>2</sup>)</b>								
Underweight(<18.0)	1.01(0.88-1.14)		0.92 (0.81 - 1.05)		1.16 (1.10-1.24)		1.03 (0.97 - 1.10)	
Normal(18.0-24.9)	1		1		1		1	
Overweight(25-29.9)	1.07 (1.01-1.13)	<0.001	1.06 (1.00 - 1.13)	<0.001	1.06 (1.03-1.09)	<0.001	1.05 (1.02 - 1.09)	<0.001
Obese(>=30)	1.21 (1.13-1.30)		1.16 (1.08 - 1.25)		1.19 (1.16-1.23)		1.11 (1.08 - 1.15)	
Missing	0.63 (0.60-0.66)		0.63 (0.60 - 0.66)		0.91 (0.89-0.93)		0.90 (0.88 - 0.92)	
<b>Asthma</b>	1.80 (1.69-1.92)	<0.001	1.63 (1.53 - 1.74)	<0.001	2.19 (2.12-2.25)	<0.001	2.08 (2.02 - 2.15)	<0.001
<b>Hypertension</b>	1.32 (1.18-1.48)	<0.001	1.26 (1.12 - 1.41)	<0.001	1.17 (1.11-1.24)	<0.001	1.19 (1.12 - 1.26)	<0.001
<b>Diabetes</b>	1.17 (1.00-1.36)	0.045	- #	-#	1.11 (1.05-1.18)	<0.001	1.12 (1.05 - 1.19)	<0.001
<b>Mental illness</b>	1.42 (1.34-1.51)	<0.001	1.32 (1.24 - 1.41)	<0.001	1.37 (1.33-1.41)	<0.001	1.26 (1.22 - 1.30)	<0.001

UOR=unadjusted odds ratio, AOR=adjusted odds ratio, CI=confidence interval, QOF=Quality and Outcomes Framework, # Diabetes not significant in the final model

## **3.6 DISCUSSION**

### **3.6.1 Principal findings**

Using a large population-based dataset this study found that the recording of smoking status during pregnancy in primary care has improved with time such that the proportion of pregnancies with a recording of smoking status during gestation was 8.8% in 2000 rising to 43.3% in 2009. The odds of a woman's smoking status being recorded during pregnancy was related to age, socioeconomic deprivation, BMI and QOF-incentivised morbidities such as asthma, diabetes, hypertension and mental illness. This indicates that even though there are no QOF targets specific to pregnancy, the QOF has had an influence on the completeness of smoking status recording during pregnancy.

### **3.6.2 Strengths and limitations**

This is the first study to assess the completeness of recording of smoking status during pregnancy in UK primary care medical records at a national level with over 200,000 pregnancies. The study is also novel in that it assesses the association between maternal characteristics and the recording of smoking status during pregnancy, taking into account the effects that the QOF had on the overall recording trends. Additionally, the code lists used to defined smoking status were quite exhaustive including medical Read codes, smoking cessation drug prescription codes and AHD codes related to smoking cessation advice, increasing the sensitivity to identify any smoking related recording in the women's primary care data. However, only electronically-coded data in primary care records were used and no free-text data (additional uncoded data that the GPs might add in patient notes to elaborate on the patient's condition),<sup>182</sup> which may provide additional information on the smoking status of women , were available.

Due to the infrequency of smoking status recordings during pregnancy the recording of smoking status throughout pregnancy was assessed compared to smaller time windows during pregnancy such as in each trimester, which may be more appropriate given that smoking status can fluctuate during pregnancy.<sup>183</sup> A potential explanation for a high proportion of pregnancies in which smoking status was not recorded could be that although this information is part of the hand-held maternity notes<sup>184</sup> (mandatory paper notes that women carry with them throughout pregnancy) it may not be transcribed onto the GP electronic records. Another reason could be that if a woman's smoking habit did not change after she became pregnant, GPs may be less likely to re-enter this information into medical records as there is no specific financial incentive for assessing and recording smoking status in pregnant women. Furthermore, as the QOF does not require GPs to record the smoking status of 'never smokers' after the age of 25, there is no financial incentive for them to update smoking status in the medical records of women who have never smoked. Similarly, ex-smokers need only be asked about their smoking status annually until they have been a non-smoker for three years. When smoking status was recalculated based on these rules, the annual trends in the completeness of smoking data during pregnancy did not vary much from the trends using the original data, however each woman only had 4.5 years of follow-up so for older women who had been non-smokers for life recording may be especially low.

### **3.6.3 Comparison with current literature**

Overall, a steady improvement has been observed in the recording of smoking status during pregnancy in the primary care data. The proportion of pregnancies with a gestational smoking record in this study increased by approximately 2% per year between 2000 and 2002. Since the late 1990s there has been an increased focus on the harms of tobacco use in the UK, with, for example, the publication of the Government White Paper 'Smoking Kills' in 1998 with a

specific objective of offering help to pregnant women to quit<sup>86</sup> and the establishment of NHS-SSS specifically tailored for pregnant women from 2001 onwards.<sup>185</sup> This changing tobacco control environment may have made these pregnant smokers more willing to approach their GPs for help to quit, and focused GPs' attention on encouraging cessation in their patients, thereby increasing the proportion of pregnant women with a smoking status record in their medical notes. The proportion of pregnancies with a recording of smoking status rose sharply from 18.0% in 2003 to 32.4% in 2004, after which it increased slowly until 2009. The most plausible explanation for this marked increase between 2003 and 2004 is GPs' awareness of the impending introduction of the 2004 GP contract.<sup>186</sup> Similar improvements in the recording of smoking status have been seen in the general population. A study using primary care data for over 300 practices throughout the UK found that, although rates of recording of smoking status in patients' electronic medical records had been increasing gradually since the year 2000, the rate of improvement accelerated from 2003, with an 88% increase observed between the first quarter of 2003 and the same period in 2004, just before the introduction of the QOF.<sup>187</sup> This suggests that the introduction of the QOF resulted in better recording of smoking status in the general population which has spilled over into greater recording in pregnancy observed in this study.

For socioeconomic deprivation, asthma and diabetes the magnitude of effect of the association with smoking status recording was observed to be stronger after the introduction of the QOF. Pre-QOF, pregnant women from the most deprived group were 17% more likely to have their smoking status recorded during gestation compared to 42% post-QOF. Smoking prevalence is generally higher in lower socioeconomic groups in both the general population as well as amongst pregnant women<sup>59</sup> and the smoking status of smokers is more likely to be recorded than that of non-smokers<sup>188-190</sup>, which likely explains more complete

recording in pregnant women from lower socioeconomic groups. Furthermore, low socioeconomic status is associated with a higher prevalence of chronic diseases such as hypertension, diabetes, asthma and depression.<sup>191</sup> The QOF encourages improved clinical management of these patients, who post-QOF may have had more frequent contacts with their GP and thus have had more chance of being asked about their smoking behaviour, increasing the gradient of the association between socioeconomic status and smoking status recording, reflecting that recording, and thus hopefully monitoring, is more complete where it is most needed.<sup>192,193</sup> Asthma is the most common pre-existing condition encountered during pregnancy<sup>194</sup> and can be exacerbated by smoking,<sup>195</sup> which may explain the high magnitude of association between asthma and recording of smoking status compared to other conditions like diabetes (which affects approximately 2-5% women of reproductive age)<sup>196</sup> and hypertension (0.6-2.7% during pregnancy).<sup>197</sup> Women with a higher BMI have an increased risk of complications during pregnancy and therefore are more likely to visit their GPs.<sup>198</sup> They are also more likely to be smokers<sup>199</sup> which in turn makes them more likely to have a recording of smoking in their primary care record.

The findings from this work are similar to those from a study in the general population which found that primary care patients with smoking-related chronic medical conditions and greater social deprivation were more likely to have a recent recording of smoking status or cessation advice in their medical records.<sup>174</sup> However, the magnitude of effect in the general population study for all morbidities was much higher than what this study found, possibly because currently pregnancy is not a QOF-incentivised condition for recording of smoking and because the pregnant population are generally healthier and younger on average than the whole population in general practice.

### **3.7 CONCLUSIONS**

In conclusion, smoking status of women during pregnancy was found to be recorded in less than half of the study population. This clearly highlights a missed opportunity in primary care considering that over three-quarters of pregnant women see their GP early in their pregnancy.<sup>167</sup>

In relation to the further work in this thesis, even for women with a recording of smoking status during pregnancy in primary care, data may not capture the changes in their smoking status accurately as over three-quarter of these women only had a single smoking related record during pregnancy. This makes it hard to establish if the women smoked throughout pregnancy or quit during the course of pregnancy. It would also mean that if a cohort of pregnant smokers was to be created using gestational smoking records, it may not include all women who may have smoked during pregnancy simply because no information was recorded. This raises questions on the utility of these data to generate population-level estimates on smoking during pregnancy which will be explored further in the following chapter.



## **4 COMPARISON OF SMOKING PREVALENCE**

### **ESTIMATES FROM THIN DATA TO OTHER DATA**

#### **SOURCES**

##### **4.1 INTRODUCTION**

As discussed earlier, reducing smoking in pregnancy to 11% or less by 2015 is one of the national goals set in the 2011 White Paper.<sup>2</sup> Information on maternal smoking is therefore important to monitor the progress towards this national goal and also to assess the effectiveness of the interventions currently in place for smoking cessation (discussed in Section 1.4.2). Electronic primary care data are collected routinely and have the power to provide estimates for the whole of the UK as well as constituent countries.<sup>149</sup> Therefore, these data such as THIN could potentially provide comprehensive and timely population-level data on smoking prevalence during pregnancy. Findings from the previous chapter show that even in recent years, smoking status was recorded in less than 50% of pregnancies. However, the completeness of the smoking data were be improved approximately 8% by making various assumptions based on the QOF recording rules discussed in Section 3.2. The next step in the quality assessment of smoking status data during pregnancy in primary care is to examine whether the prevalence obtained using these recordings in THIN is representative of the population-level prevalence of smoking in pregnancy. This is important firstly to assess the potential utility of primary care data such as THIN in providing population-level estimates of maternal smoking during pregnancy and secondly to establish an appropriate cohort of pregnant smokers which can be used for further analyses in this thesis. Hence, this chapter compares the prevalence of maternal smoking during pregnancy in THIN with the smoking prevalence measures obtained from other available data sources in the UK, with certain

assumptions based on the QOF, to assess the validity of recorded maternal smoking prevalence during pregnancy in THIN.

This study was published in the *Journal of Public Health* in October 2014 and is attached as Appendix 10.3.

#### **4.2 CURRENTLY AVAILABLE DATA SOURCES IN THE UK TO PROVIDE PREVALENCE OF MATERNAL SMOKING DURING PREGNANCY**

The UK currently has four data sources that provide population-level estimates of smoking during pregnancy. Each data source measures smoking differently, at different points in and around pregnancy and has its strengths and limitations.

Table 4-1 presents the summary of the important characteristics of these data sources and their strengths and limitations. Annual estimates for maternal smoking during pregnancy, for these data and other individual studies are described in Appendix 10.9 and were shown in Section 1.3.2, Figure 1-1. Annual estimates of maternal smoking in pregnancy from each of these data will be compared to estimates from THIN in this study.

**Table 4-1 - Summary of available data sources to measure smoking during pregnancy in the UK**

<b>Data source</b>	<b>Data collection interval</b>	<b>Country</b>	<b>Sampling frame and method</b>	<b>Sample size # (% of national births)</b>	<b>Data collection method</b>	<b>Time at which data on smoking in pregnancy are collected</b>	<b>Definition of smoking</b>	<b>Strengths</b>	<b>Limitations</b>
Infant Feeding Survey <sup>59,138,139</sup>	Every 5 years	UK (England, Scotland, Wales, Northern Ireland)	Random sample of live births in England and Scotland and all births in Wales and Northern Ireland in study period	22,400 (2.7% of all births in the UK) <sup>159,200-203</sup>	Postal survey administered by the National Health Service Information Centre	6-8 weeks after birth	Several self-reported measures available: smoking prior to pregnancy; ever smoking during pregnancy; quitting on confirmation of pregnancy; quit/cut down attempts during pregnancy; smoking at delivery.	Smoking estimates for overall UK and each constituent country Smoking status presented by socio-demographic factors Measures smoking cessation during pregnancy	Data only collected at 5 years intervals Retrospective reporting of smoking status Low response rates (approx. 52%) Results published at least a year after survey completion
Smoking Status at Time of Delivery (SATOD) <sup>60</sup>	Collected continually and reported quarterly	England	Aims to capture all live births and stillbirths	359,763 (52.1% of all births in England) <sup>159,200</sup>	Midwife-survey (in hospital maternity units)	At delivery	Self-reported smoking status at delivery	Data collected and reported at a local level	Limited to England Data collected postnatally No assessment of smoking by sociodemographic factors

Smoking Data collected as part of the Scottish Morbidity Record (SMR) <sup>61,203</sup>	Collected continually and reported by financial year	Scotland	All pregnant women attending an antenatal booking appointment (pregnancies may end in live birth or stillbirth)	57,398 (100% of all maternities in Scotland) <sup>201,203</sup>	Midwife survey (in hospital or community)	First antenatal booking appointment (usually between 8-12 weeks gestation)	Self-reported smoking status at the time of booking	Provides measures of never / ex smoking along with current smoking Provides annual rates by age and socio-economic status	Limited to Scotland Does not give estimates for the whole duration of pregnancy
Pre-school component of the Child Health Systems Programme (CHSP) <sup>61</sup>	Collected continually and reported by financial year	Scotland	Aims to capture all live births	51,746 (92% of all live births in Scotland) <sup>201,203</sup>	Survey administered by public health nurse or health visitor	Approximately 10 days after birth	Self-reported smoking status at the time of survey approximately 10 days after delivery	Provides data on smokers and non-smokers by age and socio-economic status	Limited to Scotland Data collected postnatally only Does not specifically ask about smoking during pregnancy

†Sample sizes for each wave vary therefore sample sizes for 2010 described in the table for reference

### **4.3 METHODS**

The study population included all pregnancies recorded in THIN between 2000 and 2009 in women of reproductive age. To prevent the risk of using the same pre-conception smoking status for women in their subsequent pregnancies if the smoking records were not updated only one random pregnancy per woman was chosen.

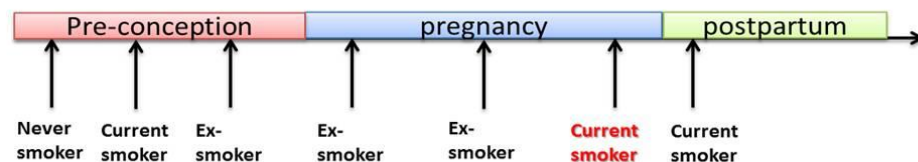
#### **4.3.1 Comparing the prevalence of smoking in pregnancy in THIN with other data sources**

For each woman all smoking status records in THIN before and during pregnancy and up to 10 days after delivery were extracted in a similar way as described in Section 3.4.2. A period of 10 days after delivery was included to allow appropriate comparisons with the Child Health Systems Programme (CHSP) data which collects smoking information approximately 10 days postpartum.<sup>61</sup> Where a Read code did not clearly indicate current smoking (e.g. 137X.00 – Cigarette consumption) further information on smoking status was assessed from the AHD and therapy files. This included the number of cigarettes smoked, or presence of prescriptions for smoking cessation medications. If no additional information was found, the recording was labelled as unknown smoking status.

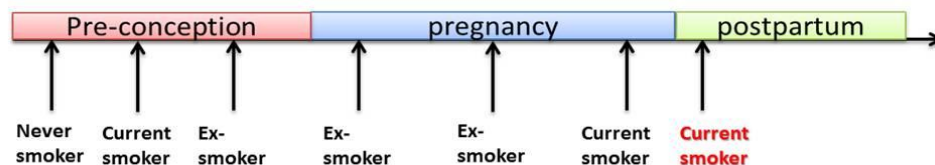
For each comparison, woman's smoking status was determined in a slightly different way (Figure 4-1). The annual prevalence of smoking during pregnancy as recorded in THIN (as a proportion of all births in that year) was then compared against the prevalence measures from the Infant Feeding Survey (IFS), Smoking status at Time of Delivery (SATOD), Scottish Morbidity Record data (SMR) and CHSP data. Each comparison made in the study used a slightly different population of women from THIN and assessed smoking status at a

different point in time in pregnancy to reflect the nature of the data collection in the source being compared (Table 4-2).

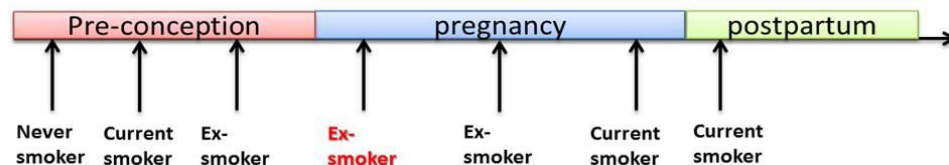
**Figure 4-1 - Example of a woman's smoking records in primary care and smoking status used for each comparison**  
**Comparison with IFS/SATOD. Latest smoking status before delivery**



**Comparison with CHSP. Latest smoking status up to 10 days postpartum**



**Comparison with SMR. Earliest smoking status in pregnancy**



Smoking status in red denotes the one used for each comparison

**Table 4-2 - THIN comparisons with the currently available data in the UK**

<b>Survey</b>	<b>Time at which survey assesses smoking prevalence</b>	<b>Years compared with THIN</b>	<b>THIN population used for comparison</b>	<b>Timing of records considered to define smoking status in THIN</b>
Infant Feeding Survey (IFS)	At delivery	2000, 2005	Data from all UK practices (n=495)	Last smoking status recording between conception and delivery
Smoking Status at Time of Delivery (SATOD)	At delivery	2006-2009	Data from English practices (n=378)	Last smoking status recording between conception and delivery
Scottish Morbidity Record (SMR)	At booking (8-12 weeks gestation)	2000-2009	Data from Scottish practices (n=63)	First smoking status recording between conception and delivery
Child Health Systems Programme (CHSP)	10 days after delivery	2001-2009	Data from Scottish practices (n=63)	Last smoking status recording between conception and 10 days after delivery



Estimates of smoking prevalence from the IFS were derived from the raw datasets of individual women's survey responses, available from the UK Data Service.<sup>204</sup> The IFS only asked about smoking status 6-8 weeks after birth so women were classified as smoking at delivery if they reported that they tried to give up smoking during pregnancy but started again before delivery, if they tried to cut down on the amount smoked during pregnancy, or if they did not try to cut down during pregnancy. Estimates of the prevalence of smoking from SATOD, SMR and CHSP were obtained from the published reports.<sup>60,61,203</sup>

#### **4.3.2 Imputing smoking status where women had no record during the gestational period**

Initially, only records of smoking status documented in THIN after the date of conception were used to determine smoking status during pregnancy. However, if a woman's smoking status was not recorded during gestation, pre-conception records of smoking status were assessed to identify women who smoked before pregnancy and may have continued during pregnancy. Based on the QOF rules for the recording of smoking status in the general population, which from April 2004 to March 2006 required the smoking status of patients aged 15 or over to be recorded at least once in primary care records, and since April 2006 have required records to be updated every 27 months, two cut-off points for including pre-conception information were used.<sup>172</sup> Firstly, a cut-off of 27 months before conception was used and women were recoded as smokers if their last smoking record in the 27 months before conception indicated smoking. Finally, if a woman did not have her smoking status recorded either during pregnancy or in the 27 months before conception, any smoking information recorded in their primary care data since registration was included.

## **4.4 RESULTS**

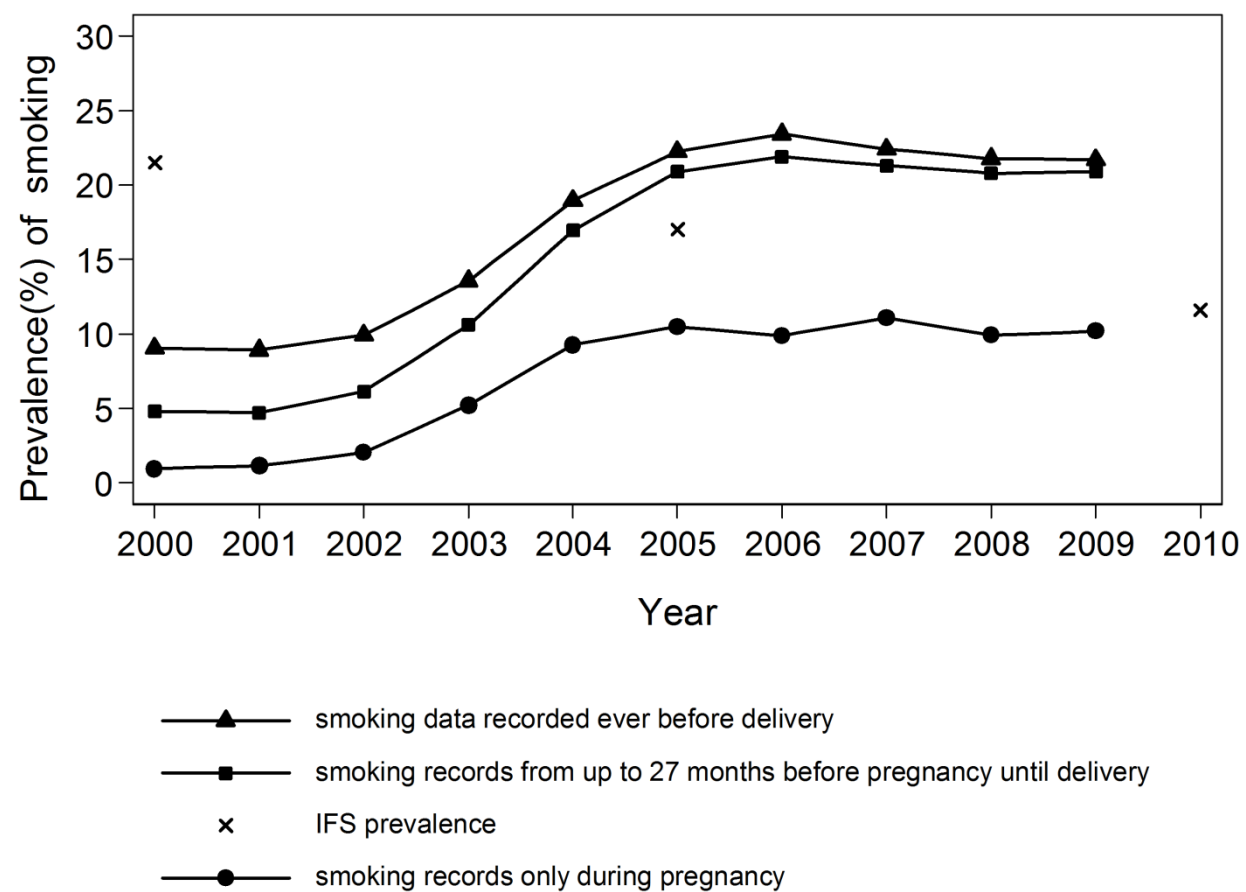
### **4.4.1 Population of pregnancies in THIN**

The total study population consisted of 215,703 pregnancies from 495 practices across the UK; 177,010 of these women were registered with a GP in England and 20,188 were in Scotland. Out of the 495 practices contributing to THIN 378 were from England and 63 were from Scotland. The mean age at conception was 29.5 years (sd 5.9 years).

### **4.4.2 Comparison with IFS data**

Figure 4-2 shows the prevalence of smoking at the time of delivery in women in THIN in relation to the corresponding measures in the IFS. Annual trends could not be compared as there were only two data points available. In 2000, none of the three prevalence estimates using THIN data were comparable to the IFS estimates. In 2005, smoking prevalence including data recorded up to 27 months before conception from THIN was slightly higher than the IFS estimate (17.0% vs. 20.9% respectively) however THIN prevalence using gestational smoking records was approximately seven percentage points lower than the IFS estimate. The THIN estimates were only available until 2009 therefore comparisons for the 2010 estimates were not possible. However, the IFS prevalence of smoking at delivery decreased to 11.6% in 2010 which is in good agreement with the THIN prevalence of (10.2%) in 2009 using gestational smoking records.

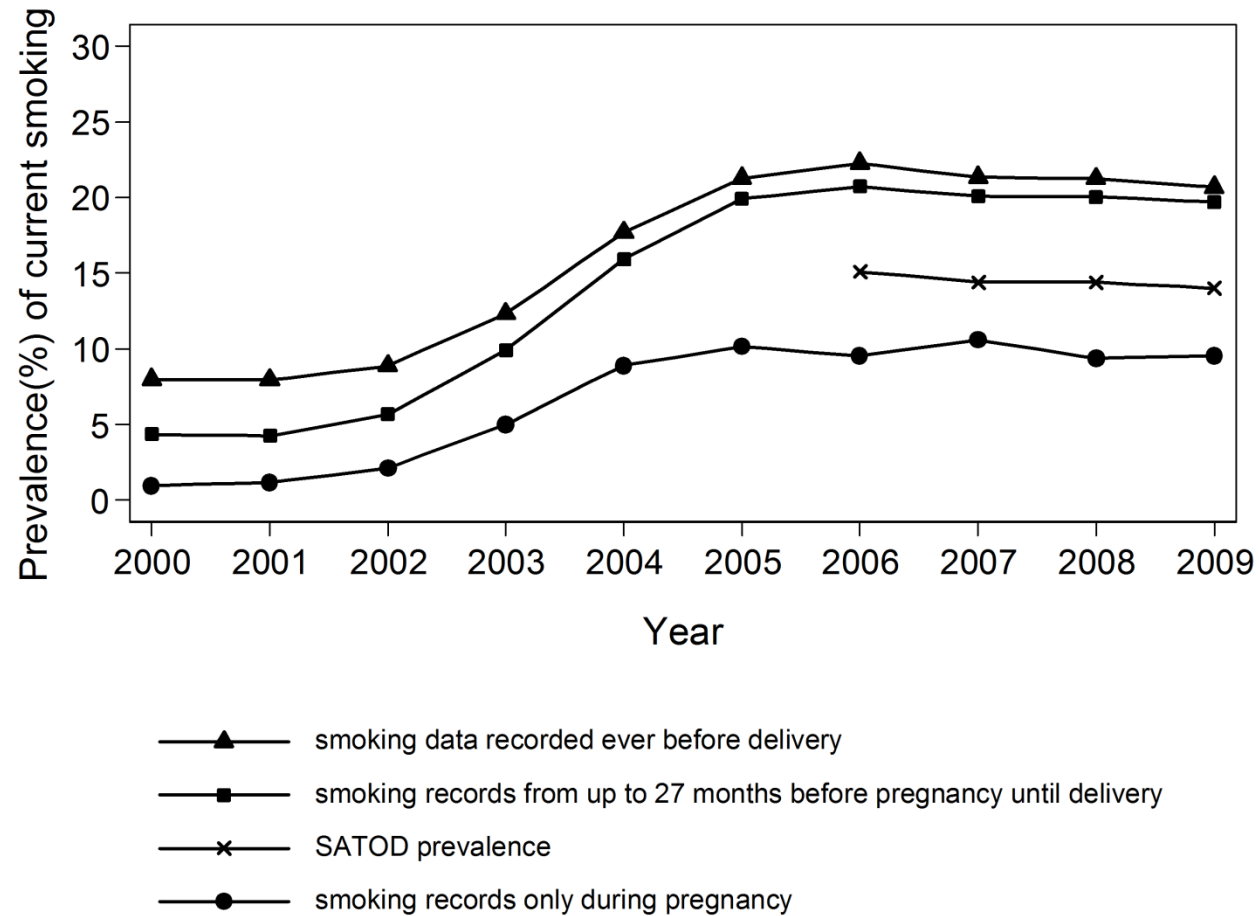
**Figure 4-2 - Comparison of maternal smoking prevalence during pregnancy from IFS and THIN**



#### **4.4.3 Comparisons with SATOD data**

When using smoking data recorded any time before delivery, the prevalence of smoking during pregnancy recorded in THIN was approximately seven percentage points higher than the SATOD estimates from 2006 to 2009. In comparison, the THIN prevalence considering data recorded up to 27 months before conception was approximately four to five percentage points higher over the four years of available data, while the THIN prevalence considering only records of smoking recorded during the gestational period was five percentage points lower than the SATOD estimates (Figure 4-3).

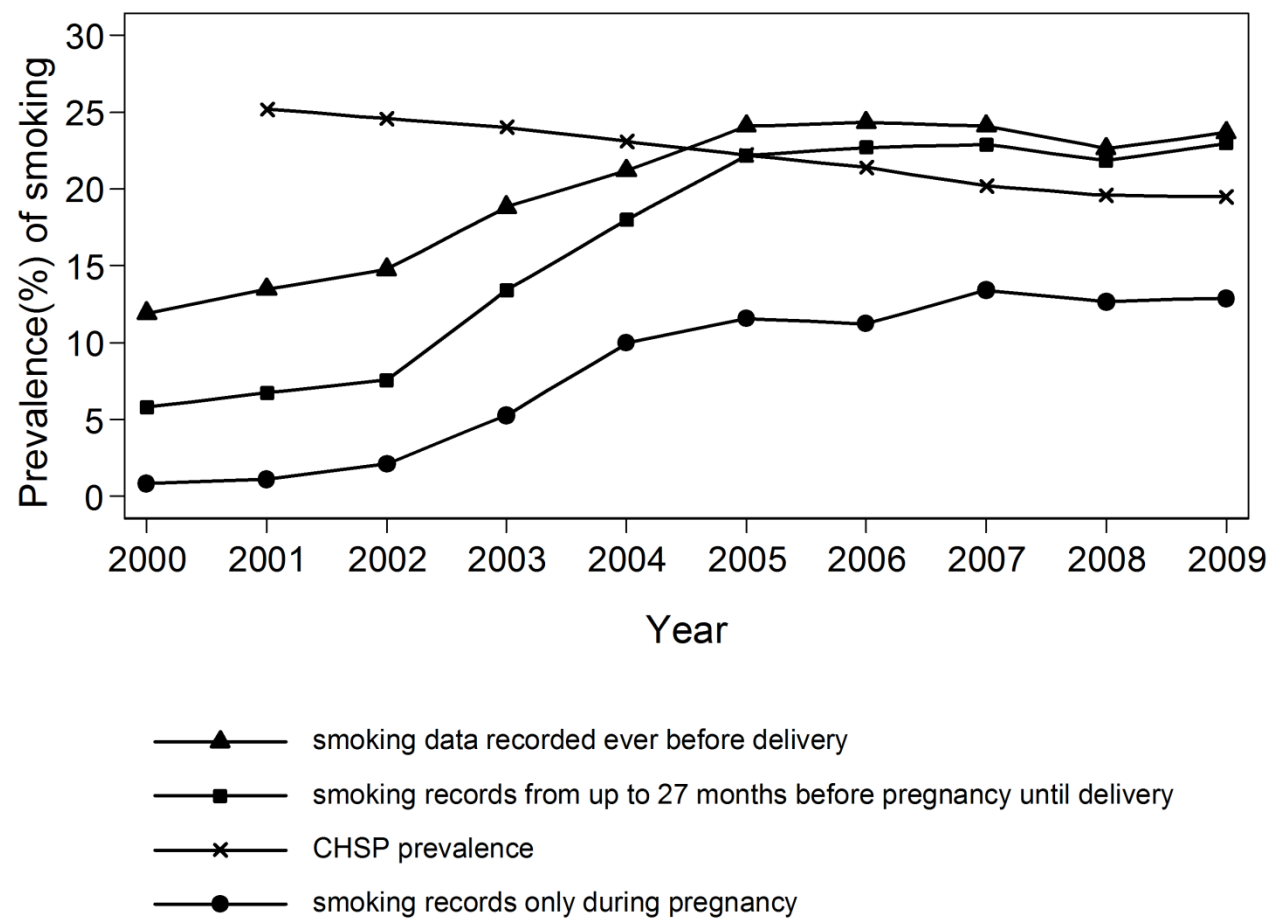
**Figure 4-3 - Comparison of maternal smoking prevalence during pregnancy from SATOD and THIN**



#### **4.4.4 Comparisons with CHSP data**

Using only records of smoking status entered during the gestational period, the THIN prevalence of maternal smoking status was low until 2004 (e.g. 43% of the CHSP prevalence of 23.1% in 2004) (Figure 4-4). It was 12.9% in 2009, approximately seven percentage points lower than the corresponding CHSP prevalence of 19.5%. Using smoking information recorded in the 27 months before pregnancy, the prevalence in CHSP and THIN converged in 2005. After this the THIN estimates were slightly higher than the CHSP estimates, such that in 2009 the THIN prevalence using data recorded up to 27 months before pregnancy was 22.9% compared to the CHSP prevalence of 19.5%. The prevalence estimates using data recorded ever before delivery were only slightly higher than the estimates using the data recorded up to 27 months before conception.

**Figure 4-4 - Comparison of maternal smoking prevalence during pregnancy from CHSP and THIN**

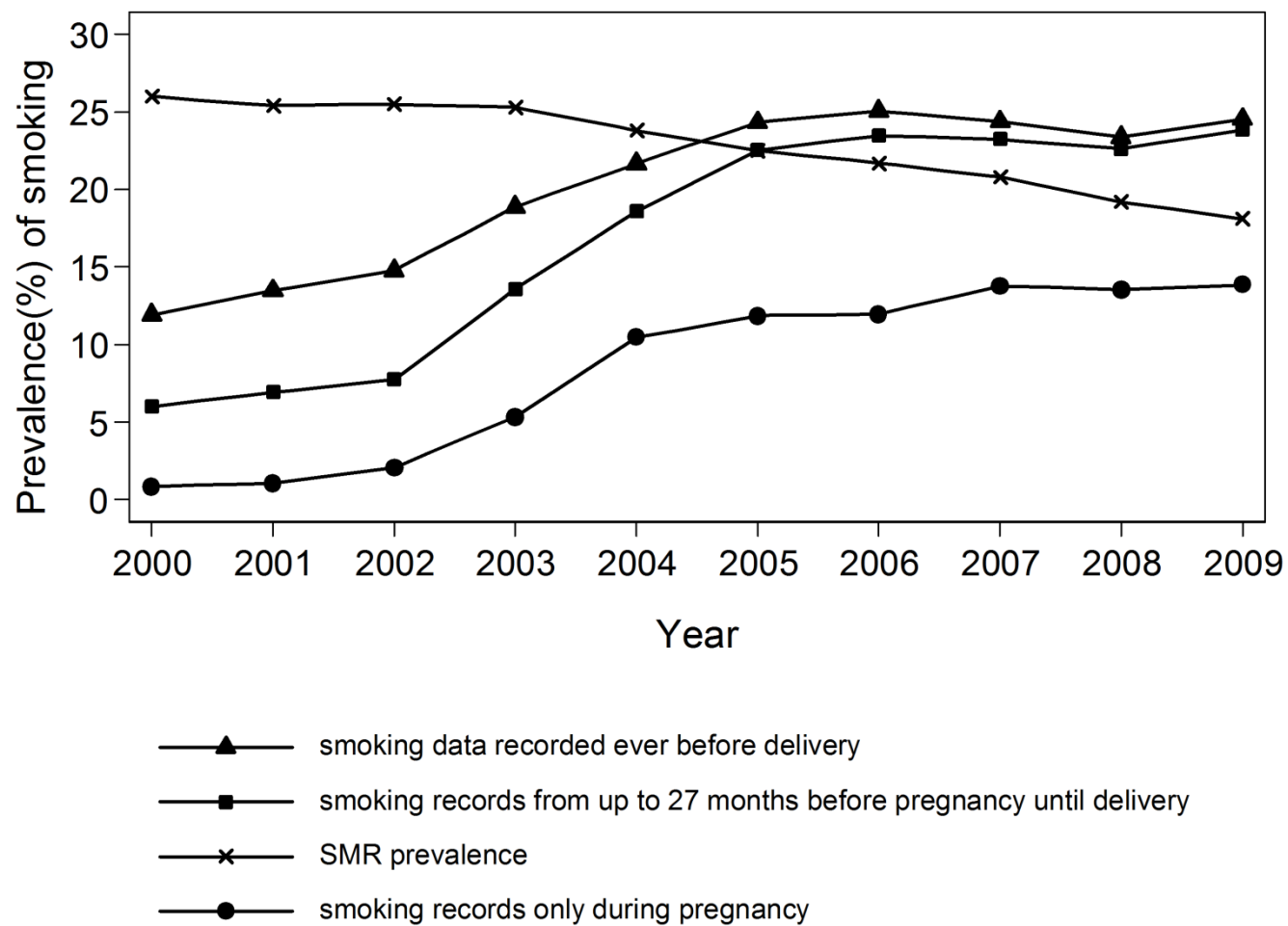


#### **4.4.5 Comparison with SMR data**

Using smoking status data recorded during the gestational period, the THIN prevalence was much lower than the SMR prevalence until 2004 (56% lower than the SMR prevalence of 23.8% in 2004, as shown in Figure 4-5). Prevalence in THIN was 13.8% in 2009 but was still 23% lower than the corresponding SMR prevalence of 18.1%. When including smoking information recorded up to 27 months before conception the two lines converged in 2005; in 2009 smoking prevalence in THIN was 23.8% using data recorded up to 27 months before conception and smoking prevalence using data recorded any time before pregnancy was 24.5% compared to the SMR prevalence of 18.1%.



**Figure 4-5 - Comparison of maternal smoking prevalence during pregnancy from SMR and THIN**



## **4.5 DISCUSSION**

### **4.5.1 Principal findings**

With current levels of completeness of smoking data in primary care records, it is not possible to produce population level estimates of smoking prevalence during pregnancy that are directly comparable to those derived from the existing data sources. The convergence between THIN estimates and estimates from other data sources has, however, improved over time. The comparability of THIN data to the SMR and CHSP surveys can be improved by the additional use of smoking status data recorded in the 27 months before conception but these to an extent may reflect smoking in general female population.

### **4.5.2 Strengths and limitations**

This is the first study to assess the potential of primary care data to provide population level estimates of smoking during pregnancy and compare it with other current data sources in the UK. As discussed earlier, fertility rates in THIN are comparable to national fertility rates<sup>153</sup> and therefore the ascertainment of pregnancies is reasonably complete. However, like the other data sources under comparison, data on smoking status recorded in THIN are self-reported and women may not accurately report their smoking behaviour, particularly during pregnancy where there may be social stigma attached to smoking.<sup>205</sup>

Underreporting of smoking during pregnancy may arguably be a particular problem in the IFS, where women are surveyed six to eight weeks after delivery.

A potential limitation of this work is the inclusion of pre-conception smoking records to predict smoking status during pregnancy, which may not be an accurate reflection of women's smoking status during pregnancy. Studies which have investigated smoking behaviour in early pregnancy indicate that many women attempt to quit when they find out they are pregnant or later during

pregnancy,<sup>206</sup> so it is unlikely that the inclusion of pre-conception records resulted in an under-estimation of smoking prevalence during pregnancy. It could however, lead to misclassification of some ex-smokers as smokers, resulting in an over-estimation of the prevalence of smoking during pregnancy in THIN. A substantial over-estimation is unlikely as approximately 35-50% of pregnancies in the UK are unplanned,<sup>207,208</sup> which means that only some women are likely to make positive behaviour changes such as quitting smoking before attempting to conceive. It may, however, hold true for some women who quit on confirmation of their pregnancy.

Another potential weakness of this study, and of primary care data, is that using primary care records it is difficult to determine the timing of smoking status ascertainment in relation to progress through gestation; this makes direct comparison with other data sources, obtained at booking or delivery, difficult. Lastly, smoking status during pregnancy is a complex and variable behaviour and it may fluctuate throughout pregnancy.<sup>183</sup> Therefore, single measures of smoking such as smoking at booking or smoking at delivery captured in SATOD, SMR and CHSP data are limited in their usefulness. Although these single measures may give a snapshot of smoking behaviour at a certain time, they may not give a complete picture of smoking behaviour throughout pregnancy. Hence, these data sources may provide population-level prevalence of maternal smoking at different points relative to pregnancy but do not contain information on changes in women's smoking status throughout pregnancy or postpartum period. IFS data assess smoking behaviour throughout pregnancy in more detail, albeit collected retrospectively. Nevertheless, these data are collected on a quinquennial basis and thus may become out of date quickly. A study with complete pregnancy follow-up and accurate assessment of smoking status and changes in women's smoking behaviour may be required for this. However, if smoking information was collected and recorded by GPs more frequently

throughout pregnancy, then primary care data may prove to be very useful to assess these changes in the smoking status of women during pregnancy but as shown in this study currently these data are not complete.

#### **4.5.3 Interpretation in light of the current literature**

To date, there are no studies assessing the validity of primary care data for quantifying the prevalence of smoking during pregnancy. A study comparing smoking prevalence recorded in THIN to smoking prevalence in the general population (measured by the General Lifestyle Survey (GLF)) found a good agreement between THIN and the GLF after 2008 and concluded that primary care data may provide an alternate means of monitoring national smoking prevalence.<sup>149</sup> Despite the smaller sample sizes at regional level, primary care data have also been shown to be a good means of monitoring regional smoking prevalence in the general population.<sup>155</sup>

The prevalence estimates of smoking during pregnancy from primary care do not accurately converge with other data sources because, at least in part, smoking status recording during pregnancy in primary care is incomplete.<sup>20 209</sup> Potential reasons for this have already been discussed in Section 3.6.3. This was shown in the previous study in this thesis which found that from 2000 to 2009 smoking status was only recorded in primary care for 28% of pregnancies. Nevertheless, this is to an extent similar to conducting a survey on a selected group of pregnant women from the population where smoking information may only be available on the women surveyed out of the whole population, which in this case is only available for women who were asked about their smoking status during pregnancy out of the whole primary care population of pregnant women.

Another possible explanation for the lower THIN prevalence could be that THIN over-represents general practices from more affluent areas of the UK. Since smoking prevalence is lower in women from more affluent groups, this may

slightly under-estimate the smoking prevalence generated using THIN data and account for some of the differences between THIN prevalence estimates and other data sources.

Whilst THIN estimates using only gestational smoking records do not approximate closely to annual prevalence from other data sources, THIN estimates using gestational smoking status show a close converging pattern with the data from SMR (collected at booking) in 2009. This is sensible as women see their GPs for initial care in pregnancy and implies that primary care data may be most useful to provide adequate data on smoking prevalence early in pregnancy, when most women see their GPs for initial care, compared to the time around delivery, when most women will be cared for essentially in secondary care facilities.

#### **4.6 CONCLUSIONS**

All existing data sources that measure smoking during pregnancy have their strengths and limitations. Primary care data have a great potential to measure smoking status during pregnancy at a population level. Although recording of gestational smoking status in THIN is improving over time, it is not adequately complete to produce maternal smoking estimates at a population level with most women just having a single record of smoking status throughout the course of pregnancy. Periodic recording of smoking status during pregnancy is important to monitor changes in smoking behaviour throughout pregnancy and to maintain and improve women's care before and after delivery. Although this information may be recorded and updated in hand-held maternity notes, there is currently no centralised recording system and the information in these notes is lost after delivery. Better integration of recording systems in primary care and midwifery services is required to improve communication and relay of relevant medical and lifestyle information including smoking status.

In terms of the further work in this thesis, it means that a cohort of pregnant smokers developed using smoking data recorded during gestation may not be representative of the UK population of pregnant smokers and some assumptions including use of pre-conception smoking records may need to be made in order to capture more women who smoke during pregnancy. Using gestational smoking records to create a cohort of smokers for studying the trends in the epidemiology of NRT prescribing in pregnant women in the later chapters will result in an underestimation of smokers. Therefore, a more exhaustive approach is needed to define the denominator of smokers for further analysis in this thesis. Smoking records from 27 months before conception were therefore included where no gestational smoking records were available. The comparability of THIN measures with prevalence measures from other data sources increased by including smoking information recorded within 27 month before conception and therefore this will provide a more appropriate denominator for further analysis in the thesis especially after 2004 as the recording of smoking status improved after the introduction of QOF. Another important consideration which was highlighted in this chapter was that even when considering the smoking records from 27 months before conception, the comparisons for earlier years i.e. 2000-2003 are not good, so it may be more appropriate to also use all pregnant women as a denominator for the later analysis in addition to pregnant smokers to rule out any bias that may arise due to the changes in smoking data quality over time.

## **5 PRESCRIBING OF NICOTINE REPLACEMENT THERAPY IN AND AROUND PREGNANCY**

### **5.1 INTRODUCTION**

As discussed in Section 1.5, NRT has been available on NHS prescription since 2001; however, it was only in 2003 that the BNF changed its instructions for NRT use in pregnancy to a caution from a contraindication.<sup>96</sup> The 2005 MHRA review concluded that despite a lack of conclusive evidence for efficacy, NRT use was likely to be less harmful than smoking,<sup>97</sup> consequently broadening the UK licensing arrangements for NRT to include pregnant women in December 2005.<sup>98</sup> It is now widely available and recommended for smoking cessation in pregnant women in the UK, based on the theoretical notion that it is safer to use NRT during pregnancy than to smoke. The BNF clearly states that the use of NRT in pregnancy is preferable to the continuation of smoking but should be used only if smoking cessation without NRT fails.<sup>210</sup>

NRT use is also recommended in guidelines for smoking cessation in pregnancy, where cessation without NRT fails.<sup>79,124</sup> However, information on NRT prescribing and use in pregnant women is lacking worldwide. In light of this, the WHO recently recommended an urgent need for studies on surveillance of current use of NRT in pregnancy.<sup>73</sup> Literature describing NRT use in pregnancy is limited to observational studies from the USA and Denmark assessing the association between NRT use during pregnancy and adverse birth outcomes. The prevalence of self-reported NRT used in the first 12 weeks of gestation was 0.3%<sup>114</sup>, 2-2.5% in 17-27 weeks of gestation in the Danish National Birth Cohort<sup>112,113</sup> and in the Pregnancy Risk Assessment Monitoring System (PRAMS) from four USA states it was 3.9% (2004).<sup>111</sup> Since then, new NRT products have been introduced and international guidelines on gestational NRT use have changed. Thus far, only a limited number of studies in the UK have assessed prescribing

and uptake of NRT during pregnancy in the UK and these studies are either too small,<sup>116</sup> providing local data<sup>116,131</sup> or only including prescribing taking place in the NHS-SSS.<sup>132</sup> It is also important to know the NRT prescribing trends for pregnant women by different maternal factors as the prevalence of maternal smoking varies by different maternal factors (e.g. age, socioeconomic status etc.<sup>59</sup>). Therefore, investigation of factors related to NRT prescribing may give an insight on the characteristics of women who attempt to quit smoking during pregnancy and whether targeted interventions are needed for women with specific characteristics. However, none of these previous studies have assessed these in detail. The generalisability of the findings from the previous is therefore limited. Furthermore, none of the previous studies have assessed changes in prescribing after the relaxation of the licensing arrangements for NRT which is important to assess the effect of this change on the prescribing rules. Therefore, this chapter aims to assess the prescribing of NRT in and around pregnancy, using the UK primary care data. This will potentially provide population-based estimates for NRT prescribing in pregnant women which can be generalisable to the whole of the UK, which previous studies have failed to do. The specific objectives for the study discussed in this chapter are:

1. To examine patterns of NRT prescribing before, during and after pregnancy
2. To calculate annual prescribing prevalence of NRT before, during and after pregnancy to inform changes in relation to the MHRA relaxation
3. To assess whether and how NRT prescribing varies by maternal characteristics

This study was published in the *British Journal of General Practice* in September 2014 and attached as Appendix 10.4.



## **5.2 METHODS**

### **5.2.1 Study population**

The study population for this analysis was restricted to all pregnancies between January 2001 and September 2009 in women of childbearing age (15-49 years) which resulted in either a live birth or a stillbirth, as NRT only became available on NHS prescription in 2001.

### **5.2.2 Extracting smoking status, NRT prescribing and other covariates**

All prescriptions for NRT were extracted, using multilex drug codes for all the NRT formulations available in the UK according to the BNF (Appendix 10.6) which may be used by the GPs to prescribe NRT in primary care.<sup>210</sup> To investigate the maternal factors that may be associated with NRT prescribing during pregnancy, data were extracted on women's age at conception, socioeconomic deprivation as measured by quintiles of the Townsend Index of deprivation,<sup>177</sup> pre-conception BMI and recorded diagnoses of medical conditions (hypertension, diabetes, asthma, and mental illness) as described in Section 3.4.3. These conditions are most prevalent in women of childbearing age and are closely related to smoking<sup>51,59,195,211,212</sup> and therefore may also influence quit attempts made using NRT.

### **5.2.3 Statistical analysis**

The overall and annual proportions of pregnancies with one or more NRT prescriptions before, during and after pregnancy were determined. This was repeated restricting the denominator to pregnancies in smokers only (making use of gestational smoking data and smoking information from 27 months before conception). A period of nine months before and after pregnancy was used to calculate prescribing prevalence, as this was similar to the average pregnancy length allowing for comparisons of period prevalence. There is no evidence of the time before and after pregnancy during which smokers are more likely to

attempt to quit. However, since nine months is a comparatively long time and smoking behaviours may fluctuate during this time, prescribing prevalence of NRT was also assessed in smaller three month windows before, during and after pregnancy. In addition, the use of different forms of NRT (patches, gum, nasal spray, lozenges, sublingual tablets, and inhalator cartridges) and combination NRT was also assessed. Oromucosal nicotine spray was first authorised for use in November 2010<sup>213</sup> and therefore was not included in this analysis.

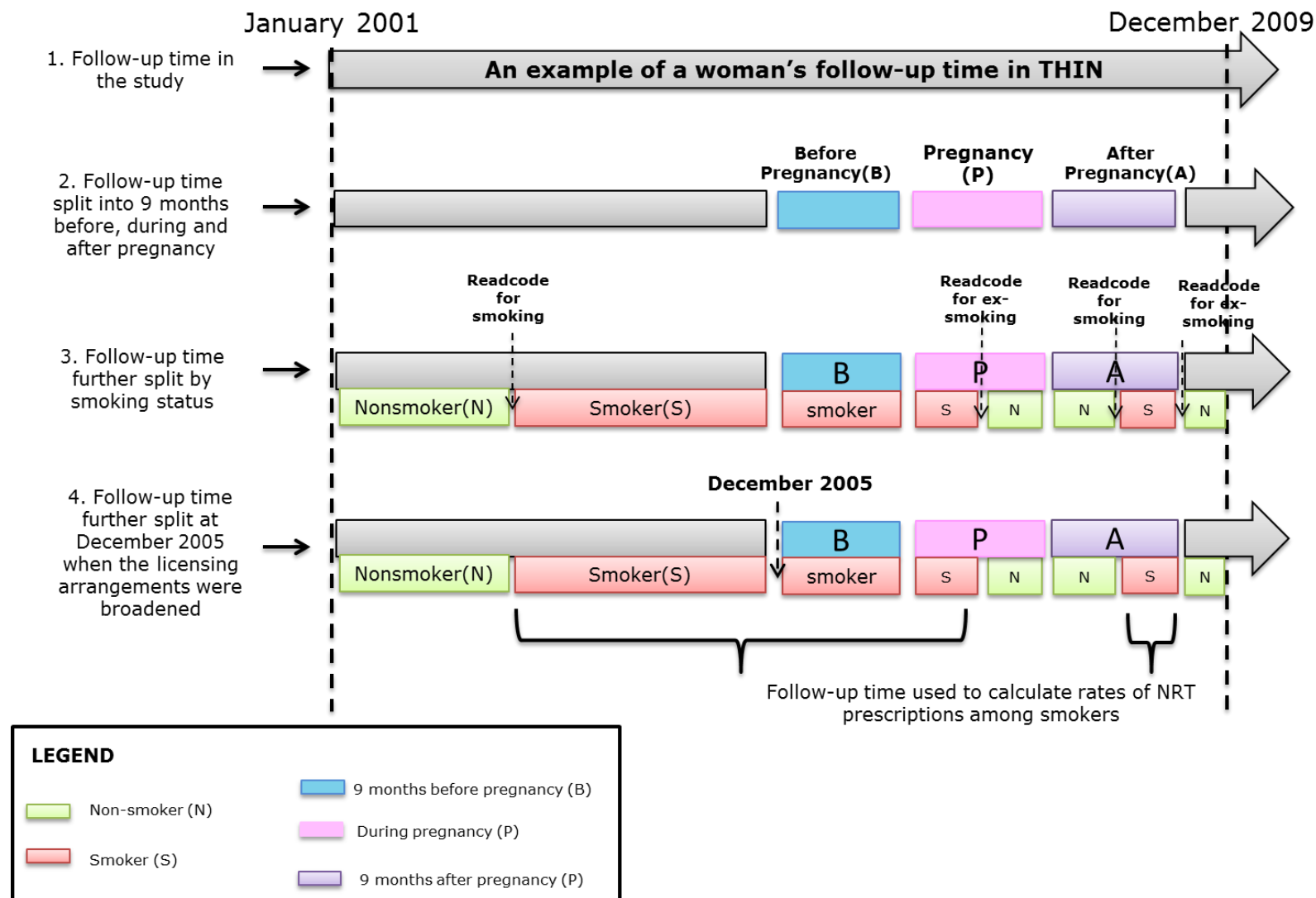
Logistic regression was used to calculate ORs for associations between women's characteristics and NRT prescribing to smokers during pregnancy, restricting the analysis to pregnancies delivered between January 2006 and December 2009 since NRT was not licensed for use in pregnancy until December 2005 and therefore prescribing was not expected to be very frequent. Likelihood ratio tests (LRT) were used to assess the associations with categorical covariates and Wald p-values were used for binary covariates. All covariates that reached statistical significance ( $p < 0.05$ ) in the univariable analysis were initially included in the multivariable analyses and each covariate was sequentially dropped from the model to assess whether the associations were still significant. Covariates that reached statistical significance ( $p < 0.05$ ) in the multivariable analysis were retained in the final model. As some women had more than one pregnancy during the study period, this potential clustering of pregnancies within women was accounted for by calculating robust CIs around the odds ratios using the clustered sandwich estimator,<sup>180,181</sup> which is explained in Section 3.4.4.

#### **5.2.4 Sensitivity analysis**

In addition to calculating overall proportions, rates of prescriptions per 1,000 person-years were also calculated as this allowed for better categorisation of time windows before, during and after pregnancy (nine months), controlling for possible fluctuations in smoking status. The study time was split into times

before, during and after pregnancy to accurately assess the rates of NRT prescribing for smokers in each of the three time periods. Smoking was treated as a time-varying covariate using lexis expansion i.e. women's smoking status was allowed to change at every point of smoking status recording in their primary care data to capture women's smoking episodes more accurately. Figure 5-1 explains the step-by-step splitting of the follow-up time for each woman by pregnancy time and smoking status. The follow-up time was further split into times before and after the relaxation of NRT licensing arrangements in December 2005. The rates of NRT prescriptions per 1,000 person-years were calculated before, during and after pregnancy in two time periods (2001 to 2005 and 2006 to 2009). Finally, rate ratios and 95% CIs were calculated to compare prescribing in smokers before and after the relaxation of licensing arrangements in the three time periods, using poisson regression.

**Figure 5-1 - Step-by-step splitting of the study follow-up time by smoking status and pregnancy time**



## **5.3 RESULTS**

### **5.3.1 Baseline characteristics**

A total of 201,465 women were identified with 255,411 pregnancies resulting in live births or stillbirths between January 2001 and December 2009, of which 45,045 (18%) were pregnancies of mothers classified as smokers. The mean age at conception was 29.5 years (sd 5.9) and the average length of pregnancy was 39.4 weeks (sd 2.2). Table 5-1 describes women's characteristics for all pregnancies and pregnancies among smokers, and NRT prescribing prevalence according to these characteristics. In the whole population, asthma, diabetes, hypertension and mental illness affected 9%, 2%, 3% and 9% of pregnancies respectively. Only the prevalence of asthma and mental illness were higher in smokers.

**Table 5-1 - Baseline characteristics of the study population**

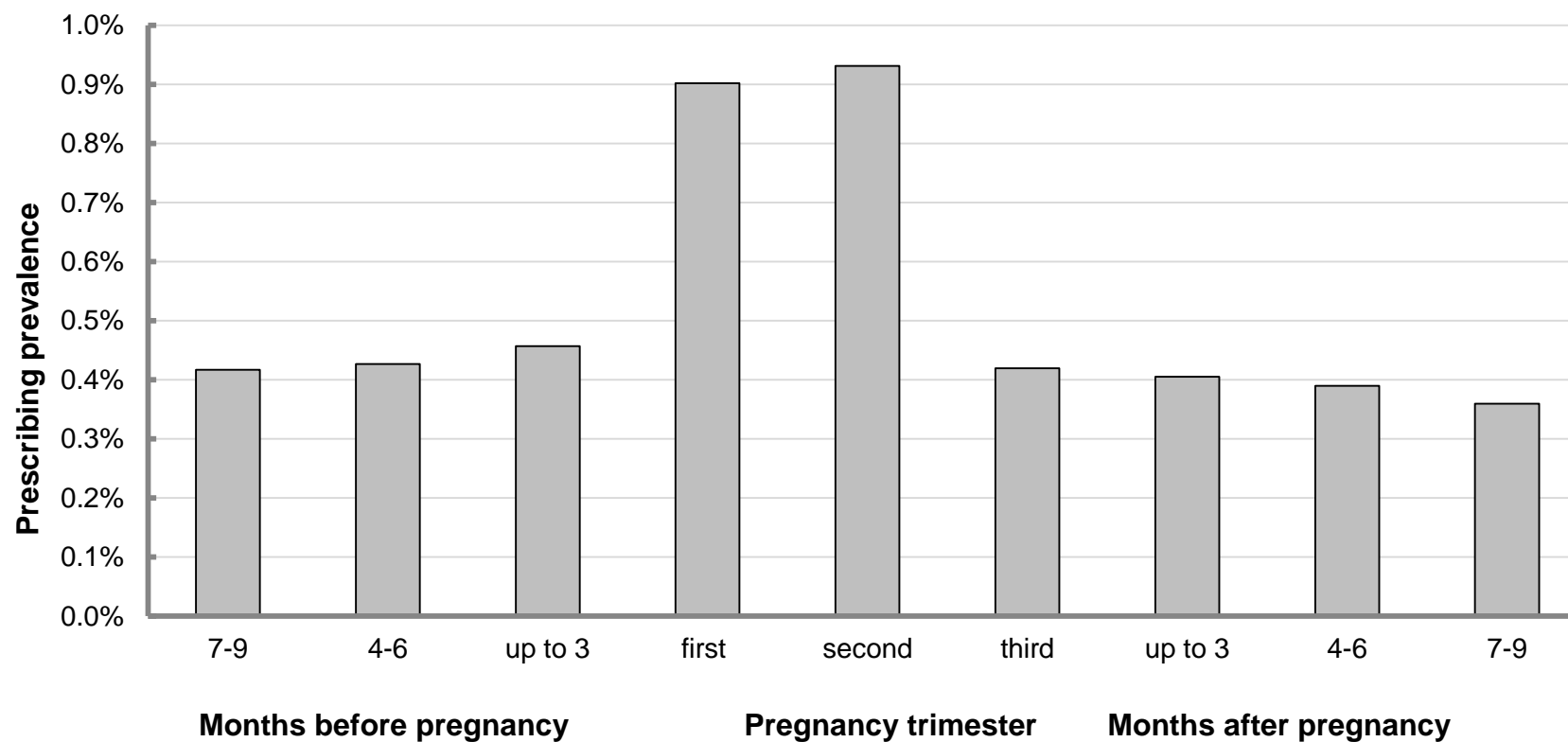
	<b>Total pregnancies (n=255,441)</b>	<b>Pregnancies with an NRT prescription (total n=4,826)</b>	<b>Pregnant smokers* (n=45,045)</b>	<b>Pregnant smokers with an NRT prescription (n=4,826)</b>
<b>Age at Conception</b>				
15-19 years	19,212	636 (3.3%)	6,716	623 (9.3%)
20-24 years	43,569	1,227 (2.8%)	12,300	1196 (9.7%)
25-29 years	69,159	1,237 (1.8%)	11,620	1223 (10.5%)
30-34 years	78,034	1,103 (1.4%)	9,246	1086 (11.7%)
35-39 years	38,764	527 (1.4%)	4,412	523 (11.9%)
40-44 years	6,384	90 (1.4%)	712	89 (12.5%)
45-49 years	319	6 (1.9%)	39	6 (15.4%)
<b>Townsend score in quintiles **</b>				
Quintile 1 – least deprived	57,859	486 (0.8%)	5,339	474 (8.9%)
Quintile 2	47,841	586 (1.2%)	6,118	582 (9.5%)
Quintile 3	49,670	921 (1.9%)	8,797	904 (10.3%)
Quintile 4	47,292	1,315 (2.8%)	11,376	1,295 (11.4%)
Quintile 5 - most deprived	36,103	1,188 (3.3%)	10,515	1,166 (11.1%)
Missing	16,676	330 (2.0%)	2,900	325 (11.2%)
<b>Pre-conception Body Mass Index</b>				
Normal(18.0-24.9)	80,003	1,502 (1.9%)	15,040	1,483 (9.9%)
Underweight(<18.0)	5,871	152 (2.6%)	1,630	151 (9.3%)
Overweight(25-29.9)	38,931	784 (2.0%)	7,306	771 (10.6%)
Obese(>=30)	26,753	617 (2.3%)	5,500	603 (11.0%)
Missing	103,883	1,771 (1.7%)	15,569	1,738 (11.2%)
<b>Asthma</b>	21,884	678 (3.1%)	5,216	670 (12.8%)
<b>Hypertension</b>	6,885	107 (1.6%)	966	107 (11.1%)
<b>Diabetes</b>	5,971	114 (1.9%)	939	114 (12.1%)
<b>Mental illness</b>	24,178	947 (3.9%)	7,166	937 (13.1%)

\*recorded as current smoker within 27 months before conception until delivery, \*\*socioeconomic status

### **5.3.2 Patterns of NRT prescribing in and around pregnancy**

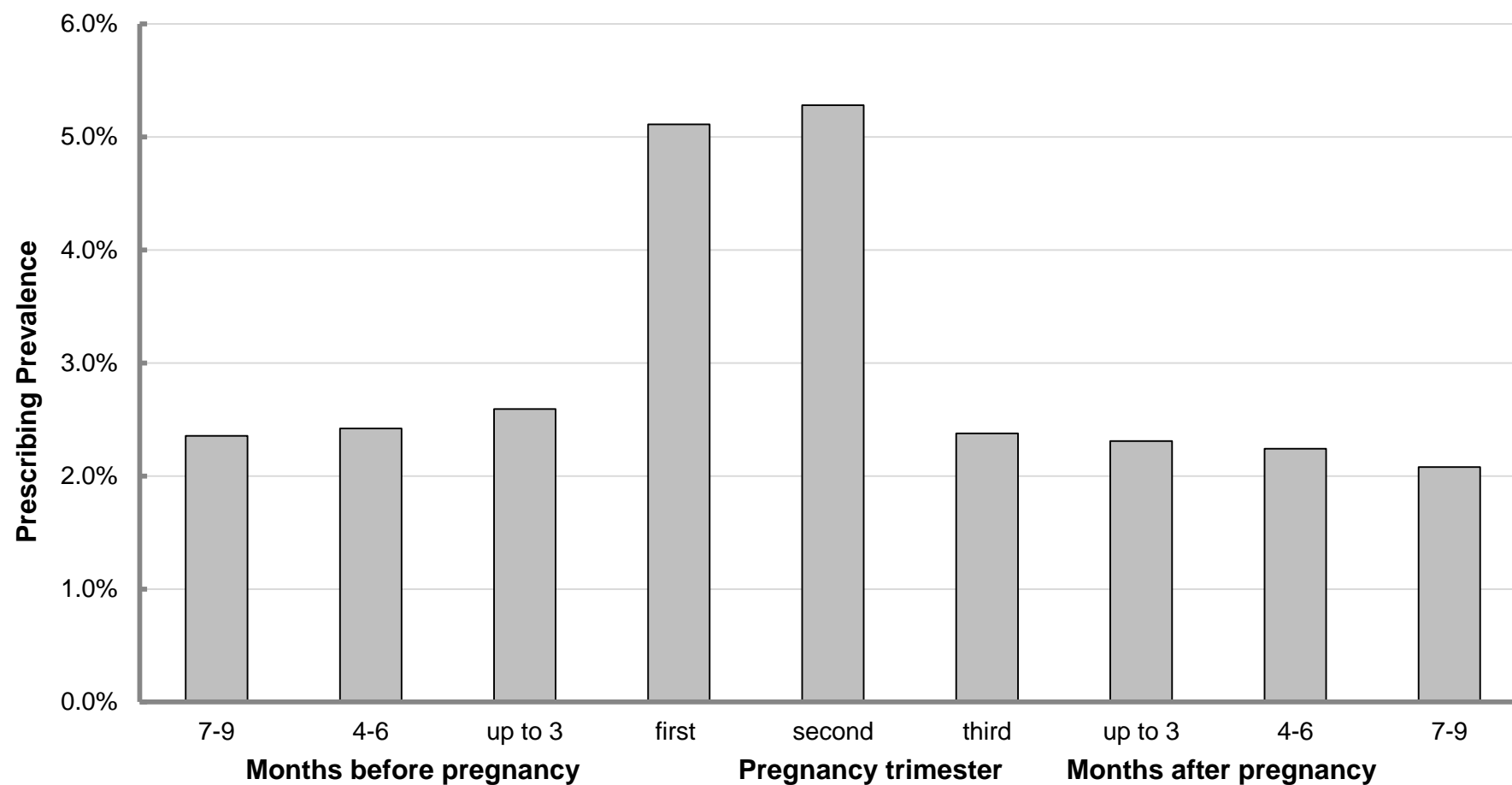
NRT was prescribed in a total of 4,826 pregnancies, which represents a prescribing prevalence of approximately 2% of all pregnancies and 11% of pregnancies in smokers. In comparison, the prescribing prevalence was 1% during both the nine months before and after pregnancy and approximately 5% in pregnancies in smokers. Figure 5-2 shows the prescribing prevalence in each three-month period before, during and after pregnancy in all pregnant women and Figure 5-3 shows the prescribing prevalence among pregnant smokers. Among smokers, NRT prescribing was more prevalent during the first and second trimester, with a prescribing prevalence of just over 5% in each compared to approximately 2.5% in the third trimester, which was similar to the periods before and after pregnancy.

**Figure 5-2 - Proportion of all pregnancies with NRT prescription in each three month period, between 2001 and 2009**



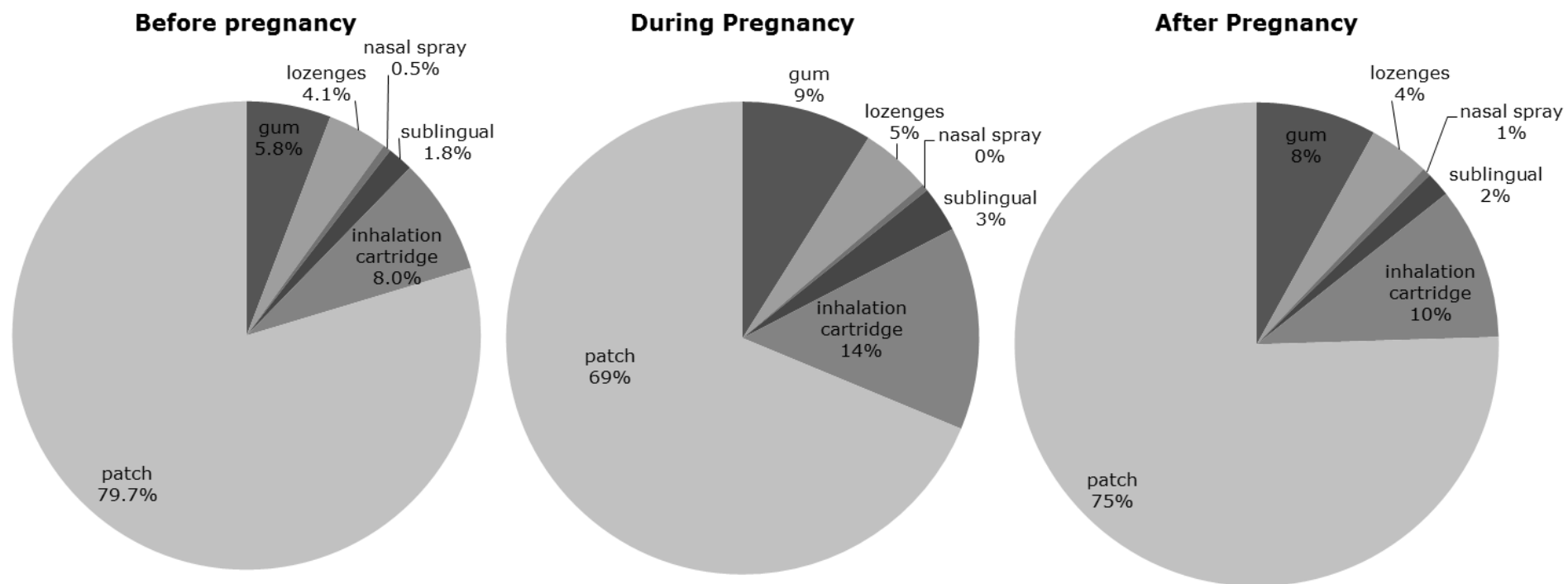


**Figure 5-3 - Proportion of pregnant smokers with NRT prescription in each three month time period, between 2001 and 2009**



Among the 4,826 women who were prescribed NRT during the nine months of pregnancy, over half of these (56%) were only issued one prescription for NRT. Another quarter of these women were prescribed NRT on two separate occasions. The maximum number of prescriptions issued during pregnancy was 26. On average, women were prescribed a total of 2 weeks' worth of NRT (IQR 1-2 weeks). The frequency of NRT prescribing nine months before and after pregnancy was similar to the pattern within pregnancy, with over half of the women receiving only a single prescription for NRT in each nine month period. In approximately two thirds of the pregnancies in which NRT was prescribed during gestation NRT prescribing was initiated only during pregnancy; there were no records of NRT prescriptions in these women's primary care data prior to the start of pregnancy. The most common form of NRT used during pregnancy was transdermal patches (approximately 70% of all prescriptions), followed by inhalator cartridges (14%), gum (9%), lozenges (5%), sublingual tablets (3%) and nasal spray (0.5%). The distribution of NRT forms prescribed before and after pregnancy was very similar. Figure 5-4 describes the distribution of different forms of NRT prescribed before, during and after pregnancy. Prescribing of combination NRT was observed in 471 (10%) of the 4,826 women where NRT was prescribed during pregnancy, 204 (8%) of 2,645 mothers with NRT prescriptions before pregnancy and 273 (11%) of 2,410 mothers with NRT prescriptions after pregnancy.

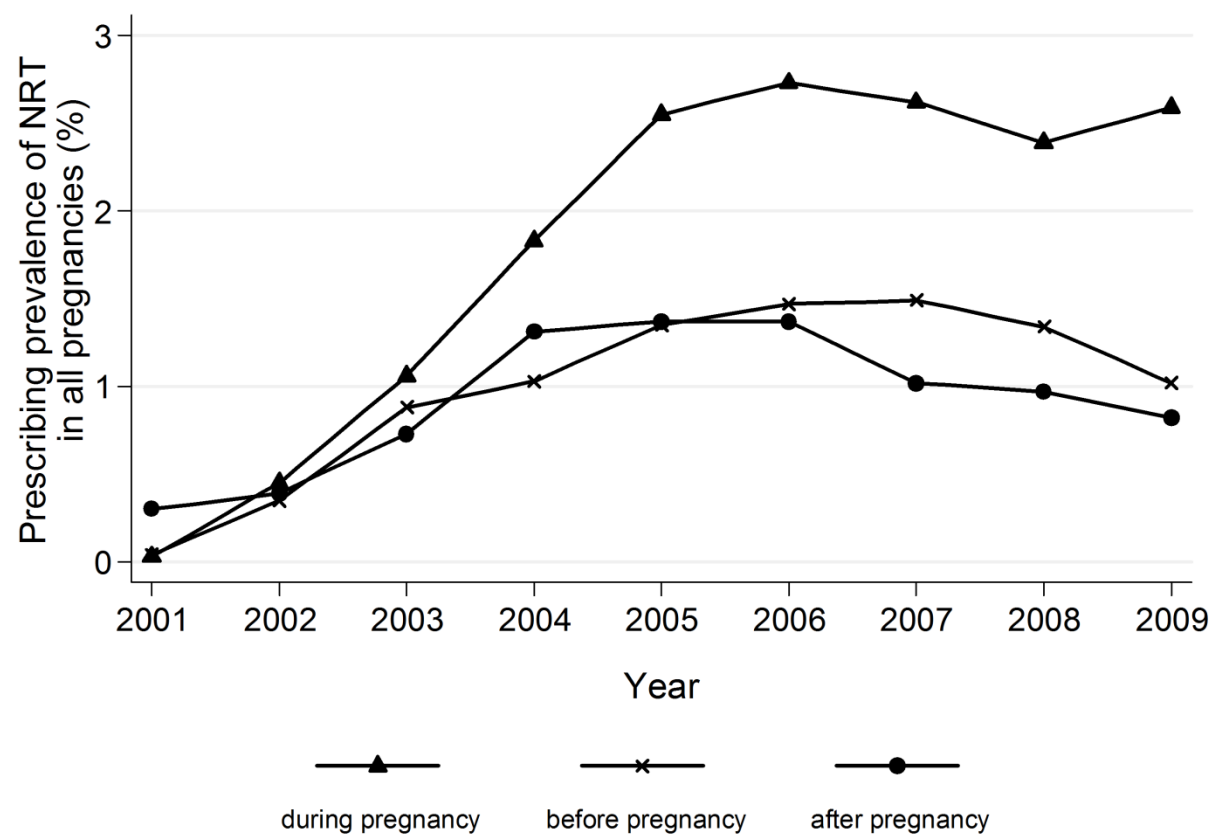
**Figure 5-4 - Use of different forms of NRT before, during and after pregnancy**



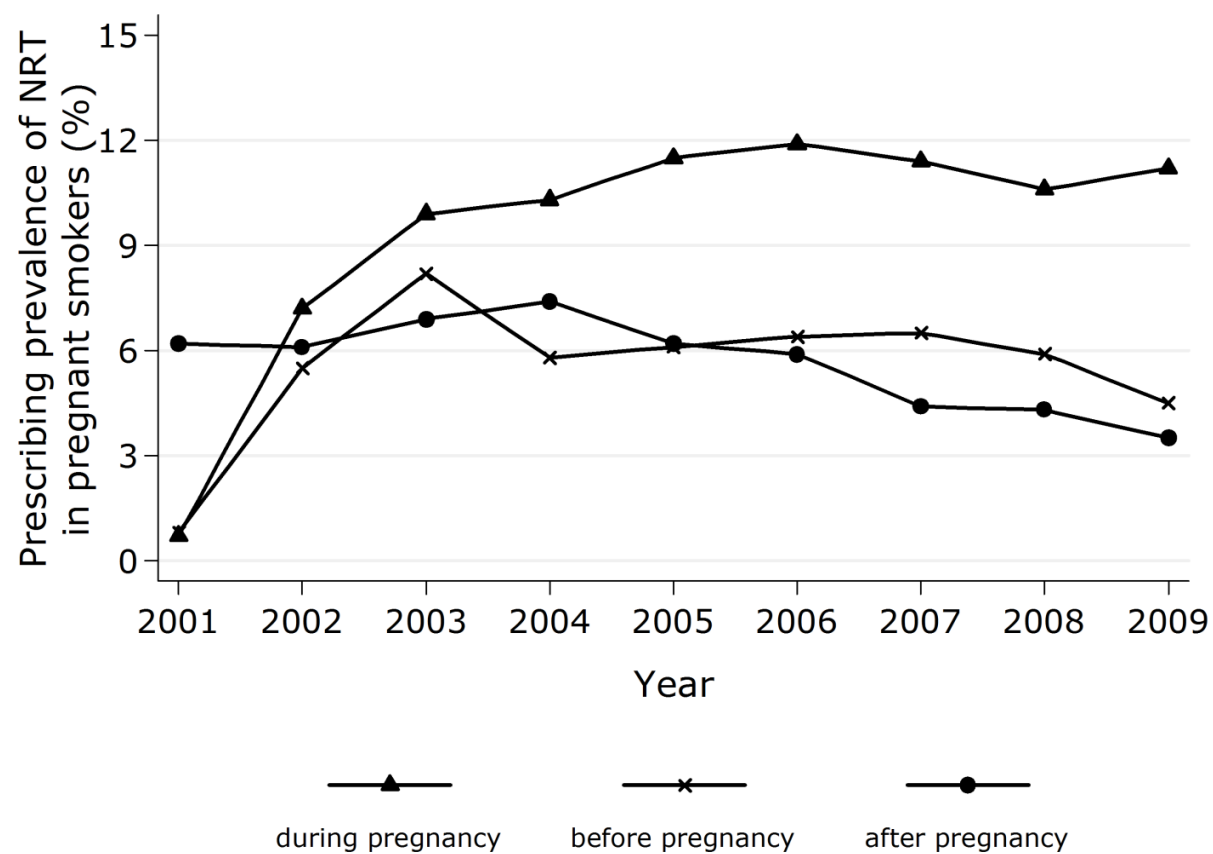
### **5.3.3 Annual prescribing of NRT before, during and after pregnancy**

Figure 5-5 shows the annual proportion of pregnancies and Figure 5-6 shows the proportion of pregnancies in smokers between 2001 and 2009 where NRT was prescribed before, during and after pregnancy. In 2001, the prescribing prevalence of NRT during pregnancy, taking all pregnancies as the denominator, was 0.03% (0.7% in pregnancies in smokers). This increased to 2.6% (11.5% in pregnancies in smokers) in 2005 after which it remained stable such that in 2009 the prescribing prevalence of NRT in all pregnancies was 2.6% (11.2% in pregnancies in smokers). The overall prescribing prevalence of NRT during pregnancy between 2001 and 2005 (i.e. before the relaxation of licensing arrangements) was 1.1 % ( 9.6% in pregnancies in smokers) and increased to 2.5% (11.1% in pregnancies in smokers) for the period of 2006-2009 (time after the relaxation of licensing arrangements). NRT prescribing prevalence in the nine months before and after pregnancy increased until 2005 after which it remained stable at around 1% (6% in smokers), with a slight decline after 2006.

**Figure 5-5 - Annual prescribing prevalence of NRT in all pregnancies**



**Figure 5-6 - Prescribing prevalence of NRT in pregnant smokers**



#### **5.3.4 Prescribing of NRT by maternal characteristics**

Table 5-2 shows the maternal characteristics associated with prescribing of NRT within pregnant smokers between 2006 and 2009. Pregnant smokers from more deprived groups were more likely to receive an NRT prescription compared to pregnant smokers from less deprived groups (OR for Quintile 5 compared to Quintile 1 = 1.33, 95% CI 1.14-1.52) and older pregnant smokers were more likely to receive NRT than younger smokers (OR for 30-35 years compared to 25-30 = 1.21, 95% CI 1.09-1.35). Pregnant smokers with a diagnosis of asthma were 34% more likely to be issued an NRT prescription in primary care compared to pregnant smokers without asthma (OR 1.34, 95% CI 1.21-1.50). In addition, pregnant smokers with a diagnosis of mental illness were 29% more likely to receive a prescription for NRT during pregnancy compared to pregnant smokers without mental illness (OR 1.29, 95% CI 1.18-1.43).

**Table 5-2 - Prescribing of NRT during pregnancy in smokers by maternal characteristics between January 2006 and December 2009**

December 2009

Demographic variables	Pregnant smokers with one or more NRT prescriptions (n=3,160)	Unadjusted Odds Ratio (95% CI)	p-value	Adjusted Odds Ratio (95% CI)**	p-value
<b>Age at conception</b>					
15-20 years	430 (10.1%)	0.91 (0.80-1.02)	<0.001	0.89 (0.78-1.00)	<0.001
20-25 years	833 (10.6%)	0.96 (0.86-1.06)		0.94 (0.85-1.04)	
25-30 years	801 (11.0%)	1		1	
30-35 years	692 (12.8%)	1.19 (1.07-1.32)		1.21 (1.09-1.35)	
35-40 years	337 (12.5%)	1.15 (1.00-1.32)		1.18 (1.03-1.35)	
40-45 years	63 (13.8%)	1.29 (0.98-1.69)		1.28 (0.97-1.69)	
45-49 years	4 (16.7%)	1.61 (0.55-4.73)		1.58 (0.53-4.71)	
<b>Townsend score</b>					
Quintile 1 (least deprived)	285 (9.4%)	1	<0.001	1	<0.001
Quintile 2	384 (10.3%)	1.10 (0.94-1.30)		1.11 (0.94-1.31)	
Quintile 3	611 (11.0%)	1.20 (1.04-1.39)		1.23 (1.05-1.43)	
Quintile 4	880 (12.2%)	1.35 (1.17-1.56)		1.39 (1.20-1.61)	
Quintile 5 (most deprived)	766 (11.6%)	1.28 (1.10-1.47)		1.33 (1.14-1.52)	
Missing	234 (12.6%)	1.39 (1.16-1.67)		1.43 (1.21-1.76)	
<b>Pre-conception Body Mass Index (kg/m<sup>2</sup>)</b>					
Normal(18.0-24.9)	1,036 (11.1%)	0.89 (0.2-1.09)	0.549	-	-
Underweight(<18.0)	104 (10.0%)	1			
Overweight(25-29.9)	532 (11.3%)	1.02 (0.91-1.35)			
Obese(>=30)	433 (11.8%)	1.06 (0.94-1.19)			
Missing	1,055 (11.4%)	1.03 (0.94-1.13)			
<b>Diabetes *</b>	86 (13.5%)	1.23 (0.98-1.56)	0.078	-	-
<b>Hypertension*</b>	71 (12.2%)	1.09 (0.85-1.41)	0.476	-	-
<b>Asthma*</b>	477 (14.4%)	1.37 (1.24-1.53)	<0.001	1.34 (1.21-1.50)	<0.001
<b>Mental illness*</b>	612 (13.9%)	1.34 (1.22-1.47)	<0.001	1.29 (1.18-1.43)	<0.001

NRT – Nicotine Replacement Therapy, CI – confidence interval, \* compared to women without the condition \*\*all covariates mutually adjusted



### **5.3.5 Sensitivity analysis**

A total of 201,465 women contributed 669,230 person-years before pregnancy, 927,952 person-years during pregnancy and 971,754 person-years after pregnancy giving a total person time of 2,568,936 years. The rate of NRT prescribing during pregnancy in smokers between 2001 and 2005 was 34.1 prescriptions per 1000 person-years (95% CI 34.1-33.0), equating to approximately 3.4% of women annually. The rate of NRT prescribing in the nine months before and after in women during pregnancy was 30% lower than the rates of prescribing during (RR 0.70, 95% CI 0.66-0.73) each. After the relaxation of licensing arrangements in December 2005 this rate of prescribing during pregnancy increased to 68.3 per 1000 person-years equating to approximately 7% of women annually. The gradient between prescribing during pregnancy and outside increased such that women were 45% less likely to receive an NRT prescription before pregnancy (RR 0.55, 95% CI 0.52-0.58) and 52% less likely to receive a prescription after pregnancy (RR 0.48, 95% CI 0.46-0.50) compared to during pregnancy.

**Table 5-3 - Time specific rates and rate ratios of NRT prescribing**

Exposure time	No. of Prescriptions	Person-years	Rate*	95% CI	RR	95% CI
<b>2001-2005</b>						
9 months before pregnancy	2,535	107,857	23.5	22.5-24.5	0.70	0.66-0.73
During pregnancy	3,701	108,476	34.1	34.1-33.0	Reference	
9 months after pregnancy	1,994	84,671	23.6	22.5-24.6	0.70	0.66-0.73
<b>2006-2009</b>						
9 months before pregnancy	2,107	561,373	37.5	35.9-39.2	0.55	0.52-0.58
During pregnancy	5,594	819,476	68.3	66.5-70.1	Reference	
9 months after pregnancy	2,892	887,083	32.6	31.4-33.8	0.48	0.46-0.50

\*rate of NRT prescribing per 1000 person-years

RR – Rate Ratio, CI – Confidence interval

Total number of women=201,465

## **5.4 DISCUSSION**

### **5.4.1 Principal findings**

After NRT was made available on NHS prescription in 2001 prescribing in and around pregnancy increased; by 2005 prescribing was twice as high during pregnancy as that in the nine months immediately before and after pregnancy, despite it being contraindicated for pregnant women. The December 2005 licence relaxation to allow prescribing in pregnancy did not further increase these trends and the prescribing prevalence during pregnancy has remained stable at 2% (11% in smokers). Women with asthma or mental illness and those from more socio-economically deprived areas were more likely to receive prescriptions during pregnancy. However, 80% women received less than 2 prescriptions, lasting two weeks on average.

### **5.4.2 Strengths and limitations**

This study presents longitudinal and contemporaneous prescribing estimates; it is the first study of NRT prescribing during pregnancy in the UK primary care and the only study internationally to assess NRT prescribing trends. The ascertainment of NRT in this study is based on prescribing data rather than the self-reported NRT use, which women may under-report.<sup>112</sup> Additionally, prescribing in the nine month periods immediately before and after pregnancy has also been assessed in this study, whereas other studies only report NRT use in trimesters 1-2.<sup>112-114,129</sup> Therefore, the findings of this study are novel in that they present the first estimates of NRT prescribing around pregnancy, which provides some information on smoking cessation attempts pre-conception and postpartum.

The data used in this study capture all NRT prescribing to pregnant women in UK primary care in practices registered in THIN. However, this may not include NRT prescribing in other settings such as local NHS Stop Smoking Services for

Pregnant women (SSSP) and NRT purchased over-the-counter or off the shelf. Only 3% of pregnant women use the SSSP on average each year<sup>214,215</sup> and a survey of all SSSPs in England conducted between April 2010 and March 2011 reported that almost half of the NRT provided by these services was issued through GPs.<sup>185</sup> In terms of self-purchased NRT, this is expected to be infrequent for several reasons. Firstly, the prevalence of medication use without health professional consultation is lower during pregnancy than when women are not pregnant.<sup>216</sup> Furthermore, all NRT packaging, clearly instructs women to consult a doctor before using this if they are pregnant. Lastly, in the UK women are entitled to free NHS prescriptions during pregnancy and the first year after delivery<sup>217</sup> so they may be more likely to get free prescriptions through GPs than paying for NRT. Hence, this study is believed to capture the majority of the prescriptions of NRT issued.

Some women may quit or relapse after delivery consequently leading to changes in the denominator of smokers and therefore the NRT estimates could be both over-estimated if more women relapse than are recorded and under-estimated if more women quit. Therefore, prescribing prevalence is also reported in all pregnancies in addition to smokers. Also, in these data over 75% of pregnant women who were classified as smokers during pregnancy and who had a recording of smoking status within the nine months after delivery were still recorded to be smokers. Hence, a substantial over-estimation or under-estimation of NRT prescribing prevalence in smokers is unlikely. The rates of NRT prescribing were also calculated, treating both smoking and pregnancy as time-varying covariates, to take into account the changes in women's smoking status over time. These rates were found to be slightly lower than the calculated NRT prescribing prevalence in smokers (~7% compared to ~11% after 2005). This is because although rates allow for more appropriate categorisation of time and exposure windows, the recording of smoking status during pregnancy is

incomplete as discussed in Chapter 3, masking the true reflection of smoking status changes over time and consequently limiting the advantage of using lexis expansion for this analysis. Nevertheless, the rate ratios using poisson regression were in concordance with the other results reiterating that NRT prescribing during pregnancy was almost double that of the prescribing before and after pregnancy in the post-relaxation period (RR 0.55 before pregnancy and RR 0.48 after pregnancy).

Another potential limitation of the study is that prescriptions provide no measures of actual medication use, compliance to the drug therapy or successful quit attempts made and some of the prescriptions issued may not have been redeemed. However, a validation study comparing the recorded prescriptions for smoking cessation medications in THIN and the NHS dispensing data between January 2004 and December 2005 reported good comparability between the two data sources indicating that prescriptions recorded for smoking cessation medications in primary care data are collected by the patients.<sup>156</sup> The only measures of compliance are available from trials. The SNAP trial reported low compliance rates in both treatment and placebo group (7.2% and 2.8% respectively using NRT for more than a month).<sup>100</sup> However, the reasons for low compliance remain unexplored. A qualitative study conducted on pregnant smokers in Australia explored barriers to NRT use and found that women with medical problems or history of obstetric complications expressed doubts about using NRT and were sceptical about its effectiveness.<sup>118</sup> However, specific reasons for low compliance rates to NRT during pregnancy have not been studied to date. Lastly, there were no measures available for nicotine dependence in the data. Assessing these measures of dependence (e.g. Fagerstrom Test for Nicotine Dependence) is difficult without surveying the study participants which would be limited by potential response biases and are rarely possible on the large population scale presented by the data in this study.

### **5.4.3 Comparison with current literature**

There are no studies internationally which have assessed the annual prescribing prevalence of NRT in pregnant women in detail. However data from nested case-control studies from the USA and Denmark assessing associations between NRT use and adverse pregnancy outcomes report the overall prescribing prevalence of NRT in all pregnancies to range from 0.3 to 4%,<sup>111-113</sup> which is very similar to the findings of this study. The findings of this study closely mirror that of the Scottish data linkage study where NRT was prescribed to 2.4% of all pregnant women<sup>131</sup>. In addition, NRT usage in pregnant smokers attending English SSSPs is reported to be 85%<sup>132</sup> and considering that only 3% of pregnant women attend these services, this also equates to 2.5%. This implies that the uptake of NRT during pregnancy in smokers is quite high (~11% of smokers) despite the lack of evidence of its effectiveness and safety.

The results of this study also demonstrate that the annual prescribing prevalence of NRT has been stable and not increased much since the changes in the licensing arrangements in December 2005, although overall prescribing in the years after the relaxation of licensing arrangements has almost doubled. The difference between the prescribing prevalence in pregnancy and the nine month periods immediately before and after pregnancy started widening after 2003. This may be attributed to the changes in prescribing indications for NRT use implemented in May 2003, when pregnancy was removed from the list of contraindications for NRT use and instead cautious use of NRT products in pregnancy was advised if smoking cessation without NRT failed.<sup>96</sup> After the relaxation of licensing arrangements of NRT in 2005 prescribing of NRT during pregnancy was almost twice as high compared to the prescribing in the nine months immediately before and after pregnancy. This may also be related to the licensing of varenicline for smoking cessation in the general non-pregnant

population in December 2006, after which a reduction in prescribing of NRT and bupropion in the general population was seen.<sup>218</sup> Alternatively, women may be more motivated to quit after finding out they are pregnant or may deliberately wait to quit until they get pregnant as they can get free NRT prescriptions during pregnancy.

The prescribing prevalence of NRT was found to be the highest in the first two trimesters during pregnancy compared to the other time periods under study and the prescribing prevalence within the third trimester was very similar to the prescribing prevalence before and after pregnancy. In a survey of all SSSPs in England between April 2010 and March 2011 assessing delivery of smoking cessation support, 60% of the SSSPs reported that there was a difference in the proportion of pregnant women seeking help by the stage of pregnancy, with the most referrals given in the first two trimesters.<sup>185</sup> This may be related to the level of motivation to quit smoking which has been shown to be higher during early pregnancy compared to late pregnancy resulting in more women seeking help at these times in pregnancy.<sup>219</sup> A study using an online database containing data on 3,880 pregnant smokers supported by one of the 44 regional SSS in England reported that 55% of all pregnant smokers (65% of pregnant NRT users) used combination NRT,<sup>132</sup> which is very high compared of 10% as shown in this work. This is mostly likely related to different baseline populations i.e. data from specialist stop smoking services compared to data from primary care. Women voluntarily attending these specialist services will likely have a higher motivation to quit which may result in more quit attempts and more NRT being prescribed compared to women attending primary care.

NICE recommends that pregnant women should initially be prescribed two weeks of NRT from their agreed stop date, with further NRT after re-assessment.<sup>79</sup> The average duration of prescription for women in this study was two weeks and most women (80%) received two or less prescriptions. One reason for this may

be that compliance was low and women did not quit or use it to quit in which case no further NRT was prescribed. Some women may have bought NRT independently after the first prescription; however, considering that women are entitled to free prescriptions during pregnancy and NRT from retailers is reasonably expensive, this is unlikely. Studies in other populations have not reported the duration of NRT use in pregnancy. However, eight to twelve weeks' use is recommended for optimal effectiveness in the general population<sup>110</sup> so it is unlikely that two weeks' use is effective for smoking cessation in pregnancy.

A study conducted in four states of the USA, in 5,716 pregnant women between the ages of 18-45 years, found NRT prescribing to be lower in pregnant smokers younger than 35 years of age compared to pregnant smokers over the age of 35.<sup>111</sup> In comparison, prescribing was assessed within 5 year age bands between 15-49 years in this study and the results were found to be similar, with NRT prescribing increasing with age; however the confidence intervals between the age categories overlapped. Advancing maternal age is associated with a higher risk for pregnancy complications<sup>220</sup> which may lead women to visit their GPs more often during pregnancy providing more opportunities to provide smoking cessation advice and prescribe NRT which may explain higher prescribing rates in these smokers compared to younger smokers. Low socioeconomic status is associated with a higher prevalence of chronic disease<sup>191</sup> and higher risk of adverse pregnancy outcomes<sup>221</sup>, which would explain why pregnant smokers in the deprived group would be prescribed more NRT than affluent groups. Asthma and mental illness are the most common conditions encountered during pregnancy<sup>194,222</sup> and are closely related to smoking, which may explain a significant association with NRT prescribing compared to other conditions.



## **5.5 CHAPTER CONCLUSIONS**

In conclusion, this study shows that the prevalence of prescribing of NRT during pregnancy, especially after the relaxation of licensing arrangements in 2005, was almost twice the prevalence of prescribing in the nine months immediately before and after pregnancy. Although studies on NRT prescribing in pregnancy are lacking worldwide, these findings give insight into prescribing in and around pregnancy and highlight that the prescribing of NRT during pregnancy is quite high. These data also show that NRT was prescribed for an average of only two weeks during pregnancy which is unlikely to be effective.

Prescribing was also found to be relatively lower before and after pregnancy, which are also important times when quitting has significant health benefits for the woman and her child. This is indicative of a possible missed opportunity to assist many young women in quitting smoking. Whilst interactions between health professionals and pregnant women should be used to discuss and offer interventions to promote smoking cessation, greater potential benefit would be derived from starting before pregnancy which should be a focus for women and health care providers.

## **6 NICOTINE REPLACEMENT THERAPY, MATERNAL SMOKING AND CONGENITAL ANOMALIES**

### **6.1 INTRODUCTION**

The findings from the previous chapter report that approximately 11% of pregnant smokers are prescribed NRT in primary care settings annually. In addition, some women may be getting their NRT directly from the SSSP and some, although a small proportion, may be buying it OTC which would make the proportions of pregnant smokers using NRT even higher. Whilst the use of NRT is now recommended for smoking cessation during pregnancy in both UK and European guidelines,<sup>79,124</sup> the evidence concerning its safety in pregnancy is still lacking. Therefore, the WHO has made a strong recommendation for more research on the safety of NRT in pregnant women.<sup>73</sup> This chapter and the following chapter (Chapter 6 and Chapter 7) address this gap in the literature by assessing the safety of NRT use during pregnancy. This chapter focuses on investigating the relationship between antenatal NRT exposure or smoking, as recorded in primary care data, and the presence of congenital anomalies in children born to women exposed to these potential risks in early pregnancy and the following chapter will focus on other birth outcomes.

The association between maternal smoking in pregnancy and congenital anomalies in infants seems to be biologically plausible. Compromised oocyte quality in mothers who smoke may be one of the possible mechanisms by which smoking causes congenital anomalies.<sup>223</sup> Another possible mechanism is the chromosomal damage and epigenetic changes leading to subtle changes in the gene expression in babies of mothers who smoke.<sup>223</sup> However, this association is currently not very clear in the literature. A large systematic review of observational studies published between 1959 to 2010 including 173,687 cases of congenital anomalies and 11,674,332 controls showed an OR of 1.01 (0.96-

1.07) for all malformations combined in relation to maternal smoking during pregnancy. However, significantly increased risks of system-specific anomalies including heart defects (OR 1.09, 95% CI 1.02-1.17), musculoskeletal defects (OR 1.16, 95% CI 1.05-1.27), orofacial clefts (OR 1.28, 95% CI 1.20-1.36), limb defects (OR 1.26, 95% CI 1.15-1.39), eye defects (OR 1.25, 95% CI 1.11-1.40) and gastrointestinal defects (OR 1.27, 95% CI 1.18-1.36) were found.<sup>28</sup>

Contrary to the systematic review, a newer study based on 1,676 cases and 3,267 controls from a total of 44,732 live births in Rhode Island between 2007 and 2010 found a significantly increased risk of congenital anomalies associated with maternal smoking (OR 1.27, 95% CI 1.05-1.55).<sup>224</sup> Similarly, a more recent case-control analysis from the Baltimore-Washington Infant Study found no statistically significant association between maternal smoking and congenital heart defects (OR 1.07, 95% CI 0.80-1.45) however an increased risk was reported for specific anomalies e.g. pulmonary valve stenosis (OR 1.35, 95% CI 1.05-1.74), truncus arteriosus (OR 1.90, 95% CI 1.04-3.45).<sup>225</sup> Another study using the PRAMS data from nine states of the USA found no increased risk of congenital heart defects in relation to maternal smoking (OR 0.50, 95% CI 0.22-1.10).<sup>226</sup> In contrast, a study from Greece including 157 infants with congenital heart defects and 208 infant without congenital heart defects born between 2006 and 2009 reported approximately a three-fold increase in the risk of congenital heart defects associated with maternal smoking during pregnancy (OR 2.75, 95% CI 1.66-4.48)<sup>227</sup> and a systematic review including all studies between 1947 to 2011 on maternal smoking and congenital heart defect found the risk of congenital heart defects to be 11% higher in children of mothers who smoked compared to non-smokers (RR 1.11, 95% CI 1.02-1.21).<sup>228</sup> Data from the National Birth Defects Prevention Study (NBDPS), USA showed no significant increase in the risk of neural tube defect in children in relation to active maternal smoking (OR 0.9, 95% CI 0.8-1.1).<sup>229</sup> Hence, to-date the evidence of the association of maternal smoking and congenital anomalies is inconclusive.

The evidence of the teratogenic safety of NRT is only limited to two studies which have assessed the association between maternal use of NRT during pregnancy and congenital anomalies in the offspring. Table 6-1 describes these studies in detail.

**Table 6-1 Summary of studies assessing congenital anomalies in relation to NRT use during pregnancy**

<b>First author, year and location</b>	<b>Study methodology</b>	<b>Sample size (Inclusion/Exclusion)</b>	<b>Exposure Assessment</b>	<b>Outcome Assessment</b>	<b>Results for NRT safety</b>
Coleman (2012), UK <sup>100</sup>	Large, double-blinded, placebo-controlled multicentre RCT	1050 participants between 16 to 50 years with pregnancies of 12-24 weeks of gestation smoking five or more cigarettes per day	4 weeks supply of Standard nicotine patch (15mg/16 hrs) versus visually identical placebo, started on the quit date	Secondary outcome: Adverse pregnancy and birth outcomes including congenital anomalies	OR for congenital anomalies associated with NRT use = 0.70 (95% CI 0.30-1.66) compared to placebo group. Estimates only based on 9 cases in the treatment group and 13 cases in the placebo group.
Morales-Suarez-Varela (2006), Denmark <sup>114</sup>	Cohort study using Danish National Birth Cohort	76,768 pregnancies between 1996 and 2002	Smoking and NRT during the first 12 weeks of pregnancy	Congenital anomalies diagnosed at birth or during the first year of life, further classified based on EUROCAT criteria <sup>230</sup>	OR 1.61 (95% CI 1.01-2.56) for congenital malformations in children born to non-smokers, who used nicotine substitutes compared to non-smokers who did not use any nicotine substitutes. When restricted to major malformations the odds ratio was 1.13(95% CI 0.62-2.07)

The SNAP trial found no association between the use of NRT during pregnancy and congenital anomalies in the offspring.<sup>100</sup> Although the SNAP trial is the biggest trial of NRT patches in pregnancy conducted so far, the primary end point was abstinence from the date of smoking cessation until delivery and therefore all the safety analyses were underpowered, especially for the more rare outcomes like congenital anomalies. This finding was based on only 22 children with congenital anomalies so this negative finding for the association between NRT use in pregnancy and congenital anomalies could be due to Type 2 error (low statistical power) in the trial to detect any association with congenital anomalies. Another important point to consider is that the mean gestational age at the time of study enrolment in the trial was about 16 weeks indicating that most of the pregnant women in the trial were given NRT after the end of the first trimester, when most of the organ development had already taken place. By contrast, the study using the Danish National Birth Cohort (DNBC) found a 61% (95% CI 1.01-2.58) increase in the risk of congenital anomalies in the babies of mothers using NRT during pregnancy compared to non-smokers but no increased risk was found when restricted to only major congenital anomalies. Although the population-based nature of the study and prospective data collection minimised the potential for ascertainment and selection bias in the study, the data on smoking and NRT use were self-reported. Furthermore, this study was conducted over a decade ago (1997-2003) after which many new forms of NRT have been introduced to the market and the prescribing of NRT in pregnancy has increased. In light of these limitations of the current literature, this chapter describes the relationship between antenatal exposure to NRT or maternal smoking described in primary care data and the presence of MCAs in children born to women exposed to these potential risks in early pregnancy.

## 6.2 METHODS

### 6.2.1 Study population

All live born children delivered between January 2001 and December 2009, with linked mother records were included in this analysis. The study population was limited to only live births because stillborn children are generally not registered with the GPs. Data before January 2001 was excluded as NRT only became available on NHS prescription in 2001.

### 6.2.2 Exposure

A variable indicating NRT exposure in early pregnancy (defined here as one month before conception until the end of the first trimester) and smoking was developed with four categories. The period of four weeks before conception was used to enable inclusion of drug prescriptions received immediately before pregnancy and potentially used around the time of conception. The first trimester of pregnancy is considered the critical period for the developments of congenital anomalies <sup>231,232</sup> and therefore only early pregnancy exposure was considered. The four exposure categories are described below:

- **Non-smoker:** All women with Read codes for never smoking or ex-smoking in their primary care records during the first trimester and within 27 months before pregnancy, with no current smoking codes in this time were classified as non-smokers.
- **NRT group:** All pregnant women with a drug code for NRT prescription during the first trimester of pregnancy or within four weeks before the estimated conception dates in their primary care records were classified as being prescribed NRT during early pregnancy. Similar to other drug safety studies, the period of four weeks before conception was included to enable the inclusion of NRT prescriptions immediately before

pregnancy and potentially used during very early pregnancy and around conception.<sup>233</sup>

- **Smoker:** If any records of current smoking were found during early pregnancy or if the latest smoking status record within 27 months before pregnancy until the end of first trimesters indicated smoking, women were categorised as being smokers during that pregnancy.
- **Unknown:** All women who did not have a recording of smoking status or NRT prescription during early pregnancy or where the smoking status records did not clearly indicate whether they were smokers or non-smokers were included in this category.

### 6.2.3 Outcome

All information on major congenital anomalies recorded at any age in children's primary care records was extracted using Read codes mapped to the EUROCAT classification system (Code list attached as Appendix 10.10).<sup>230</sup> This system identifies all conditions classified as major congenital disorders coded by the Q chapter of the International Classification of Disease version 10 (ICD-10)<sup>234</sup> and a small number of conditions in the other ICD-10 chapters and categorises them into subgroups.<sup>230</sup> Minor congenital anomalies are not very well recognised and therefore not recorded very well in primary care. Therefore, epidemiological studies only focus on assessing major congenital anomalies and so do registries. Therefore, in line with the EUROCAT classification, minor congenital anomalies (e.g. lip hypertrophy, congenital flat foot etc.) were excluded from the case definition.<sup>230</sup> Children with medical codes for teratogenic anomalies (e.g. PK80.00 – Fetal alcohol syndrome, PK84.00 Fetal valproate syndrome) were also excluded from the study population.



#### **6.2.4 Potential confounders**

Maternal age, socioeconomic status and all other maternal morbidities described in Section 3.4.3 were considered to be potential confounders due to the associations of these conditions or their treatments with congenital anomalies and maternal smoking.<sup>51,59,195,199,211,235-244</sup> In addition, epilepsy was also deemed to be an important clinical confounder for this analysis as the medical treatment for epilepsy is strongly related to congenital anomalies<sup>245,246</sup> and studies have shown epilepsy to be associated with smoking as well.<sup>247</sup> Records of diagnosed epilepsy were extracted from both the Medical and AHD files and epilepsy medication prescriptions were extracted from the Therapy file. For the purpose of this study, pregnant women were said to have epilepsy if they had a diagnostic recording of epilepsy ever before delivery and had a recording of epilepsy prescription during pregnancy or within 27 months before conception. Medical code lists and prescription code lists are attached as Appendix 10.8.11 and Appendix 10.8.12.

#### **6.2.5 Statistical analysis**

To estimate the disease burden of all major and individual system-specific congenital anomalies, absolute risks (per 10,000 live births) for the total population and each exposure group (i.e. non-smokers, smokers, NRT group and unknown group) were calculated. ORs for any major and each system-specific anomaly group were calculated for the NRT group and smokers using non-smokers as the reference group in a logistic regression model. Some women had more than one pregnancy in the study period; this was accounted for by calculating robust CIs around the OR using the clustered sandwich estimator,<sup>180,181</sup> which is explained in Section 3.4.4. In recognition of the fairly large number of exposure and outcome categories in this analysis, 99% CIs were calculated for each measure of association; exact p-values (to 3 decimal places) have also been presented for more transparent reader assessment of

associations potentially arising by chance. Adjustments were also made for potential confounders discussed above. Chi-squared tests were used to determine whether each of these confounders was associated with the exposure and with the outcome. Covariates with statistically significant associations at 5% level of significance were included in the multivariable model to obtain adjusted ORs. The reference group was then changed to smokers and ORs for MCAs in the NRT group were calculated.

## **6.2.6 Sensitivity analysis**

### *6.2.6.1 Restricting to only singleton live births*

The absolute and relative risks of overall and individual system-specific congenital anomalies were calculated, restricting the study population to only singleton live born babies, as malformations are more likely to occur in multiple births compared to singleton births.<sup>248</sup>

### *6.2.6.2 Reclassifying smokers and non-smokers based on gestational smoking status recording*

The definitions of smokers and non-smokers were restricted to only mothers who had a gestational smoking status record during early pregnancy indicating them to be a smoker or non-smoker respectively. This was done because some women who were documented to be smokers in the 27 months before conception may have given up smoking before pregnancy and therefore the definition of smokers and non-smokers during early pregnancy may result in some misclassification between these two exposure categories. The absolute risks of overall and system-specific MCA groups were calculated using only smokers and non-smokers, based on gestational records and ORs (99% CI) for MCAs in children with maternal NRT exposure during early pregnancy were calculated.

#### *6.2.6.3 Exposure window changed to 2<sup>nd</sup>/3<sup>rd</sup> trimester*

The exposure period was changed from early pregnancy to 2<sup>nd</sup>/3<sup>rd</sup> trimester and all women with NRT prescriptions in early pregnancy were excluded from the analysis. Although most of the organogenesis takes place in the first trimester, consequently increasing the risk of structural defects, some periods in the second and third trimester are also slightly sensitive for the development of congenital anomalies.<sup>249</sup> These include defects of the eye, ear, teeth, central nervous system and genitalia.<sup>250</sup> Therefore, the absolute and relative risks of overall and system-specific MCA groups for NRT group and smokers, compared to non-smokers were calculated based on 2<sup>nd</sup>/3<sup>rd</sup> trimester exposure.

#### **6.2.7 Sample size calculation**

Previous literature suggests the prevalence of MCAs to be 2.7%<sup>251</sup> and the prescribing prevalence of NRT during pregnancy has been found to be approximately 2%.<sup>252</sup> Based on these numbers, a sample size of 138,064 children with maternal NRT prescriptions in early pregnancy was needed in this study to detect an OR of 1.50 with 80% power at a 1% level of significance. The sample size to achieve this power for system-specific anomalies was much higher (e.g. 301,082 children with maternal NRT prescriptions for heart defects). Similarly, a sample of 19,041 children with smoking mothers was needed to detect an OR of 1.50 for the association between maternal smoking and presence of CAs, with 80% power at a 1% level of significance. Sample size calculations were performed in PASS 12 (Power Analysis & Sample Size Software).<sup>253</sup>

## **6.3 RESULTS**

### **6.3.1 Baseline characteristics**

A total of 232,242 live born children were included in the study population out of whom 6,480 had at least one major congenital anomaly (279 per 10,000 live births). Out of these 232,242 children 0.7% were born to mothers who were prescribed NRT , 16% to mothers who smoked during pregnancy and 49% to mothers who did not smoke during. Table 6-2 shows the baseline maternal characteristics in children with and without MCAs. The distribution of maternal age at conception, socioeconomic status and pre-conception BMI was very similar in women whose children had any MCA and women whose children did not have any MCA. The prevalence of maternal morbidities particularly epilepsy (0.4% vs. 0.7%), was found to be higher in the MCA group. Similarly, multiple births were more common in children with congenital anomalies compared to children without congenital anomalies (3.6% vs. 5.2%).

Table 6-3 presents the maternal and birth characteristics by smoking and NRT exposure. Women in the NRT group and smokers were more likely to be from socioeconomically deprived groups compared to non-smokers. Additionally, the NRT group had a higher prevalence of asthma (14.4%) compared to smokers and non-smokers (11.1% and 10.3% respectively). Similarly, mental illness was found to be most prevalent in the NRT group (20.8%) and epilepsy was found to be the highest in smokers (0.7%), followed by the NRT group (0.6%). The distribution of other morbidities was very similar across the exposure groups.

**Table 6-2 - Maternal and birth characteristics of the study population**

	All children		Children without MCAs		Children with MCAs	
	N=232,242		n=225,762		n=6,480	
	n	%	n	%	n	%
<b>Age at conception</b>						
15-19 years	12,037	5.2%	11,692	5.2%	345	5.3%
20-24 years	36,003	15.5%	34,999	15.5%	1,004	15.5%
25-29 years	59,203	25.5%	57,624	25.5%	1,579	24.4%
30-34 years	73,844	31.8%	71,822	31.8%	2,022	31.2%
35-39 years	42,477	18.3%	41,262	18.3%	1,215	18.7%
40-44 years	8,341	3.6%	8,046	3.6%	295	4.5%
45-49 years	337	0.1%	317	0.1%	20	0.3%
<b>Townsend score in quintiles</b>						
Quintile 1 (least deprived)	53,916	23.2%	52,430	23.2%	1,486	22.9%
Quintile 2	43,850	18.9%	42,653	18.9%	1,197	18.5%
Quintile 3	45,280	19.5%	43,986	19.5%	1,294	20.0%
Quintile 4	42,696	18.4%	41,490	18.4%	1,206	18.6%
Quintile 5 (most deprived)	31,884	13.7%	30,963	13.7%	921	14.3%
Missing	14,616	6.3%	14,240	6.3%	376	5.8%
<b>Pre-conception Body Mass Index (kg/m<sup>2</sup>)</b>						
normal(18.5-24.9)	73,002	31.4%	71,019	31.5%	1,983	30.6%
underweight(<18.5)	5,225	2.2%	5,071	2.2%	154	2.4%
overweight(25-29.9)	35,625	15.3%	34,626	15.3%	999	15.4%
obese(>=30)	24,594	10.6%	23,876	10.6%	718	11.1%
missing	93,796	40.4%	91,170	40.4%	2,626	40.5%
<b>Asthma</b>	19,932	8.6%	19,335	8.6%	597	9.2%
<b>Hypertension</b>	6,392	2.8%	6,165	2.7%	227	3.5%
<b>Diabetes</b>	5,490	2.4%	5,268	2.3%	222	3.4%
<b>Mental illness</b>	22,154	9.5%	21,507	9.5%	647	10.0%
<b>Epilepsy</b>	1,036	0.4%	994	0.4%	42	0.7%
<b>Multiple birth</b>	8,373	3.6%	8,038	3.6%	335	5.2%

MCAs = major congenital anomalies

**Table 6-3 - Numbers and proportions of maternal and birth characteristics by NRT exposure and smoking**

	<b>NRT group*</b>		<b>Smokers**</b>		<b>Non-smokers***</b>		<b>Unknown</b>	
	n= 1,594		n= 37,141		n=114,254		n= 79,253	
	n	%	n	%	n	%	n	%
<b>Age at conception</b>								
15-19 years	110	6.9%	3,918	10.5%	4,044	3.5%	3,965	5.0%
20-24 years	354	22.2%	9,885	26.6%	14,895	13.0%	10,869	13.7%
25-29 years	443	27.8%	10,005	26.9%	29,888	26.2%	18,867	23.8%
30-34 years	400	25.1%	8,127	21.9%	38,695	33.9%	26,622	33.6%
35-39 years	236	14.8%	4,335	11.7%	22,230	19.5%	15,676	19.8%
40-44 years	49	3.1%	846	2.3%	4,330	3.8%	3,116	3.9%
45-49 years	2	0.1%	25	0.1%	172	0.2%	138	0.2%
<b>Townsend score in quintiles</b>								
Quintile 1 (least deprived)	152	9.5%	4,573	12.3%	29,060	25.4%	20,131	25.4%
Quintile 2	219	13.7%	5,120	13.8%	23,056	20.2%	15,455	19.5%
Quintile 3	339	21.3%	7,281	19.6%	22,382	19.6%	15,278	19.3%
Quintile 4	438	27.5%	9,303	25.0%	19,090	16.7%	13,865	17.5%
Quintile 5 (most deprived)	338	21.2%	8,524	23.0%	12,731	11.1%	10,291	13.0%
Missing	108	6.8%	2,340	6.3%	7,935	6.9%	4,233	5.3%
<b>Pre-conception BMI (kg/m<sup>2</sup>)</b>								
Normal (18.5-24.9)	495	31.1%	12,535	33.7%	44,568	39.0%	15,404	19.4%
Underweight (<18.5)	49	3.1%	1,277	3.4%	2,733	2.4%	1,166	1.5%
Overweight (25-29.9)	262	16.4%	6,011	16.2%	21,472	18.8%	7,880	9.9%
Obese (>=30)	223	14.0%	4,553	12.3%	14,369	12.6%	5,449	6.9%
Missing	565	35.4%	12,765	34.4%	31,112	27.2%	49,354	62.3%
<b>Asthma</b>	230	14.4%	4,116	11.1%	11,764	10.3%	3,822	4.8%
<b>Hypertension</b>	36	2.3%	793	2.1%	3,731	3.3%	1,832	2.3%
<b>Diabetes</b>	45	2.8%	746	2.0%	3,324	2.9%	1,375	1.7%
<b>Mental illness</b>	331	20.8%	5,882	15.8%	9,095	8.0%	6,846	8.6%
<b>Epilepsy</b>	9	0.6%	248	0.7%	497	0.4%	282	0.4%
<b>Multiple birth</b>	47	2.9%	1,290	3.5%	4,021	3.5%	3,015	3.8%

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy, \*\*\* No smoking in early pregnancy

### **6.3.2 Absolute risks of major and system-specific congenital anomalies**

Table 6-4 presents the numbers and absolute risks of any major and system-specific congenital anomalies in the total population and also stratified by maternal exposures. The absolute risk of MCAs in the NRT group was higher than non-smokers (364/10,000 live births compared to 273/10,000 live births). Similar increases in the risk were seen in the most common anomaly groups in the NRT group like heart, limb, genital and urinary defects. The absolute risks of MCAs in smokers were found to be very similar to the non-smokers with slightly higher risk in the more rare anomalies such as abdominal anomalies (5/10,000 live births in smoking group compared to 1/10,000 live births in the reference group).

**Table 6-4 - Absolute risks of major congenital anomalies by NRT exposure and maternal smoking**

	All children		NRT group*		Smokers**		Non-smokers***		Unknown	
	N= 232,242		n= 1,594		n= 37,141		n=114,254		n= 79,253	
	n ‡	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000
All MCAs combined	6,480	279	58	364	1,009	272	3,121	273	2,292	289
Heart	2,021	87	15	94	327	88	999	87	680	86
Limb	1,243	54	11	69	183	49	623	55	426	54
Genital system	1,077	46	12	75	158	43	507	44	400	50
Urinary system	622	27	6	38	89	24	304	27	223	28
Chromosomal	438	19	3	19	53	14	216	19	166	21
Musculoskeletal	416	18	5	31	64	17	196	17	151	19
Oro-facial cleft	348	15	2	13	57	15	158	14	131	17
Digestive system	347	15	5	31	44	12	174	15	124	16
Nervous system	359	15	3	19	58	16	170	15	128	16
Other malformations§	316	14	2	13	45	12	150	13	119	15
Eye	256	11	1	6	32	9	120	11	103	13
Respiratory system	188	8	10	63	32	9	89	8	57	7
Genetic	176	8	0	-	21	6	82	7	73	9
Abdominal wall	61	3	0	-	20	5	17	1	24	3
Ear, face & neck	41	2	0	-	8	2	15	2	18	2

MCA = Major Congenital Anomalies

‡ each case may have more than one system anomaly, therefore total of all system-specific anomalies may vary

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy, \*\*\* no smoking in early pregnancy

§ e.g. Asplenia, conjoined twins etc.



### **6.3.3 Relative risks of major and system specific congenital anomalies**

Table 6-5 shows the adjusted ORs for overall and each system specific major congenital anomaly comparing the NRT group and smokers to non-smokers. The OR for MCAs in the NRT group was 1.34 (99% CI 0.94-1.91, p-value 0.034) compared with non-smokers. There was no increased risk of MCAs in smokers compared to non-smokers (OR 0.99, 99% CI 0.89-1.09, p-value 0.819) compared to non-smokers. The ORs for system-specific anomalies were broadly similar to the overall findings. At 99% confidence interval, odds ratios showed no increased risk of any system specific congenital anomaly in the NRT group compared to non-smokers except respiratory system anomalies (OR 7.61, 99% CI 2.93-19.74, p-value <0.001). However, this was based on a very small number of exposed cases (10 cases of respiratory system anomaly) as shown in Table 6-4.

Table 6-6 presents the ORs for major congenital anomalies in the NRT group compared to smokers. The relative risk of major congenital anomalies in NRT group was not appreciably altered when the reference group was changed to smokers (OR 1.35, 99% CI 0.94-1.93 for overall MCAs).

**Table 6-5 - Adjusted odds ratio for major congenital anomalies by maternal NRT and smoking exposure**

	NRT group*¥		Smokers**¥		Unknown¥	
	n= 1,594		n=37,141		n= 79,253	
	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value
All MCAs combined	1.34 (0.94-1.91)	0.034	0.99 (0.89-1.09)	0.815	1.06 (0.98-1.15)	0.032
Heart	1.08 (0.55-2.13)	0.757	1.02 (0.86-1.21)	0.787	0.99 (0.87-1.13)	0.861
Limb	1.31 (0.59-2.88)	0.380	0.94 (0.75-1.17)	0.487	0.99 (0.84-1.16)	0.847
Genital system	1.66 (0.78-3.55)	0.082	0.92 (0.72-1.18)	0.411	1.14 (0.96-1.36)	0.047
Urinary system	1.43 (0.49-4.16)	0.385	0.92 (0.67-1.26)	0.511	1.05 (0.83-1.34)	0.523
Chromosomal	1.03 (0.23-4.64)	0.961	0.85 (0.56-1.28)	0.313	1.09 (0.83-1.42)	0.424
Musculoskeletal	1.89 (0.58-6.16)	0.166	1.03 (0.70-1.52)	0.826	1.13 (0.85-1.49)	0.268
Oro-facial cleft	0.86 (0.14-5.37)	0.828	1.05 (0.69-1.58)	0.748	1.20 (0.88-1.64)	0.123
Digestive system	2.01 (0.62-6.49)	0.125	0.76 (0.49-1.19)	0.118	1.02 (0.75-1.38)	0.873
Nervous system	1.17 (0.26-5.24)	0.792	0.98 (0.65-1.47)	0.904	1.13 (0.83-1.53)	0.314
Other malformations <sup>\$</sup>	0.96 (0.15-6.02)	0.952	0.92 (0.59-1.44)	0.654	1.14 (0.83-1.56)	0.296
Eye	0.56 (0.04-7.47)	0.567	0.77 (0.45-1.30)	0.197	1.23 (0.87-1.75)	0.121
Respiratory system	7.61 (2.93-19.74)	<0.001	1.07 (0.62-1.86)	0.745	0.93 (0.60-1.44)	0.683
Genetic	-	-	0.85 (0.44-1.65)	0.532	1.26 (0.83-1.92)	0.150
Abdominal wall	-	-	2.27 (0.94-5.44)	0.016	1.87 (0.81-4.30)	0.053
Ear, face & neck	-	-	1.62 (0.49-5.37)	0.300	1.68(0.68-4.14)	0.138

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy, ¥Reference category = non-smokers during early pregnancy, ‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes and epilepsy, <sup>\$</sup> e.g. Asplenia, conjoined twins etc. MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence interval

**Table 6-6 - Adjusted odds ratio for major congenital anomalies in the NRT group compared to smokers**

	NRT group*	
	n=1,594	
	AOR ‡ (99% CI)	p-value
All MCAs combined	1.35 (0.94-1.93)	0.032
Heart	1.06 (0.54-2.11)	0.813
Limb	1.39 (0.62-3.10)	0.292
Genital system	1.80 (0.83-3.90)	0.051
Urinary system	1.55 (0.52-4.61)	0.297
Chromosomal	1.20 (0.26-5.61)	0.750
Musculoskeletal	1.83 (0.55-6.06)	0.195
Oro-facial cleft	0.81 (0.13-5.18)	0.774
Digestive system	2.63 (0.78-2.11)	0.041
Nervous system	1.19 (0.25-5.47)	0.770
Other malformations <sup>§</sup>	1.04 (0.16-6.68)	0.962
Eye	0.73 (0.05-10.01)	0.759
Respiratory system	7.10 (2.60-19.38)	<0.001
Genetic	-	-
Abdominal wall	-	-
Ear, face & neck	-	-

¥Reference category – smokers during early pregnancy

\* NRT=nicotine replacement therapy prescription in early pregnancy

‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes, epilepsy, <sup>§</sup> e.g. Asplenia, conjoined twins etc.

MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence intervals

### **6.3.4 Sensitivity analysis**

#### *6.3.4.1 Restricting to only singleton live births*

Table 6-7 shows the absolute risks of all major and system specific congenital anomalies in singleton live-born children by NRT and smoking exposure. Similar to the main results, the absolute risk of MCAs was higher in the NRT group compared with non-smokers (356/10,000 live births compared to 270/10,000 live births). Similar increases in the risk were seen for the most common anomalies in the NRT group like heart, limb, genital and urinary defects but the absolute risk differences were very small.

Table 6-8 shows the adjusted ORs for overall and each system specific major congenital anomaly group in singleton live-born children comparing the NRT group and smokers to non-smokers. The effect estimates remained unaltered with no increased risk of congenital anomalies in the NRT group and smokers compared with non-smokers.

**Table 6-7 - Absolute risks of major congenital anomalies by NRT exposure and maternal smoking in singleton live borns**

	All children		NRT group*		Smokers**		Non-smokers***		Unknown	
	N= 223,869		n= 1,547		n= 35,851		n=110,233		n= 76,238	
	n ‡	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000
All MCAs combined	6,145	274	55	356	959	267	2,973	270	2,158	283
Heart	1,868	83	14	90	307	86	927	84	620	81
Limb	1,199	54	11	71	177	49	604	55	407	53
Genital system	1,020	46	12	78	152	42	482	44	374	49
Urinary system	597	27	6	39	85	24	296	27	210	28
Chromosomal	425	19	3	19	51	14	208	19	163	21
Musculoskeletal	398	18	5	32	62	17	187	17	144	19
Oro-facial cleft	333	15	2	13	54	15	149	14	128	17
Digestive system	330	15	5	32	44	12	166	15	115	15
Nervous system	347	16	3	19	56	16	163	15	125	16
Other malformations§	306	14	2	13	44	12	144	13	116	15
Eye	241	11	1	6	30	8	114	10	96	13
Respiratory system	176	8	8	52	28	8	86	8	54	7
Genetic	168	8	-	-	19	5	81	7	68	9
Abdominal wall	55	2	0	-	19	5	15	1	21	3
Ear, face & neck	41	2	0	-	8	2	15	1	18	2

MCA = Major Congenital Anomalies, NRT = nicotine replacement therapy

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy, \*\*\* no smoking in early pregnancy

‡ each case may have more than one system anomaly, therefore total of all system-specific anomalies may vary

§ e.g. Asplenia, conjoined twins etc.

**Table 6-8 - Adjusted odds ratio for major congenital anomalies by maternal NRT and smoking exposure in singleton live-born children**

	NRT group*¥		Smokers**¥		Unknown¥	
	n= 1,547		n=35,851		n= 76,238	
	AOR*‡ (99% CI)	p-value	AOR*‡ (99% CI)	p-value	AOR*‡ (99% CI)	p-value
All MCAs combined	1.31 (0.91-1.87)	0.053	0.98 (0.89-1.08)	0.684	1.06 (0.98-1.15)	0.038
Heart	1.07 (0.53-2.15)	0.797	1.02 (0.86-1.22)	0.708	0.98 (0.85-1.12)	0.660
Limb	1.33 (0.61-2.94)	0.340	0.94 (0.75-1.18)	0.465	0.98 (0.83-1.15)	0.699
Genital system	1.73 (0.81-3.68)	0.063	0.93 (0.73-1.19)	0.451	1.13 (0.94-1.35)	0.079
Urinary system	1.46 (0.50-4.24)	0.359	0.90 (0.65-1.25)	0.423	1.03 (0.81-1.29)	0.757
Chromosomal	1.07 (0.24-4.80)	0.909	0.85 (0.56-1.28)	0.312	1.11 (0.85-1.45)	0.319
Musculoskeletal	1.97 (0.611-6.36)	0.135	1.05 (0.71-1.55)	0.742	1.13 (0.85-1.51)	0.265
Oro-facial cleft	0.91 (0.14-5.74)	0.900	1.07 (0.70-1.62)	0.677	1.25 (0.91-1.70)	0.066
Digestive system	2.07 (0.64-6.69)	0.110	0.79 (0.51-1.24)	0.182	0.99 (0.73-1.36)	0.966
Nervous system	1.21 (0.27-5.44)	0.745	0.98 (0.65-1.48)	0.923	1.15 (0.84-1.56)	0.244
Other malformations <sup>\$</sup>	0.98 (0.16-6.18)	0.983	0.94 (0.59-1.47)	0.709	1.16 (0.84-1.59)	0.244
Eye	0.59 (0.04-7.81)	0.596	0.76 (0.44-1.30)	0.186	1.21 (0.84-1.73)	0.168
Respiratory system	6.36 (2.43-16.63)	<0.001	0.99 (0.56-1.76)	0.977	0.92 (0.59-1.44)	0.644
Genetic	-	-	0.78 (0.40-1.53)	0.350	1.19 (0.78-1.82)	0.285
Abdominal wall	-	-	2.25 (0.90-5.59)	0.022	1.83 (0.76-4.39)	0.074
Ear, face & neck	-	-	1.75 (0.55-5.60)	0.213	1.69 (0.66-4.40)	0.151

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy

¥Reference category = non-smokers during early pregnancy, ‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes and epilepsy MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence interval

<sup>\$</sup> e.g. Asplenia, conjoined twins etc.

#### *6.3.4.2 Reclassifying smokers and non-smokers based on gestational smoking status recording*

When the smoker and non-smoker groups were reclassified to women with a gestational smoking status recording in their primary care data indicating such behaviour only 3% were classified as smokers and 8% as non-smokers. The absolute risk of CAs in smokers was now higher compared to the risk using a broader definition (298/10,000 live births compared to 272/10,000 live births). However, the association between NRT exposure, smoking during early pregnancy and MCAs remained unchanged with no significant association between NRT exposure and smoking compared to non-smokers apart from respiratory anomalies where the risk of MCAs was over six times higher in the NRT group compared to definitive smokers during early pregnancy (OR 6.49, 99% CI 2.35-17.87, p-value <0.001). Table 6-9 presents the absolute risks of congenital anomalies by each exposure group and Table 6-10 presents adjusted ORs for NRT and smoking exposure, based on a restricted definition of smokers and non-smokers.

**Table 6-9 - Absolute risks of major congenital anomalies by NRT exposure and maternal smoking, using only gestational smoking records**

	All children		NRT group*		Smokers**		Non-smokers***		Unknown	
	N= 232,242		n= 1,594		n= 198		n=547		n= 205,602	
	n ‡	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000
All MCAs combined	6,480	279	58	364	198	298	547	297	5,677	276
Heart	2,021	87	15	94	116	84	330	91	1,560	86
Limb	1,243	54	11	69	73	53	192	53	967	54
Genital system	1,077	46	12	75	57	41	172	48	836	46
Urinary system	622	27	6	38	31	22	97	27	488	27
Chromosomal	438	19	3	19	21	15	70	19	344	19
Musculoskeletal	416	18	5	31	24	17	59	16	328	18
Oro-facial cleft	348	15	2	13	29	21	50	14	267	15
Digestive system	347	15	5	31	21	15	60	17	261	14
Nervous system	359	15	3	19	27	19	51	14	278	15
Other malformations§	316	14	2	13	26	19	35	10	253	14
Eye	256	11	1	6	9	6	42	12	204	11
Respiratory system	188	8	10	63	16	12	33	9	129	7
Genetic	176	8	0	-	7	5	28	8	141	8
Abdominal wall	61	3	0	-	5	4	9	2	47	3
Ear, face & neck	41	2	0	-	2	1	5	3	34	2

MCA = Major Congenital Anomalies, NRT = nicotine replacement therapy

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy, \*\*\* no smoking in early pregnancy

‡ each case may have more than one system anomaly, therefore total of all system-specific anomalies may vary

§ e.g. Asplenia, conjoined twins etc.



**Table 6-10 - Adjusted odds ratio for major congenital anomalies by maternal NRT and smoking exposure using only gestational smoking records**

	NRT exposed group*¥		Smokers**¥		Unknown¥	
	n= 22,814		n=1,113		n= 19,038	
	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value
All MCAs combined	1.22 (0.84-1.77)	0.156	1.00 (0.80-1.25)	0.978	0.93 (0.82-1.04)	0.096
Heart	1.04 (0.52-2.06)	0.886	0.92 (0.69-1.23)	0.485	0.96 (0.81-1.12)	0.506
Limb	1.34 (0.59-2.98)	0.353	1.03 (0.72-1.48)	0.817	1.00 (0.82-1.23)	0.543
Genital system	1.56 (0.72-3.38)	0.138	0.84 (0.56-1.26)	0.265	0.98 (0.79-1.22)	0.788
Urinary system	1.42 (0.48-4.21)	0.408	0.85 (0.49-1.45)	0.435	1.00 (0.76-1.34)	0.951
Chromosomal	1.00 (0.22-4.62)	0.996	0.86 (0.45-1.66)	0.566	0.98 (0.70-1.38)	0.901
Musculoskeletal	1.99 (0.59-6.70)	0.145	1.09 (0.58-2.07)	0.710	1.13 (0.78-1.63)	0.396
Oro-facial cleft	0.86 (0.13-5.57)	0.842	1.44 (0.78-2.68)	0.127	1.07 (0.71-1.62)	0.661
Digestive system	1.85 (0.56-6.18)	0.185	0.90 (0.46-1.75)	0.692	0.86 (0.59-1.25)	0.314
Nervous system	1.26 (0.27-5.81)	0.700	1.30 (0.69-2.44)	0.279	1.12 (0.76-1.66)	0.447
Other malformations\$	1.31 (0.20-8.61)	0.707	1.95 (0.98-3.92)	0.013	1.45 (0.91-2.30)	0.041
Eye	0.52 (0.04-6.97)	0.512	0.52 (0.20-1.34)	0.075	0.98 (0.63-1.52)	0.907
Respiratory system	6.49 (2.35-17.87)	<0.001	1.22 (0.54-2.78)	0.532	0.78 (0.47-1.29)	0.210
Genetic	-	-	0.70 (0.23-2.09)	0.401	0.99 (0.58-1.68)	0.954
Abdominal wall	-	-	0.89 (0.20-3.85)	0.838	1.07 (0.41-2.75)	0.849
Ear, face & neck	-	-	0.53 (0.05-7.01)	0.391	1.03 (0.26-4.01)	0.957

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy

¥Reference category = non-smokers during early pregnancy, ‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes and epilepsy MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence interval

\$ e.g. Asplenia, conjoined twins etc.

#### *6.3.4.3 Exposure window changed to 2<sup>nd</sup>/3<sup>rd</sup> trimester*

When NRT exposure in the 2<sup>nd</sup>/3<sup>rd</sup> trimester was assessed the absolute risks of MCAs in the NRT group were lower than the risks in early pregnancy (235/10,000 live births compared to 370/10,000 live births) and also the risk in all live births (279/10,000 live births). However, the association between NRT exposure, smoking during early pregnancy and MCAs remained unchanged with no significant association between NRT exposure and smoking compared to non-smokers. Table 6-11 presents the absolute risks of MCAs by each exposure group in 2<sup>nd</sup>/3<sup>rd</sup> trimester and Table 6-12 presents adjusted odds ratio for NRT exposure and smoking in 2<sup>nd</sup>/3<sup>rd</sup> trimester.

**Table 6-11 - Absolute risks of major congenital anomalies by NRT exposure and maternal smoking during 2<sup>nd</sup>/3<sup>rd</sup> trimester**

	All children		NRT exposed group*		Smokers**		Non-smokers***		Unknown	
	N=230,648		n= 1,827		n= 37,250		n=112,419		n= 79,152	
	n ‡	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000	n	n/10,000
All MCAs combined	6,422	278	43	235	1,024	275	3,070	273	2,285	289
Heart	2,021	87	15	94	327	88	999	87	680	86
Limb	1,243	54	11	69	183	49	623	55	426	54
Genital system	1,077	46	12	75	158	43	507	44	400	50
Urinary system	622	27	6	38	89	24	304	27	223	28
Chromosomal	438	19	3	19	53	14	216	19	166	21
Musculoskeletal	416	18	5	31	64	17	196	17	151	19
Oro-facial cleft	345	15	2	13	57	15	158	14	131	17
Digestive system	347	15	5	31	44	12	174	15	124	16
Nervous system	359	15	3	19	58	16	170	15	128	16
Other malformations§	316	14	2	13	45	12	150	13	119	15
Eye	256	11	1	6	32	9	120	11	103	13
Respiratory system	188	8	10	63	32	9	89	8	57	7
Genetic	176	8	-	-	21	6	82	7	73	9
Abdominal wall	61	3	-	-	20	5	17	1	24	3
Ear, face & neck	41	2	-	-	8	2	15	2	18	2

MCA = Major Congenital Anomalies, NRT = nicotine replacement therapy

\*NRT=nicotine replacement therapy prescription in late pregnancy, \*\*smoking in pregnancy, \*\*\* no smoking in pregnancy

‡ each case may have more than one system anomaly, therefore total of all system-specific anomalies may vary

§ e.g. Asplenia, conjoined twins etc.

**Table 6-12 - Adjusted odds ratio for major congenital anomalies by maternal NRT and smoking exposure during 2<sup>nd</sup>/3<sup>rd</sup> trimester**

	NRT exposed group*¥		Smokers**¥		Unknown¥	
	n= 1,827		n= 37,250		n= 79,152	
	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value	AOR‡ (99% CI)	p-value
All MCAs combined	0.85 (0.57-1.26)	0.285	1.00 (0.91-1.10)	0.936	1.06 (0.99-1.14)	0.041
Heart	1.08 (0.55-2.13)	0.757	1.02 (0.86-1.21)	0.787	0.99 (0.87-1.13)	0.861
Limb	1.31 (0.59-2.88)	0.380	0.94 (0.75-1.17)	0.487	0.99 (0.84-1.16)	0.847
Genital system	1.66 (0.78-3.55)	0.082	0.82 (0.72-1.18)	0.411	1.14 (0.96-1.36)	0.047
Urinary system	1.43 (0.49-4.16)	0.385	0.92 (0.67-1.27)	0.511	1.06 (0.84-1.33)	0.523
Chromosomal	1.02 (0.23-4.65)	0.961	0.85 (0.56-1.28)	0.313	1.09 (0.83-1.41)	0.424
Musculoskeletal	1.89 (0.58-6.16)	0.166	1.03 (0.70-1.52)	0.826	1.13 (0.85-1.49)	0.268
Oro-facial cleft	0.86 (0.14-5.37)	0.828	1.05 (0.69-1.59)	0.748	1.20 (0.88-1.64)	0.123
Digestive system	2.01 (0.62-6.49)	0.125	0.76 (0.49-1.19)	0.118	1.02 (0.75-1.38)	0.873
Nervous system	1.17 (0.26-5.24)	0.792	0.98 (0.65-1.47)	0.904	1.13 (0.83-1.53)	0.314
Other malformations <sup>\$</sup>	0.96 (0.15-6.02)	0.952	0.93 (0.59-1.44)	0.654	1.14(0.83-1.56)	0.296
Eye	0.56 (0.04-7.47)	0.567	0.77 (0.45-1.30)	0.197	1.23 (0.87-1.75)	0.121
Respiratory system	7.61 (2.93-19.74)	<0.001	1.07 (0.62-1.86)	0.745	0.93 (0.60-1.44)	0.683
Genetic	-	-	0.85 (0.44-1.66)	0.532	1.26 (0.83-1.92)	0.150
Abdominal wall	-	-	3.62 (1.54-8.47)	<0.001	2.04 (0.89-4.61)	0.025
Ear, face & neck	-	-	1.52 (0.45-5.16)	0.376	1.60 (0.58-4.43)	0.230

\*NRT=nicotine replacement therapy prescription in late pregnancy, \*\*smoking in pregnancy

¥Reference category = non-smokers during early pregnancy, ‡ adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes and epilepsy MCAs= Major Congenital Anomalies, AOR = Adjusted Odds Ratio, CI = confidence interval

<sup>\$</sup> e.g. Asplenia, conjoined twins etc.

## **6.4 DISCUSSION**

### **6.4.1 Principal findings**

This study found that NRT exposure during early pregnancy was not associated with an increased risk of overall and system-specific MCAs in the offspring compared with non-smokers and smokers except for an increased risk of respiratory anomalies; however this finding was based on only 10 cases exposed to NRT. These findings remained unaltered when the population was restricted to only singleton live-borns and to women with a gestational smoking status recording in their primary care data. No increased risks of MCAs were found with 2<sup>nd</sup>/3<sup>rd</sup> trimester NRT exposure.

### **6.4.2 Strengths and limitations**

This is the largest study to date to investigate the association between NRT prescribing in pregnant women and the presence of MCAs in their offspring. Because the study was based on routinely collected population-based data, the ascertainment of congenital anomaly cases was independent of the exposure variable minimising the potential for selection bias in the study.

Although in the UK congenital anomalies are diagnosed in secondary care, major diagnoses should be communicated to the patients' general practitioners resulting in a primary care record for MCAs. The prevalence of MCAs in THIN has been shown to be highly comparable to EUROCAT data<sup>157</sup>. Furthermore, MCA diagnosis using clinical coding in electronic primary care data has also been validated against doctor-provided written records reported directly from the general practice.<sup>158</sup>

The study was unable to assess MCAs in pregnancies that ended in stillbirth as congenital anomalies are not comprehensively detected and are poorly recorded for stillborn children. Nevertheless, this exclusion of stillborn children is unlikely to cause substantial underestimation of the cases of MCAs or bias the

associations under study because the prevalence of stillbirth in the UK is only 0.6%<sup>254</sup> out of which 8-14% can be attributed to MCAs.<sup>255,256</sup> The study also did not include any miscarriages as most of the miscarriages take place early in pregnancy<sup>257</sup> when women may not know that they are pregnant and therefore it is not possible to ascertain MCAs in these.

Previous studies have used women's self-reports to define NRT exposure which is subject to reporting errors and bias.<sup>100,114</sup> In contrast, the measurement of NRT exposure in this study was based on recorded GP prescribing. As discussed earlier, in the UK women can access NRT in settings other than the GP practice, which means that some women in the smokers /non-smokers category may have received NRT from pharmacies or SSSPs, not documented in the GP records. This may bias the estimates towards null. However, as discussed in Section 5.4, OTC purchasing of NRT is assumed to be infrequent and GP data include SSSP prescribing as well, therefore any misclassification in the exposure will be minimal and non-differential.

Measuring actual drug consumption in any large population-based study is difficult and is a limitation in previous studies.<sup>114</sup> Similarly, in primary care data it is not possible to establish if the women actually used the NRT that was prescribed. However, women are generally more motivated to quit during pregnancy<sup>258</sup> and NRT is only prescribed after a discussion on potential benefits and harms and if the woman agrees to use it.<sup>79</sup> Although data from RCTs show low compliance to NRT especially during pregnancy<sup>100,106</sup> most of these report a median duration of at least two weeks for NRT use.<sup>107-109</sup> The average duration of prescribed NRT was two weeks on average as discussed in Section 5.3.2, therefore it is assumed that women did comply with the NRT prescription. Also, the exposure time of two weeks is fairly short and if there is a higher risk of MCAs with longer NRT exposure this study may not have been able to capture it.

Similarly, ascertaining accurate smoking status is difficult in studies, especially in pregnant women as there is a high potential for misreporting due to the social stigma attached to smoking in pregnancy. All the previous studies investigating the association between maternal smoking and MCAs have relied on self-reported smoking status through interviews or surveys, as biochemical validation is practically difficult and expensive in population-based studies.<sup>28</sup> Similarly, in primary care data it is not possible to be completely certain about the accuracy of the smoking status records in women's electronic notes, as entries are not biochemically validated and are also based on self-reports of women. In this study pre-conception records were also included to ascertain women's smoking status during early pregnancy which may result in misclassification of some non-smokers as smokers and bias the effect estimates towards null. However, a substantial misclassification is unlikely as approximately 35-50% of pregnancies in the UK are unplanned,<sup>31, 32</sup> which means that only some women are likely to make positive behaviour changes such as quitting smoking before attempting to conceive. To address this issue the risks of MCAs were recalculated using only gestational smoking records to define smokers and non-smokers and the findings remained unchanged.

Congenital anomaly is a rare condition and from previous work it is known that NRT prescribing among pregnant women is also rare.<sup>252</sup> Therefore, only 1,594 children had mothers with NRT prescriptions in early pregnancy which although did not provide adequate power (post-hoc power: 60%) but was still about 5 times bigger than the previous study.<sup>114</sup> The number of NRT exposed cases of MCA was also 6 times higher than the Danish study (58 vs 11 cases). Nevertheless, much larger numbers are needed to assess the association between NRT exposure and specific anomaly groups.

### **6.4.3 Interpretation and conclusion in light of the current literature**

In this study the odds of major congenital anomalies in offspring of women prescribed NRT was 34% higher compared to non-smokers, although this finding was not statistically significant. Similarly, the absolute risks of system-specific anomalies were also generally higher than in the overall population and smokers, although these differences were small. A potential explanation for this finding may be that women who were prescribed NRT during pregnancy may be heavier smokers for some part of their pregnancy or immediately before their pregnancy and found it difficult to quit without pharmacotherapy<sup>259,260</sup> leading to confounding by indication. Although data on the exact time of NRT prescription in pregnancy was available, there is still inadequate information in the data regarding the smoking intensity of women before getting an NRT prescription. Therefore, it is difficult to completely separate the effects of smoking for some part of pregnancy from the effects of NRT. Additionally, despite adjustments in the analysis for sociodemographic factors and maternal morbidities, women prescribed NRT may have differed in unrecorded ways. Thus, unmeasured confounding factors may have contributed to the higher OR point estimate for NRT.

The only observational study on NRT and congenital anomalies, using the DNBC, showed that the women who used NRT in the first 12 weeks of pregnancy, but did not smoke, were more likely to have infants with congenital anomalies (OR 1.61, 95% CI 1.01-2.58) compared to non-smokers however when the analysis was only restricted to MCAs no association was found (OR 1.13, 95% CI 0.62-2.07).<sup>114</sup> The exposure time in the DNBC study was very similar to this study (i.e. early pregnancy) and despite the different exposure definition (self-reported NRT use in the DNBC study and GP prescribed NRT in this study) both the studies did not find any significantly increased risk of major congenital anomalies in relation to NRT, which is reassuring. In comparison, the SNAP trial



assessed NRT use at a later stage of pregnancy and reported a 30% lower likelihood of congenital anomalies in the NRT group compared to placebo group; however the results were not statistically significant and based on a very small number of events (9 events in NRT group compared to 13 events in placebo group).<sup>100</sup> When the exposure time in this study was changed to 2<sup>nd</sup>/3<sup>rd</sup> trimester NRT exposure the association between NRT and major CAs was did not become statistically significant, which mirrors the findings of the SNAP trial.

For mothers who smoked during early pregnancy this study found no association with congenital anomalies in their infants. This is very similar to the results from a large meta-analysis of 172 observational studies on maternal smoking in pregnancy with a total of 173,687 malformation cases and 11,674,332 controls, which found the OR for all congenital anomalies to be 1.01 (95% CI 0.96-1.07).<sup>28</sup> However, the magnitude of effect for system-specific anomaly groups were slightly different e.g. the systematic review found a significantly increased risk of heart defects associated with maternal smoking (OR 1.09, 95% CI 1.02-1.17).<sup>28</sup> In comparison, this study found an increase of 2% in the risk of heart defects associated with maternal smoking (OR 1.02, 99% CI 0.86-1.21), which was not statistically significant. In line with the findings of this chapter, the Baltimore-Washington Infant Study also did not find a statistically significant association between maternal smoking and congenital heart defects (OR 1.07, 95% CI 0.80-1.45).<sup>225</sup> The meta-analysis also found a higher risk of musculoskeletal defects, orofacial clefts, limb defects, eye defects and gastrointestinal defects<sup>28</sup> contrary to the findings reported here. A potential explanation for the difference in the estimates could be the very large sample size in the meta-analysis compared to this study and the use of 99% confidence intervals compared to the standard 95% CIs presented in the meta-analysis. A recent study on Greece based on 167 children with congenital heart defects found a three-fold increase in the risk of congenital heart defects associated with

maternal smoking<sup>227</sup> which is higher compared to the findings reported in this chapter and other available literature. This study, however, collected smoking exposure in the first trimester retrospectively after the delivery which increases the potential for recall bias. Additionally, no adjustments were made for other maternal co-morbidities (e.g. epilepsy), and socioeconomic status which may be important confounders.<sup>238,246,261</sup> The risk of nervous system anomalies was not found to be higher with maternal smoking (OR 0.98, 95% CI 0.65-1.47). Correspondingly, the OR for neural tube defects, which is the most common nervous system anomaly, in the NBDPS study, a national study from the US, was found to be 0.9 (95% CI 0.8-1.11).<sup>262</sup>

The limited evidence of maternal exposure to NRT during pregnancy and the risk of congenital anomalies in the offspring has not shown any significant associations between these factors. This study with much larger numbers than any other previous study did not find a protective or harmful effect of NRT during pregnancy. Therefore, it may be likely that there is no true association between NRT exposure during pregnancy and congenital anomalies in the offspring. However, it is difficult to be completely certain in the absence of adequate statistical power, for which an even larger study is required. Furthermore, other birth outcomes also need to be assessed in relation to NRT and smoking during pregnancy before making conclusions about the overall safety of the drug during pregnancy.

## **7 NICOTINE REPLACEMENT THERAPY, MATERNAL SMOKING IN PREGNANCY AND OTHER BIRTH OUTCOMES**

### **7.1 INTRODUCTION**

The previous chapter investigated and described the association between exposure to NRT and maternal smoking as recorded in primary care data and congenital anomalies. This chapter focuses on examining the relationship between NRT exposure, maternal smoking and other birth outcomes to comprehensively assess the safety of NRT in pregnancy.

Maternal smoking during pregnancy has been associated with several adverse birth outcomes including stillbirth, low birth weight and other birth outcomes as discussed in Section 1.1.1. Approximately 4-7% of stillbirths in developed countries can be attributed to maternal smoking.<sup>29</sup> A population-based study from Australia with a total sample of 191,941 births reported the risk of stillbirth to be twice as high in smokers compared to non-smokers after 34 weeks of gestation.<sup>263</sup> Similar results were reported by a Danish study assessing the risk of stillbirth in 25,012 singleton children of pregnant women between September 1989 and August 1996.<sup>264</sup> In addition, a meta-analysis of four studies from Australia, Sweden, Canada and the USA found maternal smoking to increase the risk of stillbirth by 36%.<sup>29</sup>

Maternal smoking has also been linked to low birth weight in infants and has been reported as one of the most important preventable causes of low birth weight.<sup>265</sup> A Dutch study from the early 1990s including approximately 800 pregnant women reported a 19g reduction in birth weight for each cigarette smoked in the day while pregnant.<sup>266</sup> As discussed in Section 1.1.1.2 recent data from the developed countries reports a reduction of 165g in birth weight

associated with maternal smoking.<sup>19</sup> This was even greater for heavy smokers where the birth weight reduced by 226g compared to non-smokers.<sup>20</sup> Whilst there is clear evidence of the association of smoking with outcomes like stillbirth and low birth weight the understanding of the relationship between maternal smoking and the mode of delivery is vague. There are very few studies examining this relationship. A recent study conducted in Germany using a perinatal database including 170,254 singleton pregnancies found no increased risk of caesarean section associated with maternal smoking.<sup>31</sup> Similar results were found in smaller hospital-based studies from Spain and Hong Kong with no statistically significant association between maternal smoking and caesarean section.<sup>267,268</sup> A cross-sectional study from the UK using 15,288 births from the Millenium Cohort Data also did not find any effect of smoking on whether a woman had medical intervention at birth (OR 1.003, 95% CI 0.88-1.44) or caesarean section (OR 1.15, 95% CI 0.95-1.39).<sup>269</sup> However, a study conducted in a maternity unit at St. Marys hospital, Portsmouth, UK on 400 smoking mothers and 400 non-smoking mothers showed that the risk of caesarean section was twice as high in smokers compared to non-smokers.<sup>270</sup> Similarly, a recent study conducted in Israel, including approximately 6000 pregnancies, reported the risk of any operative or instrumental intervention to be higher in smokers compared to non-smokers OR 1.24 (95% CI 1.01–1.52).<sup>32</sup>

The studies examining the association between NRT and these birth outcomes are even more limited. To date, there is only one observational study that has assessed the association between maternal NRT use and stillbirth.<sup>113</sup> Other evidence comes from RCTs of NRT patches and gum with inadequate power to assess safety outcomes.<sup>100,107,109</sup> Data from the DNBC suggest no increased risk of stillbirth associated with NRT use in the first 27 weeks of pregnancy (HR = 0.57, 95%CI 0.28-1.16) compared to those who did not use NRT and did not smoke). In comparison, women who both smoked and used NRT had an HR of

0.83 (95%CI 0.34-2.00) compared with non-smoking women who did not use NRT.<sup>113</sup> A meta-analysis of three RCTs assessing stillbirth as a secondary outcome also reported similar findings with no increased risk of stillbirth associated with NRT use compared to placebo (pooled OR 1.98, 95% CI 0.55-7.07).<sup>101</sup> Table 7-1 summarises the studies assessing NRT and birth outcomes including stillbirth, birth weight and mode of delivery.

The few studies assessing the association between NRT and birth weight present mixed evidence. Data from the observational studies report either no association between NRT and birth weight<sup>112</sup> or show an increased risk of low birth weight associated with NRT use.<sup>111</sup> In comparison, data from the trials report either no significant effect of NRT on infant's birth weight<sup>100,107,108</sup> or report higher birth weight in babies born to women randomised to NRT compared to the placebo group (mean difference 337g, ( $p < 0.01$ )<sup>109</sup> (Table 7-1).

The association between NRT and caesarean section has only been investigated in the SNAP trial which found a 45% increased risk of caesarean section associated with NRT use compared to placebo (Table 7-1).

**Table 7-1 - Summary of studies assessing the association between NRT use and birth outcomes**

First author, year and location	Study methodology	Sample size (Inclusion/Exclusion)	Exposure Assessment	Outcome Assessment	Results for NRT safety
<b>NRT and stillbirth</b>					
Strandberg-Larsen (2008), Denmark <sup>113</sup>	Cohort study using Danish National Birth Cohort	87,032 pregnancies between 1996-2002	NRT self-reported usage, total number of weeks with NRT use during the first 27 weeks of gestation, NRT type used	Stillbirth, defined as any foetus that did not breathe or show any other signs of life at birth after a minimum of 20 weeks of gestation, derived from The Civil Registration System and Danish Medical Birth Registry	Women who used NRT during pregnancy had a HR of 0.57 (95%CI 0.28-1.16) for still birth compared to those who did not use NRT. Women who both smoked and used NRT had a HR of 0.83 (95%CI 0.34-2.00) compared with non-smoking women who did not use NRT
Coleman (2012), UK <sup>100</sup>	Large, double-blinded, placebo-controlled multicentre RCT	1050 participants between 16 to 50 years with pregnancies of 12-24 weeks of gestation smoking five or more cigarettes per day	4 weeks supply of Standard nicotine patch (15mg/16 hrs) versus visually identical placebo, started on the quit date	Secondary outcome: Adverse pregnancy and birth outcomes including stillbirth	5 cases in NRT group and 2 cases in the placebo group. Stillbirth – OR 2.59 (95% CI 0.50-13.4)
Oncken (2008), Connecticut and Massachusetts <sup>109</sup>	Prospective, randomised, double-blind placebo-controlled clinical trial.	100 women randomised to nicotine gum and 94 to placebo	Individualised behavioural counselling and 6 week treatment with 2mg nicotine gum versus placebo	Stillbirth as a secondary outcome	2 cases in the NRT group and 0 cases in the placebo group. Stillbirth – OR 4.55 (0.22- 93.63)

Pollack (2007), North Carolina, USA <sup>107</sup>	An open-labelled non-placebo, randomised trial	Cognitive Behavioural Therapy (CBT)-only (n=59) versus CBT+NRT (n=122) in pregnant women between 13 and 25 weeks of gestation.	Control: received a "Quit kit" (which contained a booklet, water bottle, straws, candy, exercise band, and stress management tape), as well as 3 counselling sessions from a "support specialist" based on motivational interviewing, trans theoretical model and social cognitive theory. Intervention: as above plus an option of NRT by patch, gum or lozenge. Participants could change mode of administration if they wished.	Stillbirth as a secondary outcome	1 cases in the CBT+NRT group and 1 case in the only CBT group. OR 0.49 (0.03- 7.66)
<b>NRT and low birth weight</b>					
Coleman (2012), UK <sup>100</sup>	Large, double-blinded, placebo-controlled multicentre RCT	1050 participants between 16 to 50 years with pregnancies of 12-24 weeks of gestation smoking five or more cigarettes per day	4 weeks supply of Standard nicotine patch (15mg/16 hrs) versus visually identical placebo, started on the quit date	Secondary outcome: Adverse pregnancy and birth outcomes including birth weight	Low birth weight – OR 1.38 (95% CI 0.90-2.09), mean difference in birth weight=-0.05 (95% CI -0.17, 0.08).

Lassen (2010), Denmark <sup>112</sup>	Cohort study using Danish National Birth Cohort, a nationwide study of pregnant women and their offspring including 101,042 pregnancies between 1996 and 2002	72,761 pregnancies between 1996 and 2002	NRT self-reported usage, total number of weeks with NRT use during the first 27 weeks of gestation, NRT type used	Offspring Birth weight in mothers using NRT	Total NRT use not significantly associated with changes in birth weight (b=0.25g per week of NRT use (95%CI -2.31, 2.81)). Simultaneous use of >1 product associated with a statistically insignificant decrease in birth weight (b=-10.73g per week of NRT use (95% CI -26.51,5.05))
Gaither (2009), North Carolina, USA <sup>111</sup>	Cross-sectional study using data from 2004 Phase V Pregnancy Risk Assessment Monitoring System	6,041 women between the ages of 18-45 years out of which 5,716 included in the final analysis	Smoking, NRT prescription Versus Non-smoking women during pregnancy	Low birth weight defined as <2500g at birth)	After the adjustment for age, marital status, education and race/ethnicity women recommended NRT had twice the risk of low birth weight compared to non-smokers (OR=1.95, 95%CI 1.10-3.46)
Oncken (2008), Connecticut and Massachusetts <sup>109</sup>	Prospective, randomised, double-blind placebo-controlled clinical trial.	100 women randomised to nicotine gum and 94 to placebo	Individualised behavioural counselling and 6 week treatment with 2mg nicotine gum versus placebo	Offspring birth weight	Mean difference in the birth weight between offspring of mothers using NRT versus mothers on placebo=337g (p<0.001)



Pollack (2007), North Carolina, USA <sup>107</sup>	An open-labelled non-placebo, randomised trial	Cognitive Behavioural Therapy (CBT)-only (n=59) versus CBT+NRT (n=122) in pregnant women between 13 and 25 weeks of gestation.	Control: received a "Quit kit" (which contained a booklet, water bottle, straws, candy, exercise band, and stress management tape), as well as 3 counselling sessions from a "support specialist" based on motivational interviewing, trans theoretical model and social cognitive theory. Intervention: as above plus an option of NRT by patch, gum or lozenge. Participants could change mode of administration if they wished.	Birth weight	The mean difference between the CBT+NRT and CBT only arm in the birth weight = -71g (p=0.51)
Wisborg (2000), Denmark <sup>108</sup>	Double-blinded, placebo-controlled RCT	Pregnant women who smoked ten or more cigarettes after the first trimester (250) were randomly assigned to receive nicotine patches (124) or placebo patches (126).	Women randomized to nicotine were treated with 15-mg patches (16 hours/day) for 8 weeks, and 10-mg patches (16 hours/day) for 3 weeks.	Birth weight	Mean difference between NRT and placebo group (186 g, 95% CI 35-336 g. RR for low birth weight with NRT use during pregnancy =0.40, (95% CI 0.10-1.10)
<b>NRT and mode of delivery</b>					

Coleman (2012), UK <sup>100</sup>	Large, double-blinded, placebo-controlled multicentre RCT	1050 participants between 16 to 50 years with pregnancies of 12-24 weeks of gestation smoking five or more cigarettes per day	4 weeks supply of Standard nicotine patch (15mg/16 hrs) versus visually identical placebo, started on the quit date	Secondary outcome: Adverse pregnancy and birth outcomes including mode of delivery	Caesarean section delivery – OR 1.45 (95% CI 1.05-2.01)
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Given the dearth of information on the safety of NRT use during pregnancy and the inconclusive evidence arising from the limited literature available, this chapter focuses on examining the associations between NRT and smoking exposure during pregnancy as recorded in primary care and adverse birth outcomes. The specific objectives for this chapter are:

1. To examine the risk of stillbirth and fetal death (stillbirth and miscarriage) associated with maternal NRT and smoking exposure during pregnancy as described in primary care data
2. To assess the association between maternal NRT and smoking exposure during pregnancy, as recorded in primary care data, with birth weight
3. To assess the association between maternal NRT and smoking exposure during pregnancy as described in primary care data and mode of delivery

## **7.2 METHODS**

### **7.2.1 Study population**

The study population used for assessing stillbirth and mode of delivery was the same as described in Section 5.2.1 i.e. all pregnancies between January 2001 and September 2009 in women of childbearing age (15-49 years) which resulted in either a live birth or a stillbirth.

For low birth weight all live born children delivered between January 2001 and December 2009 with linked mother records and a recording for birth weight in their primary care records were included in the analysis. Stillborn children only constituted 0.07% of the total population and were excluded from this analysis as there may be higher risks of fetal growth restriction in stillborns compared to liveborns.

### **7.2.2 Exposure**

Two different time windows were used to classify the study population into one of the exposure categories: NRT group, smoker, non-smoker and unknown.

Firstly, early pregnancy NRT and smoking exposure (defined as exposure between four weeks before conception until the end of the first trimester), as recorded in primary care data, was assessed as described in Section 6.2.2.

Additionally, the exposure window was expanded to the whole course of pregnancy until delivery to assess the effects of NRT or smoking exposure any time during pregnancy on stillbirth. This exposure window was then also used for assessing the risk of low birth weight and the mode of delivery as fetal growth takes place throughout pregnancy.

### **7.2.3 Outcomes**

#### *7.2.3.1 Stillbirth*

Stillbirth was defined as a baby born with no signs of life at or after 28 weeks of gestation, in accordance with the WHO definition.<sup>271</sup> Information on stillbirth was extracted from the birth outcome variable pre-defined in the mother-child linked data, which has been described in Section 2.5.

A variable combining both stillbirth and miscarriage was created, called fetal death to assess the effect of NRT and smoking exposure on overall fetal death. It should however be noted that the information on miscarriages in these data is not complete which may have implications on the results.

#### *7.2.3.2 Birth weight*

Firstly, birth weight was also used as a continuous variable to examine the change in birth weight by each category of exposure. Then, low birth weight was

defined as a live born baby with a birth weight of less than 2500g (2.5kg) according to the WHO definition of low birth weight.<sup>11</sup>

#### *7.2.3.3 Mode of delivery*

Mode of delivery was also pre-defined in the mother-child linked file and categorised as normal delivery, assisted delivery and caesarean section. All pregnancies where there was no record of caesarean delivery or an assisted delivery were categorised as normal deliveries.

### **7.2.4 Statistical analysis**

#### *7.2.4.1 Stillbirth*

The absolute risk of stillbirth was calculated by dividing the total number of stillbirths by the number of stillbirths and live births combined. Logistic regression was used to compute ORs and corresponding 99% CIs for stillbirth for the NRT group and smokers, using non-smokers as the reference group. Maternal age, Townsend quintile, maternal diabetes, hypertension, asthma, pre-conception body mass index and mental illnesses were considered as potential confounders based on the previous literature.<sup>195,199,211,242-244,272-274</sup> The covariates which had a significant statistical association with the exposure and the outcomes in chi-squared tests were included in the final model. The potential clustering of pregnancies among mothers was accounted for using the clustered sandwich estimator<sup>180,181</sup> The reference group was then changed to smokers and the ORs were re-calculated. This analysis was then repeated using the entire pregnancy until the outcome as the exposure time for NRT and smoking.

To estimate the association between NRT and smoking exposure during pregnancy with fetal death (defined here as stillbirth and miscarriages) the risk of fetal death was calculated for NRT and smoking exposure during the entire

pregnancy time until the outcome, using the analysis techniques described above.

#### *7.2.4.2 Birth weight*

The association between NRT exposure maternal smoking during pregnancy and birth weight was analysed using a multiple linear regression model, treating birth weight as a continuous outcome. Only complete case analysis was conducted i.e. only babies with a recording of birth weight were included in this analysis. Potential confounding factors (described above) and clustering were adjusted for in the analysis. The regression co-efficient ( $\beta$ ) represents the average change in birth weight in grams associated with NRT group and smoking in relation to non-smokers. The risk of low birth weight for the NRT group and smokers was calculated in a similar fashion using univariable and multivariable logistic regression models as described above.

#### *7.2.4.3 Mode of delivery*

A multinomial logistic regression model (for categorical study outcomes) was used to obtain relative risk ratios (RRR) for assisted delivery and caesarean section relative to normal delivery in the NRT group, smokers and unknown categories compared to non-smokers. This model extends logistic regression by estimating the effect of one or more exposure variables on the probability that the outcome is in a particular category.<sup>275</sup> Robust CIs were calculated and appropriate adjustments in the RRRs for potential confounders were made in the same way as described above.

### **7.2.5 Sensitivity analysis**

#### *7.2.5.1 Reclassifying smokers and non-smokers based on gestational smoking status recording*

Similar to the previous chapter, the definition of smokers was restricted to only mothers who had a gestational smoking record during pregnancy and the non-smokers to mothers who had a gestational record in their primary care data indicating them to be non-smokers. This was done for both the early pregnancy exposure and exposure throughout pregnancy. The absolute and relative risks of stillbirth, low birth weight and different modes of delivery were re-calculated using this definition.

#### *7.2.5.2 Risk of low birth weight stratified by pre-term birth*

Since birth weight is directly related to gestational age<sup>276</sup> the risk of low birth weight was further stratified by whether the baby was born preterm or not. Preterm birth was defined as babies born alive before 37 weeks of pregnancy in line with the WHO definition<sup>277</sup> and deliveries occurring at or after 37 weeks of gestation were classified as term deliveries for purposes of this analysis. Unadjusted and adjusted ORs and corresponding CIs were calculated separately for preterm and term deliveries.

### **7.2.6 Sample size calculations**

The prevalence of stillbirth in the UK is estimated to be approximately 5/1000 live and stillbirths.<sup>159</sup> Based on the known prescribing prevalence of NRT and maternal smoking during pregnancy from previous chapters, a sample size of 96,641 children with mothers prescribed NRT was needed to detect an OR of 1.50 with 80% power at 1% level of significance. For maternal smoking, a sample size of 12,903 children with mothers who smoked during pregnancy was needed to detect an OR of 1.50, with 80% power at 1% level of significance.

Considering the standard deviation of birth weight in general population to be 466g,<sup>278</sup> a sample size of 7,646 babies will have 80% power to detect a mean difference of 150g with a two-sided level of significance of 5%. The prevalence of low birth weight in the UK in 2009 was approximately 7%.<sup>279</sup> In light of this, and the smoking and NRT prescribing prevalence from the previous chapter, a sample size of 43,029 children with mothers prescribed NRT was needed to detect an OR of 1.50 with 80% power at 1% level of significance. For smoking exposure a sample of 5,907 children with maternal smoking exposure was needed to detect an OR of 1.50 with 80% power at 1% level of significance.

## **7.3 RESULTS**

### **7.3.1 Stillbirth**

#### *7.3.1.1 Baseline characteristics*

The study population included 255,441 pregnancies delivered between 2001 and 2009 out of which 1,044 ended in stillbirths, giving a prevalence of 4/1,000 live and stillbirths. Pregnancies that were conceived at later ages (>35 years) resulted in a higher prevalence of stillbirth. The prevalence of stillbirths was also higher in pregnant women with diabetes and mental illness (3.5% and 11.9% respectively). The distribution of socioeconomic status, pre-conception BMI, and the prevalence of chronic illnesses like asthma and hypertension were comparable in women with stillbirth and those with live births.



**Table 7-2 - Baseline characteristics for all pregnancies, by live birth and stillbirth**

	All pregnancies		Live births		Stillbirths	
	N=255,441		N=254,397		N=1,044	
	n	%	n	%	n	%
<b>Age at conception</b>						
15-19 years	14,141	5.5%	14,066	5.5%	75	7.2%
20-24 years	40,879	16.0%	40,703	16.0%	176	16.9%
25-29 years	65,029	25.5%	64,796	25.5%	233	22.3%
30-34 years	79,959	31.3%	79,683	31.3%	276	26.4%
35-39 years	45,765	17.9%	45,543	17.9%	222	21.3%
40-44 years	9,179	3.6%	9,122	3.6%	57	5.5%
45-49 years	489	0.2%	484	0.2%	5	0.5%
<b>Townsend score in quintiles</b>						
Quintile 1 (least deprived)	57,859	22.7%	57,658	22.7%	201	19.3%
Quintile 2	47,841	18.7%	47,664	18.7%	177	17.0%
Quintile 3	49,670	19.4%	49,465	19.4%	205	19.6%
Quintile 4	47,292	18.5%	47,086	18.5%	206	19.7%
Quintile 5 (most deprived)	36,103	14.1%	35,902	14.1%	201	19.3%
Missing	16,676	6.5%	16,622	6.5%	54	5.2%
<b>Pre-conception Body Mass Index (kg/m<sup>2</sup>)</b>						
Normal(18.5-24.9)	80,016	31.3%	79,737	31.3%	279	26.7%
Underweight(<18.5)	5,856	2.3%	5,825	2.3%	31	3.0%
Overweight(25-29.9)	38,945	15.2%	38,785	15.2%	160	15.3%
Obese(>=30)	26,741	10.5%	26,595	10.5%	146	14.0%
Missing	103,883	40.7%	103,455	40.7%	428	41.0%
<b>Asthma</b>	21,884	8.6%	21,802	8.6%	82	7.9%
<b>Hypertension</b>	6,885	2.7%	6,848	2.7%	37	3.5%
<b>Diabetes</b>	5,971	2.3%	5,930	2.3%	41	3.9%
<b>Mental illness</b>	24,178	9.5%	24,054	9.5%	124	11.9%

### *7.3.1.2 Association between NRT and smoking exposure in early pregnancy and stillbirth*

Table 7-3 presents the odds of stillbirth in relation to NRT exposure and maternal smoking during early pregnancy. The prevalence of stillbirth in the study population was found to be 4/1,000 live and stillbirths. The absolute risk of stillbirth was 4/1,000 live and stillbirths amongst the NRT group and 5/1000 live and stillbirths among smokers.

In the unadjusted analysis there was no statistically significant increased risk of stillbirth associated with NRT exposure during early pregnancy. However, women who smoked during early pregnancy were 35% more likely to have stillbirths compared to non-smokers (OR 1.35, 99% CI 1.08-1.68). The association between NRT exposure in early pregnancy and stillbirth did not reach statistical significance when adjusted for the potential confounders (OR 1.19, 99% CI 0.47-3.01). The association between maternal smoking and stillbirth was, however, still significant after adjusting for maternal age at conception, Townsend quintile, pre-conception BMI, diabetes and mental illness, with a 27% increase in the risk of stillbirth associated with maternal smoking during early pregnancy (OR 1.27, 99% CI 1.01-1.60).

When the reference group was changed to smokers, no increased risk of stillbirth was found for NRT exposure in comparison to smoking (OR 0.94, 99% CI 0.36-2.38).

**Table 7-3 – Risk of stillbirth by NRT and smoking exposure only during early pregnancy**

	<b>Total population</b>	<b>Stillbirths</b>	<b>Unadjusted OR</b>	<b>p-value</b>	<b>Adjusted OR</b>	<b>p-value</b>
	<b>N=255,441</b>	<b>n (%)</b>	<b>(99% CI)</b>		<b>(99%CI)‡</b>	
Non-smoker***	125,261	450 (0.4%)	1		1	
NRT-exposed group *	1,759	8 (0.4%)	1.26 (0.50-3.18)	0.508	1.19 (0.47-3.01)	0.622
Smoker**	41,603	201 (0.5%)	1.35 (1.08-1.68)	<0.001	1.27 (1.01-1.60)	0.007
Unknown	86,818	385 (0.4%)	1.23 (1.03-1.48)	0.002	1.20 (1.00-1.45)	0.010

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy , \*\*\*non-smokers during early pregnancy

‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births

OR=Odds ratio, CI= confidence interval

*7.3.1.3 Association between NRT, smoking exposure during the entire pregnancy and stillbirth*

When the exposure time was expanded to include any NRT prescribing or smoking until delivery the absolute risks were similar.

No increased risk of stillbirth was found to be associated with NRT exposure (adjusted OR 1.67, 99% CI 0.94-2.99) (Table 7-4). Maternal smoking any time during pregnancy was also not found to be associated with an increased risk of stillbirth (OR 1.19, 99% CI 0.95-1.52).

When the reference group was changed to smokers, no increased risk of stillbirth was found in the NRT group in comparison to smoking (OR 1.39, 99% CI 0.76-2.53).

**Table 7-4 – Risk of stillbirth by NRT and smoking exposure throughout pregnancy**

	<b>Total population</b> <b>N=255,441</b>	<b>Stillbirths</b> <b>n (%)</b>	<b>Unadjusted OR</b> <b>(99% CI)</b>	<b>p-value</b>	<b>Adjusted OR</b> <b>(99%CI) ‡</b>	<b>p-value</b>
Non-smoker***	123,356	447 (0.4%)	1			
NRT-exposed group *	3,254	21 (0.6%)	1.79 (1.00-3.18)	0.010	1.67 (0.94-2.99)	0.022
Smoker**	42,089	193 (0.5%)	1.26 (1.00-1.58)	0.001	1.19 (0.95-1.52)	0.046
Unknown	86,742	383 (0.4%)	1.22 (1.01-1.45)	0.002	1.18 (0.98-1.43)	0.018

\*NRT=nicotine replacement therapy prescription any time during pregnancy, \*\*smoking any time during pregnancy, \*\*\*non-smokers during pregnancy ‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births  
OR=Odds ratio, CI= confidence interval

#### *7.3.1.4 Association between NRT, smoking exposure and fetal death*

Table 7-5 presents the unadjusted and adjusted odds ratios for fetal death in relation to NRT and maternal smoking exposure during pregnancy. The prevalence of stillbirth and miscarriages together was the highest among current smokers (20.8%) and the lowest in the NRT group (9.4%).

NRT exposure during pregnancy was found to have a protective effect on fetal death such that it reduced the risk of fetal death by half (OR 0.44, 99% CI 0.38-0.51) in comparison to non-smokers. Smoking was found to increase the risk of fetal death by 16% (OR 1.16, 99% CI 1.11-1.21) when compared to the risk in non-smokers.

**Table 7-5 – Risk of fetal death by NRT and smoking exposure throughout pregnancy**

	<b>Total population</b>	<b>Fetal death</b>	<b>Unadjusted OR</b>	<b>p-value</b>	<b>Adjusted OR‡</b>	<b>p-value</b>
	<b>N=311,802</b>	<b>n (%)</b>	<b>(99% CI)</b>		<b>(99%CI)</b>	
Non-smoker***	150,175	25,962 (17.3%)	1		1	
NRT group *	5,234	491 (9.4%)	0.50 (0.44-0.56)	<0.001	0.44 (0.38-0.50)	<0.001
Smoker**	50,643	10,560 (20.8%)	1.26 (1.22-1.30)	<0.001	1.16 (1.11-1.21)	<0.001
Unknown	105,750	20,392 (19.3%)	1.14 (1.11-1.17)	<0.001	0.95 (0.74-1.21)	0.571

\*NRT=nicotine replacement therapy prescription any time during pregnancy, \*\*smoking any time during pregnancy, \*\*\*non-smokers during pregnancy ‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births  
OR=Odds ratio, CI= confidence interval

#### *7.3.1.5 Sensitivity analysis*

The results from the sensitivity analysis were very similar to the main results showing no statistically significant increased risk of stillbirth in the NRT group in both early pregnancy (OR 1.44, 99% CI 0.54-3.82) and throughout pregnancy (OR 1.95, 99% CI 1.00-3.63). Similarly, the risk of stillbirth increased by 78% in mothers who smoked in early pregnancy (OR 1.78, 99% CI 1.04-3.02). This effect decreased when exposure throughout pregnancy was assessed (OR 1.47, 99% CI 0.96-2.25).



**Table 7-6 – Risk of stillbirth by NRT and smoking exposure only during early pregnancy, using only gestational smoking records**

	<b>Total population N=255,441</b>	<b>Stillbirths n (%)</b>	<b>Unadjusted OR (99% CI)</b>	<b>p-value</b>	<b>Adjusted OR (99%CI)‡</b>	<b>p-value</b>
Non-smoker***	20,068	59 (0.3%)	1		1	
NRT-exposed group *	1,759	8 (0.4%)	1.55 (0.59-4.09)	0.246	1.44 (0.54-3.82)	0.336
Smoker**	7,381	41 (0.6%)	1.89 (1.13-3.20)	0.002	1.78 (1.04-3.02)	0.005
Unknown	226,233	936 (0.4%)	1.41 (0.99-1.99)	0.011	1.37 (0.96-1.93)	0.020

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy , \*\*\*non-smokers during early pregnancy

‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births

OR=Odds ratio, CI= confidence interval

**Table 7-7 – Risk of stillbirth by NRT and smoking exposure throughout pregnancy, using only gestational smoking records**

	<b>Total population</b>	<b>Stillbirths</b>	<b>Unadjusted OR</b>	<b>p-value</b>	<b>Adjusted OR</b>	<b>p-value</b>
	<b>N=255,441</b>	<b>n (%)</b>	<b>(99% CI)</b>		<b>(99%CI) ‡</b>	
Non-smoker***	32,203	101 (0.3%)	1		1	
NRT-exposed group *	3,254	21 (0.6%)	1.79 (1.00-3.18)	0.010	1.95 (1.00-3.63)	0.006
Smoker**	12,126	60 (0.5%)	1.32 (1.06-1.66)	0.001	1.47 (0.96-2.25)	0.019
Unknown	207,757	862 (0.4%)	1.22 (1.01-1.45)	0.002	1.31 (1.00-1.72)	0.018

\*NRT=nicotine replacement therapy prescription any time during pregnancy, \*\*smoking any time during pregnancy, \*\*\*non-smokers during pregnancy ‡adjusted for maternal age, Townsend score, diabetes, mental illness and Body Mass Index, multiple births  
OR=Odds ratio, CI= confidence interval

### **7.3.2 Low birth weight**

#### *7.3.2.1 Baseline characteristics*

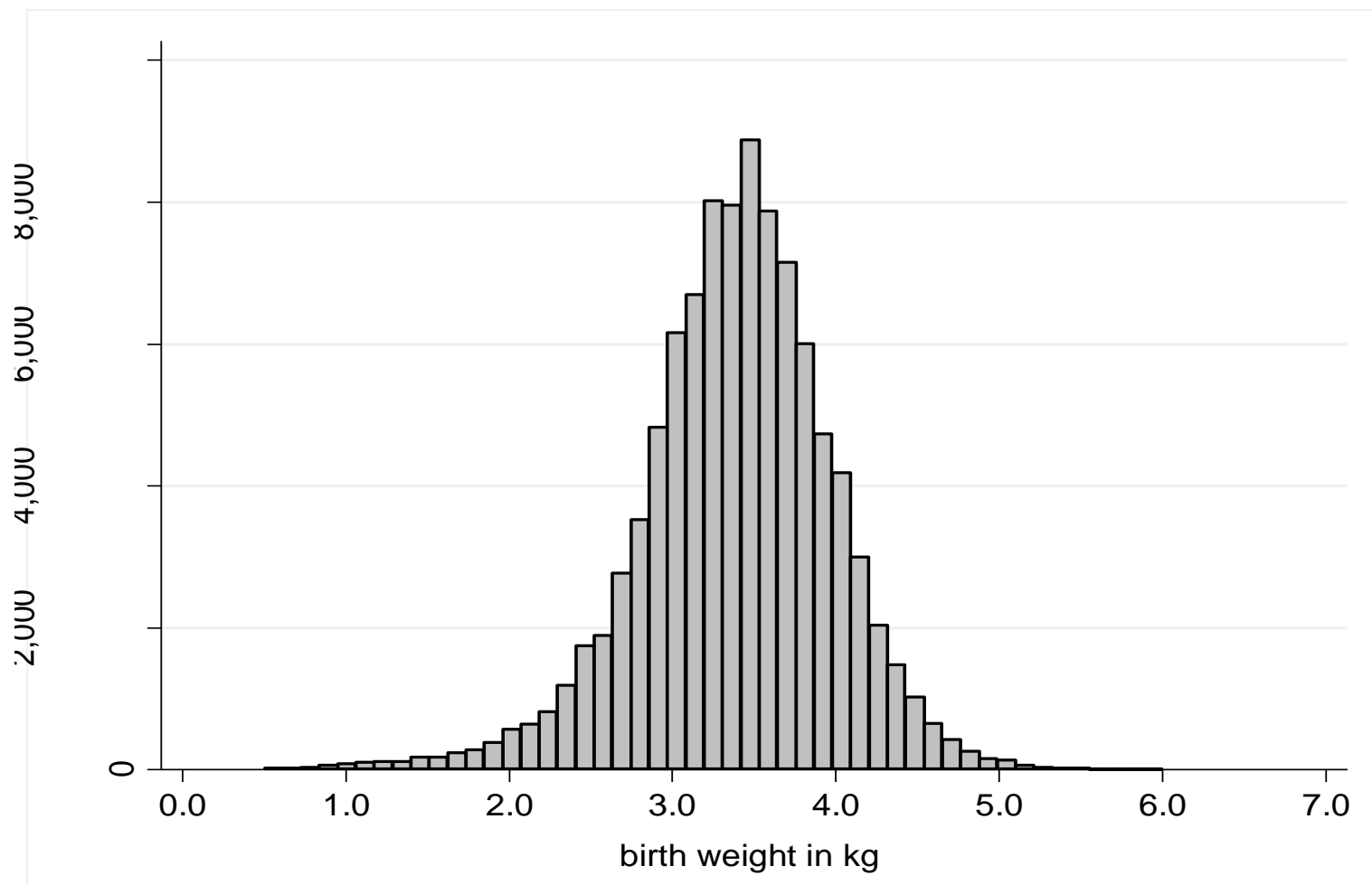
A total of 96,782 children with linked maternal records had their birth weight recorded in THIN out of a total population of 232,242 live born children. The distribution of maternal characteristics in children with a recording of birth weight and without a recording of birth weight was highly comparable however the proportion of missing maternal BMI data was lower in children with who had a recording of birth weight compared to those without a recording of birth weight (35.4% compared with 44.0%) (Table 7-8).

**Table 7-8 - Recording of birth weight and maternal characteristics**

	All births (N=232,242)		Birth weight recorded (96,872)		No birth weight recorded (135,370)	
	N	%	n	%	n	%
<b>Age at conception</b>						
15-19 years	12,037	5.2%	4,900	5.1%	7,137	5.3%
20-24 years	36,003	15.5%	15,031	15.5%	20,972	15.5%
25-29 years	59,203	25.5%	24,722	25.5%	34,481	25.5%
30-34 years	73,844	31.8%	30,791	31.8%	43,053	31.8%
35-39 years	42,477	18.3%	17,917	18.5%	24,560	18.1%
40-44 years	8,341	3.6%	3,376	3.5%	4,965	3.7%
45-49 years	337	0.1%	135	0.1%	202	0.1%
<b>Townsend score in quintiles</b>						
Quintile 1 (most affluent)	53,916	23.2%	22,061	22.8%	31,855	23.5%
Quintile 2	43,850	18.9%	17,839	18.4%	26,011	19.2%
Quintile 3	45,280	19.5%	19,390	20.0%	25,890	19.1%
Quintile 4	42,696	18.4%	18,109	18.7%	24,587	18.2%
Quintile 5 (most deprived)	31,884	13.7%	13,053	13.5%	18,831	13.9%
Missing	14,616	6.3%	6,420	6.6%	8,196	6.1%
<b>Pre-conception Body Mass Index</b>						
Normal(18.5-24.9)	73,002	31.4%	32,813	33.9%	40,189	29.7%
Underweight(<18.5)	5,225	2.2%	2,317	2.4%	2,908	2.1%
Overweight(25-29.9)	35,625	15.3%	16,254	16.8%	19,371	14.3%
Obese(>=30)	24,594	10.6%	11,233	11.6%	13,361	9.9%
Missing	93,796	40.4%	34,255	35.4%	59,541	44.0%
<b>Asthma</b>	19,932	8.6%	9,002	9.3%	10,930	8.1%
<b>Hypertension</b>	6,392	2.8%	2,910	3.0%	3,482	2.6%
<b>Diabetes</b>	5,490	2.4%	2,400	2.5%	3,090	2.3%
<b>Mental illness</b>	22,154	9.5%	10,131	10.5%	12,023	8.9%
<b>Multiple births</b>	8,373	3.6%	3,361	3.5%	5,012	3.7%

In the 96,782 children with a recording of birth weight, the mean birth weight was 3.41kgs (sd 0.59) and the mean gestational age was 40 weeks (sd 2.11). Figure 7-1 presents a histogram of the birth weight (in kilograms) of the 96,782 children with a recording of birth weight. Birth weight was normally distributed with no skewing towards high or low birth weight. Table 7-9 presents the maternal characteristics of children with normal and low birth weight.

**Figure 7-1 - Histogram of birth weight in the study population**



**Table 7-9 - Baseline characteristics by birth weight**

	All live births (N=96,872)		Normal birth weight (N=90,670)		Low birth weight (N= 6,202)	
	N	%	n	%	n	%
<b>Age at conception</b>						
15-19 years	4,900	5.1%	4,549	5.0%	351	5.7%
20-24 years	15,031	15.5%	14,007	15.4%	1,024	16.5%
25-29 years	24,722	25.5%	23,231	25.6%	1,491	24.0%
30-34 years	30,791	31.8%	28,950	31.9%	1,841	29.7%
35-39 years	17,917	18.5%	16,695	18.4%	1,222	19.7%
40-44 years	3,376	3.5%	3,124	3.4%	252	4.1%
45-49 years	135	0.1%	114	0.1%	21	0.3%
<b>Townsend score in quintiles</b>						
Quintile 1 (least deprived)	22,061	22.8%	20,862	23.0%	1,199	19.4%
Quintile 2	17,839	18.4%	16,791	18.5%	1,048	16.9%
Quintile 3	19,390	20.0%	18,201	20.1%	1,189	19.2%
Quintile 4	18,109	18.7%	16,811	18.5%	1,298	20.9%
Quintile 5 (most deprived)	13,053	13.5%	12,006	13.2%	1,047	16.9%
Missing	6,420	6.6%	5,999	6.6%	421	6.8%
<b>Pre-conception Body Mass Index (kg/m<sup>2</sup>)</b>						
Normal(18.5-24.9)	32,813	33.9%	30,667	33.8%	2,146	34.6%
Underweight(<18.5)	2,317	2.4%	2,008	2.2%	309	5.0%
Overweight(25-29.9)	16,254	16.8%	15,310	16.9%	944	15.2%
Obese(>=30)	11,233	11.6%	10,644	11.7%	589	9.5%
Missing	34,255	35.4%	32,041	35.3%	2,214	35.7%
<b>Asthma</b>	9,002	9.3%	8,298	9.2%	704	11.4%
<b>Hypertension</b>	2,910	3.0%	2,501	2.8%	409	6.6%
<b>Diabetes</b>	2,400	2.5%	2,207	2.4%	193	3.1%
<b>Mental illness</b>	10,131	10.5%	9,354	10.3%	777	12.5%
<b>Multiple births</b>	3,361	3.50%	1,823	2.0%	1,538	24.8%

#### *7.3.2.2 Association between maternal NRT and smoking exposure during pregnancy and birth weight*

Table 7-10 describes the change in mean birth weight for the NRT group and smokers compared to non-smokers. NRT exposure during pregnancy was associated with a statistically significant decrease in birth weight of 176g compared to non-smokers ( $\beta = -176\text{g}$ , 99% CI -221g, -131g). In comparison, smoking during pregnancy was associated with a statistically significant decrease in birth weight of 120g compared to non-smokers ( $\beta = -123\text{g}$ , 99% CI -136g, -109g).

When the baseline was changed to smokers, the NRT group was found to have slightly reduced birth weight compared to smokers ( $\beta = -5\text{g}$ , 99% CI -9g, -0.7g).



**Table 7-10 - The association between NRT and smoking exposure during pregnancy and mean birth weight**

	Unadjusted change in mean birth weight (g)		Adjusted change in mean birth weight(g)	
	$\beta$ (99% CI)	p-value	$\beta$ (99% CI)*	p-value
<b>NRT group *</b>	-211 (-258, -164)	<0.001	-176 (-221,-131)	<0.001
<b>Smoker**</b>	-143 (-157, -129)	<0.001	-123 (-136,-109)	<0.001
<b>Unknown</b>	-30 (-41,-19)	<0.001	-28 (-39,-17)	<0.001

Non-smokers during early pregnancy considered as baseline

\*NRT=nicotine replacement therapy prescription in pregnancy, \*\*smoking in pregnancy

‡Adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index

CI = confidence interval, OR = Odds ratio

#### *7.3.2.3 Association between NRT exposure, smoking and low birth weight*

Table 7-11 presents the prevalence of low birth weight by NRT and smoking exposure in mothers and the corresponding unadjusted and adjusted odds ratios (99% CI). The prevalence of low birth weight was the highest in the NRT group followed by smokers (11.0% and 9.0% respectively). Compared to non-smokers, children born to women in the NRT group were over twice as likely and children born to smokers were 64% more likely to have low birth weight. When adjusted for potential confounders, the risk of low birth weight in the NRT group was 93% higher compared to non-smokers (OR 1.93, 99% CI 1.48-2.53). Similarly, the risk of low birth weight in smokers was 69% higher (OR 1.69, 99% CI 1.53-1.86) compared to non-smoking mothers. When the reference group was changed to smokers, there was no increased risk of low birth weight in the NRT group compared to smokers (OR 1.24, 99% CI 0.97-1.59) ( $p=0.023$ ).

**Table 7-11 – Risk of low birth weight by NRT and smoking exposure during pregnancy**

	<b>Total population</b> <b>N=96,872</b>	<b>Low birth weight</b> <b>n (%)</b>	<b>Unadjusted OR</b> <b>(99% CI)</b>	<b>p-value</b>	<b>Adjusted OR</b> <b>(99%CI) ‡</b>	<b>p-value</b>
Non-smoker***	49,452	2,796 (5.6%)	1		1	
NRT group *	1,223	135 (11.0%)	2.07 (1.63-2.63)	<0.001	1.93 (1.48-2.53)	<0.001
Smoker**	16,135	1,445 (9.0%)	1.64 (1.50-1.79)	<0.001	1.69 (1.53-1.86)	<0.001
Unknown	30,062	1,826 (6.1%)	1.08 (0.99-1.16)	0.014	1.09 (0.99-1.18)	0.015

\*NRT=nicotine replacement therapy prescription in pregnancy, \*\*smoking in pregnancy, \*\*\*non-smokers during pregnancy

‡ Adjusted for maternal age, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index

CI = confidence interval, OR = Odds ratio

#### 7.3.2.4 Sensitivity analysis

##### 7.3.2.4.1 Maternal NRT and smoking during pregnancy and birth weight, using only gestational smoking records

Table 7-12 describes the change in mean birth weight for NRT group and smokers compared to non-smokers, using only gestational smoking records. NRT exposure during pregnancy was still associated with a statistically significant decrease in birth weight of 168g compared to non-smokers ( $\beta = -168\text{g}$ , 99% CI -214g, -122g). In comparison, smoking during pregnancy was associated with a statistically significant decrease in birth weight of 139g compared to non-smokers ( $\beta = -139\text{g}$ , 99% CI -165g, -113g).

**Table 7-12 - The association between NRT and smoking exposure during pregnancy and mean birth weight, using only gestational smoking records**

	Unadjusted change in mean birth weight (g)		Adjusted change in mean birth weight(g)	
	$\beta$ (99% CI)	p-value	$\beta$ (99% CI)*	p-value
<b>NRT group *</b>	-207 (-255, -158)	<0.001	-168 (-214,-122)	<0.001
<b>Smoker**</b>	-168 (-194, -141)	<0.001	-139 (-165,-113)	<0.001
<b>Unknown</b>	-26 (-41,-12)	<0.001	-22 (-35,-8)	<0.001

Non-smokers during early pregnancy considered as baseline

\*NRT=nicotine replacement therapy prescription in pregnancy, \*\*smoking in pregnancy

‡Adjusted for maternal age at conception, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index

CI = confidence interval, OR = Odds ratio

#### 7.3.2.4.2 Reclassifying smokers and non-smokers based on gestational smoking status recording

Table 7-13 presents the prevalence of low birth weight by NRT and smoking exposure in mothers and the corresponding unadjusted and adjusted ORs (99% CI) using only gestational smoking status records. The prevalence of low birth weight across the exposure groups was very similar to the main analysis (11.0% in the NRT group and 9.4% in smokers). After adjusting for potential confounders children born to women in the NRT group were 88% more likely (OR 1.88, 99% CI 1.42-2.49) and children born to smokers were 73% more likely (OR 1.73, 99% CI 1.45-2.06) to be of low birth weight compared to children born to non-smokers during pregnancy.

**Table 7-13 - Unadjusted and adjusted Odds ratio for low birth weight by NRT and smoking exposure, using only definitive smokers and non-smokers**

	<b>Total population N=96,872</b>	<b>Low birth weight n (%)</b>	<b>Unadjusted OR (99% CI)</b>	<b>p-value</b>	<b>Adjusted OR (99%CI) ‡</b>	<b>p-value</b>
Non-smoker***	13,088	740 (5.6%)	1		1	
NRT-exposed group *	1,223	135 (11.0%)	2.07 (1.48-2.03)	<0.001	1.88 (1.42-2.49)	<0.001
Smoker**	4,622	435 (9.4%)	1.73 (1.60-2.67)	<0.001	1.73 (1.45-2.06)	<0.001
Unknown	77,939	4,892 (6.3%)	1.12 (1.00-1.24)	0.006	1.13 (0.99-1.24)	0.012

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy, \*\*\*non-smokers during early pregnancy

‡ Adjusted for maternal age, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index

CI = confidence interval, OR = Odds ratio

#### 7.3.2.4.3 Risk of low birth weight stratified by pre-term birth

Table 7-14 shows the risk of low birth weight by NRT and smoking exposure stratified by preterm birth. Both maternal NRT and smoking exposure during pregnancy were found to be associated with low birth weight in babies in both preterm and term births. However, the risk of low birth weight was slightly higher in term births.

When direct comparisons were made with smokers in both term and pre-term birth, NRT was not found to have any statistically significant increased risk (OR 1.31, 99% CI 0.79-2.20 for pre-term birth and OR 0.99, 99% CI 0.68-1.46 for term births).



**Table 7-14 - Unadjusted and adjusted odds ratio for low birth weight by NRT and smoking exposure, stratified by preterm birth**

	<b>Unadjusted OR (99% CI)</b>	<b>p-value</b>	<b>Adjusted OR (95% CI) ‡</b>	<b>p-value</b>
<b>Term birth</b>				
<b>Non-smoker***</b>	1		1	
<b>NRT group *</b>	2.18 (1.54-3.10)	<0.001	1.82 (1.25-2.66)	<0.001
<b>Smoker**</b>	1.96 (1.73-2.22)	<0.001	1.83 (1.59-2.09)	<0.001
<b>Unknown</b>	1.14 (1.00-1.27)	0.006	1.09 (0.97-1.24)	0.053
<b>Pre-term birth</b>				
<b>Non-smoker***</b>	1		1	
<b>NRT group *</b>	1.77 (1.10-2.85)	0.002	2.00 (1.21-3.31)	<0.001
<b>Smoker**</b>	1.28 (1.09-1.51)	<0.001	1.52 (1.27-1.82)	<0.001
<b>Unknown</b>	1.00 (0.87-1.15)	0.972	1.06 (0.91-1.23)	0.354

\*NRT=nicotine replacement therapy prescription in early pregnancy, \*\*smoking in early pregnancy, \*\*\*non-smokers during early pregnancy

‡Adjusted for maternal age, Townsend score, maternal hypertension, diabetes, asthma, mental illness, Body Mass Index

CI = confidence interval, OR = Odds ratio

### **7.3.3 Mode of delivery**

A total of 255,441 pregnancies among a cohort of 201,465 mothers were identified. Approximately three-quarters of all pregnancies (76.5%) were delivered through normal vaginal delivery, 6.2% through assisted delivery and 17.3% through caesarean section. Compared to the normal and assisted deliveries, women with caesarean sections were older and more obese and had a higher prevalence of hypertension, diabetes and mental illness. Table 7-15 presents the baseline characteristics of women in all three outcome groups. Asthma and mental illness were found to be most common in current smokers and the NRT group. In addition, approximately 50% mothers in smokers group and NRT group were more deprived (Townsend quintile 4 and 5). Table 7-16 presents maternal characteristics by NRT exposure and smoking among the study population. Women prescribed NRT and smokers were more likely to be from younger and more deprived groups. Additionally, the prevalence of asthma and mental illness was the highest among pregnant women who smoked during pregnancy or were prescribed NRT during pregnancy.

The prevalence of assisted delivery was found to be the highest in non-smokers (6.7%) however it wasn't very different in other exposure groups (5.2% in NRT group and 5.7% in smokers and unknown group). Similarly, the prevalence of caesarean section was also found to be the highest in non-smokers (18.3%).

**Table 7-15 - Baseline characteristics for all modes of delivery**

Baseline characteristics	All		Normal delivery		Assisted delivery		Caesarean delivery	
	N=255,441		n=195,523		n=15,835		n=44,083	
	n	%	n	%	n	%	n	%
<b>Age at conception</b>								
15-19 years	14,141	5.5%	11,776	6.0%	974	6.2%	1,391	3.2%
20-24 years	40,879	16.0%	33,271	17.0%	2,452	15.5%	5,156	11.7%
25-29 years	65,029	25.5%	50,717	25.9%	4,271	27.0%	10,041	22.8%
30-34 years	79,959	31.3%	59,892	30.6%	5,187	32.8%	14,880	33.8%
35-39 years	45,765	17.9%	33,182	17.0%	2,494	15.7%	10,089	22.9%
40-44 years	9,179	3.6%	6,374	3.3%	429	2.7%	2,376	5.4%
45-49 years	489	0.2%	311	0.2%	28	0.2%	150	0.3%
<b>Townsend score in quintiles</b>								
Quintile 1 (least deprived)	57,859	22.7%	43,195	22.1%	4,028	25.4%	10,636	24.1%
Quintile 2	47,841	18.7%	35,996	18.4%	3,274	20.7%	8,571	19.4%
Quintile 3	49,670	19.4%	37,889	19.4%	3,147	19.9%	8,634	19.6%
Quintile 4	47,292	18.5%	36,933	18.9%	2,601	16.4%	7,758	17.6%
Quintile 5 (most deprived)	36,103	14.1%	28,657	14.7%	1,785	11.3%	5,661	12.8%
Missing	16,676	6.5%	12,853	6.6%	1,000	6.3%	2,823	6.4%
<b>Pre-pregnancy Body Mass Index (kg/m<sup>2</sup>)</b>								
Normal(18.5-24.9)	80,016	22.7%	62,131	31.8%	5,724	36.1%	12,161	27.6%
Underweight(<18.5)	5,856	18.7%	4,737	2.4%	391	2.5%	728	1.7%
Overweight(25-29.9)	38,945	19.4%	28,914	14.8%	2,385	15.1%	7,646	17.3%
Obese(>=30)	26,741	18.5%	18,732	9.6%	1,222	7.7%	6,787	15.4%
Missing	103,883	14.1%	81,009	41.4%	6,113	38.6%	16,761	38.0%
<b>Asthma</b>	21,884	22.7%	16,358	8.4%	1,414	8.9%	4,112	9.3%
<b>Hypertension</b>	6,885	18.7%	4,385	2.2%	422	2.7%	2,078	4.7%
<b>Diabetes</b>	5,971	19.4%	3,588	1.8%	356	2.2%	2,027	4.6%
<b>Mental illness</b>	24,178	18.5%	18,338	9.4%	1,385	8.7%	4,455	10.1%

**Table 7-16 - Baseline characteristics by NRT and smoking exposure during pregnancy**

	<b>All pregnancies</b>		<b>NRT group*</b>		<b>Smokers**</b>		<b>Non-smokers***</b>		<b>Unknown</b>	
	N=255,441		n=3,254		n=42,089		n=123,356		n=86,742	
	n	%	n	%	n	%	n	%	n	%
<b>Age at conception</b>										
15-19 years	14,141	5.5%	306	9.4%	4,649	11.0%	4,558	3.7%	4,628	5.3%
20-24 years	40,879	16.0%	791	24.3%	11,421	27.1%	16,387	13.3%	12,280	14.2%
25-29 years	65,029	25.5%	847	26.0%	11,282	26.8%	32,383	26.3%	20,517	23.7%
30-34 years	79,959	31.3%	773	23.8%	8,980	21.3%	41,389	33.6%	28,817	33.2%
35-39 years	45,765	17.9%	447	13.7%	4,767	11.3%	23,692	19.2%	16,859	19.4%
40-44 years	9,179	3.6%	83	2.6%	944	2.2%	4,717	3.8%	3,435	4.0%
45-49 years	489	0.2%	7	0.2%	46	0.1%	230	0.2%	206	0.2%
<b>Townsend score in quintiles</b>										
Quintile 1 – least deprived	57,859	22.7%	334	10.3%	5,141	12.2%	30,828	25.0%	21,556	24.9%
Quintile 2	47,841	18.7%	381	11.7%	5,886	14.0%	24,779	20.1%	16,795	19.4%
Quintile 3	49,670	19.4%	620	19.1%	8,258	19.6%	24,084	19.5%	16,708	19.3%
Quintile 4	47,292	18.5%	884	27.2%	10,478	24.9%	20,636	16.7%	15,294	17.6%
Quintile 5 - most deprived	36,103	14.1%	804	24.7%	9,624	22.9%	14,068	11.4%	11,607	13.4%
Missing	16,676	6.5%	231	7.1%	2,702	6.4%	8,961	7.3%	4,782	5.5%
<b>Pre-conception Body Mass Index (kg/m<sup>2</sup>)</b>										
Normal(18.0-24.9)	80,016	22.7%	1,017	31.3%	14,127	33.6%	48,171	39.1%	16,701	19.3%
Underweight(<18.0)	5,856	18.7%	101	3.1%	1,491	3.5%	2,984	2.4%	1,280	1.5%
Overweight(25-29.9)	38,945	19.4%	515	15.8%	6,860	16.3%	23,060	18.7%	8,510	9.8%
Obese(>=30)	26,741	18.5%	405	12.4%	5,104	12.1%	15,375	12.5%	5,857	6.8%
Missing	103,883	14.1%	1,216	37.4%	14,507	34.5%	33,766	27.4%	54,394	62.7%
<b>Asthma</b>	21,884	22.7%	404	12.4%	4,868	11.5%	12,416	10.1%	4,196	4.9%
<b>Hypertension</b>	6,885	18.7%	70	2.3%	882	2.1%	3,965	3.2%	1,968	2.3%
<b>Diabetes</b>	5,971	19.4%	70	2.6%	865	2.0%	3,548	2.9%	1,488	1.7%
<b>Mental illness</b>	24,178	18.5%	625	19.0%	6,549	15.5%	9,604	7.8%	7,400	8.5%

\*NRT=nicotine replacement therapy prescription in pregnancy, \*\*smoking in pregnancy, \*\*\* No smoking in pregnancy,

**Table 7-17 - Breakdown of mode of deliveries by NRT and smoking exposure**

<b>Mode of delivery</b>	<b>Total</b>	<b>NRT group*</b>	<b>Smokers**</b>	<b>Non-smokers***</b>	<b>Unknown</b>
	<b>N=255,441</b>	<b>n=3,254</b>	<b>n=42,089</b>	<b>n=123,356</b>	<b>n=86,742</b>
<b>Normal</b>	195,523 (76.5%)	2,551 (78.4%)	33,019 (78.5%)	92,452 (75%)	67,501 (77.8%)
<b>Assisted</b>	15,835 (6.2%)	159 (4.9%)	2,415 (5.7%)	8,355 (6.8%)	4,909 (5.7%)
<b>C-section</b>	44,083 (17.3%)	544 (16.7%)	6,658 (15.8%)	22,549 (18.3%)	14,332 (16.5%)

\*NRT=nicotine replacement therapy prescription in pregnancy, \*\*smoking in pregnancy, \*\*\* No smoking in pregnancy

Table 7-18 presents the unadjusted and adjusted RRRs for each mode of delivery for NRT and smoking exposure during pregnancy compared to non-smokers. In the unadjusted analysis pregnant women who were prescribed NRT during pregnancy had a 31% reduced risk of assisted delivery (RRR 0.69, 99% CI 0.55-0.85) and 13% reduced risk of caesarean sections (RRR 0.87, 99% CI 0.77-0.99) compared to non-smokers. Smokers had consistently decreased risks of both assisted delivery and caesarean section compared with women from the referent group (non-smokers). After adjusting for maternal characteristics, NRT exposure during pregnancy was still significantly associated with a 25% reduction in the risk of assisted delivery however the association between NRT exposure and caesarean section was not statistically significant ( $p=0.566$ ).

When the reference category was changed to current smokers, the relative risk of assisted delivery in the NRT group decreased by 12%, however this was not statistically significant. Similarly, the relative risk of caesarean section in the NRT group compared to smokers was 1.01 (99% CI 0.89-1.16) which indicated no statistically significant association.

**Table 7-18 - Unadjusted and adjusted relative risk ratios of each mode of delivery relative to normal delivery by NRT and smoking exposure during pregnancy compared to non-smokers**

	Unadjusted				Adjusted ‡			
	Assisted Delivery		C-section		Assisted delivery		C-section	
	RRR (99% CI)	p-value	RRR (99% CI)	p-value	RRR(99% CI)	p-value	RRR(99% CI)	p-value
Non-smoker***	1		1		1		1	
NRT group *	0.69 (0.55-0.85)	<0.001	0.87 (0.77-0.99)	0.005	0.75 (0.60-0.93)	<0.001	0.97 (0.85-1.10)	0.566
Smoker**	0.80 (0.75-0.86)	<0.001	0.83 (0.80-0.86)	<0.001	0.85 (0.80-0.91)	<0.001	0.96 (0.92-1.00)	0.004
Unknown	0.80 (0.77-0.84)	<0.001	0.87 (0.84-0.90)	<0.001	0.84 (0.80-0.88)	<0.001	0.92 (0.89-0.95)	<0.001

\*NRT=nicotine replacement therapy prescription in pregnancy, \*\*smoking in pregnancy, \*\*\* No smoking in pregnancy, ‡adjusted for maternal age, Townsend score, diabetes, asthma, hypertension, mental illness, RRR= Relative Risk Ratio, CI=Confidence Interval

**Table 7-19 - Unadjusted and adjusted relative risk ratios of each mode of delivery relative to normal delivery in non-smokers and the NRT group compared to smokers**

	Unadjusted				Adjusted ‡			
	Assisted Delivery		C-section		Assisted delivery		C-section	
	RRR (95% CI)	p-value	RRR (95% CI)	p-value	RRR(95% CI)	p-value	RRR(95% CI)	p-value
Non-smoker***	1.24 (1.16-1.32)	<0.001	1.21 (1.16-1.26)	<0.001	1.18 (1.10-1.26)	<0.001	1.05 (1.00-1.09)	0.007
NRT group *	0.85 (0.68-1.06)	0.060	1.06 (0.93-1.20)	0.491	0.88 (0.70-1.08)	0.118	1.01 (0.89-1.16)	0.733
Smoker**	1		1		1		1	
Unknown	1.00 (0.93-1.06)	0.864	1.05 (1.00-1.10)	0.002	0.99 (0.92-1.05)	0.599	0.96 (0.92-1.00)	0.016

\*NRT=nicotine replacement therapy prescription in pregnancy, \*\*smoking in pregnancy, \*\*\* No smoking in pregnancy, ‡adjusted for maternal age, Townsend score, diabetes, asthma, hypertension, mental illness



#### *7.3.3.1 Sensitivity analysis*

When smokers and non-smokers were reclassified based on the presence of gestational smoking status records, the proportion of total smokers reduced to 4.8% and non-smokers to 12.6%. However, the distribution of normal, assisted and caesarean deliveries remained similar to the main analysis.

In the unadjusted analysis women in the NRT group had a 31% reduced risk of assisted delivery (RRR 0.69, 99% CI 0.55-0.85) and a 13% reduced risk of caesarean sections (RRR 0.87, 99% CI 0.77-0.99) compared to non-smokers. Smokers had consistently decreased risks of both assisted delivery and caesarean section compared with women from the referent group (non-smokers). After adjusting for maternal characteristics, NRT exposure during pregnancy was significantly associated with a 32% reduction in the risk of assisted delivery, however the association between NRT exposure and caesarean section was not statistically significant anymore ( $p=0.120$ ).

**Table 7-20 - Unadjusted and adjusted relative risk ratios of each mode of delivery relative to normal delivery by NRT and smoking exposure during pregnancy compared to non-smokers, using definitive smokers and non-smokers**

	Unadjusted				Adjusted ‡			
	Assisted Delivery		C-section		Assisted delivery		C-section	
	RRR (99% CI)	p-value	RRR (99% CI)	p-value	RRR(99% CI)	p-value	RRR(99% CI)	p-value
Non-smoker***	1		1		1		1	
NRT group *	0.63 (0.51-0.79)	<0.001	0.84 (0.74-0.96)	0.005	0.68 (0.54-0.85)	<0.001	0.92 (0.81-1.05)	0.120
Smoker**	0.71 (0.64-0.80)	<0.001	0.76 (0.70-0.82)	<0.001	0.76 (0.68-0.86)	<0.001	0.88 (0.81-0.95)	<0.001
Unknown	0.81 (0.76-0.86)	<0.001	0.88 (0.85-0.92)	<0.001	0.82 (0.77-0.87)	<0.001	0.91 (0.87-0.95)	<0.001

\*NRT=nicotine replacement therapy prescription in pregnancy, \*\*smoking in pregnancy, \*\*\* No smoking in pregnancy, ‡adjusted for maternal age, Townsend score, diabetes, asthma, hypertension, mental illness, RRR= relative risk ratio, CI=confidence interval

## **7.4 DISCUSSION**

### **7.4.1 Principal findings**

This study, using a large population based dataset, found no significant association between NRT exposure during the first trimester, and any time during pregnancy, and stillbirth. However, maternal smoking during early pregnancy was found to increase the risk of stillbirth by 27%. In contrast, maternal smoking any time during pregnancy did not significantly increase the risk of stillbirth. Compared to non-smokers, the risk of low birth weight babies was 93% higher in the NRT group and 69% higher in smokers. The mean birth weight in babies in the NRT group was 176g lower than those of non-smoker, and the mean birth weight in the smokers group was 123g lower than those of non-smokers. However, there was no statistically significant difference between the risk of low birth weight in the NRT group and smokers. The study did not find a significantly increased risk of assisted delivery or caesarean section in the NRT group compared to smokers and no significant risk of caesarean section in current smokers compared to non-smokers. However, it found that the risk of assisted delivery decreased by 25% in the NRT group and 15% in smokers compared to non-smokers.

### **7.4.2 Strengths and limitations**

This is the first population-based report to assess the effects of NRT on adverse birth outcomes in the UK and the largest international study conducted thus far. Furthermore, since these data are prospectively recorded the potential for recall bias is greatly minimised. The measurement of drug exposure in the study was based on GP prescribing records rather than self-reports, reducing the potential for recall bias. However, the exposure measurement may still be subject to misclassification, which has been discussed in detail in Section 6.4.2.

Due to the paucity of smoking records during pregnancy, it was not possible to accurately ascertain smoking status at each stage of pregnancy. Therefore if there was any medical record indicating smoking during pregnancy women were assumed to be smoking during that pregnancy. Some of these women may have quit during the course of pregnancy but given the fluctuations of smoking status in pregnancy and the risk of relapse,<sup>183</sup> these women were still categorised as smokers. Therefore, the risk of adverse birth outcomes in relation to maternal smoking during pregnancy may be slightly underestimated. However, the potential for misclassification between the exposure groups cannot be completely eliminated from the previous Danish studies as well because smoking status was self-reported between 12-16 weeks of gestation and was then assumed to be constant until the end of pregnancy. In contrast, the findings reported here are based on the effects of NRT and smoking during the entire pregnancy in addition to early pregnancy as recorded in primary care data. However, for some women there was only a smoking record in the first trimester and therefore the effect estimates may not differ greatly between the two exposure windows. Furthermore, data on intensity of smoking was not complete which limited the ability of the study to examine any dose response effects of maternal smoking on adverse birth outcomes.

Whilst there may be confounding-by-indication by women's smoking intensity in that women who were prescribed NRT may be heavier smokers to start with, pregnant women getting NRT prescriptions could also be the women modifying their potentially harmful exposures for the better health of the baby. These could include smoking, alcohol use, dietary habits or other unmeasured factors. Although the ORs have been adjusted for a number of potential confounders, other unmeasured factors like labour and delivery complications, and household smoking were not adjusted for as enough information was not available in the data. Furthermore, the duration of NRT prescription in these data was relatively

short i.e. two weeks so if there is truly a beneficial or harmful effect of NRT this may be slightly underestimated.

Stillborn babies are usually not registered in primary care. Therefore, the ascertainment of stillbirth in this study is based on the documentation of such events in maternal primary care records. Approximately 97% of deliveries in England and Wales in 2011 took place in the NHS hospitals, maternity units and maternity wings<sup>280</sup> and all the delivery information recorded in the inpatient data should, but may not always, be transferred onto the primary care records. Therefore, this study may have missed cases of stillbirth. Nevertheless, the prevalence of stillbirth in this study was 4/1,000 live and stillbirths, which is comparable to the national prevalence of 5.2/1,000 births in the UK in 2009.<sup>159</sup> A study assessing the completeness of maternity data in UK primary and secondary care between 1998 and 2009 in one general practice found that birth weight and mode of delivery were recorded in only about 14% of 1,212 pregnancies with a linked child record in the primary care data (THIN) compared to 61% of the 3,255 pregnancies in secondary care data (Hospital Episodes Statistics (HES)).<sup>281</sup> The study discussed in this chapter however has data from approximately 500 practices from across the UK and had birth weight recorded for 42% of the babies with linked maternal records in THIN. Nevertheless, using a population of cases with a recording of birth weight, the prevalence of low birth weight was found to be 6.4% which is highly comparable to the national average of about 7%.<sup>279,282</sup> Furthermore, birth weight when plotted graphically was found to be normally distributed indicating that the selected population was broadly representative of the overall population and the presence of birth weight record did not differ by low or high birth weight. Additionally, the maternal characteristics in children with a recording of birth weight were highly comparable to the maternal characteristics in children without a recording of birth weight in primary care again indicating that this selected sample was

representative of the overall population and therefore any selection bias is unlikely to be present.

The prevalence of caesarean sections and assisted deliveries in this study was found to be much lower than the national prevalence of approximately 25% and 12% respectively in 2009.<sup>283,284</sup> All the pregnancies where no caesarean section or assisted delivery was recorded were assumed to be delivered through normal vaginal delivery, over-estimating the proportion of normal deliveries. This in turn may result in non-differential misclassification of the outcome and consequently bias the effect estimate towards null.

### **7.4.3 Comparison with current literature**

#### *7.4.3.1 NRT and stillbirth*

NRT exposure during early pregnancy or any time during the entire pregnancy was not found to be associated with an increased risk of stillbirth. The study including 87,032 pregnancies from the DNBC, with information on smoking and NRT use in the first trimester, found that for women who used NRT there was no statistically significant increase in the risk of stillbirth (HR 0.57, 95% CI 0.28-1.16) compared to non-smokers.<sup>113</sup> The non-smoker group in their study included ex-smokers who quit before conception but may be using NRT in pregnancy to avoid a smoking relapse. This may have resulted in misclassification of their exposure variable and under-estimate the effects of NRT use in pregnancy. Despite the differences in the exposure window and definition of stillbirth, the Danish study found very similar results to the ones presented in this chapter. The association between NRT exposure and stillbirth did not reach statistical significance, which is in line with the SNAP trial results<sup>100</sup> and the pooled estimates from the meta-analysis<sup>101</sup> again suggesting that the use of NRT does not significantly increase the risk of stillbirth.

The study found that smoking during early pregnancy increases the risk of stillbirth, which is consistent with the current literature. The study using DNBC found the risk of stillbirth to be 46% higher in smokers (HR 1.46, 95% CI 1.17-1.82) compared to non-smokers using smoking information from the first trimester.<sup>113</sup> Similarly, another Danish study based on a cohort of 25,102 live born singleton children collected smoking data before 30 weeks of gestation and found the risk of stillbirth to be twice as high compared to non-smokers.<sup>264</sup> . These differences could be attributed to the use of slightly different definitions of stillbirth, ascertainment of smoking status, which was mostly self-reported in these studies and also the use of different populations with slightly different prevalence of maternal smoking and stillbirth. In addition, the choice of confounders in each of the previous studies and their definitions and data quality may also contribute to the slight difference in the effect estimates of these studies.

Other studies which assessed smoking at the end of pregnancy or where the exact time of smoking assessment was not specified found the risk of stillbirth in smokers to be 34%<sup>285</sup> to over two fold <sup>29,264,273,286,287</sup> higher compared to non-smokers. In contrast, when the exposure window was expanded to the whole of pregnancy in this study, smoking was not found to be associated with an increase in stillbirth. A population-based cohort study from Sweden reported a significant interaction between gestational age and the effects of smoking; As pregnancy advanced, the risk of stillbirth associated with smoking decreased.<sup>288</sup> This may partly explain the lack of statistically significant association between smoking and stillbirth considering the complete duration of pregnancy.

Smoking reduces fetal oxygenation through increased blood levels of carboxyhaemoglobin and impairment of oxygen unloading.<sup>264</sup> This along with prostacyclin synthesis increases vascular resistance and decreases fetal blood flow. Nicotine in tobacco smoke is also postulated to cause vasoconstriction.<sup>264</sup>

All these effects collectively result in fetal growth restriction and placental complications, which are the most important causes of still birth.<sup>288,289</sup> Thus, this association seems to be biologically plausible. However, from the findings of this study and the previous study it does not seem likely that nicotine alone can result in stillbirth. The study also highlights that the effects of smoking may be more harmful to the immature foetus and placenta.

Although no significant associations were found between NRT and smoking exposure during pregnancy and fetal death, maternal smoking is an important risk factor for miscarriage which may contribute to these fetal deaths. A recent meta-analysis of 98 observational studies concluded that any active smoking during pregnancy was associated with an increased risk of miscarriage (RR 1.23, 95% CI 1.16-1.30).<sup>30</sup> Although the prevalence of smoking may be higher in women having miscarriages, the extent to which details of a miscarriage event is documented in primary care is currently not known. However, many women may not know that they are pregnant at the time of the miscarriage and therefore the recording and ascertainment of such events in the data is not expected to be complete. The reported prevalence of miscarriage in studies is 20%.<sup>290,291</sup> However, only 13% of pregnancies were recorded to end in miscarriage in the primary care data. This may explain the lack of statistically significant associations between smoking and fetal death found in the study.

#### *7.4.3.2 NRT and birth weight*

NRT exposure during pregnancy was found to be associated with a reduction in birth weight compared to not smoking with a 74% increased risk of low birth weight in babies of mothers prescribed NRT compared to non-smokers. A study using the PRAMS data to assess the association between NRT use and adverse birth outcomes in approximately 6,000 women in the USA found the risk of having a low birth weight baby in NRT users to be about two fold compared to



non-smokers,<sup>111</sup> which is very similar to the findings of this study. Contrary to the findings reported in this chapter, a study using the DNBC found no significant association between the duration of NRT use, type of NRT product used and offspring birth weight.<sup>112</sup> However, the Danish study primarily assessed NRT use within the first 27 weeks of pregnancy which limits the validity of the findings as fetal weight gain essentially takes place in the second and third trimester and the effects of smoking on fetal growth are more pronounced in the late stages of pregnancy.<sup>292,293</sup> Results from the trials report inconclusive evidence regarding the use of NRT during pregnancy and birth weight with some trials reporting no association between NRT use and birth weight<sup>100,107</sup> and some reporting higher birth weights in the NRT groups compared to placebo groups.<sup>108,109</sup> However, the interpretation of these findings from the trials is complicated by their inadequate power to assess safety outcomes and is highly dependent on compliance and adherence to treatments in both arms.

The study reiterates that smoking during pregnancy has a negative effect on fetal growth such that the risk of low birth weight was 63% higher in smokers compared to non-smokers and babies of smokers weighed 120g less than babies of non-smokers. This is consistent with previous studies which also found a decrease in birth weight of approximately 160g in babies of smokers compared to non-smokers.<sup>19,20</sup>

The risk of low birth weight associated with NRT and smoking were not found to be very different in the pre-term and term babies. This implies that the risk of low birth weight associated with NRT and smoking exposure holds regardless of gestational age. There are several proposed mechanisms by which smoking and NRT may affect birth weight. Nicotine is water soluble and consequently can pass through the placenta into the developing fetal circulation that is unable to metabolise nicotine in the same way as a fully developed adult system.

Therefore, the concentration of nicotine builds up over pregnancy in the

placental tissues and amniotic fluids.<sup>294</sup> Nicotine concentrations are reported to be 15% higher in the fetal circulation and 88% higher in the amniotic fluids than in the maternal circulation in smokers.<sup>295</sup> Therefore, although NRT may deliver lower concentrations of nicotine in the blood than smoking the concentrations in fetal circulation will still be higher than the maternal circulation. This may result in poor oxygen and nutrient delivery to the fetus resulting in poor organ development and low birth weight.<sup>294</sup> A case-control study using magnetic resonance imaging (MRI) to assess organ growth and overall fetal growth in 26 pregnant women found lower brain volumes, kidney volumes, impaired lung growth and total fetal volumes in smoking mothers compared to non-smoking mothers, indicating poor organ development.<sup>294</sup> Another study based on 7,098 pregnant women in Rotterdam, the Netherlands found an association between maternal smoking and reduced fetal head circumference, abdominal circumference and femur length.<sup>296</sup> An alternative proposed mechanism could be the suppression of appetite in mothers again leading to poor nutrient intake and inadequate nutrient delivery to the foetus. Lastly, the structure of nicotine is very similar to acetylcholine, which is one of the main enzymes in the nervous system and also regulates cell growth in the developing fetus.<sup>112,297</sup> Hence, it may alter cell growth signalling in the fetus leading to impaired growth and low birth weight.<sup>274</sup> Carbon monoxide in cigarettes may worsen this by causing fetal hypoxia.<sup>294</sup>

This study found no added benefit of using NRT over smoking in relation to birth weight and the risk of low birth weight was slightly higher in the nicotine group in comparison to smokers. This association may be confounded by how nicotine-dependent these women in the NRT group were and how intensely they smoked before NRT prescription, which has been discussed in detail in Section 6.4.2. Also, detailed information on NRT use and compliance was not available and it may be possible that women used NRT and smoked as well, or had periods of

relapses between NRT. These possibilities cannot be completely ruled out.

Lastly, there may also be some residual confounding through weight loss during pregnancy as maternal weight changes during pregnancy are directly related to infant birth weight<sup>298</sup> and NRT is known to suppress appetite<sup>299</sup> which may reduce maternal weight or other unmeasured factors, information for which was not available in the current data.

#### *7.4.3.3 NRT and mode of delivery*

The SNAP trial found a 45% increase in the risk of caesarean section deliveries with NRT use compared to placebo, however adherence to the therapy was low in both NRT and placebo group and the rate of abstinence from the quit date until delivery was less than 10%.<sup>100</sup> Furthermore, the study was adequately powered to assess abstinence but not the safety of NRT therefore this finding may be solely due to chance as the authors have discussed. In contrast, this study found no increased risk of caesarean section in the NRT group compared to current smokers or non-smokers. Nicotine is postulated to affect the maternal circulation of the placenta which can cause a consequent impairment of oxygen transfer to the fetus leading to an increased need for operative interventions for delivery such as caesarean section or assisted delivery.<sup>32</sup> However, the cardiovascular effects of NRT on both the mother and the fetus are very small<sup>300,301</sup>, which is reflected in the study findings. Furthermore, a hospital-based case-control study from France, based on approximately 600 women, aimed to examine the risk factors for caesarean section found similar results with no significant associations between maternal smoking and caesarean section.<sup>302</sup>

The only study to examine the association between smoking and assisted delivery<sup>269</sup> was based on the longitudinal Millennium Cohort from the UK and found no association between maternal smoking during pregnancy and the risk of assisted deliveries (OR 1.003, 95% CI 0.88-1.14). However, the findings from

this chapter paradoxically report a small protective effect of NRT and smoking exposure on assisted deliveries such that the risk of caesarean section reduced by 28% in NRT group and 15% in smokers compared to non-smokers. There may be several explanations for this finding; it may be simply due to the misclassification of some assisted deliveries as normal deliveries in current smokers, due to unmeasured confounding, or smoking may truly reduce the risk of assisted deliveries just like its incongruous protective effect on pre-eclampsia.<sup>10,303</sup>. Nevertheless the absolute risk of assisted deliveries in NRT group, smokers and non-smokers was not very different (4.8%, 5.7% and 6.8% respectively) making this difference in the risk less clinically relevant.

## **7.5 CHAPTER CONCLUSIONS**

This chapter as a whole aimed to assess different birth outcomes in relation to NRT and maternal smoking during pregnancy and found no increased risk of stillbirth in the NRT group compared to non-smokers, which is encouraging. In contrast, maternal smoking during pregnancy was found to increase the risk of stillbirth. Women who were prescribed NRT or smoked during pregnancy had higher risks of having a low birth weight baby compared to non-smokers. Lastly, the risk of caesarean sections in the NRT group and smokers was found to be similar to non-smokers however the risk of assisted deliveries was lower in comparison to non-smokers. Based on these findings it can be said that NRT exposure during pregnancy has no increased risks of stillbirth, low birth weight and caesarean section in comparison to maternal smoking. Nevertheless, these findings represent NRT exposure as recorded in general practice data only and therefore need to be interpreted with caution due to the limitations discussed above. Other immediate and long-term neonatal and paediatric outcomes need to be examined carefully before NRT can be considered to be completely safe during pregnancy.

## **8 OVERALL CONCLUSIONS, IMPLICATIONS AND FUTURE DIRECTIONS FOR RESEARCH**

The overall aims of this thesis were to assess the potential usefulness of primary care data to inform assessment of smoking behaviours in pregnant women at a population level and to investigate the prescribing and safety of NRT among pregnant women. This concluding chapter summarises key findings from the research presented in this thesis, highlights clinical and public health implications and makes recommendations for future public health practice and research areas in relation to maternal smoking ascertainment (Section 8.1) and NRT prescribing and safety (Section 8.2).

### **8.1 QUALITY OF MATERNAL SMOKING STATUS DATA DURING PREGNANCY IN PRIMARY CARE**

#### **8.1.1 Summary of main findings**

Having smoking status recorded in a pregnant women's medical records is not only useful for clinical management, but can also increase the potential utility of primary care data in informing national smoking estimates for pregnant women in a cost-effective and timely manner. The studies in this thesis have highlighted several features of the recording of smoking status during pregnancy in primary care data which must be taken into account when using these data to study the trends in the epidemiology of smoking or the provision of smoking cessation treatments. It showed that the recording of smoking status during pregnancy is incomplete and only present in less than 30% of the pregnant population under study. Therefore currently, certain informed assumptions need to be made to enhance the utility of these data for assessing smoking and smoking cessation treatment among pregnant women at a population level. Two such assumptions based on the QOF rules were tested in this thesis i.e. including smoking records

from 27 months before conception and smoking records ever before delivery to determine the smoking status for pregnancies where there was no gestational smoking record available. Smoking estimates using the 27 months assumption were generally found to have better comparability to other available data sources and therefore smoking records from 27 months before conception were considered to determine smoking status during pregnancy where gestational smoking status was missing. At an individual level, however, women do not have enough records of smoking status during pregnancy to assess changes in their smoking status throughout pregnancy.

### **8.1.2 Implications for further research**

Data from this thesis suggest that the completeness of smoking status recording during pregnancy in primary care data is improving over the years with about 40% women with smoking status recorded during pregnancy in 2009. Further research demonstrating this trend in future years may strengthen the utility of THIN for research on smoking in relation to pregnancy.

#### *8.1.2.1 Statistical methods for missing data*

In this thesis simple imputations were made for missing smoking data using assumptions based on QOF recording rules to provide an appropriate population of smokers for analysis. An alternative approach could be to use multiple imputation techniques to statistically impute smoking status during pregnancy, for which first the patterns of missing data will need be to be assessed (e.g. missing at random, missing not at random, missing by age, sex, disease or any other factors). Data on smoking could be imputed based on multinomial regression techniques.<sup>304</sup> Finally the results from these multiple imputation techniques can be compared from the results in this thesis to assess the validity of both approaches. This could be done by reviewing the records of a random group of pregnant women from general practices or surveying pregnant women

and comparing the self-reported smoking prevalence in this subgroup to the prevalence using recorded and imputed smoking status to investigate the potential validity of primary care data to predict smoking status during pregnancy. However, data anonymity in THIN may make this difficult and may also require substantial manpower, training and resources. An alternative approach could be to use the Additional Information Services (AIS) offered by THIN to provide more information to researchers which includes anonymised patient or GP questionnaires, copies of patient-related correspondence, laboratory tests etc.<sup>163</sup> This service can be used to collect self-reported smoking information from pregnant women to calculate smoking prevalence and validate the approaches discussed above. However, this may involve payments which may not always be available in projects.

#### *8.1.2.2 Use of free text data*

GPs may sometimes record more details on smoking status as free text data, which were not available for use for the purposes of this research. Free-text information from primary care records has been previously used to estimate death rates<sup>305</sup> and the incidence of rheumatoid arthritis<sup>306</sup> previously. However, no studies have assessed the utility of these data to improve estimates of smoking prevalence in pregnancy or wider general population. Nevertheless, researchers in the Division of Epidemiology and Public Health, University of Nottingham are currently analysing free text records in detail and have found that a lot of smoking information is recorded in the free text in primary care data (Vishal Basra, personal communication, 3<sup>rd</sup> February 2014). Such free text data are available to researchers, subject to relevant payments, and may provide more in-depth data on smoking status and fluctuations occurring during pregnancy and add to the partially incomplete coded information on smoking status during pregnancy.

#### *8.1.2.3 Mixed methods research*

This thesis investigated maternal characteristics related to the completeness of maternal smoking status recording in pregnancy. GP characteristics such as gender, training, smoking status may influence the recording of smoking status in the general population.<sup>307,308</sup> Similarly, certain practice characteristics (e.g. location, catchment area and staffing etc.) may also influence the recording and provision of smoking cessation advice.<sup>309</sup> However, more research is needed on the influence of these factors on the recording of smoking status and provision and recording of smoking cessation advice in pregnant women. Therefore mixed-methods research using both qualitative and quantitative studies on the patient, caregiver and practice attributes may provide some valuable insights into how smoking status is recorded during pregnancy.

#### *8.1.2.4 Using other primary care data to answer similar questions*

There are other larger primary care datasets available for research purposes in the UK such as QRESEARCH and the Clinical Practice Research Database (CPRD) formerly known as the GPRD, which is also linked to the maternity data from Hospital Episode Statistics (HES), and the Office for National Statistics (ONS) data. The CPRD currently has over 650 practices and data on over 5 million patients<sup>310</sup> and QRESEARCH contains data from over 600 practices.<sup>144</sup> The methods used here to define smoking status and investigate the quality of data can be applied to these other datasets when assessing the trends in maternal smoking prevalence and these larger datasets can be used for external validation of the associations between NRT and birth outcomes in future once pregnancy cohort is established in these data.

#### *8.1.2.5 Potential linkage with midwives notes*

Midwives are the main point of contact for women during pregnancy and are also responsible along with other health care team members for assessing and



documenting the smoking status of pregnant women. A recent study assessing the consistency and completeness of maternity hand-held notes in the UK analysed 63 different sets of hand-held notes currently in use in the UK and found that smoking related questions were part of all these notes.<sup>184</sup> Therefore, smoking status recording in the hand-held midwives notes may be more complete than primary care data. However, currently there is no research investigating how complete this information is in the midwives' notes. Also since there is no centralised recording and documenting system for midwives this information is not at hand after delivery. Therefore, electronic linkages between midwives notes and primary care data, or electronic imaging or transmission of midwives notes into the GP data, may be very useful not only to assess smoking and smoking cessation treatments during pregnancy but to also provide a detailed description of other events occurring during pregnancy to supplement and augment the information already present in primary care data. The Maternity Data Set by the Health and Social Care Information Centre<sup>311</sup> could be used as a template for this to extract maternity data, which could then be linked to primary care data.

### **8.1.3 Implications for clinical practice and policy**

Given the detrimental effects of maternal smoking during pregnancy, more accurate and up-to-date recording of smoking status in the pregnant population is vital in planning and delivering health services and other interventions to promote smoking cessation. The antenatal care model in the UK is midwife-led where midwives are responsible for care of women during pregnancy. However, current guidelines recommend that monitoring of smoking status during pregnancy should be a shared responsibility between all healthcare professionals involved in the care of pregnant women, including the GPs and midwives.<sup>74,79,165</sup> The Royal College of Midwives recommends that during pregnancy midwives should have full confidential access to a woman's written and electronic records

and GPs should ensure that all significant and relevant information is copied into women's hand-held maternity records.<sup>166</sup> Similarly, relevant information collected by midwives during pregnancy should also be communicated to the GPs and fed back into the electronic primary care records. Therefore, appropriate methods should be introduced to improve communication and documentation of such information between the midwives and GPs during pregnancy. One such method could be the use of electronic tools, such as digital pens, to complete hand-held maternity records which may then also transmit data to other central sources such as primary care. This will enable continuity of care and better communication between the GPs and midwives without requiring any extra time and effort.

Electronic patient-reported outcomes (e-PROs) is a fairly new concept in e-Health research where patients can report their health outcomes electronically.<sup>312</sup> ePROs are commonly used in clinical trials where patients can report the intensity, frequency, duration of symptoms (e.g. the Pulmonary Artery Hypertension – Symptoms and Impact (PAHSYMPACT) which measures the symptoms and impact of pulmonary artery hypertension using an electronic device), physiological measures (peak expiratory flow using a peak flow meter device which can transmit information directly to a central database).<sup>313</sup> Several modes of data collection can be used for this such as digital pens, smart phones, tablets, mobile applications and web-based responses etc.<sup>313</sup> ePROs are now being integrated into clinical care especially for cancer patients and the compliance to such tools has been reported to be good.<sup>314</sup> This concept could also be integrated in primary care data to obtain a detailed snapshot of several outcomes including smoking behaviour during pregnancy by giving women more control of their data and allowing them to enter their information themselves. This is in the early stages of development in the UK<sup>312</sup> but may be a useful tool in future to monitor patterns and trends of maternal smoking during pregnancy.

Based on the results from this work, it can be observed that the recording of smoking status improved in conditions which were included in the QOF such as diabetes, asthma, hypertension etc. This raises an important issue of whether pregnancy should be included as a condition in the QOF to record smoking status, given the current gaps in the recording of smoking status in pregnant women in primary care. Although some women may go to a midwife directly, according to the National Perinatal Epidemiology Unit 77% of women see their GP first for pregnancy care.<sup>167</sup> This may be an opportune time for the GPs to assess and document women's smoking status and provide brief advice and guidance on the resources available to quit. Therefore, including smoking status and cessation advice in pregnancy as a QOF recording target and linking payments to it may not only increase this recording in primary care data but also make the GPs more vigilant of monitoring smoking during pregnancy and providing referrals to interventions and services that are proven to work, thereby decreasing the overall smoking prevalence a little, if not substantially.

## **8.2 PRESCRIBING AND SAFETY OF NRT IN PREGNANCY**

### **8.2.1 Summary of main findings**

Trends in NRT prescribing, its use and safety were the gaps in the current literature highlighted by the WHO in the recent recommendations for the prevention and management of tobacco use in pregnancy.<sup>73</sup> Three studies in this thesis focused on these highlighted areas and assessed the prescribing of NRT in and around pregnancy across the UK and safety outcomes: major congenital anomalies, stillbirth, birth weight and mode of delivery.

The prescribing of NRT in and around pregnancy has increased substantially following its availability as an NHS prescription; however, the annual prescribing prevalence plateaued after the relaxation of licensing arrangements in 2005. Nevertheless, overall prescribing in the post-relaxation period was found to be

about twice as high compared to prescribing in the pre-relaxation period. The prescribing prevalence of NRT during pregnancy was almost double that of the prescribing prevalence in the nine months immediately before and after pregnancy; however, most women only had a record of single NRT prescription during pregnancy, lasting two weeks on average. Prescribing of NRT was also found to increase with greater socio-economic deprivation and the presence of comorbidities like asthma and mental illness.

No increased risk of congenital anomalies was found in the NRT group compared to smokers or non-smokers except for respiratory anomalies however this estimate was based on only 10 exposed cases. The risk of stillbirth in the NRT group was similar to non-smokers, which is encouraging. In contrast, maternal smoking during pregnancy was found to increase the risk of stillbirth. Contrarily, women who were prescribed NRT or who smoked during pregnancy had higher risks of having a low birth weight baby compared to non-smokers. Lastly, the risk of caesarean sections in the NRT group and current smokers was found to be similar to non-smokers, however the risk of assisted deliveries was lower in comparison to non-smokers.

## **8.2.2 Implications for further research**

### *8.2.2.1 Potential data linkages*

Currently primary care data such as THIN are one of the best available resources in the UK to examine population-level trends and patterns of NRT prescribing during pregnancy. Data from the NHS-SSS may only represent a subgroup of very motivated pregnant women. However, access to these data may provide useful information not only on the patterns and success of NRT use but also on other cessation interventions. A potential-linkage system between primary care and the NHS-SSS data may be useful in describing NRT use during pregnancy throughout the UK. Moreover, it will also give a more detailed account of quit

attempts made by women both during and outside pregnancy and the outcome of those quit attempts. However, no such links exist presently. NRT data can also be obtained from other data sources like OTC sales data which are available commercially (e.g. Electronic Point of Sales scanner data<sup>140</sup>) and the ePACT data which monitor electronic drug prescribing. However, currently these data do not have any specific information on sales and dispensing to pregnant women.

Women get free prescriptions during pregnancy as discussed earlier in the thesis and therefore if pregnant women are flagged up in these sales and prescribing data, then these data may be able to supplement the estimates from primary care data and give a more comprehensive picture of NRT prescribing and use during pregnancy in the UK.

Information on birth weight and mode of delivery in this work was missing for a substantial number of pregnancies. As indicated earlier, this information is expected to be more complete in secondary care data. Therefore, potential linkages between primary and secondary data may present more accurate estimates and reduce the proportion of missing data substantially. The CPRD primary care data have now been linked to HES and HES maternity, and HES linkages with THIN data have now been completed for approximately 70 practices with more practices being added with every release. This will not only improve the information on these selected outcomes but will also provide information on a number of labour and delivery events and complications which may be important when assessing the impact of drugs or smoking in future. The completeness and quality of the exposure data (smoking and NRT) can also be improved by potential linkages suggested above.

#### *8.2.2.2 Qualitative research*

Apart from these objective measures of NRT prescribing it is also important to combine subjective measures (such as self-reported use of NRT and outcomes of

quit attempts). The only qualitative study assessing women's perspectives on barriers and facilitators of smoking cessation using NRT was conducted on a small selected sample of pregnant smokers in Australia.<sup>118</sup> Therefore, qualitative studies using focus groups of pregnant smokers may therefore help explore the barriers and facilitators that pregnant women experience in using NRT. This may also provide more information on women's choices of NRT forms, as each form has a slightly different dose of NRT and mechanism of action which may have implications for the safety of the drug. It will also be instrumental in exploring the socio-demographic characteristics of women in relation to NRT prescribing in more detail which will help policy makers and public health professionals in tailoring these services and targeting special groups to encourage smoking cessation.

#### *8.2.2.3 Larger studies*

Although this was one of the biggest studies to determine the association between NRT, maternal smoking and congenital anomaly a bigger sample size is required to provide more power to the analysis and generate more precise risk estimates associated with smoking and NRT use. Therefore, a study using more recent primary care data, with more practices, more pregnancies and longer follow-up time, using similar methods is warranted. This will improve the precision of the estimates. However, considering the prevalence of congenital anomalies, the statistical power of epidemiological studies may always be limited in assessing the risks for system-specific anomaly groups especially the more rare ones.

#### *8.2.2.4 Other outcomes*

In addition to the outcomes assessed in this thesis other immediate and long-term neonatal and paediatric outcomes such as neonatal intensive care admissions, neonatal deaths, respiratory infections in early life etc., need to be

examined carefully before NRT can be deemed to be completely safe during pregnancy. The only available estimates for the association between nicotine replacement therapy and neonatal outcomes comes from trials<sup>100</sup> and currently the evidence is inconclusive. A meta-analysis of three trials of NRT in pregnancy found a pooled OR of 0.94 (95% CI 0.64-1.88) for neonatal intensive care admissions and 0.28 (95% CI 0.06-1.41) for neonatal death.<sup>101</sup>

### **8.2.3 Implications for clinical practice and policy**

Considering that NRT use in the general population for smoking cessation is recommended for at least eight to twelve weeks, two weeks of NRT may not be truly helpful for women to quit smoking. The findings also indicated that only 1% of women of reproductive age who smoke are prescribed NRT before they get pregnant, indicating a missed opportunity to assist many young women in quitting smoking. Whilst interactions between health professionals and women during pregnancy should be used to discuss and offer interventions to promote smoking cessation, greater potential benefit would be derived from starting before pregnancy which should be a focus for women and health care providers.

Currently, NRT use is recommended by the national guidelines for smoking cessation aid during pregnancy, where pregnant women cannot quit without NRT.<sup>79</sup> However, NRT should not be considered as a panacea for smoking cessation during pregnancy and smoking cessation without pharmacotherapy should be encouraged to help pregnant women quit. Health care professionals need to encourage women to quit before pregnancy to reduce the risks associated with any kind of nicotine exposure to the foetus. Also given, the effectiveness of NRT outside pregnancy it's use during postpartum period can be encouraged more to prevent postpartum relapse in women who quit during pregnancy.

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# 10 APPENDICES

## 10.1 COMPLETENESS OF MATERNAL SMOKING STATUS RECORDING

### DURING PREGNANCY IN UNITED KINGDOM PRIMARY CARE DATA

OPEN ACCESS Freely available online



## Completeness of Maternal Smoking Status Recording during Pregnancy in United Kingdom Primary Care Data

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### Abstract

**Background:** Given the health impacts of smoking during pregnancy and the opportunity for primary healthcare teams to encourage pregnant smokers to quit, our primary aim was to assess the completeness of gestational smoking status recording in primary care data and investigate whether completeness varied with women's characteristics. As a secondary aim we assessed whether completeness of recording varied before and after the introduction of the Quality and Outcomes Framework (QOF).

**Methods:** In The Health Improvement Network (THIN) database we calculated the proportion of pregnancies ending in live births or stillbirths where there was a recording of maternal smoking status for each year from 2000 to 2009. Logistic regression was used to assess variation in the completeness of maternal smoking recording by maternal characteristics, before and after the introduction of QOF.

**Results:** Women had a record of smoking status during the gestational period in 28% of the 277,552 pregnancies identified. In 2000, smoking status was recorded in 9% of pregnancies, rising to 43% in 2009. Pregnant women from the most deprived group were 17% more likely to have their smoking status recorded than pregnant women from the least deprived group before QOF implementation (OR 1.17, 95% CI 1.10–1.25) and 42% more likely afterwards (OR 1.42, 95% CI 1.37–1.47). A diagnosis of asthma was related to recording of smoking status during pregnancy in both the pre-QOF (OR 1.63, 95% CI 1.53–1.74) and post-QOF periods (OR 2.08, 95% CI 2.02–2.15). There was no association between having a diagnosis of diabetes and recording of smoking status during pregnancy pre-QOF however, post-QOF diagnosis of diabetes was associated with a 12% increase in recording of smoking status (OR 1.12, 95% CI 1.05–1.19).

**Conclusion:** Recording of smoking status during pregnancy in primary care data is incomplete though has improved over time, especially after the implementation of the QOF, and varies by maternal characteristics and QOF-incentivised morbidities.

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### Introduction

Smoking during pregnancy has a well-documented negative effect on the health of a mother and her baby [1] and smoking cessation during pregnancy has been linked to a reduction in maternal and fetal complications in addition to its wider health benefits [2,3]. Current recommendations emphasise that all healthcare workers involved in a pregnant woman's care (e.g. midwives, general practitioners (GPs), practice nurses and obstetricians) should assess the woman's smoking status at the earliest possible stage of pregnancy and offer cessation advice and a referral to specialist stop smoking advisers for women who smoke [4–8]. Documentation of a woman's smoking status in her medical records is recommended to enable her

healthcare team to offer appropriate support throughout the pregnancy [7].

In the United Kingdom (UK) women must be registered with a GP in order to receive antenatal care and, although most antenatal contacts are with midwives, an estimated 77% of women see their GPs first for confirmation of pregnancy before attending an antenatal booking appointment with a midwife [9]. This first contact with a GP and subsequent visits during pregnancy could potentially be used as an opportunity for assessing and recording the smoking status of pregnant women.

In April 2004, a new contract for GPs was implemented which introduced a number of pay-for-performance targets known as the Quality and Outcomes Framework (QOF) [10]. Approximately 8% of the QOF points (worth around £10,000) per year per

practice are related to the recording of smoking status and delivery of smoking cessation advice [11,12]. GPs are required to document patients' smoking status at least once every 27 months, or every 15 months where the patient has hypertension, diabetes, asthma and certain other smoking-related morbidities. A detailed description of QOF targets is available elsewhere [13].

In the population as a whole the recording of patients' smoking status is more complete after the introduction of QOF [14,15]. However, the QOF sets no specific incentives for the recording of smoking status in pregnant women. Having smoking status recorded in a pregnant women's medical records is not only useful for clinical management, but also increases opportunities for health professionals to provide smoking cessation interventions throughout pregnancy and afterwards. Therefore, our primary aim was to assess the completeness of recording of smoking status during pregnancy in primary care medical records over time and investigate whether completeness varied with women's socio-demographic and health-related characteristics. Additionally, our secondary aim was to investigate whether, despite having no specific targets for pregnancy, there was an increase in the completeness of smoking status recording during pregnancy in UK primary care after the introduction of the QOF.

## Methods

### Data source and study population

The Health Improvement Network (THIN) is an electronic primary care database containing anonymised patient records from general practices across the UK, covering approximately 5.7% of the UK population [16]. The version of THIN used for this study contains data from 495 practices with a combined total of approximately 9.5 million patients, including approximately 2 million women of reproductive age (defined here as age 15–49 years) [16]. The recorded population prevalence of smoking in THIN has been previously validated at both national and regional levels [14,15] and fertility rates in THIN are highly comparable to national fertility rates [17]. For the work reported here, our study population included all pregnancies recorded in THIN between 2000 and 2009 in women of reproductive age which resulted in either a live birth or a stillbirth.

### Smoking status and maternal characteristics

Records of maternal smoking status during pregnancy were identified using Read codes [18]. These included codes for current, never, and ex-smoking, codes indicating the type or number of cigarettes smoked, and codes indicating smoking cessation interventions delivered to patients. Women were also considered to be smokers if they had a prescription for a smoking cessation drug (nicotine replacement therapy, bupropion or varenicline) in their medical records during pregnancy. This method of classifying smoking status in electronic primary care data has been previously validated [14]. Code lists are available from the authors on request.

To investigate the factors that may be associated with the recording of maternal smoking status during pregnancy, data were extracted on women's age at conception, socioeconomic deprivation as measured by quintiles of the Townsend Index of material deprivation [19], body mass index (BMI) before conception and recorded diagnoses, during or before the pregnancy, of morbidities common in pregnancy in which the recording of smoking status has been specifically incentivised by the QOF (hypertension, diabetes, asthma, and mental illness which included depression, anxiety, bipolar disorder, schizophrenia and other psychoses). When extracting data on BMI and maternal morbidities before

pregnancy, we only considered recent recordings of BMI and comorbidities before pregnancy (27 months prior to pregnancy, in line with the QOF recording rules). Missing data for Townsend quintile and BMI were included as separate categories in the analyses.

### Statistical analyses

The prevalence of smoking status recording during pregnancy was calculated for each year from 2000 to 2009 as the number of pregnancies with at least one recording of smoking status during the gestational period divided by the total number of pregnancies delivered in that year. These data were plotted graphically.

Since April 2006 the QOF has not required GPs to record the smoking status of patients after the age of 25 years if they have been a never smoker until that age [20]. After 2008, if a patient who once smoked has been recorded as an ex-smoker for three years, GPs need no longer check and update the patient's smoking status records. Therefore, we recalculated the proportion of pregnancies with missing gestational smoking status data to take these rules into account. For women who only had records of being a never smoker up to age 25 and who did not have a record of smoking during a subsequent pregnancy we imputed a never smoking record during gestation. Similarly, for women who had no smoking status records during gestation but who were recorded as ex-smokers for three consecutive years before the conception we imputed an ex-smoking record during gestation. We then recalculated the annual proportion of pregnancies with a recording of smoking status during the gestational period.

We used logistic regression to calculate odds ratios (ORs) for associations between women's characteristics and the recording of smoking status during pregnancy. All covariates that reached statistical significance ( $p < 0.05$ ) in the univariable analysis were initially included in the multivariable analyses. Covariates that reached statistical significance ( $p < 0.05$ ) in the multivariable analysis were retained in the final model. As some women had more than one pregnancy during the study period that contributed to our analyses, we accounted for this potential clustering of pregnancies within women by calculating robust confidence intervals (CIs) around our odds ratios using the clustered sandwich estimator to allow for intragroup correlation [21,22]. As the introduction of the QOF incentivised the recording of smoking status in patients with smoking-related chronic conditions, we expected the QOF to be an effect modifier of the association between recording of smoking status during pregnancy and these morbidities. We therefore carried out logistic regression for two separate time periods: before the implementation of the QOF (January 2000–April 2004) and after the implementation of the QOF (April 2004–December 2009). We visually compared the magnitude, precision and significance of the odds ratios for each maternal factor in the pre and post-QOF periods in order to assess whether the association between maternal factors and the recording of smoking status during pregnancy changed after the QOF was introduced. All analyses were performed using Stata version 12.0 (StataCorp LP, College Station, TX).

### Ethics Statement

Ethical approval for use of the THIN data was provided by the THIN Scientific Review Committee (reference number 11-047).

## Results

### Baseline characteristics

We identified 215,703 women with pregnancies resulting in live births or stillbirths between January 2000 and December 2009. Of

these, 162,295 (75.0%) women had only one pregnancy, 46,062 (21.5%) had two pregnancies and 7,346 (3.5%) had three or more pregnancies, giving a total of 277,552 pregnancies. The mean age at conception was 29.5 years (standard deviation 5.9) and the average length of pregnancy was 39.4 weeks (standard deviation 2.2). Table 1 describes the baseline characteristics of the study population in the pre-QOF and post-QOF time periods. The overall prevalence of diagnosed asthma, diabetes, hypertension and mental illness within the study population was approximately 8%, 2%, 2.5% and 9% respectively. Information on socioeconomic status was missing for 6% of the total pregnancies and information on BMI was missing for 42% of pregnancies.

#### Completeness of maternal smoking records

A record of smoking status at any point during the gestational period was present in 76,569 (28%) of the 277,552 pregnancies. Of the 76,569 pregnancies in which smoking status was recorded, 913 (1.2%) only had a recording for smoking cessation drug prescription with no accompanying Read codes indicating smoking status. In 56,605 (20.4%) pregnancies, women had their smoking status recorded only once during the gestational period, whereas in 19,964 (7%) pregnancies smoking status was recorded more than once. Figure 1 shows the proportion of pregnancies with smoking status recorded during gestation from 2000 to 2009.

In 2000, smoking status was recorded during the gestational period for only 1,943 (8.8%) of the total 22,111 pregnancies. This proportion increased steadily to 18% in 2003 and a steep point change was observed in 2004 with the proportion rising to 32.3%. After 2004 it increased steadily on an annual basis such that the proportion of pregnancies with smoking status recorded during gestation in 2009 was 43.3% (13,360 out of 30,880 pregnancies).

When data for never smoking and ex-smoking were imputed based on QOF rules, the overall proportion of pregnancies with a record of smoking status during gestation increased to 32.1%. In 2000, smoking status was recorded during gestation for only 11.0% of pregnancies which increased to 35.8% in 2004 and 49.2% in 2009 (Figure 1).

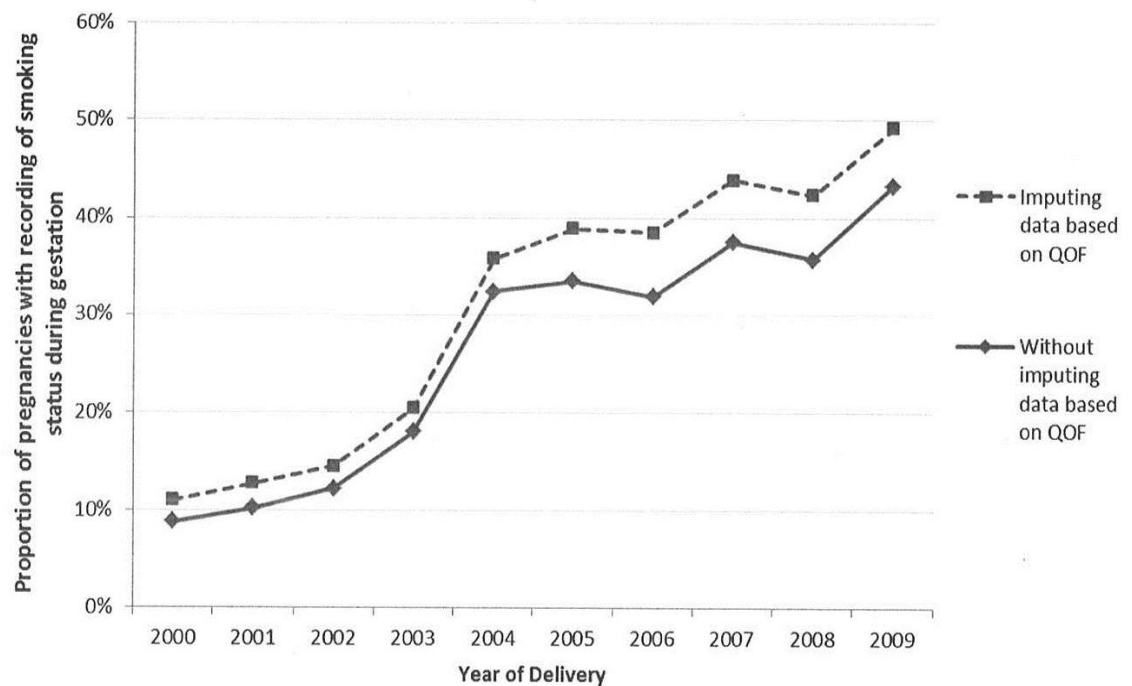
#### Factors associated with recording of maternal smoking status during pregnancy

Table 2 shows variations in the recording of smoking status during pregnancy by women's sociodemographic characteristics and morbidities in the pre-QOF and post-QOF time periods. Overall, the strength of the associations between all maternal characteristics and recording of smoking status during gestation was higher in the post-QOF period compared to pre-QOF period. The recording of smoking status during pregnancy varied with socioeconomic status such that pregnant women from the most

**Table 1.** Baseline characteristics of the study population.

	Pre-QOF(January 2000– March 2004)			Post-QOF (April 2004– December 2009)		
	Total pregnancies (n = 98,373)	Pregnancies with a gestational smoking record (n = 12,381)		Total pregnancies (n = 179,179)	Pregnancies with a gestational smoking record (n = 64,188)	
<b>Age at Conception</b>						
15–19 years	5,529	953	(17.2%)	9,854	4,856	(14.8%)
20–24 years	14,809	2,202	(14.9%)	29,323	12,607	(14.9%)
25–29 years	25,732	3,175	(12.3%)	45,416	16,758	(15.7%)
30–34 years	32,621	3,750	(11.5%)	54,574	17,437	(17.4%)
35–39 years	16,614	1,944	(11.7%)	32,778	10,296	(9.9%)
40–44 years	2,907	338	(11.6%)	6,868	2,123	(19.8%)
45–49 years	161	19	(11.8%)	366	111	(15.9%)
<b>Townsend Score in quintiles</b>						
Quintile 1 - most affluent	24,760	2,850	(11.5%)	38,815	11,733	(16.5%)
Quintile 2	19,288	2,277	(11.8%)	32,962	11,025	(14.8%)
Quintile 3	18,592	2,317	(12.5%)	35,209	12,542	(14.9%)
Quintile 4	17,128	2,279	(13.3%)	33,982	13,114	(15.7%)
Quintile 5 - most deprived	13,252	1,964	(14.8%)	25,742	10,915	(17.4%)
Missing	5,353	694	(13.0%)	12,469	4,859	(9.9%)
<b>Pre-conception Body Mass Index</b>						
Normal(18.0–24.9)	26,663	3,948	(14.8%)	59,267	21,209	(15.9%)
Underweight(<18.0)	1,968	293	(14.9%)	4,355	1,714	(14.4%)
Overweight(25–29.9)	11,923	1,867	(15.7%)	29,476	10,957	(16.5%)
Obese(>= 30)	7,125	1,240	(17.4%)	20,993	8,406	(14.8%)
Missing	50,694	5,033	(9.9%)	65,088	21,902	(14.9%)
<b>Asthma</b>	6,537	1,297	(19.8%)	16,807	8,911	(15.7%)
<b>Hypertension</b>	2,372	377	(15.9%)	4,962	1,959	(17.4%)
<b>Diabetes</b>	1,345	194	(14.4%)	4,864	1,857	(9.9%)
<b>Mental illness</b>	8,717	1,439	(16.5%)	17,294	7,373	(19.8%)

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**Figure 1. Annual proportion of pregnancies in THIN with smoking status recorded during gestation (2000–2009).**  
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deprived group (quintile 5) were 17% more likely to have their smoking status recorded during pregnancy than pregnant women from the most affluent group (quintile 1) before the implementation of the QOF (OR 1.17, 95% CI 1.10–1.25) and 42% more likely afterwards (OR 1.42, 95% CI 1.37–1.47). Similarly, pre-QOF pregnant women with a diagnosis of asthma were 63% more likely to have their smoking status recorded during pregnancy than pregnant women without asthma (OR 1.63, 95% CI 1.53–1.74) and post-QOF pregnant women with asthma were over twice as likely to have their smoking status recorded during pregnancy (OR 2.08, 95% CI 2.02–2.15). Having a diagnosis of diabetes was not associated with the recording of gestational smoking status pre-QOF (unadjusted OR 1.17, 95% CI 1.00–1.36), ( $p = 0.290$ ). However, post-QOF it was associated with a 12% increase in the odds of recording of gestational smoking status (OR 1.12, 95% CI 1.05–1.19). Recording of smoking status during pregnancy was also related to hypertension and mental illness. In both time periods the odds of a woman having her smoking status recorded during pregnancy were greater at younger ages compared with older ages and great in overweight and obese women. However, the magnitude of effects and corresponding CIs in the pre-QOF and post-QOF periods overlapped.

## Discussion

Using a large population-based dataset we found that the recording of smoking status during pregnancy in primary care has improved with time such that the proportion of pregnancies with a recording of smoking status during gestation was 8.8% in 2000 rising to 43.3% in 2009. The odds of a woman's smoking status being recorded during pregnancy was related to age, socioeco-

nomic deprivation, BMI and QOF-incentivised morbidities such as asthma, diabetes, hypertension and mental illness.

The proportion of pregnancies with a gestational smoking record increased by approximately 2% per year between 2000 and 2002. Since the late 1990s there has been an increased focus on the harms of tobacco use in the UK, with, for example, the publication of the Government white paper 'Smoking Kills' in 1998 [1], the establishment of NHS Stop Smoking Services in 1999 [23], and the availability of smoking cessation medications on NHS prescriptions from 2001 [24]. This changing tobacco control environment may have made these pregnant smokers more willing to approach their GPs for help to quit, and focused GPs' attention on encouraging cessation in their patients, thereby increasing the proportion of pregnant women with a smoking status record in their medical notes. The proportion of pregnancies with a recording of smoking status rose sharply from 18.0% in 2003 to 32.4% in 2004, after which it increased slowly until 2009. The most plausible explanation for this marked increase between 2003 and 2004 is GPs' awareness of the impending introduction of the 2004 GP contract [25]. Similar improvements in the recording of smoking status have been seen in general population. A study using primary care data for over 300 practices throughout the UK found that, although rates of recording of smoking status in patients' electronic medical records had been increasing gradually since the year 2000, the rate of improvement accelerated from 2003, with an 88% increase observed between the first quarter of 2003 and the same period in 2004, just before the introduction of the QOF [26]. This suggests that the introduction of the QOF resulted in better recording of smoking status in the general population which has spilled over into the greater recording in pregnancy observed in our study.



**Table 2.** Odds of having smoking status recorded during gestation by women's characteristics before and after the QOF implementation.

	Pre-QOF(January 2000–March 2004)				Post-QOF(April 2004–December 2009)			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Age</b>								
15–19	1.48 (1.37–1.60)		1.56 (1.44–1.70)		1.66 (1.59–1.74)		1.62 (1.54–1.69)	
20–24	1.24 (1.17–1.32)		1.22 (1.15–1.30)		1.29 (1.25–1.32)		1.24 (1.20–1.28)	
25–29	1	<0.001	1	<0.001	1	<0.001	1	<0.001
30–34	0.92 (0.87–0.97)		0.95 (0.91–1.00)		0.80 (0.78–0.82)		0.84 (0.82–0.86)	
35–39	0.94 (0.88–0.99)		0.99 (0.93–1.05)		0.78 (0.75–0.80)		0.83 (0.80–0.85)	
40–44	0.93 (0.83–1.05)		0.99 (0.88–1.12)		0.76 (0.72–0.81)		0.80 (0.76–0.85)	
45–49	0.95 (0.59–1.53)		0.99 (0.61–1.60)		0.74 (0.59–0.93)		0.77 (0.61–0.97)	
<b>Townsend Score</b>								
Quintile 1 (most affluent)	1		1		1		1	
Quintile 2	1.03 (0.78–1.09)		1.01 (0.95–1.07)		1.16 (1.12–1.19)		1.12 (1.09–1.16)	
Quintile 3	1.09 (1.03–1.16)	<0.001*	1.03 (0.97–1.10)	<0.001*	1.28 (1.24–1.32)	<0.001*	1.18 (1.14–1.21)	<0.001*
Quintile 4	1.18 (1.11–1.25)		1.07 (1.00–1.13)		1.45 (1.40–1.49)		1.26 (1.22–1.30)	
Quintile 5 (most deprived)	1.34 (1.25–1.42)		1.17 (1.10–1.25)		1.69 (1.64–1.75)		1.42 (1.37–1.47)	
Missing	1.14 (1.04–1.25)		1.06 (0.97–1.16)		1.47 (1.41–1.54)		1.34 (1.29–1.40)	
<b>Body Mass Index</b>								
Underweight (<18.0)	1.01(0.88–1.14)		0.92 (0.81–1.05)		1.16 (1.10–1.24)		1.03 (0.97–1.10)	
Normal (18.0–24.9)	1		1		1		1	
Overweight (25.0–29.9)	1.07 (1.01–1.13)	<0.001	1.06 (1.00–1.13)	<0.001	1.06 (1.03–1.09)	<0.001	1.05 (1.02–1.09)	<0.001
Obese (≥30)	1.21 (1.13–1.30)		1.16 (1.08–1.25)		1.19 (1.16–1.23)		1.11 (1.08–1.15)	
Missing	0.63 (0.60–0.66)		0.63 (0.60–0.66)		0.91 (0.89–0.93)		0.90 (0.88–0.92)	
<b>Asthma</b>	1.80 (1.69–1.92)	<0.001	1.63 (1.53–1.74)	<0.001	2.19 (2.12–2.25)	<0.001	2.08 (2.02–2.15)	<0.001
<b>Hypertension</b>	1.32 (1.18–1.48)	<0.001	1.26 (1.12–1.41)	<0.001	1.17 (1.11–1.24)	<0.001	1.19 (1.12–1.26)	<0.001
<b>Diabetes</b>	1.17 (1.00–1.36)	0.045	†	†	1.11 (1.05–1.18)	<0.001	1.12 (1.05–1.19)	<0.001
<b>Mental illness</b>	1.42 (1.34–1.51)	<0.001	1.32 (1.24–1.41)	<0.001	1.37 (1.33–1.41)	<0.001	1.26 (1.22–1.30)	<0.001

OR = odds ratio, CI = confidence interval, QOF = Quality and Outcomes Framework.

\*p-value for trend.

†Diabetes not significant in the final model.

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For socioeconomic deprivation, asthma and diabetes the magnitude of effect of the association with smoking status recording was observed to be stronger after the introduction of the QOF. Pre-QOF, pregnant women from the most deprived group were 17% more likely to have their smoking status recorded during gestation compared to 42% post-QOF. Smoking prevalence is generally higher in lower socioeconomic groups in both the general population as well as amongst pregnant women [27] and the smoking status of smokers is more likely to be recorded than that of non-smokers [28–30], which likely explains more complete recording in pregnant women from lower socioeconomic groups. Furthermore, low socioeconomic status is associated with a higher prevalence of chronic diseases such as hypertension, diabetes, asthma and depression [31]. The QOF encourages improved clinical management of these patients, who post-QOF may have had more frequent contacts with their GP and thus have had more chance of being asked about their smoking behaviour, increasing the gradient of the association between socioeconomic status and smoking status recording, reflecting that recording, and thus hopefully monitoring, is more complete where it is most needed [32,33]. Asthma is the most common pre-existing

condition encountered during pregnancy [34] and is closely related to smoking, which may explain the high magnitude of association between asthma and recording of smoking status compared to other conditions like diabetes (which affects approximately 2–5% in women of reproductive age) [35] and hypertension (0.6–2.7% during pregnancy) [36]. Women with a higher BMI have an increased risk of complications during pregnancy and therefore are more likely to visit their GPs [37]. They are also more likely to be smokers which in turn will affect the completeness of recording of their smoking status. Our findings are similar to those from a study in the general population which found that primary care patients with smoking-related chronic medical conditions and greater social deprivation were more likely to have a recent recording of smoking status or cessation advice in their medical records [38]. However, the magnitude of effect in this general population study for all morbidities much higher than that which we found, presumably because currently pregnancy is not a QOF-incentivised condition for recording of smoking.

To our knowledge this is the first study to assess the completeness of recording of smoking status during pregnancy in UK primary care medical records at a national level, using a large

population-based dataset with over 200,000 pregnancies. A potential limitation of our study is that due to the infrequency of smoking status recordings during pregnancy we did not assess recording of smoking status in smaller windows during pregnancy such as in each trimester, which may be more appropriate given that smoking status fluctuates during pregnancy [39]. Furthermore, we only assessed electronically-coded data in primary care records to examine the recording of smoking status during pregnancy and did not have access to free text or midwives' notes to ascertain smoking status; these may provide additional information on the smoking status of women during pregnancy. A potential explanation for the high proportion of pregnancies in which smoking status was not recorded could be that if a woman's smoking habit did not change after she became pregnant, GPs might be less likely to re-enter this information into medical records as there is no specific financial incentive for recording smoking status in pregnant women. Furthermore, as the QOF does not require GPs to record the smoking status of 'never smokers' after the age of 25, there is no financial incentive for them to update smoking status in the medical records of women who have never smoked. Similarly, ex-smokers need only be asked about their smoking status annually until they have been a non-smoker for three years. However, when we recalculated smoking status based on these rules, the annual trends in the completeness of smoking data during pregnancy did not vary much from the trends using the original data.

The current antenatal model in the UK is a midwife-led care one, where midwives are the main point of contact for women during pregnancy [9,40]. The National Institute for Health and Clinical Excellence (NICE) recommends that all pregnant women should have their smoking status recorded at the first antenatal booking appointment with the midwife and that all smokers should be referred to a stop smoking service and this should be recorded in the hand-held records which women in the UK carry with them throughout their pregnancy [7,41]. Data from a qualitative study of midwives in Glasgow, Scotland, suggested that they view it as part of their role to collect this smoking data at the booking appointment [42]. However, the means of recording of maternity data and provision of smoking cessation information during antenatal visits varies from practice to practice and we do not

know whether, or how completely, smoking status data entered onto hand-held records get transferred to a woman's electronic primary care medical record for future reference.

As the current guidelines recommend, monitoring of smoking status during pregnancy should be a shared responsibility between all healthcare professionals involved in the care of pregnant women, including GPs and midwives [4,5,7]. The Royal College of Midwives recommends that during pregnancy midwives should have full confidential access to a woman's written and electronic records and GPs should ensure that all significant and relevant information is copied into a woman's hand-held maternity records [8]. Similarly, relevant information collected by midwives during pregnancy should also be communicated to the GPs and fed back into the electronic primary care records. Therefore, we recommend that appropriate methods should be introduced to improve communication and documentation of such information between the midwives and the GPs during pregnancy. One such strategy could be inclusion of pregnancy in the QOF as a condition where smoking status and smoking cessation advice should be recorded in the electronic primary care record. Primary care is the central hub in the current UK health care system and increasing the assessment and complete documentation of smoking status in primary care will not only increase opportunities for providing smoking cessation advice and interventions during pregnancy, but is also important to maintain continuity of care throughout and beyond pregnancy for both a woman's health and that of her children.

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## Author Contributions

Conceived and designed the experiments: LS TC IJT KF. Performed the experiments: NND. Analyzed the data: NND. Contributed reagents/materials/analysis tools: NND LS. Wrote the paper: NND IJT TC KF LS.

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## 10.2 SMOKING CESSATION ADVICE RECORDED DURING PREGNANCY IN UNITED KINGDOM PRIMARY CARE

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### RESEARCH ARTICLE

### Open Access

# Smoking cessation advice recorded during pregnancy in United Kingdom primary care

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## Abstract

**Background:** United Kingdom (UK) national guidelines recommend that all pregnant women who smoke should be advised to quit at every available opportunity, and brief cessation advice is an efficient and cost-effective means to increase quit rates. The Quality and Outcomes Framework (QOF) implemented in 2004 requires general practitioners to document their delivery of smoking cessation advice in patient records. However, no specific targets have been set in QOF for the recording of this advice in pregnant women. We used a large electronic primary care database from the UK to quantify the pregnancies in which women who smoked were recorded to have been given smoking cessation advice, and the associated maternal characteristics.

**Methods:** Using The Health Improvement Network database we calculated annual proportions of pregnant smokers between 2000 and 2009 with cessation advice documented in their medical records during pregnancy. Logistic regression was used to assess variation in the recording of cessation advice with maternal characteristics.

**Results:** Among 45,296 pregnancies in women who smoked, recorded cessation advice increased from 7% in 2000 to 37% in 2004 when the QOF was introduced and reduced slightly to 30% in 2009. Pregnant smokers from the youngest age group (15–19) were 21% more likely to have a record of cessation advice compared to pregnant smokers aged 25–29 (OR 1.21, 95% CI 1.10–1.35) and pregnant smokers from the most deprived group were 38% more likely to have a record for cessation advice compared to pregnant smokers from the least deprived group (OR 1.38, 95% CI 1.14–1.68). Pregnant smokers with asthma were twice as likely to have documentation of cessation advice in their primary care records compared to pregnant smokers without asthma (OR 1.97, 95% CI 1.80–2.16). Presence of comorbidities such as diabetes, hypertension and mental illness also increased the likelihood of having smoking cessation advice recorded. No marked variations were observed in the recording of cessation advice with body mass index.

**Conclusion:** Recorded delivery of smoking cessation advice for pregnant smokers in primary care has increased with some fluctuation over the years, especially after the implementation of the QOF, and varies with maternal characteristics.

**Keywords:** Pregnancy, Smoking, Primary care, Smoking cessation advice

## Background

Smoking during pregnancy is harmful to both the mother and the unborn child and is associated with substantial morbidities such as ectopic pregnancy, premature rupture of membranes, pre-eclampsia, placental abruption, still-birth, low birth weight, premature birth and childhood

asthma [1–5]. Data from the 2010 Infant Feeding Survey show that 26% of mothers in the United Kingdom (UK) smoked at some point before or during their pregnancy and 12% of women smoked throughout their pregnancy [6]. Given the high proportion of mothers currently smoking during pregnancy and the resulting health impacts, reducing smoking during pregnancy in the UK is a national priority [7].

Offering smokers brief cessation advice lasting no more than five minutes during routine consultations with a general practitioner (GP), during which doctors make clear

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that smoking is harmful and offer help with cessation [8], is one of the simplest and most cost-effective tools to reduce the burden of smoking in the general population and increases rates of quitting by two-thirds compared to unassisted quit rates of 4% (OR 1.66, 95% CI 1.42-1.94) [9]. In pregnant women, cessation rates with brief advice have been low (5-9%) compared with intense advice and counselling (14-17%) [10,11]. However, physician advice to quit has been cited by pregnant women as one of the most important factors which influences their decision to stop smoking [12] and has been recommended in the recent World Health Organisation guidance for the management of tobacco use in pregnancy [13]. Current UK guidelines also recommend that smoking cessation advice should be offered at every available opportunity by health professionals who come into contact with pregnant women, including GPs and midwives, as only after smoking and smoking cessation is raised can it be possible to refer women on for the more intensive behavioural support or other smoking cessation therapies that are known to work [14-17]. The Quality and Outcomes Framework (QOF) introduced in UK primary care in 2004 financially rewards GPs for offering cessation advice to smokers and documenting this advice in the patients' electronic medical records [18]. However, there are no specific QOF targets for offering and recording cessation advice to pregnant women who smoke and little is known about the frequency with which smoking cessation advice is indeed routinely delivered and recorded by primary care health professionals during pregnancy. Data from Health Education Authority (HEA) surveys carried out in the 1990s showed that less than half the women interviewed who were smokers received cessation advice from a health professional [19], and another study conducted in 200 antenatal clinics in Leicester, UK reported that only 34% of current smokers received advice from their GP, 19% from a midwife, 12% from an obstetrician, 9% from family and friends and 26% received no advice at all [20].

Given the national guidelines and the effectiveness of smoking cessation advice in increasing quit rates, we aimed to determine the proportion of pregnant smokers with smoking cessation advice recorded in their electronic primary care records in recent UK data. In addition, we aimed to investigate whether socioeconomic factors and women's existing medical conditions in pregnancy were associated with this recording.

## Methods

### Data source and study population

The Health Improvement Network (THIN) is an electronic primary care database containing anonymised patient records from general practices across the UK [21]. THIN was set up by Cegedim Strategic Data (CSD) Medical Research UK, formerly known as Epidemiology and

Pharmacology Information Core (EPIC) and provides data for research purposes. The University of Nottingham has a license to use data from EPIC, subject to approval from the Scientific Review Committee (SRC) which reviews the ethics and research protocol. Ethical approval for the study was obtained from the THIN Scientific Review Committee (reference number 11-047).

The version of THIN used for this study covered approximately 5.7% of the population and contained data from 495 practices with a nationally representative sample of women of reproductive age (defined here as aged 15-49 years) [21]. Fertility rates in THIN are very similar to national fertility rates [22] and the population prevalence of smoking recorded in THIN has been previously validated at both national and regional levels [23,24]. Our study population included all pregnancies recorded in THIN from 2000 to 2009 in women of reproductive age which resulted in either a live birth or a stillbirth, and where women were considered to be smokers during pregnancy. Women were defined as smokers if they had a Read code [25] indicating smoking recorded in their medical records or a drug code for nicotine replacement therapy (NRT) during their pregnancy, or, in the absence of recording during pregnancy, if their last recorded Read code in the 27 months prior to pregnancy indicated smoking as defined in more detail previously [26].

### Recording of smoking cessation and women's characteristics

Our main outcome of interest was whether pregnant women identified as smokers had Read codes [25] for smoking cessation advice recorded in their THIN records during the period of their pregnancy. Code lists are available from the authors on request.

Data were also extracted on women's age at the start of their pregnancy, socioeconomic deprivation as measured by quintiles of the Townsend Index of deprivation [27] based on their home postcode, body mass index (BMI) before their pregnancy and morbidities common in pregnancy for which the recording of smoking status has been specifically incentivised by the QOF (hypertension, diabetes, asthma, and mental illness which included depression, anxiety, bipolar disorder, schizophrenia and other psychoses), during pregnancy or within 27 months before conception in line with the QOF recording rules [28]. A summary variable was also created for the presence of at least one chronic condition out of the morbidities under study. Missing data for Townsend quintile and BMI were included in separate categories in the analyses.

### Statistical analysis

Across the whole study period, annual proportions of pregnant smokers with records of smoking cessation advice were calculated as the number of pregnancies



among smokers with recorded smoking cessation advice divided by the total number of pregnancies among smokers who gave birth in that year.

To investigate the factors associated with the recording of smoking cessation advice delivered to pregnant smokers we used data from 2006 to 2009, as the proportion of pregnant smokers given smoking cessation advice in primary care only stabilised after 2006 (as seen in Figure 1). Firstly, using univariable logistic regression, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for the association between each variable (age at pregnancy, Townsend quintile, BMI category, asthma, diabetes, hypertension and mental illness) and whether or not smoking cessation advice was recorded during pregnancy. Covariates that were significantly associated with the recording of smoking cessation advice in the univariable model ( $p < 0.05$ ) were considered for inclusion in the final multivariable model. As some women had more than one pregnancy during the study period that contributed to our analyses, we accounted for this potential clustering of pregnancies within women by calculating robust confidence intervals (CIs) around our odds ratios using the clustered sandwich estimator to allow for intragroup correlation [29,30]. All analyses were completed using Stata version 11.0 (StataCorp LP, College Station, TX).

## Results

### Baseline characteristics

We identified 45,296 pregnancies in 39,781 women resulting in a live birth or stillbirth from 2000 to 2009 and where women were classified as smokers during pregnancy. Of these 4,826 also had NRT prescribed during pregnancy for smoking cessation. The mean age at conception was 27 years (standard deviation 6.17) and 48.6% of the pregnancies included in the study were in women in the two most deprived quintiles of the Townsend Index of deprivation. Smoking cessation advice was recorded in 12,454 (27.5%) of all pregnancies under study and half of

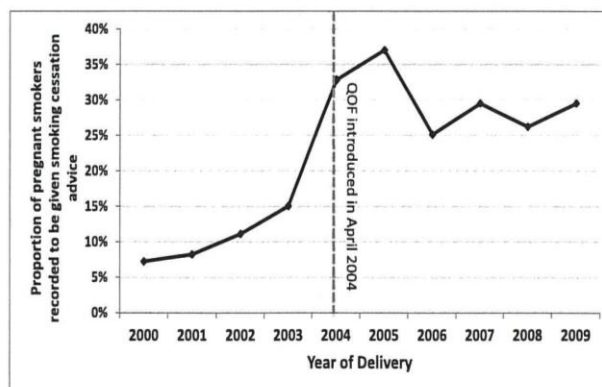
the pregnancies (49.5%) where women also received an NRT prescription during pregnancy. Table 1 describes the baseline characteristics of the study population.

### Annual trends in recorded smoking cessation advice in primary care

Figure 1 shows the annual proportions of pregnant smokers with smoking cessation advice recorded in their primary care medical records during pregnancy from 2000 to 2009. Overall, there has been an increase in this proportion over time. The proportion of pregnant smokers with recorded smoking cessation advice in 2000 was only 7%. This doubled to 15% in 2003, after which a steep increase was observed in 2004 with the proportion rising to 33%. The proportion of pregnant smokers with recorded smoking cessation advice peaked in 2005 at 37%, after which it stabilised at between 26-29% in the period of 2006–2009.

### Factors associated with the recording of smoking cessation advice in pregnancy

Table 2 shows variations in the odds of smoking cessation advice being recorded during pregnancy by women's sociodemographic characteristics and morbidities. Pregnant smokers from the youngest age group (15–19) and the oldest age group (45–49) were more likely to be recorded as having received smoking cessation advice compared to pregnant smokers between the age of 25 and 29 years (OR 1.21 (95% CI 1.10-1.35) and OR 2.37 (95% CI 1.11-5.10) respectively). Recording also varied with socioeconomic status, such that pregnant smokers from the most deprived group (quintile 5) were 38% more likely to have smoking cessation advice recorded in their primary care records than pregnant women from the least deprived quintile (OR 1.38, 95% CI 1.14-1.68). In addition, recorded smoking cessation advice was higher in pregnant smokers with morbidities, such that pregnant smokers with asthma were almost twice as likely to have been recorded as having received smoking cessation advice compared to



**Figure 1** Annual proportions of pregnant smokers with smoking cessation advice recorded in their primary care records (2000–2009).

**Table 1 Baseline characteristics of the study population (pregnant smokers)**

	Total pregnancies (N = 45,296)	Recorded smoking cessation advice (%*) (N = 12,454)
<b>Age at conception</b>		
15-19 years	5,019	1,538 (30.6%)
20-24 years	12,180	3,355 (27.5%)
25-29 years	12,005	3,153 (26.3%)
30-34 years	9,736	2,613 (26.8%)
35-39 years	5,254	1,457 (27.7%)
40-44 years	1,048	317 (30.2%)
45-49 years	54	21 (38.9%)
<b>Townsend score in quintiles</b>		
Quintile 1 - most affluent	5,380	1,293 (24.0%)
Quintile 2	6,156	1,625 (26.4%)
Quintile 3	8,842	2,360 (26.7%)
Quintile 4	11,432	3,303 (28.9%)
Quintile 5 - most deprived	10,572	3,141 (29.7%)
Missing	5,380	1,293 (24.0%)
<b>Pre-conception body mass index</b>		
Normal (18.0-24.9)	19,579	5,144 (26.3%)
Underweight (<18.0)	2,106	588 (27.9%)
Overweight (25-29.9)	8,897	2,547 (28.4%)
Obese (>=30)	6,338	1,874 (29.6%)
Missing	8,302	2,301 (27.7%)
<b>Asthma</b>	5,238	2,102 (40.1%)
<b>Hypertension</b>	969	315 (32.5%)
<b>Diabetes</b>	942	310 (32.9%)
<b>Mental illness</b>	7,193	2,184 (30.4%)
<b>At least one of above morbidities**</b>	12,577	4,177 (33.2%)

\*% with recorded smoking cessation advice as a proportion of all pregnancies in smokers within each variable strata.

\*\*Recording of medical conditions including asthma, hypertension, diabetes and mental illness.

pregnant smokers without asthma (OR 1.97, 95% CI 1.80-2.16). Similarly, pregnant smokers with hypertension and diabetes were, respectively, 32% (OR 1.32, 95% CI 1.09-1.60) and 24% (OR 1.24, 95% CI 1.03-1.50) more likely to have smoking cessation advice recorded in their medical records compared to smokers without these morbidities. The presence of at least one of the above morbidities (diabetes, hypertension, asthma, mental illness) increased the likelihood of recording of smoking cessation advice for pregnant smokers by 49% (OR 1.49, 95% CI 1.39-1.60).

## Discussion

Using a large population-based dataset, we have shown that the proportion of pregnant smokers recorded as

having been advised to quit in primary care increased from 7% in 2000 to 30% in 2009, with substantial increases in the rate of recording around the time of the introduction of the QOF in 2004. We also found smoking cessation advice was more likely to be recorded in pregnant smokers from more deprived socioeconomic groups, among pregnant teenagers and women over age 45 years, and among women with asthma, diabetes, hypertension and mental illness.

Whilst national trends in the delivery of smoking cessation advice have been assessed in the general population [31,32], this is the first study to assess this advice recording during pregnancy in primary care. Our study provides estimates for the delivery of smoking cessation advice during pregnancy in routine GP consultations to complement survey data, which may over-estimate physician behaviours such as delivering smoking cessation advice [33] and may be limited by small sample sizes and non-probability sampling techniques [19,20]. However, we acknowledge that the recording of smoking cessation advice in a pregnant woman's medical records may not always be acknowledged and interpreted as advice to quit by the women, and we do not know whether it was acted upon and resulted in a cessation attempt. The concept of smoking cessation advice is very subjective and different GPs may have different opinions on what constitutes effective advice. This may vary from a detailed discussion on smoking cessation strategies to only a brief mention of smoking during the consultation [34]. Indeed it is possible that in some cases smoking or smoking cessation may not actually have been discussed at all in the consultation and therefore we cannot be completely sure of the degree to which these Read codes represent the nature and extent of the advice delivered to pregnant smokers [32,34]. Additionally, GPs commonly address an average of two to three different medical problems during a single consultation [35,36]. However, the clinical coding does not necessarily reflect the breadth of the consultation and only the dominant topics of the visit may be coded [37]. Therefore, it is possible that smoking cessation advice was provided as part of the consultation yet not recorded electronically in women's primary care notes. Furthermore, defining women as smokers based on NRT prescriptions may result in over-estimation of the cessation advice recording as prescribing of NRT is more likely to be accompanied or preceded by the delivery of smoking cessation advice. However, only 10% of the smokers in our study were identified based on NRT prescriptions. Moreover, only 50% of women who received NRT also had a record of smoking cessation advice, and therefore it would not affect the proportion of smokers with cessation advice substantially.

In the UK health care system midwives are the main point of contact for most women during pregnancy [37,38]



**Table 2 Odds ratios of receiving smoking cessation advice by women's characteristics and morbidities between 2006 and 2009**

	Pregnant smokers (n = 27,959)	Pregnant smokers with smoking cessation advice (n = 7,716)		Unadjusted		Adjusted	
		n	%	OR (95% CI)	p-value	OR (95% CI)	p-value
<b>Age at conception</b>							
15-19	3,169	957	30.2	1.19 (1.08-1.32)	0.008	1.21 (1.10-1.35)	0.001
20-24	7,738	2,127	27.5	1.05 (0.96-1.14)		1.04 (0.96-1.13)	
25-29	7,542	2,006	26.6	1		1	
30-34	5,639	1,535	27.2	1.03 (0.95-1.12)		1.05 (0.96-1.14)	
35-39	3,166	872	27.5	1.05 (0.95-1.15)		1.07 (0.97-1.17)	
40-44	671	203	30.3	1.20 (1.00-1.43)		1.18 (0.98-1.41)	
45-49	34	16	47.1	2.45 (1.21-4.98)		2.37 (1.11-5.10)	
<b>Townsend score</b>							
Quintile 1 (most affluent)	3,047	711	23.3	1.00	<0.001*	1.00	<0.001*
Quintile 2	3,745	1,005	26.8	1.21 (1.07-1.35)		1.19 (1.06-1.34)	
Quintile 3	5,532	1,480	26.8	1.20 (1.06-1.36)		1.18 (1.04-1.35)	
Quintile 4	7,191	2,075	28.9	1.33 (1.16-1.53)		1.29 (1.13-1.48)	
Quintile 5 (most deprived)	6,583	1,989	30.2	1.42 (1.17-1.72)		1.38 (1.14-1.68)	
Missing	1,861	456	24.5	1.07 (0.89-1.28)		1.03 (0.85-1.24)	
<b>Body mass index</b>							
Underweight (<18.0)	11,893	3,196	26.9	1.10 (0.97-1.25)	<0.001	1.08 (0.95-1.22)	<0.001
Normal (18.0-24.9)	1,334	385	28.9	1		1	
Overweight (25.0-29.9)	5,689	1,645	28.9	1.11 (1.03-1.19)		1.09 (1.01-1.18)	
Obese (≥30)	4,218	1,252	29.7	1.15 (1.06-1.24)		1.08 (0.99-1.16)	
Missing	4,825	1,238	25.7	0.94 (0.87-1.01)		0.92 (0.83-1.01)	
<b>Asthma</b>	3,317	1,368	41.2	2.02 (1.85-2.2)	<0.001	1.97 (1.80 - 2.16)	<0.001
<b>Hypertension</b>	580	200	34.5	1.39 (1.16-1.67)	<0.001	1.32 (1.09 - 1.60)	<0.001
<b>Diabetes</b>	635	208	32.8	1.29 (1.07-1.55)	0.008	1.24 (1.03 - 1.50)	0.015
<b>Mental illness</b>	4,390	1,314	29.9	1.15 (1.06-1.24)	0.001	1.09 (1.01 - 1.18)	0.019

OR Odds ratio, CI Confidence interval, \*p-value for trend.

and guidelines indicate that midwives should ask about women's smoking status at the first antenatal booking appointment (usually between 8–12 weeks), and provide smoking cessation advice and referral if warranted [39]. This information should be documented in women's hand-held notes (mandatory paper records that women should carry throughout pregnancy as part of the UK's National Health Service antenatal care). However, there are no existing studies to show the extent to which this information is transferred to their electronic primary care records. We may, therefore, have underestimated the proportion of smokers in fact receiving cessation advice.

Our study is novel in that it investigates the maternal characteristics associated with the recording of smoking cessation advice during pregnancy. We found a significant increase in recorded smoking cessation advice with increasing deprivation quintile. A similar trend was seen in a study which examined the impact of the QOF on the recording of smoking advice in the general adult

population - smokers from the most deprived quintile were 20% more likely to have a record of smoking cessation advice than smokers in the least deprived quintile [31]. This may be related to a poorer overall health status, higher prevalence of illness in more deprived smokers [40], or generally heavier smoking habits in this group [6], resulting in more GP visits and consequently more opportunities for the delivery and recording of smoking cessation advice. We also found that pregnant smokers in the youngest (15–19 years) and the oldest (45–49 years) age groups were more likely to have smoking cessation advice recorded during pregnancy. Although the latter was only a very small group of women, pregnancies in the 45–49 age groups are generally high-risk, resulting in more GP visits than normal pregnancies, which will make smoking cessation more important and result in more opportunities for providing smoking cessation advice. The prevalence of smoking during pregnancy is generally higher in younger women [6], and teenagers also have generally higher-risk

pregnancies compared with women of average childbearing age [41,42]. According to the Infant Feeding Survey 2010, levels of smoking during pregnancy were the highest among mothers under the age of 20 in England and Scotland [6], which may explain higher smoking cessation advice documentation in this very young group in our study. The presence of comorbidities such as asthma, diabetes, hypertension and mental illness was also related to recording of smoking cessation advice delivery in our study. The effect of asthma was the strongest, such that pregnant smokers with asthma were twice as likely to have cessation advice recorded in their primary care records compared to non-asthmatics. This is consistent with a general population study which showed that presence of comorbidities was strongly related to the recording of cessation advice in primary care in the general population. However, the magnitude of effect for the morbidities was much higher than that found in our study [31], which may be because pregnant women are generally younger and healthier compared to the general adult population.

In our study, the proportion of pregnant smokers with smoking cessation advice recorded in their medical records during their pregnancy doubled between 2003 and 2004 suggesting that, despite having no specific target for recording of smoking cessation advice during pregnancy, the QOF has increased the occurrence of such activity. This marked increase between 2003 and 2004 can be attributed to the introduction of the 2004 GP contract as the negotiations for this contract started between 2002 and 2003 [43]. A general population study using primary care data from over 300 practices throughout the UK to assess the effect of the QOF on recording of smoking status and smoking cessation advice found that although rates of recording of smoking cessation advice in patients' electronic medical records had been increasing gradually since the year 2000, the rate of improvement accelerated from 2003, with a 3-fold increase observed between the first quarter of 2003 and the same period in 2004, just before the introduction of the QOF (Risk Ratio (RR) 3.03, 95% CI 2.98-3.09) [44]. This may be evidence that historically GPs have not documented their delivery of smoking cessation advice in patients' primary care records and after the introduction of QOF in 2004 the documentation of such advice improved. Data collected by semi-structured interviews in antenatal clinics at one UK hospital in the mid-1990s found that 34% of pregnant smokers reported receiving advice to quit from their GP [20]. Similarly, annual surveys between 1992 and 1999 conducted on pregnant women throughout England found that the proportion of pregnant smokers who received advice from a health professional ranged from 38%-55% [19]. Patient recall is known to be biased towards over-reporting in questions about smoking cessation advice [33,45], which may explain why estimates from these

surveys are higher than our estimates from THIN data presented here. However, the large difference between the proportion of women with cessation advice recorded in THIN prior to 2004 and these survey estimates suggests that the introduction of the QOF may have resulted in an improvement in the recording of advice, which GPs were already giving but not documenting [34]. Despite these uncertainties in the interpretation of the data presented here, the observation that only approximately one-third of smokers have the delivery of cessation advice recorded in their primary care medical records suggests there is substantial room for improvement in the provision of this important health advice, particularly during pregnancy.

## Conclusions

In conclusion, although there are no specific targets to encourage GPs to deliver and document smoking cessation to pregnant women, the effects of smoking-related QOF targets in the general population appear to have increased the overall recording of smoking cessation advice during pregnancy as well with some fluctuations over the years. Pregnancy offers a strategic opportunity for health professionals to promote smoking cessation and motivate women to give up as women are generally more receptive to cessation interventions [46], therefore every opportunity to encourage smoking cessation should be seized by the health care professionals even if it is in the form of brief advice lasting less only a few minutes. The inclusion in the QOF of a target on smoking cessation advice specifically during pregnancy may result in the topic of smoking being raised more frequently, more advice being given and recorded and more pregnant smokers being referred on for specialist support with quitting smoking.

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

NND, LJT, TC and LS conceived the idea for the study and analyses, which was conducted using a dataset created under supervision of LJT of women in their potential childbearing years from The Health Improvement Network database. BH carried out the data management and analysis under supervision by NND and LS and wrote the first draft of the manuscript. LJT and TC provided interpretations at different stages of the project and helped to draft the manuscript. All authors read and approved full drafts and the final manuscript.

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## 10.3 A COMPARISON OF UK PRIMARY CARE DATA WITH OTHER NATIONAL DATA SOURCES FOR MONITORING THE PREVALENCE OF SMOKING DURING PREGNANCY

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### A comparison of UK primary care data with other national data sources for monitoring the prevalence of smoking during pregnancy

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#### ABSTRACT

**Background** We aimed to assess the potential usefulness of primary care data in the UK for estimating smoking prevalence in pregnancy by comparing the primary care data estimates with those obtained from other data sources.

**Methods** In The Health Improvement Network (THIN) primary care database, we identified pregnant smokers using smoking information recorded during pregnancy. Where this information was missing, we used smoking information recorded prior to pregnancy. We compared annual smoking prevalence from 2000 to 2012 in THIN with measures from the Infant Feeding Survey (IFS), Smoking At Time of Delivery (SATOD), Child Health Systems Programme (CHSP) and Scottish Morbidity Record (SMR).

**Results** Smoking estimates from THIN data converged with estimates from other sources after 2004, though still do not agree completely. For example, in 2012 smoking prevalence at booking was 11.6% in THIN using data recorded only during pregnancy, compared with 19.6% in SMR data. However, the use of smoking data recorded up to 27 months before conception increased the THIN prevalence to 20.3%, improving the comparability.

**Conclusions** Under-recording of smoking status during pregnancy results in unreliable prevalence estimates from primary care data and needs improvement. However, in the absence of gestational smoking data, the inclusion of pre-conception smoking records may increase the utility of primary care data. One strategy to improve gestational smoking status recording in primary care could be the inclusion of pregnancy in the Quality and Outcome's Framework as a condition for which smoking status and smoking cessation advice must be recorded electronically in patient records.

**Keywords** primary care, pregnancy and childbirth disorders, smoking

#### Introduction

Smoking in pregnancy is an important preventable cause of poor health outcomes for women and their babies.<sup>1,2</sup> In March 2011, the UK Government white paper entitled 'Healthy lives healthy people: A tobacco control plan for England' set out a national goal to reduce the prevalence of smoking throughout pregnancy to 11% or less by 2015.<sup>3</sup> It is therefore crucial to collect data on maternal smoking to monitor progress towards this national goal. The UK currently has four data sources that provide population-level estimates of smoking during pregnancy. Each

measures smoking differently and has its strengths and limitations. The Infant Feeding Survey (IFS) measures smoking at

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delivery, retrospectively, at 6–8 weeks postpartum in the UK.<sup>4–6</sup> The smoking at the time of delivery (SATOD) data measure smoking behaviour at the time of delivery,<sup>7</sup> whereas the Child Health Systems Programme (CHSP) Pre-School Component measures maternal smoking around delivery usually within 10 days postpartum.<sup>8</sup> In comparison, data from the Scottish Morbidity Records (SMR) measure smoking at the time of first antenatal appointment. Electronic primary care records contain routinely collected information on medical diagnoses, prescriptions and other data such as patients' smoking status,<sup>9</sup> and thus could potentially provide comprehensive and timely population-level data on smoking prevalence during pregnancy. In April 2004, a contract for UK general practitioners (GPs) (family physicians) was implemented; this introduced pay-for-performance targets known as the Quality and Outcomes Framework (QOF)<sup>10</sup> according to which the recording of smoking status and recorded delivery of smoking cessation advice can generate revenue of up to £10 000 per year per practice.<sup>11,12</sup> Consequently, the recording of smoking status in primary care data has improved such that, outside of pregnancy, UK primary care data are a valid source of data to monitor smoking prevalence at a population level both nationally and regionally.<sup>13,14</sup> However, the potential use of these data for generating estimates of smoking during pregnancy at a population level is yet to be studied. In an earlier study, we found that the recording of smoking status during pregnancy is relatively incomplete; in 2009, only 43% of women had a record for smoking status during pregnancy.<sup>15</sup> However, in this previous work, we found that the utility of incomplete individual-level smoking status data could be improved by making various assumptions which reflected data recording practices encouraged by the QOF.<sup>15</sup> Consequently, in this paper, we test similar assumptions to assess the potential usefulness of primary care data for estimating the population smoking prevalence in pregnancy by comparing estimates from primary care data with those obtained from other available data sources.

## Methods

### Data source and study population

The Health Improvement Network (THIN) is an electronic primary care database containing anonymized patient records from general practices across the UK. It is representative of the UK population in terms of patient demographics and the prevalence of common illnesses.<sup>16</sup> The version of THIN used for this study contained data from 570 practices, covering ~6% of the UK population.<sup>9</sup> Our study population included all women of reproductive age (defined as 15–49<sup>17</sup>) in THIN with pregnancies ending in live births or stillbirths from 2000 to 2012. Pregnancies ending in miscarriage were

not included in the study population as many of these occur early in pregnancy when women may not know they are pregnant. Therefore, they may not be reported to the doctor, or if they are reported, the first consultation indicating the pregnancy may be for reporting the miscarriage, when ascertainment of smoking status would only be retrospective. For women with more than one pregnancy during the study time, one pregnancy was chosen at random for analysis to prevent any clustering effects.

### Comparing the prevalence of smoking in pregnancy in THIN with other data sources

For each woman, we extracted all records of smoking status recorded in THIN using Read codes<sup>18</sup> before and during pregnancy and up to 10 days after delivery (e.g. 137R.00—Current smoker). Where a Read code did not clearly indicate current smoking (e.g. 137X.00—Cigarette consumption), we assessed whether smoking status could be derived from any additional information recorded, such as the number of cigarettes smoked, or the presence of prescriptions for smoking cessation medications. If no additional information was found, the recording was labelled as unknown smoking status. Code lists are available from the authors on request.

Using a previously validated algorithm,<sup>13</sup> we used the extracted Read codes to determine each woman's smoking status during their pregnancy. The annual prevalence of smoking during pregnancy as recorded in THIN (as a proportion of all births in that year) was then compared against the prevalence measures from the IFS, SATOD, SMR and CHSP. A detailed description of each of these data sources is provided in Table 1.

Each comparison used a slightly different population of women from THIN and assessed smoking status at a different point in time in pregnancy to reflect the nature of the data collection in the source being compared (see Table 2). Estimates of smoking prevalence from the IFS were derived from the 'raw' data sets of individual women's survey responses, available from the UK Data Service.<sup>24</sup> The IFS only asked about smoking status retrospectively, so women were classified as smoking at delivery if they reported that they tried to give up smoking during pregnancy but started again before delivery, if they tried to cut down on the amount smoked during pregnancy, or if they did not try to cut down during pregnancy. Estimates of the prevalence of smoking from SATOD, SMR and CHSP data were obtained from published reports.

### Imputing smoking status where women had no record during the gestational period

Initially, we used only records of smoking status documented in the primary care record after the date of conception to

**Table 1** Summary of available data sources to measure smoking during pregnancy in the UK

Data source	Data collection interval	Country	Sampling frame and method	Sample size <sup>a</sup> (% of national births)	Data collection method	Time at which data on smoking in pregnancy are collected	Definition of smoking	Strengths	Limitations
Infant Feeding Survey <sup>4-6</sup>	Every 5 years	UK (England, Scotland, Wales, Northern Ireland)	Random sample of live births in England and Scotland and all births in Wales and Northern Ireland in study period	22 400 (2.7% of all births in the UK) <sup>19-23</sup>	Postal survey administered by the National Health Service Information Centre	6-8 weeks after birth	Several self-reported measures available: smoking prior to pregnancy; ever smoking during pregnancy; quitting on confirmation of pregnancy; quit/cut down attempts during pregnancy; smoking at delivery	Smoking estimates for overall UK and each constituent country presented by sociodemographic factors (~52%) Measures smoking cessation during pregnancy Data collected and reported at a local level	Data only collected at 5 years intervals Retrospective reporting of smoking status Low response rates (~52%) Results published at least a year after survey completion Limited to England Data collected postnatally No assessment of smoking by sociodemographic factors
Smoking Status at Time of Delivery (SATOD) <sup>7</sup>	Collected continually and reported quarterly	England	Aims to capture all live births and stillbirths	359 763 (52.1% of all births in England) <sup>19,22</sup>	Midwife survey (in hospital maternity units)	At delivery	Self-reported smoking status at delivery	Provides measures of never/ex smoking along with current smoking Provides annual rates by age and socio-economic status	Limited to Scotland Does not give estimates for the whole duration of pregnancy Limited to Scotland Data collected postnatally only Does not specifically ask about smoking during pregnancy
Smoking Data collected as part of the Scottish Morbidity Record (SMR) <sup>8</sup>	Collected continually and reported by financial year	Scotland	All pregnant women attending an antenatal booking appointment (pregnancies may end in live birth or stillbirth)	57 398 (100% of all maternities in Scotland) <sup>20,23</sup>	Midwife survey (in hospital or community)	First antenatal booking appointment (usually between 8-12 weeks gestation)	Self-reported smoking status at the time of booking	Provides measures of never/ex smoking along with current smoking Provides annual rates by age and socio-economic status	Limited to Scotland Does not give estimates for the whole duration of pregnancy Limited to Scotland Data collected postnatally only Does not specifically ask about smoking during pregnancy
Preschool component of the Child Health Systems Programme (CHSP) <sup>9</sup>	Collected continually and reported by financial year	Scotland	Aims to capture all live births	51 746 (92% of all live births in Scotland) <sup>20,23</sup>	Survey administered by public health nurse or health visitor	Approximately 10 days after birth	Self-reported smoking status at the time of survey ~10 days after delivery	Provides data on smokers and non-smokers by age and socio-economic status	Limited to Scotland Data collected postnatally only Does not specifically ask about smoking during pregnancy

<sup>a</sup>Sample sizes for each wave vary therefore sample sizes for 2010 described in the table for reference.



**Table 2** THIN comparisons with the currently available data in the UK

Survey	Time at which survey assesses smoking prevalence	Years compared with THIN	THIN population used for comparison	Timing of records considered to define smoking status in THIN
Infant Feeding Survey (IFS)	At delivery	2000, 2005, 2010	Data from all UK practices ( $n = 570$ )	Last smoking status recording between conception and delivery
Smoking Status at Time of Delivery (SATOD)	At delivery	2006–2012	Data from English practices ( $n = 420$ )	Last smoking status recording between conception and delivery
Scottish Morbidity Record (SMR)	At booking (8–12 weeks gestation)	2000–2012	Data from Scottish practices ( $n = 85$ )	First smoking status recording between conception and delivery
Child Health Systems Programme (CHSP)	10 days after delivery	2001–2012	Data from Scottish practices ( $n = 85$ )	Last smoking status recording between conception and 10 days after delivery

determine smoking status during pregnancy. However, if a woman's smoking status was not recorded during gestation, we used pre-conception records of smoking status to identify women who might have smoked during pregnancy. Based on the QOF rules for the recording of smoking status in the general population, which from April 2004 to March 2006 required the smoking status of patients aged 15 or over to be recorded at least once in primary care records, and since April 2006 have required records to be updated every 27 months, we used two cut-off points for including information from pre-conception records.<sup>25</sup> Firstly, we used a cut-off of 27 months before conception and recoded women as smokers if their last smoking record in the 27 months before conception indicated smoking. Finally, if a woman did not have her smoking status recorded either during pregnancy or in the 27 months before conception, we included any smoking information recorded in their primary care data since they registered with their practice.

All analyses were conducted in Stata 12.0 (StataCorp LP, College Station, TX, USA). Ethical approval was obtained from the THIN Scientific Review Committee (Reference number 11-047).

## Results

### Population of pregnancies and smoking in THIN

We identified 310 043 women with one or more pregnancies ending in a live birth or stillbirth from 2000 to 2012; 246 730 of these women were registered with a GP in England and 34 442 were in Scotland. The mean age at conception was 29.5 years (standard deviation 5.9 years). Only 30% of women had their smoking status recorded at least once during pregnancy and of these women 75% only had a single record.

### Comparison with IFS data

Figure 1a shows the prevalence of smoking at the time of delivery in women in THIN compared with the prevalence measures in the IFS. Annual trends could not be compared as there were only three data points available. In 2000, none of the three prevalence estimates using THIN data were comparable with the IFS estimates. In 2005, smoking prevalence including data recorded up to 27 months before conception from THIN was slightly higher than the IFS estimate (17.0 versus 20.6%, respectively). In 2010, the IFS prevalence of smoking at the time of delivery decreased further to 11.6%, while the THIN prevalence using data recorded up to 27 months before conception remained similar (19.9%). In comparison, the IFS prevalence for 2010 was ~3 percentage points higher than the THIN prevalence using only smoking data recorded during pregnancy (11.6% in the IFS compared with 9.3% in THIN).

### Comparison with SATOD data

When using smoking data recorded any time before delivery, the prevalence of smoking during pregnancy recorded in THIN was ~7 percentage points higher than the SATOD estimates from 2006 to 2012. In comparison, the THIN prevalence considering data recorded up to 27 months before conception was ~4–5 percentage points higher over the 6 years of available data, while the THIN prevalence considering only records of smoking recorded during the gestational period was 4–5 percentage points lower than the SATOD estimates (Fig. 1b).

### Comparison with CHSP data

Using only records of smoking status entered during the gestational period, the THIN prevalence of maternal smoking was low until 2004 (e.g. 44% of the CHSP prevalence of 23.1% in

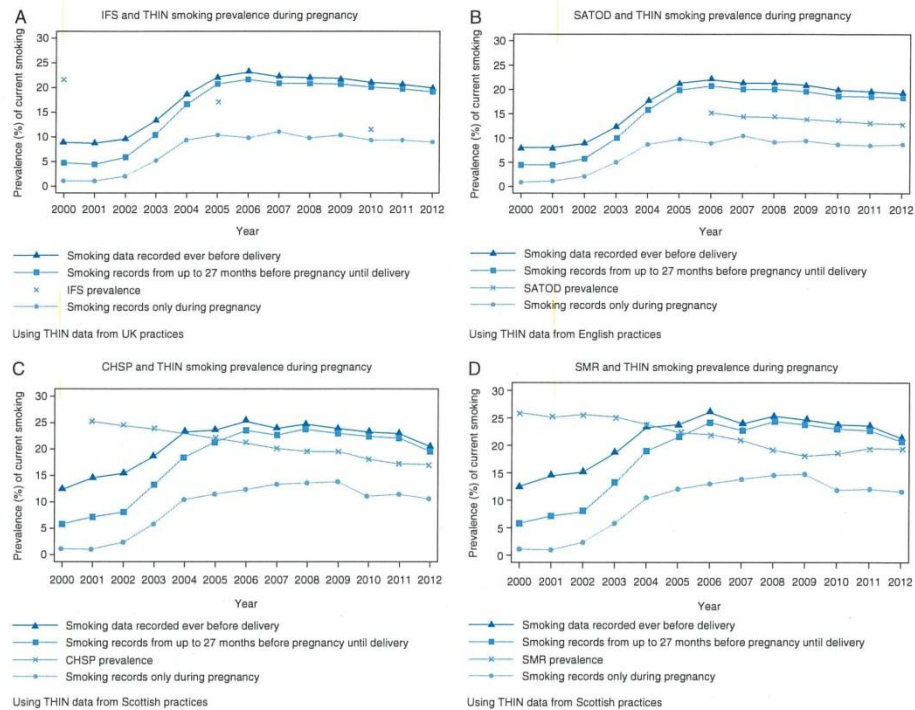


Fig. 1 Comparison of smoking prevalence from currently available data sources and THIN.

2004) (Fig. 1c). It was 10.5% in 2012, ~7 percentage points lower than the corresponding CHSP prevalence of 17.1%. Using smoking information recorded in the 27 months before pregnancy, the prevalence in CHSP and THIN converged in 2005. After this, the THIN estimates were slightly higher than the CHSP estimates, such that in 2012 the THIN prevalence using data recorded up to 27 months before pregnancy was 19.9% compared with the CHSP prevalence of 17.1%. The prevalence estimates using data recorded ever before delivery were only slightly higher than the estimates using data recorded up to 27 months before conception.

#### Comparison with SMR data

Using smoking status data recorded during the gestational period, the THIN prevalence was much lower than the SMR prevalence until 2004 (THIN prevalence = 10.6% compared with SMR prevalence of 23.8% in 2004, as shown in Fig. 1d).

Prevalence in THIN was 11.6% in 2012 but was still 40% lower than the corresponding SMR prevalence of 19.6%. When including smoking information recorded up to 27 months before conception, the two lines converged between 2004 and 2005; in 2012, smoking prevalence in THIN was 20.3% using data recorded up to 27 months before conception and smoking prevalence using data recorded any time before pregnancy was 21.3% compared with the SMR prevalence of 19.3%.

## Discussion

### Main findings

We found that, with current levels of completeness of smoking data in primary care records, it is not possible to produce population level estimates for smoking prevalence during pregnancy that are directly comparable with those



derived from existing surveys. The convergence between THIN estimates and estimates from other data sources has, however, improved over time especially following the introduction of the QOF. Data from the IFS show good agreement with smoking at delivery in women in 2010 as recorded in THIN based on smoking status records entered in the electronic medical record during pregnancy. THIN data, using smoking data recorded up to 27 months before conception, show good agreement with SMR estimates in the final year of the study period.

#### What is already known on the topic

To date, there are no studies assessing the validity of primary care data for quantifying the prevalence of smoking during pregnancy. A study comparing smoking prevalence recorded in THIN to smoking prevalence in the general population [measured by the General Lifestyle Survey (GLF)] found a good agreement between THIN and the GLF after 2008 and concluded that primary care data may provide an alternate means of monitoring national smoking prevalence.<sup>18</sup> Despite the smaller sample sizes at regional level, primary care data have also been shown to be a good means of monitoring regional smoking prevalence in the general population.<sup>19</sup>

If primary care data were valid to monitor smoking prevalence during pregnancy, there would be several advantages of using these data to do so. All women in the UK must be registered with a GP in pregnancy to receive free antenatal care, so their records will be available in GP research databases. THIN data are routinely collected, have a lag of only 3–8 months before clinical data become available to researchers, and have the statistical power to provide estimates for the whole UK as well as constituent countries.<sup>18</sup>

#### What this study adds

The prevalence estimates of smoking during pregnancy from primary care do not accurately converge with other data sources because, at least in part, smoking status recording during pregnancy in primary care is incomplete.<sup>20</sup> If a woman's status did not change after she became pregnant (e.g. a non-smoker before pregnancy remained a non-smoker during pregnancy, or a smoker continued to smoke), GPs might be less likely to re-enter this information, which may account for the low completeness. Furthermore, in the UK, smoking status during pregnancy is primarily ascertained by midwives and recorded in women's handheld maternity records [mandatory paper records that women carry throughout pregnancy as part of the UK's National Health Service (NHS) antenatal care]. While the National Institute for Health and Clinical Excellence (NICE) recommends that midwives

and others involved in the care of pregnant women assess and document women's smoking status in their maternity records,<sup>26,27</sup> this information is not routinely entered into primary care records as the documentation in midwives' notes is not usually transcribed onto the electronic primary care records. This was clearly reflected in our previous study which found that from 2000 to 2009 smoking status was only recorded in primary care for 28% of pregnancies.<sup>20</sup> In the current study, smoking status was only recorded for 30% of pregnancies.

Another possible explanation for the lower THIN prevalence could be that THIN over-represents general practices from more affluent areas of the UK. Since smoking prevalence is lower in women from more affluent groups, this may slightly under-estimate the smoking prevalence generated using THIN data and account for some of the differences between THIN prevalence estimates and other data sources.

While THIN estimates using only gestational smoking records do not approximate closely to annual prevalence from other data sources, THIN estimates using smoking data from up to 27 months pre-conception are comparable with the SMR data (smoking status recorded at booking) in 2012. GP data may be most useful to provide adequate data on smoking prevalence early in pregnancy, when most women see their GPs for initial care, compared with the time around delivery, when most women will be cared for essentially in secondary care facilities.

#### Limitations

This is the first study to assess the potential of primary care data to provide population-level estimates of smoking during pregnancy and compare it with other current data sources in the UK. Fertility rates in THIN are comparable with national fertility rates<sup>28</sup> and therefore our ascertainment of pregnancies is valid. However, like the other data sources under comparison, data on smoking status recorded in THIN are self-reported and women may not accurately report their smoking behaviour, particularly during pregnancy where there may be social stigma attached to smoking.<sup>29</sup>

A potential limitation of our study was the inclusion of pre-conception smoking records to predict smoking status during pregnancy, which may not be an accurate reflection of women's smoking status during pregnancy. Studies which have investigated smoking behaviour in early pregnancy indicate that many women attempt to quit when they find out they are pregnant or later during pregnancy,<sup>30</sup> so it is unlikely that the inclusion of pre-conception records resulted in an under-estimation of smoking prevalence during pregnancy. It could however, lead to misclassification of some ex-smokers

as current smokers, resulting in an over-estimation of the prevalence of current smoking during pregnancy in THIN. We believe that a substantial over-estimation is unlikely as ~35–50% of pregnancies in the UK are unplanned,<sup>31,32</sup> which means that only some women are likely to make positive behaviour changes such as quitting smoking before attempting to conceive. It may, however, hold true for some women who quit on confirmation of their pregnancy.

Another potential weakness of our study, and of primary care data itself, is that it is difficult to determine the timing of smoking status ascertainment in relation to progress through gestation; this makes direct comparison with other data sources, obtained at booking or delivery, difficult. Lastly, smoking status during pregnancy is a complex and variable behaviour and it may fluctuate throughout pregnancy.<sup>33</sup> Therefore, single measures of smoking such as smoking at booking or smoking at delivery captured in SATOD, SMR and CHSP data are limited in their usefulness. Although they may give a snapshot of smoking behaviour at a certain time, they may not give a complete picture of smoking behaviour throughout pregnancy. IFS data assess smoking behaviour throughout pregnancy in more detail, albeit collected retrospectively. However, these data are collected on a quinquennial basis and thus may become out of date quickly. If smoking information was collected and recorded by GPs more frequently throughout pregnancy, then primary care data may prove to be very useful to assess the population-level burden of maternal smoking throughout pregnancy. However, as shown in this study, currently these data are not desirably complete.

### Conclusion

All existing data sources that measure smoking during pregnancy have their strengths and limitations. Primary care data have a great potential to measure smoking status during pregnancy at a population level, but this potential appears to be greatest for measuring smoking prevalence in early pregnancy around the time of booking appointments. Although recording of gestational smoking status in THIN is improving over time, it is not adequately complete to produce maternal smoking estimates at a population level with most women just having a single recording of smoking status throughout the course of pregnancy. Periodic recording of smoking status during pregnancy is important to monitor changes in smoking behaviour throughout pregnancy and to maintain and improve women's care before and after delivery. Although this information may be recorded and updated in handheld maternity notes, there is currently no centralized recording system and the information in these notes is lost after delivery. Better integration of recording systems in primary care and midwifery services is required

to improve communication and relay of relevant medical and lifestyle information including smoking status. One strategy to improve this recording in primary care may be the inclusion of pregnancy in the QOF as a condition where smoking status and smoking cessation advice should be recorded in the electronic primary care records. This will not only increase opportunities for healthcare professionals to provide smoking cessation advice and interventions, but could also provide valuable data for the evaluation of the effectiveness of these interventions and monitoring progress towards meeting national prevalence targets.

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## 10.4 PRESCRIBING OF NICOTINE REPLACEMENT THERAPY IN AND AROUND PREGNANCY: A POPULATION-BASED STUDY USING PRIMARY CARE DATA

### Research

Nafeesa N Dhalwani, Lisa Szatkowski, Tim Coleman, Linda Fiaschi, and Laila J Tata

## Prescribing of nicotine replacement therapy in and around pregnancy:

a population-based study using primary care data

### Abstract

#### Background

Licensing arrangements for nicotine replacement therapy (NRT) in the UK were broadened in 2005 to allow prescribing to pregnant smokers. However, estimates of NRT prescribing in pregnant females in the UK are currently lacking.

#### Aim

To assess trends in NRT prescribing around pregnancy, and variation in prescribing by maternal characteristics.

#### Design and setting

Population-based descriptive study using pregnancy data from The Health Improvement Network primary care database, 2001–2012.

#### Method

NRT prescriptions were identified during pregnancy and in the 9 months before and after. Annual prescribing prevalence was calculated. Logistic regression was used to assess females' likelihood of receiving prescriptions by maternal characteristics.

#### Results

Of 388 142 pregnancies studied, NRT was prescribed in 7551 for an average duration of 2 weeks. The prescribing prevalence of NRT increased from 0.03% (0.7% in smokers) in 2001 to 2.6% (11.4% in smokers) in 2005, after which it remained stable. Prescribing prevalence of NRT before and after pregnancy was half the prevalence during pregnancy. The odds of prescribing NRT during pregnancy in smokers increased with socioeconomic deprivation (OR = 1.29, 95% CI = 1.15 to 1.45 in the most compared with the least deprived group). Prescribing was 33% higher in pregnant smokers with asthma (OR = 1.33, 95% CI = 1.22 to 1.45) and mental illness (OR = 1.33, 95% CI = 1.23 to 1.44) compared with smokers without these diagnoses.

#### Conclusion

NRT prescribing is higher during pregnancy compared with before and after, and is higher in smokers from more socioeconomically deprived groups, those with asthma or those diagnosed mental illness.

#### Keywords

nicotine replacement therapy; pregnancy; prescribing; smoking cessation.

### INTRODUCTION

Smoking in pregnancy is related to several adverse outcomes for both mothers and their children.<sup>1,2</sup> In the UK, 26% of mothers smoke directly before or during their pregnancy, and 12% continue to smoke throughout.<sup>3</sup> Similar prevalence has been reported in Australia and the US (11.7% and 10.7% respectively).<sup>4,5</sup> Therefore, reducing smoking in pregnancy is a global public health priority.<sup>6</sup>

Nicotine replacement therapy (NRT) is a pharmacological smoking cessation aid which became available on prescription from the UK NHS in April 2001.<sup>7</sup> It was initially contraindicated during pregnancy because of a lack of evidence for its safety.<sup>8</sup> To date there is no conclusive evidence on its effectiveness during pregnancy,<sup>9</sup> and studies of NRT safety during pregnancy are inconclusive.<sup>10–12</sup> Nevertheless, expert consensus is that NRT is likely to be less harmful than smoking during pregnancy and, with various caveats, NRT has been recommended by international guidelines when smoking cessation without NRT is unsuccessful.<sup>13–16</sup>

Literature describing NRT use in pregnancy is limited to observational studies from the US and Denmark assessing the association of NRT use during pregnancy and adverse birth outcomes. The prevalence of self-reported NRT used in the first 12 weeks of gestation was 0.3%,<sup>17</sup>

2–2.5% in 17–27 weeks of gestation in the Danish National Birth Cohort,<sup>18,19</sup> and in the Pregnancy Risk Assessment Monitoring System (PRAMS) from four US states it was 3.9% (2004).<sup>2</sup> Since their publication, new NRT products have been introduced and international guidelines on gestational NRT use have changed. In 2013, the World Health Organization (WHO) recommended an urgent need for studies on the surveillance of current NRT use in pregnancy.<sup>16</sup>

In December 2005, UK licensing arrangements were changed to allow prescribing of NRT to pregnant smokers.<sup>16</sup> As a result, NRT can now be prescribed to pregnant females by GPs, midwives, or other licensed health professionals working in NHS Stop Smoking Services (SSS) after discussing the risks and benefits of using the drug in pregnancy. Although it can also be bought directly from pharmacies or other retailers such as supermarkets, all drug packaging retains warnings against its use in pregnancy without prior GP consultation. Most NRT is probably received via GP prescription, as half of NRT provided by pregnancy SSSs is issued via the patient's GP.<sup>16</sup>

Thus far, only two UK studies have assessed NRT use in pregnancy.<sup>20,21</sup> One of these studies only presents local data from Tayside, Scotland,<sup>21</sup> and the second was only among females attending NHS SSS in England.<sup>20</sup> Given that only 3% of all

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### How this fits in

Pregnancy is an opportunistic time to offer smoking cessation interventions to females. This study is the first to quantify prescribing of nicotine replacement therapy before, during, and after pregnancy in the UK. Prescribing prevalence of nicotine replacement therapy during pregnancy was 11% among smokers, double the prescribing prevalence before and after pregnancy. However, most females received only 2 weeks of nicotine replacement therapy during pregnancy. Prescribing was higher in pregnant smokers from more deprived areas and in smokers with diagnoses of asthma or mental illness.

pregnant females attend SSSs, this will have excluded most pregnant smokers.<sup>22,23</sup> In this study, UK prescribing of NRT is quantified before, during, and after pregnancy using a nationally representative sample, and the

characteristics of females who receive NRT prescriptions are investigated.

### METHOD

#### Data source and study population

The Health Improvement Network (THIN), an electronic database containing anonymised patient records from general practices across the UK, was used for this study, covering approximately 6% of the population,<sup>24</sup> representative of the UK population in terms of demographics, prevalence of common illnesses, and fertility rates.<sup>25,26</sup> Prevalence of smoking and prescribing of smoking cessation medications in the general population in THIN has been validated against national data.<sup>27,28</sup> The study population included all pregnancies between January 2001 and December 2012 in females of childbearing age (15–49 years), resulting in a live birth or a stillbirth.

#### Outcome and covariates

The smoking status of females was determined using Read Codes<sup>29</sup> recorded from 27 months before conception up to the end of pregnancy, based on the recording rules in the GP contract,<sup>30</sup> which is described in detail elsewhere.<sup>31</sup> Multilex Drug Codes for all NRT formulations available in the UK according to the *British National Formulary* (BNF) were used for NRT prescriptions.<sup>32</sup> Code lists are available from the authors on request.

To investigate factors associated with NRT prescribing, data were extracted on females' age at conception, socioeconomic deprivation (Townsend Index),<sup>33</sup> pre-conception body mass index (BMI), and diagnoses of medical conditions (hypertension, diabetes, asthma, and mental illness, which included depression, anxiety, bipolar disorder, schizophrenia, and other psychoses) during or before pregnancy. These conditions were selected as they are closely related to smoking,<sup>34–36</sup> and may influence quit attempts.

#### Statistical analysis

Overall and annual proportions of pregnancies, and pregnancies among smokers, with one or more NRT prescriptions before, during and after pregnancy were determined. There is no evidence of the time before and after pregnancy during which smokers are more likely to attempt to quit, therefore the 9 months before and after pregnancy were used to calculate prescribing prevalence, as these were similar to the average pregnancy length, allowing for comparisons of period

Table 1. Baseline characteristics of the study population

	Total pregnancies, n = 388 142	NRT prescribed, total n = 7551 [% of pregnancies with NRT prescription]	Pregnancies among smokers,* n = 71 685	NRT prescribed, n = 7551 [% of pregnancies among smokers with NRT prescription]
<b>Age at conception, years</b>				
5–19	27 365	930 (3.4)	9898	930 (9.4)
20–24	66 484	1962 (3.0)	19 869	1962 (9.9)
25–29	105 967	2004 (1.9)	19 188	2004 (10.4)
30–34	118 031	1664 (1.4)	14 534	1664 (11.4)
35–39	59 541	832 (1.4)	6952	832 (12.0)
40–44	10 222	152 (1.5)	1203	152 (12.4)
45–49	532	7 (1.3)	61	7 (11.5)
<b>Townsend score in quintiles<sup>33</sup></b>				
Quintile 1 – most affluent	83 203	722 (0.9)	7970	722 (9.1)
Quintile 2	71 045	925 (1.3)	9511	925 (9.7)
Quintile 3	76 619	1432 (1.9)	14 291	1432 (10.0)
Quintile 4	73 470	2068 (2.8)	18 097	2068 (11.4)
Quintile 5 – most deprived	55 653	1875 (3.4)	16 925	1875 (11.1)
Missing	28 152	529 (1.9)	4891	529 (10.8)
<b>Pre-conception body mass index, kg/m<sup>2</sup></b>				
Normal (18.0–24.9)	118 832	2266 (1.9)	22 888	2266 (9.9)
Underweight (<18.0)	8614	256 (3.0)	2353	256 (10.9)
Overweight (25–29.9)	58 693	1237 (2.1)	11 664	1237 (10.6)
Obese (≥30)	42 281	992 (2.3)	9191	992 (10.8)
Missing	159 722	2800 (1.8)	25 789	2800 (10.9)
<b>Asthma</b>	33 724	1061 (3.1)	8188	1061 (13.0)
<b>Hypertension</b>	9992	154 (1.5)	1420	154 (10.8)
<b>Diabetes</b>	10 752	224 (2.1)	1798	224 (12.5)
<b>Mental illness</b>	37 055	1567 (4.2)	11 624	1567 (13.3)

\*Smoker classified as those with a record of current smoking at some point within the 27 months before conception until delivery. <sup>33</sup>Socioeconomic status. NRT = nicotine replacement therapy.

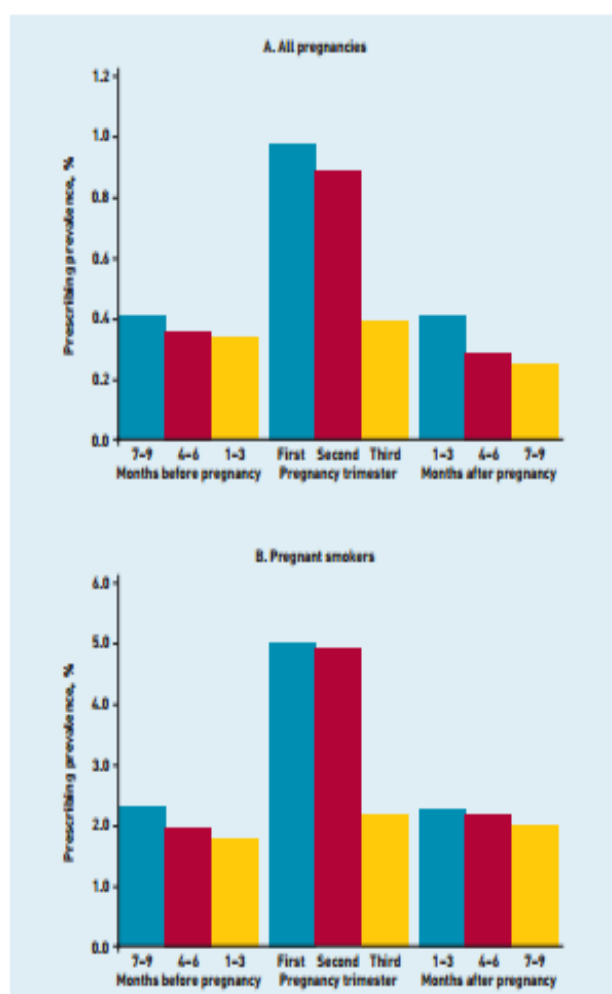


Figure 1. Proportion of overall pregnancies and smokers with NRT prescriptions in each 3-month time period, between 2001 and 2012.

prevalence. As smoking behaviours may fluctuate during a 9-month period, 3-month windows were also assessed during and around pregnancy. The use of different forms of NRT (patches, gum, nasal spray, lozenges, sublingual tablets, inhalator cartridges, and combination) was assessed. Logistic regression was used to calculate ORs for associations between females' characteristics and prescribing of NRT to smokers during pregnancy, restricting to pregnancies delivered from January 2006, after relaxation of licensing arrangements.<sup>10</sup> All covariates reaching statistical significance at the 5% level in univariable models were included in the multivariable analysis and each covariate was sequentially dropped from the model to assess whether it remained statistically significant, retaining only those that were. Some females had more than one

pregnancy during the study period and there may be potential clustering of females within practices; this was accounted for by using generalised estimating equations (GEE) with an exchangeable correlation structure which provided best estimates of the population-level associations with maternal characteristics despite potential dependence between pregnancy, that is accounting for clustered data.<sup>10</sup> Analyses were performed using Stata (version 12.0).

## RESULTS

### Baseline characteristics

Between 2001 and 2012, 388 142 pregnancies were identified resulting in live births or stillbirths, of which 71 685 (18.5%) were in smokers. Mean age at conception was 29.6 years (SD 5.9). Table 1 describes females' characteristics for all pregnancies and pregnancies among smokers, and NRT prescribing according to these characteristics.

### Patterns of NRT prescribing in and around pregnancy

NRT was prescribed in 7551 pregnancies, which represented a prescribing prevalence of 2% of all pregnancies and 11% of pregnancies in smokers. In comparison, the prescribing prevalence was 1% during the 9 months before and after pregnancy overall, and 5% in smokers. Figure 1 shows the prescribing prevalence in 3-month periods outside pregnancy and by trimester. NRT prescribing among smokers was most frequent during the first and second trimesters at just over 5%, compared with 2% in the third trimester.

Among the pregnancies where NRT was prescribed, over half (55%) had only one prescription issued, 25% had two prescriptions, and 20% had three or more prescriptions. The maximum number of prescriptions issued during pregnancy was 26. On average, females were prescribed a total of 2 weeks' worth of NRT (interquartile range 1–2 weeks). The prescription frequency and length of NRT issued in the 9 months before and after pregnancy was similar to pregnancy time.

In two-thirds of the pregnancies in which NRT was prescribed, it was initiated only during pregnancy, with no evidence of NRT prescribing prior to the start of pregnancy. The most common form of NRT used during pregnancy was transdermal patches (65% of all prescriptions), followed by inhalator cartridges (17%), gum (8%), lozenges (6%), sublingual tablets (2%), oromucosal spray (0.7%), and nasal spray (0.3%). Combination NRT was used in 14% of pregnancies where

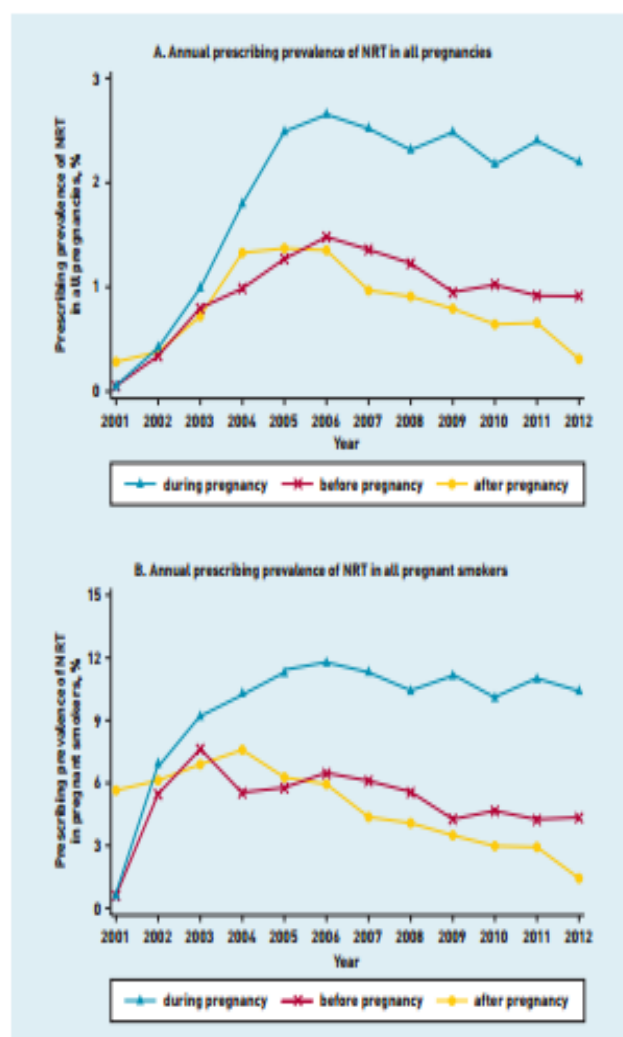


Figure 2. Annual prescribing prevalence of NRT between 2001 and 2012.

NRT was prescribed. The distribution of NRT forms prescribed before and after pregnancy was very similar.

#### Annual prescribing of NRT before, during, and after pregnancy

Figure 2 shows the proportion of pregnancies between 2001 and 2012 in which NRT was prescribed before, during, and after pregnancy. In 2001, the prescribing prevalence of NRT in all pregnancies during gestation was 0.03% (0.7% of pregnancies among smokers). This increased to 2.6% (11.4% among smokers) in 2005, after which it remained stable. The proportion of pregnancies with NRT prescriptions issued in the 9 months before and after pregnancy increased until 2004, after which it remained stable at around 1% (6% among smokers) with a gradual decline in prescribing prevalence after 2006.

#### Prescribing of NRT by maternal characteristics

Table 2 shows the maternal characteristics associated with prescribing in pregnant smokers between 2006 and 2012. Prescribing was higher in older compared with younger age groups (OR for 40–44 years = 1.27, 95% CI = 1.03 to 1.58, compared with the 25–29-year age group). Pregnant smokers from more socioeconomically deprived groups were more likely to receive prescriptions compared with less deprived groups (OR for quintile 5 compared with quintile 1 = 1.29, 95% CI = 1.15 to 1.45). Pregnant smokers with a diagnosis of asthma or mental illness were 33% more likely to be prescribed compared with pregnant smokers without these morbidities.

#### DISCUSSION

##### Summary

After NRT was made available on NHS prescription in 2001, prescribing in and around pregnancy increased; by 2005 prescribing was twice as high during pregnancy as in the 9 months immediately before and after pregnancy, despite being contraindicated for pregnant females. The December 2005 licence relaxation to allow prescribing in pregnancy did not further increase these trends and the prescribing prevalence during pregnancy has remained stable at 2% (11% in smokers). Females with asthma or mental illnesses and those from more socioeconomically-deprived areas were more likely to receive prescriptions during pregnancy. Eighty per cent of females received  $\leq 2$  prescriptions.

##### Strengths and limitations

Using a large population-based data source, longitudinal and contemporaneous prescribing estimates are presented; this is the first study of NRT prescribing during pregnancy in the UK and the only study internationally that has assessed prescribing trends. Ascertainment of NRT use is based on prescribing data rather than self-reported NRT use, which females may under-report.<sup>11</sup> Prescribing in 9-month periods immediately before and after pregnancy was also assessed, whereas other studies only report NRT use in trimesters one and two.<sup>14,17</sup> Therefore, the present estimates of NRT prescribing around pregnancy are novel in providing population-level information on smoking cessation attempts pre-conception and postpartum for the first time.

The present study data capture all NRT prescribing to pregnant females in UK primary care in practices registered

**Table 2. Prescribing of NRT in pregnant smokers by maternal characteristics between January 2006 and December 2012**

Demographic variables	Pregnancies among smokers with one or more NRT prescriptions, n = 5756, n (%)	Unadjusted odds ratio (95% CI)	P-value	Adjusted odds ratio (95% CI)*	P-value
<b>Age at conception, years</b>					
15–19	721 (9.9)	0.92 (0.84 to 1.01)		0.93 (0.84 to 1.03)	
20–24	1533 (10.2)	0.94 (0.88 to 1.02)	<0.001	0.93 (0.86 to 1.00)	<0.001
25–29	1537 (10.7)	1.00		1.00	
30–34	1222 (11.9)	1.12 (1.04 to 1.22)		1.13 (1.04 to 1.23)	
35–39	616 (12.2)	1.16 (1.05 to 1.28)		1.17 (1.05 to 1.30)	
40–44	122 (13.3)	1.28 (1.05 to 1.56)		1.27 (1.03 to 1.58)	
45–49	5 (10.9)	1.01 (0.40 to 2.58)		1.12 (0.43 to 2.94)	
<b>Townsend score</b>					
Quintile 1 (least deprived)	505 (9.2)	1.00		1.00	
Quintile 2	696 (10.1)	1.10 (0.98 to 1.25)	<0.001*	1.09 (0.96 to 1.24)	<0.001*
Quintile 3	1101 (10.3)	1.14 (1.01 to 1.27)		1.19 (1.05 to 1.34)	
Quintile 4	1405 (11.8)	1.35 (1.19 to 1.48)		1.37 (1.22 to 1.54)	
Quintile 5 (most deprived)	1428 (11.3)	1.25 (1.13 to 1.39)		1.29 (1.15 to 1.45)	
Missing	421 (11.4)	1.27 (1.10 to 1.45)		1.33 (1.15 to 1.54)	
<b>Pre-conception body mass index, kg/m<sup>2</sup></b>					
Underweight	206 (11.0)	1.12 (0.96 to 1.30)			
Normal	1786 (10.4)	1.00	0.614	-	-
Overweight	976 (11.2)	1.06 (0.97 to 1.14)			
Obese	806 (11.1)	1.06 (0.96 to 1.15)			
Missing	1982 (10.8)	1.02 (0.95 to 1.09)			
<b>Diabetes</b>	193 (13.2)	1.26 (1.08 to 1.47)	0.075	-	-
<b>Hypertension</b>	114 (11.3)	1.04 (0.86 to 1.27)	0.660	-	-
<b>Asthma</b>	845 (13.8)	1.36 (1.26 to 1.48)	<0.001	1.33 (1.22 to 1.45)	<0.001
<b>Mental illness</b>	1181 (13.7)	1.38 (1.29 to 1.48)	<0.001	1.33 (1.23 to 1.44)	<0.001

NRT = nicotine replacement therapy. \*Percentages of pregnancies in smokers with NRT prescription. All covariates mutually adjusted. P-value for trend.

in THIN. These data may not include NRT prescribing in other settings such as local NHS Stop Smoking Services for Pregnant females (SSSP) and NRT purchased in pharmacies or retailers. A survey of all SSSPs in England conducted between April 2010 and March 2011 reported that almost half of the NRT provided by these services was issued through GPs.<sup>48</sup> In terms of self-purchased NRT, the authors believe this will be infrequent for several reasons. Firstly, the prevalence of medication use without health professional consultation is lower during pregnancy than when females are not pregnant.<sup>41</sup> Furthermore, all packages of NRT clearly instruct females to consult a doctor before using them if they are pregnant. Lastly, in the UK females are entitled to free NHS prescriptions during pregnancy,<sup>49</sup> so they are more likely to get free prescriptions through GPs than paying for NRT. Hence, the authors believe that this study captures most prescriptions of NRT issued and provides valuable information on prescribing patterns during pregnancy.

Potential changes in smoking habits were not accounted for over the study, and therefore this study has also presented proportions for all pregnancies. Some females may quit or relapse after delivery consequently leading to changes in the baseline smokers; NRT estimates could therefore be overestimated if more females relapse than are recorded, and underestimated if more females quit. In the present data, however, over 75% of pregnant females who were classified as smokers during pregnancy and who had a recording of smoking status within the 9 months after delivery were still recorded as smokers. Therefore, a substantial overestimation or underestimation is unlikely.

#### Comparison with existing literature

The present study data suggest that UK prescribing of NRT during pregnancy increased between 2001 and 2005, after which it plateaued. Despite NRT use being recommended in smoking cessation guidelines for pregnant females in several



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### Ethical approval

Ethical approval for this study was obtained from the THIN Scientific Review Committee (reference number 11-047).

### Provenance

Freely submitted; externally peer reviewed.

### Competing interests

Tim Coleman was paid to attend a symposium arranged by Pierre Fabre Laboratories, France in 2012. The other authors have declared no competing interests.

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countries,<sup>14,15</sup> no other studies thus far have assessed the annual prescribing prevalence of NRT during pregnancy for comparison. Studies from the US, Denmark, and Scotland report an overall prescribing prevalence of between 0.3% and 4%.<sup>1,10,11</sup> NRT use in pregnant smokers attending English SSSs is reported to be 85%<sup>10</sup> and considering that only 3% of pregnant females attend these services, this equates to 2.5%, which is similar to the present findings.

The National Institute for Health and Care Excellence (NICE) recommends that pregnant females should initially be prescribed 2 weeks of NRT from their agreed stop date with further NRT after re-assessment.<sup>7</sup> The average duration of prescription for females in the present study was 2 weeks and most females (80%) received two or fewer prescriptions. One reason for this may be that compliance was low and females did not quit or use it to quit, in which case no further NRT was prescribed. Some females may have bought NRT independently after the first prescription; however, considering that females are entitled to free prescriptions during pregnancy and NRT from retailers is reasonably expensive, this is unlikely. Studies in other populations have not reported the duration of NRT use in pregnancy. However, 8–12 weeks' use is recommended for optimal effectiveness in the general population,<sup>4</sup> so it is unlikely that 2 weeks' use is effective for smoking cessation in pregnancy.

A study including 5716 pregnant females from the US showed NRT prescribing to be lower in pregnant smokers aged <35 years compared with pregnant smokers aged ≥35 years,<sup>3</sup> which is similar to the present findings. Low socioeconomic status is associated with a higher prevalence of chronic disease<sup>16</sup> and higher risk of adverse pregnancy outcomes,<sup>15</sup> which could explain why pregnant smokers in the deprived group in this study were prescribed NRT more often than affluent groups. Asthma and mental illness are the most common medical conditions encountered during pregnancy,<sup>14,17</sup> and are closely related to smoking, which may explain the significant association with NRT prescribing compared

with other conditions.

The English SSSPs study reported that 55% of all pregnant smokers (65% of pregnant NRT users) used combination NRT,<sup>10</sup> which is high compared with the present estimate of 14%. This is mostly likely related to different baseline populations. Females voluntarily attending these specialist services likely have a higher motivation to quit, which may result in more quit attempts and more NRT being prescribed compared with females attending primary care.

It is unfortunate that NRT prescribing prevalence outside pregnancy began to decline considering the demonstrated effectiveness of NRT,<sup>18</sup> however, this may be related to the licensing of varenicline for smoking cessation in the non-pregnant population in December 2006, after which a reduction in NRT and bupropion prescribing was seen in the general population.<sup>19</sup>

### Implications for practice

Pregnancy offers a strategic opportunity for health professionals to promote smoking cessation as females are generally more receptive to cessation interventions and are more likely to attempt to quit smoking because of the potential foetal harm associated with smoking during pregnancy.<sup>20</sup> The study findings give insight into the prescribing in and around pregnancy, which is important for policy makers and GPs to monitor and promote smoking cessation in females of childbearing age. The study shows that NRT was prescribed for an average of only 2 weeks during pregnancy, which is unlikely to be effective considering that NRT use in the general population for smoking cessation is recommended for at least 8–12 weeks. It is also highlighted that only 1% of smokers who are not yet pregnant receive NRT, which indicates missed opportunities to assist young females to quit, despite the reported effectiveness of NRT outside pregnancy. Although interactions between health professionals and females during pregnancy should be used to discuss and offer interventions to promote smoking cessation, greater potential benefit would result from starting before pregnancy which should be a prioritised focus for females and healthcare providers.

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## 10.5 MEDICAL READ CODES FOR SMOKING

Medcode	Description
137L.00	Current non-smoker
1371.11	Non-smoker
63C5.00	Maternal tobacco abuse
137a.00	Pipe tobacco consumption
137..00	Tobacco consumption
137X.00	Cigarette consumption
6893.00	Tobacco usage screen
68T..00	Tobacco usage screen
137Y.00	Cigar consumption
137Z.00	Tobacco consumption NOS
ZV4K000	[V]Tobacco use
745H000	Nicotine replacement therapy using nicotine patches
8H7i.00	Referral to smoking cessation advisor
6791.00	Health ed. - smoking
E251.00	Tobacco dependence
137Q.00	Smoking started
137H.00	Pipe smoker
137M.00	Rolls own cigarettes
1372.11	Occasional smoker
137h.00	Minutes from waking to first tobacco consumption
137c.00	Thinking about stopping smoking
E251200	Tobacco dependence, episodic
137d.00	Not interested in stopping smoking
E251z00	Tobacco dependence NOS
745H100	Nicotine replacement therapy using nicotine gum
1374.00	Moderate smoker - 10-19 cigs/d
8HTK.00	Referral to stop-smoking clinic
9007.00	Stop smoking monitor verb.inv.
137f.00	Reason for restarting smoking
ZRBm211	FTND - Fagerstrom test for nicotine dependence
8I39.00	Nicotine replacement therapy refused
137b.00	Ready to stop smoking
137e.00	Smoking restarted
745Hy00	Other specified smoking cessation therapy
8CAg.00	Smoking cessation advice provided by community pharmacist
1373.00	Light smoker - 1-9 cigs/day
13p5.00	Smoking cessation programme start date
38DH.00	Fagerstr test for nicotine dep
E251000	Tobacco dependence, unspecified

8B3Y.00	Over the counter nicotine replacement therapy
745H200	Nicotine replacement therapy using nicotine inhalator
137J.00	Cigar smoker
67A3.00	Pregnancy smoking advice
137R.00	Current smoker
ZV6D800	[V]Tobacco abuse counselling
8BP3.00	Nicotine replacement therapy provided by community pharmacis
E251100	Tobacco dependence, continuous
8B3f.00	Nicotine replacement therapy provided free
8B2B.00	Nicotine replacement therapy
8I2I.00	Nicotine replacement therapy contraindicated
13p0.00	Negotiated date for cessation of smoking
ZRaM.11	MFS - Motives for smoking scale
8HkQ.00	Referral to NHS stop smoking service
ZRaO.11	OFS - Occasions for smoking scale
67H6.00	Brief intervention for smoking cessation
JRaO.00	Occasions for smoking scale
8CAL.00	Smoking cessation advice
137..11	Smoker - amount smoked
137P.11	Smoker
ZRBm200	Fagerstrom test for nicotine dependence
137V.00	Smoking reduced
137C.00	Keeps trying to stop smoking
13p5000	Practice based smoking cessation programme start date
ZRh4.00	Reasons for smoking scale
1372.00	Trivial smoker - < 1 cig/day
8IAj.00	Smoking cessation advice declined
745H300	Nicotine replacement therapy using nicotine lozenges
137m.00	Failed attempt to stop smoking
1376.00	Very heavy smoker - 40+cigs/d
137Q.11	Smoking restarted
137P.00	Cigarette smoker
ZRaM.00	Motives for smoking scale
ZG23300	Advice on smoking
9008.00	Stop smoking monitor phone inv
ZRh4.11	RFS - Reasons for smoking scale
137G.00	Trying to give up smoking
67H1.00	Lifestyle advice regarding smoking
745H400	Smoking cessation drug therapy
1375.00	Heavy smoker - 20-39 cigs/day
ZRaO.00	Occasions for smoking scale
E251300	Tobacco dependence in remission
1378.00	Ex-light smoker (1-9/day)
137A.00	Ex-heavy smoker (20-39/day)

137S.00	Ex smoker
137I.00	Ex roll-up cigarette smoker
137j.00	Ex-cigarette smoker
1379.00	Ex-moderate smoker (10-19/day)
137N.00	Ex pipe smoker
137B.00	Ex-very heavy smoker (40+/day)
137K.00	Stopped smoking
1377.00	Ex-trivial smoker (<1/day)
137T.00	Date ceased smoking
137F.00	Ex-smoker - amount unknown
137K000	Recently stopped smoking
137O.00	Ex cigar smoker
1371.00	Never smoked tobacco
13p4.00	Smoking free weeks
9N4M.00	DNA - Did not attend smoking cessation clinic
9005.00	Stop smoking monitor 2nd lettr
13p2.00	Smoking status between 4 and 52 weeks
9003.00	Stop smoking monitor default
900A.00	Stop smoking monitor.chck done
900..12	Stop smoking monitoring admin.
E023.00	Nicotine withdrawal
ZV11600	[V]Personal history of tobacco abuse
13p6.00	Carbon monoxide reading at 4 weeks
900Z.00	Stop smoking monitor admin.NOS
13p..00	Smoking cessation milestones
137g.00	Cigarette pack-years
900..11	Stop smoking clinic admin.
9001.00	Attends stop smoking monitor.
13p3.00	Smoking status at 52 weeks
9N2k.00	Seen by smoking cessation advisor
9006.00	Stop smoking monitor 3rd lettr
9002.00	Refuses stop smoking monitor
900..00	Anti-smoking monitoring admin.
4I90.00	Expired carbon monoxide concentration
8HBM.00	Stop smoking face to face follow-up
745H.00	Smoking cessation therapy
745Hz00	Smoking cessation therapy NOS
137D.00	Admitted tobacco cons untrue ?
13p1.00	Smoking status at 4 weeks
9004.00	Stop smoking monitor 1st lettr
137E.00	Tobacco consumption unknown
9009.00	Stop smoking monitoring delete

## 10.6 MULTILEX DRUG CODES FOR SMOKING CESSATION MEDICATIONS

Drugcode	Generic name
92309998	BUPROPION mr tab 150mg
92311998	BUPROPION mr tab 150mg
93447992	NICONIL
96930992	NICONIL PATCH 15 MG
96924992	NICONIL PATCH 30 MG
83326998	NICOTINE BITARTRATE sf loz 1mg
82527998	NICOTINE BITARTRATE sf loz 1mg
87922998	NICOTINE BITARTRATE sf loz 2mg
82526998	NICOTINE BITARTRATE sf loz 2mg
82603998	NICOTINE BITARTRATE sublingual tab 2mg
82604998	NICOTINE BITARTRATE sublingual tab 2mg
96845992	NICOTINE TRANSDERMAL PATCH 20CM
96844992	NICOTINE TRANSDERMAL PATCH 30CM
82473998	NICOTINE chewing gum 2mg
82506998	NICOTINE chewing gum 2mg
89112998	NICOTINE chewing gum 2mg
82502998	NICOTINE chewing gum 2mg
82475998	NICOTINE chewing gum 2mg
95727998	NICOTINE chewing gum 2mg
82504998	NICOTINE chewing gum 2mg
98904998	NICOTINE chewing gum 2mg
82476998	NICOTINE chewing gum 2mg
82503998	NICOTINE chewing gum 2mg
91248998	NICOTINE chewing gum 2mg
82505998	NICOTINE chewing gum 2mg
82474998	NICOTINE chewing gum 2mg
82498998	NICOTINE chewing gum 4mg
82472998	NICOTINE chewing gum 4mg
82469998	NICOTINE chewing gum 4mg
82499998	NICOTINE chewing gum 4mg
82497998	NICOTINE chewing gum 4mg
95727997	NICOTINE chewing gum 4mg
91248997	NICOTINE chewing gum 4mg
82496998	NICOTINE chewing gum 4mg
98904997	NICOTINE chewing gum 4mg
82470998	NICOTINE chewing gum 4mg
82471998	NICOTINE chewing gum 4mg
89110998	NICOTINE chewing gum 4mg
82501998	NICOTINE chewing gum 4mg



88291998	NICOTINE inh cartridge 10mg
88288998	NICOTINE inh cartridge 10mg
89863998	NICOTINE loz 0.35mg
92840997	NICOTINE loz 0.35mg
92840998	NICOTINE mint flav chew gum 2mg
92841998	NICOTINE mint flav chew gum 2mg
95727996	NICOTINE mint flav chew gum 4mg
98904996	NICOTINE mint flav chew gum 4mg
82490998	NICOTINE nasal spray 10mg/ml
92657998	NICOTINE nasal spray 10mg/ml
92836998	NICOTINE nasal spray 10mg/ml
83272998	NICOTINE patch 10mg
97739997	NICOTINE patch 10mg
82494998	NICOTINE patch 10mg
97763997	NICOTINE patch 10mg
98581997	NICOTINE patch 11mg/24 hr
92892997	NICOTINE patch 11mg/24 hr
97673997	NICOTINE patch 14mg
82510998	NICOTINE patch 14mg
82771998	NICOTINE patch 14mg
88005997	NICOTINE patch 14mg
82509998	NICOTINE patch 14mg
97737997	NICOTINE patch 14mg
97740997	NICOTINE patch 14mg
84468998	NICOTINE patch 14mg
97763996	NICOTINE patch 15mg
83271998	NICOTINE patch 15mg
82492998	NICOTINE patch 15mg
97739996	NICOTINE patch 15mg
82770998	NICOTINE patch 21mg
97737996	NICOTINE patch 21mg
84466998	NICOTINE patch 21mg
88005996	NICOTINE patch 21mg
82508998	NICOTINE patch 21mg
82507998	NICOTINE patch 21mg
97673996	NICOTINE patch 21mg
97740996	NICOTINE patch 21mg
98581998	NICOTINE patch 22mg/24 hr
92892998	NICOTINE patch 22mg/24 hr
83270998	NICOTINE patch 25mg
83273998	NICOTINE patch 25mg
97763998	NICOTINE patch 5mg
97739998	NICOTINE patch 5mg
82495998	NICOTINE patch 5mg

82723998	NICOTINE patch 7mg
97673998	NICOTINE patch 7mg
97740998	NICOTINE patch 7mg
82511998	NICOTINE patch 7mg
84469998	NICOTINE patch 7mg
97737998	NICOTINE patch 7mg
82512998	NICOTINE patch 7mg
88005998	NICOTINE patch 7mg
82429998	NICOTINE patch+gum 15mg + 2mg
82428998	NICOTINE patch+gum 15mg + 2mg
84442998	NICOTINE sf loz 1.5mg
84443998	NICOTINE sf loz 1.5mg
81928998	NICOTINE sf loz 1.5mg
82707998	NICOTINE sf loz 1.5mg
91248996	NICOTINE sf loz 1mg
98430998	NICOTINE sf loz 1mg
91162998	NICOTINE sf loz 2mg
92889990	NICOTINE sf loz 2mg
87920998	NICOTINE sf loz 2mg
91384998	NICOTINE sf loz 2mg
83301998	NICOTINE sf loz 4mg
82706998	NICOTINE sf loz 4mg
87919998	NICOTINE sf loz 4mg
92888990	NICOTINE sf loz 4mg
98082998	NICOTINE sf loz 4mg
91848998	NICOTINE sf loz 4mg
92840996	NICOTINE sublingual tab 2mg
82500998	NICOTINE sublingual tab 2mg
92841997	NICOTINE sublingual tab 2mg
85397998	VARENICLINE tabs 1mg
85400998	VARENICLINE tabs 1mg
85401998	VARENICLINE tabs 500 micrograms
85398998	VARENICLINE tabs 500 micrograms
85403998	VARENICLINE tabs 500micrograms + 1mg
85399998	VARENICLINE tabs 500micrograms + 1mg

## 10.7 AHD CODES FOR SMOKING

Ahd code	Description
1003040000	Smoking
1064100000	Advice given

## 10.8 CODE LISTS FOR

### COMORBIDITIES

#### 10.8.1 Medical READ codes for

#### Diabetes Mellitus

Medcode	Description
C101000	Diabetes mellitus, juvenile type, with ketoacidosis
C108311	Type I diabetes mellitus with multiple complications
C108600	Insulin dependent diabetes mellitus with gangrene
C10E311	Type I diabetes mellitus with multiple complications
C108112	Type 1 diabetes mellitus with ophthalmic complications
C108300	Insulin dependent diabetes mellitus with multiple complicatn
C108F11	Type I diabetes mellitus with diabetic cataract
C108E00	Insulin dependent diabetes mellitus with hypoglycaemic coma
C108012	Type 1 diabetes mellitus with renal complications
C10EJ11	Type I diabetes mellitus with neuropathic arthropathy
C108912	Type 1 diabetes mellitus maturity onset
C10E800	Type 1 diabetes mellitus - poor control
C10EM00	Type 1 diabetes mellitus with ketoacidosis
C10E700	Type 1 diabetes mellitus with retinopathy
C108D00	Insulin dependent diabetes mellitus with nephropathy
C10EH00	Type 1 diabetes mellitus with arthropathy
C10EA00	Type 1 diabetes mellitus without complication
C107000	Diabetes mellitus, juvenile +peripheral circulatory disorder
C101y00	Other specified diabetes mellitus with ketoacidosis
C100011	Insulin dependent diabetes mellitus
C108.00	Insulin dependent diabetes mellitus
C108F12	Type 1 diabetes mellitus with diabetic cataract
C10EA12	Insulin-dependent diabetes without complication
C10EB11	Type I diabetes mellitus with mononeuropathy
C10EP11	Type I diabetes mellitus with exudative maculopathy
C108512	Type 1 diabetes mellitus with ulcer
C108D12	Type 1 diabetes mellitus with nephropathy
C101.00	Diabetes mellitus with ketoacidosis
C108C12	Type 1 diabetes mellitus with polyneuropathy
C102.00	Diabetes mellitus with hyperosmolar coma
C10C.00	Diabetes mellitus autosomal dominant
C10E712	Insulin dependent diabetes mellitus with retinopathy

C10E612	Insulin dependent diabetes mellitus with gangrene
C108100	Insulin-dependent diabetes mellitus with ophthalmic comps
C108312	Type 1 diabetes mellitus with multiple complications
C108411	Unstable type I diabetes mellitus
C108.13	Type I diabetes mellitus
C10ED11	Type I diabetes mellitus with nephropathy
C108111	Type I diabetes mellitus with ophthalmic complications
C108712	Type 1 diabetes mellitus with retinopathy
C108F00	Insulin dependent diabetes mellitus with diabetic cataract
C108H12	Type 1 diabetes mellitus with arthropathy
C108A11	Type I diabetes mellitus without complication
C108000	Insulin-dependent diabetes mellitus with renal complications
C108B00	Insulin dependent diabetes mellitus with mononeuropathy
C108C00	Insulin dependent diabetes mellitus with polyneuropathy
C108C11	Type I diabetes mellitus with polyneuropathy
K081.00	Nephrogenic diabetes insipidus
C10E211	Type I diabetes mellitus with neurological complications
C10EP00	Type 1 diabetes mellitus with exudative maculopathy
C10EK11	Type I diabetes mellitus with persistent proteinuria
C10EC00	Type 1 diabetes mellitus with polyneuropathy
C10E412	Unstable insulin dependent diabetes mellitus
C10EN11	Type I diabetes mellitus with ketoacidotic coma
C10EB12	Insulin dependent diabetes mellitus with mononeuropathy
C10E212	Insulin-dependent diabetes mellitus with neurological comps
C108812	Type 1 diabetes mellitus - poor control
C108G11	Type I diabetes mellitus with peripheral angiopathy
C10EE00	Type 1 diabetes mellitus with hypoglycaemic coma
C108J12	Type 1 diabetes mellitus with neuropathic arthropathy
C10E511	Type I diabetes mellitus with ulcer
C10E.12	Insulin dependent diabetes mellitus
C108500	Insulin dependent diabetes mellitus with ulcer
C108E12	Type 1 diabetes mellitus with hypoglycaemic coma
C108212	Type 1 diabetes mellitus with neurological complications
C10EC12	Insulin dependent diabetes mellitus with polyneuropathy
C108911	Type I diabetes mellitus maturity onset
C108B12	Type 1 diabetes mellitus with mononeuropathy
C108E11	Type I diabetes mellitus with hypoglycaemic coma
C10E300	Type 1 diabetes mellitus with multiple complications
C10E600	Type 1 diabetes mellitus with gangrene
C108700	Insulin dependent diabetes mellitus with retinopathy

C10z000	Diabetes mellitus, juvenile type, + unspecified complication	C10EE11	Type I diabetes mellitus with hypoglycaemic coma
C108800	Insulin dependent diabetes mellitus - poor control	C108G12	Type 1 diabetes mellitus with peripheral angiopathy
C10E200	Type 1 diabetes mellitus with neurological complications	C10EF12	Insulin dependent diabetes mellitus with diabetic cataract
C10E112	Insulin-dependent diabetes mellitus with ophthalmic comps	C10ED00	Type 1 diabetes mellitus with nephropathy
C108900	Insulin dependent diabetes maturity onset	C10EL11	Type I diabetes mellitus with persistent microalbuminuria
C10E011	Type I diabetes mellitus with renal complications	C10EC11	Type I diabetes mellitus with polyneuropathy
ZRbH.00	Perceived control of insulin-dependent diabetes	C104000	Diabetes mellitus, juvenile type, with renal manifestation
C10EH12	Insulin dependent diabetes mellitus with arthropathy	C10ED12	Insulin dependent diabetes mellitus with nephropathy
C10E400	Unstable type 1 diabetes mellitus	C10E411	Unstable type I diabetes mellitus
C10E.11	Type I diabetes mellitus	C108611	Type I diabetes mellitus with gangrene
C10E611	Type I diabetes mellitus with gangrene	C10E711	Type I diabetes mellitus with retinopathy
ZC2C900	Dietary advice for type I diabetes	C10EB00	Type 1 diabetes mellitus with mononeuropathy
C108200	Insulin-dependent diabetes mellitus with neurological comps	C10EH11	Type I diabetes mellitus with arthropathy
C10E812	Insulin dependent diabetes mellitus - poor control	C10EG11	Type I diabetes mellitus with peripheral angiopathy
C108D11	Type I diabetes mellitus with nephropathy	C10G000	Secondary pancreatic diabetes mellitus without complication
C10EK00	Type 1 diabetes mellitus with persistent proteinuria	66An.00	Diabetes type 1 review
C108H00	Insulin dependent diabetes mellitus with arthropathy	C10E312	Insulin dependent diabetes mellitus with multiple complicat
C108811	Type I diabetes mellitus - poor control	C10EF00	Type 1 diabetes mellitus with diabetic cataract
C10EQ00	Type 1 diabetes mellitus with gastroparesis	C108.12	Type 1 diabetes mellitus
C10E111	Type I diabetes mellitus with ophthalmic complications	C10G.00	Secondary pancreatic diabetes mellitus
C10EL00	Type 1 diabetes mellitus with persistent microalbuminuria	C10EJ00	Type 1 diabetes mellitus with neuropathic arthropathy
C10EE12	Insulin dependent diabetes mellitus with hypoglycaemic coma	C10E512	Insulin dependent diabetes mellitus with ulcer
C108211	Type I diabetes mellitus with neurological complications	C108H11	Type I diabetes mellitus with arthropathy
C108.11	IDDM-Insulin dependent diabetes mellitus	C108400	Unstable insulin dependent diabetes mellitus
C10E100	Type 1 diabetes mellitus with ophthalmic complications	C10EM11	Type I diabetes mellitus with ketoacidosis
C108A12	Type 1 diabetes mellitus without complication	C10EN00	Type 1 diabetes mellitus with ketoacidotic coma
C10E012	Insulin-dependent diabetes mellitus with renal complications	C10E.00	Type 1 diabetes mellitus
C106000	Diabetes mellitus, juvenile, + neurological manifestation	C105000	Diabetes mellitus, juvenile type, + ophthalmic manifestation
C10FS00	Maternally inherited diabetes mellitus	C101z00	Diabetes mellitus NOS with ketoacidosis
C10E911	Type I diabetes mellitus maturity onset	C10y000	Diabetes mellitus, juvenile, + other specified manifestation
C108711	Type I diabetes mellitus with retinopathy	C10EG00	Type 1 diabetes mellitus with peripheral angiopathy
C108J11	Type I diabetes mellitus with neuropathic arthropathy	C10E900	Type 1 diabetes mellitus maturity onset
C108511	Type I diabetes mellitus with ulcer	C108412	Unstable type 1 diabetes mellitus
C101100	Diabetes mellitus, adult onset, with ketoacidosis	C108B11	Type I diabetes mellitus with mononeuropathy
C10EA11	Type I diabetes mellitus without complication	ZC2C911	Diet advice for insulin-dependent diabetes
C10E811	Type I diabetes mellitus - poor control	C108A00	Insulin-dependent diabetes without complication
C108011	Type I diabetes mellitus with renal complications	C10E500	Type 1 diabetes mellitus with ulcer
C10E912	Insulin dependent diabetes maturity onset	C108612	Type 1 diabetes mellitus with gangrene
C10E000	Type 1 diabetes mellitus with renal complications	C102000	Diabetes mellitus, juvenile type, with hyperosmolar coma
C10EF11	Type I diabetes mellitus with diabetic cataract	C109700	Non-insulin dependent diabetes mellitus - poor control
		C109300	Non-insulin-dependent diabetes mellitus with multiple comps

C10FF11	Type II diabetes mellitus with peripheral angiopathy	C107200	Diabetes mellitus, adult with gangrene
C104100	Diabetes mellitus, adult onset, with renal manifestation	C109400	Non-insulin dependent diabetes mellitus with ulcer
C109E11	Type II diabetes mellitus with diabetic cataract	C109F12	Type 2 diabetes mellitus with peripheral angiopathy
C109111	Type II diabetes mellitus with ophthalmic complications	C10C.11	Maturity onset diabetes in youth
C109411	Type II diabetes mellitus with ulcer	C109J00	Insulin treated Type 2 diabetes mellitus
C109E12	Type 2 diabetes mellitus with diabetic cataract	C109.11	NIDDM - Non-insulin dependent diabetes mellitus
C10ER00	Latent autoimmune diabetes mellitus in adult	C109E00	Non-insulin depend diabetes mellitus with diabetic cataract
C10F111	Type II diabetes mellitus with ophthalmic complications	C109511	Type II diabetes mellitus with gangrene
C109312	Type 2 diabetes mellitus with multiple complications	C10FK00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus
C10F611	Type II diabetes mellitus with retinopathy	C10FF00	Type 2 diabetes mellitus with peripheral angiopathy
C10F211	Type II diabetes mellitus with neurological complications	C109.13	Type II diabetes mellitus
C10FP00	Type 2 diabetes mellitus with ketoacidotic coma	C109600	Non-insulin-dependent diabetes mellitus with retinopathy
C109H11	Type II diabetes mellitus with neuropathic arthropathy	C109G00	Non-insulin dependent diabetes mellitus with arthropathy
C109C11	Type II diabetes mellitus with nephropathy	C109012	Type 2 diabetes mellitus with renal complications
C109900	Non-insulin-dependent diabetes mellitus without complication	C10F911	Type II diabetes mellitus without complication
ZC2CA11	Dietary advice non-insulin-dependent diabetes	C107100	Diabetes mellitus, adult, + peripheral circulatory disorder
C105100	Diabetes mellitus, adult onset, + ophthalmic manifestation	C109D00	Non-insulin dependent diabetes mellitus with hypoglyca coma
C109C00	Non-insulin dependent diabetes mellitus with nephropathy	C109000	Non-insulin-dependent diabetes mellitus with renal comps
C10F600	Type 2 diabetes mellitus with retinopathy	C10F500	Type 2 diabetes mellitus with gangrene
C109A11	Type II diabetes mellitus with mononeuropathy	66Ao.00	Diabetes type 2 review
C10F011	Type II diabetes mellitus with renal complications	C109D12	Type 2 diabetes mellitus with hypoglycaemic coma
C100112	Non-insulin dependent diabetes mellitus	C109412	Type 2 diabetes mellitus with ulcer
C109200	Non-insulin-dependent diabetes mellitus with neuro comps	C10FQ11	Type II diabetes mellitus with exudative maculopathy
C10FQ00	Type 2 diabetes mellitus with exudative maculopathy	C10FG11	Type II diabetes mellitus with arthropathy
C10F400	Type 2 diabetes mellitus with ulcer	C10F900	Type 2 diabetes mellitus without complication
C10FL11	Type II diabetes mellitus with persistent proteinuria	C109.12	Type 2 diabetes mellitus
C109712	Type 2 diabetes mellitus - poor control	C109.00	Non-insulin dependent diabetes mellitus
C109B00	Non-insulin dependent diabetes mellitus with polyneuropathy	C10FN00	Type 2 diabetes mellitus with ketoacidosis
C10FE11	Type II diabetes mellitus with diabetic cataract	C10FH00	Type 2 diabetes mellitus with neuropathic arthropathy
C109100	Non-insulin-dependent diabetes mellitus with ophthalm comps	C109G11	Type II diabetes mellitus with arthropathy
C109112	Type 2 diabetes mellitus with ophthalmic complications	C109500	Non-insulin dependent diabetes mellitus with gangrene
C10F100	Type 2 diabetes mellitus with ophthalmic complications	C10FC00	Type 2 diabetes mellitus with nephropathy
C10FG00	Type 2 diabetes mellitus with arthropathy	C10F.11	Type II diabetes mellitus
C100111	Maturity onset diabetes	C10F711	Type II diabetes mellitus - poor control
C10FM11	Type II diabetes mellitus with persistent microalbuminuria	C10F300	Type 2 diabetes mellitus with multiple complications
C10FR00	Type 2 diabetes mellitus with gastroparesis	C10FE00	Type 2 diabetes mellitus with diabetic cataract
C109212	Type 2 diabetes mellitus with neurological complications	C10F311	Type II diabetes mellitus with multiple complications
C109612	Type 2 diabetes mellitus with retinopathy	C106100	Diabetes mellitus, adult onset, + neurological manifestation
C10F511	Type II diabetes mellitus with gangrene	C10D.11	Maturity onset diabetes in youth type 2
C109G12	Type 2 diabetes mellitus with arthropathy	C10z100	Diabetes mellitus, adult onset, + unspecified complication
		C109J11	Insulin treated non-insulin dependent diabetes mellitus

C109J12	Insulin treated Type II diabetes mellitus	C10FP11	Type II diabetes mellitus with ketoacidotic coma
C10F000	Type 2 diabetes mellitus with renal complications	C106.13	Diabetes mellitus with polyneuropathy
ZC2CA00	Dietary advice for type II diabetes	C10N000	Secondary diabetes mellitus without complication
C10y100	Diabetes mellitus, adult, + other specified manifestation	C100.00	Diabetes mellitus with no mention of complication
C109211	Type II diabetes mellitus with neurological complications	C107z00	Diabetes mellitus NOS with peripheral circulatory disorder
C109C12	Type 2 diabetes mellitus with nephropathy	C10zz00	Diabetes mellitus NOS with unspecified complication
C10FM00	Type 2 diabetes mellitus with persistent microalbuminuria	2G5C.00	Foot abnormality - diabetes related
C109F11	Type II diabetes mellitus with peripheral angiopathy	66AJ100	Brittle diabetes
C109912	Type 2 diabetes mellitus without complication	8I84.00	Did not complete XPERT diabetes structured education program
C10C.12	Maturity onset diabetes in youth type 1	L180100	Diabetes mellitus during pregnancy - baby delivered
C10D.00	Diabetes mellitus autosomal dominant type 2	9OLL.00	XPERT diabetes structured education programme completed
C109512	Type 2 diabetes mellitus with gangrene	66AQ.00	Diabetes: shared care programme
C109A00	Non-insulin dependent diabetes mellitus with mononeuropathy	C350011	Bronzed diabetes
C109611	Type II diabetes mellitus with retinopathy	C10N100	Cystic fibrosis related diabetes mellitus
C10FN11	Type II diabetes mellitus with ketoacidosis	9NM0.00	Attending diabetes clinic
C109B12	Type 2 diabetes mellitus with polyneuropathy	C103000	Diabetes mellitus, juvenile type, with ketoacidotic coma
C109H12	Type 2 diabetes mellitus with neuropathic arthropathy	2G51100	Foot abnormality - non-diabetes
C10FH11	Type II diabetes mellitus with neuropathic arthropathy	2G5D.00	Foot abnormality - non-diabetes
C109911	Type II diabetes mellitus without complication	9OLZ.00	Diabetes monitoring admin.NOS
C10FD11	Type II diabetes mellitus with hypoglycaemic coma	L180200	Diabetes mellitus in puerperium - baby delivered
C10FA11	Type II diabetes mellitus with mononeuropathy	8CR2.00	Diabetes clinical management plan
C10F411	Type II diabetes mellitus with ulcer	C105y00	Other specified diabetes mellitus with ophthalmic complicatn
C109711	Type II diabetes mellitus - poor control	9NiD.00	Did not attend DESMOND diabetes structured education program
C109B11	Type II diabetes mellitus with polyneuropathy	9h41.00	Excepted from diabetes qual indicators: Patient unsuitable
C109K00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	679L.00	Health education - diabetes
C10FB11	Type II diabetes mellitus with polyneuropathy	8I82.00	Did not complete DAFNE diabetes structured education program
C10F200	Type 2 diabetes mellitus with neurological complications	918T.00	Diabetes key contact
C109D11	Type II diabetes mellitus with hypoglycaemic coma	2126300	Diabetes resolved
C10F.00	Type 2 diabetes mellitus	C104y00	Other specified diabetes mellitus with renal complications
C109311	Type II diabetes mellitus with multiple complications	9OL1.00	Attends diabetes monitoring
C10FJ00	Insulin treated Type 2 diabetes mellitus	9OL2.00	Refuses diabetes monitoring
C10FL00	Type 2 diabetes mellitus with persistent proteinuria	8H4e.00	Referral to diabetes special interest general practitioner
C109A12	Type 2 diabetes mellitus with mononeuropathy	9N0n.00	Seen in community diabetes specialist clinic
C10FD00	Type 2 diabetes mellitus with hypoglycaemic coma	8Hj5.00	Referral to XPERT diabetes structured education programme
C10FB00	Type 2 diabetes mellitus with polyneuropathy	8H7f.00	Referral to diabetes nurse
C109011	Type II diabetes mellitus with renal complications	8Hj0.00	Referral to diabetes structured education programme
C10FA00	Type 2 diabetes mellitus with mononeuropathy	9OL7.00	Diabetes monitor.verbal invite
C10FC11	Type II diabetes mellitus with nephropathy	ZRBa.00	Education score - diabetes
C10FJ11	Insulin treated Type II diabetes mellitus	66AP.00	Diabetes: practice programme
ZC2C800	Dietary advice for diabetes mellitus	9OLB.00	Attended diabetes structured education programme
C10F700	Type 2 diabetes mellitus - poor control	9OLF.00	Diabetes structured education programme completed
		9OL3.00	Diabetes monitoring default

9OL9.00	Diabetes monitoring deleted	8HI4.00	Referral to community diabetes specialist nurse
8HTe.00	Referral to diabetes preconception counselling clinic	C104z00	Diabetes mellitus with nephropathy NOS
ZL62500	Referral to diabetes nurse	9OL5.00	Diabetes monitoring 2nd letter
8Hj3.00	Referral to DAFNE diabetes structured education programme	F372.00	Polyneuropathy in diabetes
8I83.00	Did not complete DESMOND diabetes structured educat program	Cyu2300	[X]Unspecified diabetes mellitus with renal complications
C100100	Diabetes mellitus, adult onset, no mention of complication	3882.00	Diabetes well being questionnaire
C107.00	Diabetes mellitus with peripheral circulatory disorder	C10y.00	Diabetes mellitus with other specified manifestation
8I81.00	Did not complete diabetes structured education programme	C10..00	Diabetes mellitus
8Hj1.00	Family/carer referral to diabetes structured education prog	7276.00	Pan retinal photocoagulation for diabetes
C100000	Diabetes mellitus, juvenile type, no mention of complication	9OLJ.00	DAFNE diabetes structured education programme completed
66AU.00	Diabetes care by hospital only	ZRB6.00	Diabetes wellbeing questionnaire
L180000	Diabetes mellitus - unspec whether in pregnancy/puerperium	C106y00	Other specified diabetes mellitus with neurological comps
9M00.00	Informed consent for diabetes national audit	C10M000	Lipoatrophic diabetes mellitus without complication
9NiE.00	Did not attend XPERT diabetes structured education programme	3883.00	Diabetes treatment satisfaction questionnaire
C106.00	Diabetes mellitus with neurological manifestation	8CS0.00	Diabetes care plan agreed
C104.00	Diabetes mellitus with renal manifestation	C103.00	Diabetes mellitus with ketoacidotic coma
C103z00	Diabetes mellitus NOS with ketoacidotic coma	C108y00	Other specified diabetes mellitus with multiple comps
9OL..00	Diabetes monitoring admin.	2BBF.00	Retinal abnormality - diabetes related
C105.00	Diabetes mellitus with ophthalmic manifestation	C314.11	Renal diabetes
Cyu2.00	[X]Diabetes mellitus	9OL6.00	Diabetes monitoring 3rd letter
9OLC.00	Family/carer attended diabetes structured education prog	66AJ.11	Unstable diabetes
L180.00	Diabetes mellitus during pregnancy/childbirth/puerperium	9OL8.00	Diabetes monitor.phone invite
212H.00	Diabetes resolved	C10yy00	Other specified diabetes mellitus with other spec comps
C135.00	Diabetes insipidus	ZRB4.00	Diabetes clinic satisfaction questionnaire
C106z00	Diabetes mellitus NOS with neurological manifestation	F171100	Autonomic neuropathy due to diabetes
C106.12	Diabetes mellitus with neuropathy	ZRB5.11	DTSQ - Diabetes treatment satisfaction questionnaire
C107.12	Diabetes with gangrene	8B3I.00	Diabetes medication review
9OLG.00	Attended XPERT diabetes structured education programme	9OLA.11	Diabetes monitored
9OLH.00	Attended DAFNE diabetes structured education programme	9NN9.00	Under care of diabetes specialist nurse
3881.00	Education score - diabetes	9NiA.00	Did not attend diabetes structured education programme
66A8.00	Has seen dietician - diabetes	C135.12	Diabetes insipidus - pituitary
9OL4.00	Diabetes monitoring 1st letter	R102.11	[D]Prediabetes
Kyu0300	[X]Glomerular disorders in diabetes mellitus	K01x100	Nephrotic syndrome in diabetes mellitus
C103y00	Other specified diabetes mellitus with coma	C102z00	Diabetes mellitus NOS with hyperosmolar coma
9NI4.00	Seen by general practitioner special interest in diabetes	66AX.00	Diabetes: shared care in pregnancy - diabetol and obstet
C10yz00	Diabetes mellitus NOS with other specified manifestation	9h4..00	Exception reporting: diabetes quality indicators
C10z.00	Diabetes mellitus with unspecified complication	L180400	Diabetes mellitus in puerperium - baby previously delivered
C103100	Diabetes mellitus, adult onset, with ketoacidotic coma	ZRB5.00	Diabetes treatment satisfaction questionnaire
9OLM.00	Diabetes structured education programme declined	8Hj4.00	Referral to DESMOND diabetes structured education programme
C108z00	Unspecified diabetes mellitus with multiple complications	9OLA.00	Diabetes monitor. check done
8Hg4.00	Discharged from care of diabetes specialist nurse	ZV65312	[V]Dietary counselling in diabetes mellitus
		ZRB6.11	DWBQ - Diabetes wellbeing questionnaire

679R.00	Patient offered diabetes structured education programme
90LK.00	DESMOND diabetes structured education programme completed
C10N.00	Secondary diabetes mellitus
8BL2.00	Patient on maximal tolerated therapy for diabetes
Cyu2000	[X]Other specified diabetes mellitus
C10zy00	Other specified diabetes mellitus with unspecified comps
C105z00	Diabetes mellitus NOS with ophthalmic manifestation
C100z00	Diabetes mellitus NOS with no mention of complication
C107y00	Other specified diabetes mellitus with periph circ comps
66Af.00	Patient diabetes education review
C102100	Diabetes mellitus, adult onset, with hyperosmolar coma
C10M.00	Lipoatrophic diabetes mellitus
66AR.00	Diabetes management plan given
L180300	Diabetes mellitus during pregnancy - baby not yet delivered
C107.11	Diabetes mellitus with gangrene
9M10.00	Informed dissent for diabetes national audit
90L...11	Diabetes clinic administration
2G51000	Foot abnormality - diabetes related
66A9.00	Understands diet - diabetes
L180z00	Diabetes mellitus in pregnancy/childbirth/puerperium NOS
9h42.00	Excepted from diabetes quality indicators: Informed dissent
8CP2.00	Transition of diabetes care options discussed
ZRB4.11	CSQ - Diabetes clinic satisfaction questionnaire
9NiC.00	Did not attend DAFNE diabetes structured education programme
L180800	Diabetes mellitus arising in pregnancy
L180900	Gestational diabetes mellitus
Q44B.00	Syndrome of infant of mother with gestational diabetes
ZC2CB00	Dietary advice for gestational diabetes
L180811	Gestational diabetes mellitus
14F4.00	H/O: Admission in last year for diabetes foot problem
Lyu2900	[X]Pre-existing diabetes mellitus, unspecified
1434.00	H/O: diabetes mellitus
L180700	Pre-existing malnutrition-related diabetes mellitus
L180500	Pre-existing diabetes mellitus, insulin-dependent
L180X00	Pre-existing diabetes mellitus, unspecified
ZV13F00	[V]Personal history of gestational diabetes mellitus
L180600	Pre-existing diabetes mellitus, non-insulin-dependent
C10AX00	Malnutrit-relat diabetes mellitus with other spec comps
Cyu2100	[X]Malnutrit-relat diabetes mellitus with other spec comps
C10A200	Malnutrition-related diabetes mellitus with renal complicatn
C10A300	Malnutrit-related diabetes mellitus wth ophthalmic complicat

C10A100	Malnutrition-related diabetes mellitus with ketoacidosis
C10A000	Malnutrition-related diabetes mellitus with coma
C10A500	Malnutritn-relat diabetes melitus wth periph circul complctn
C10A700	Malnutrition-related diabetes mellitus without complications
C10A.00	Malnutrition-related diabetes mellitus
Cyu2200	[X]Malnutrit-related diabetes mellitus with unspec compics
C10AW00	Malnutrit-related diabetes mellitus with unspec compics
C10A600	Malnutrition-related diabetes mellitus with multiple comps
C10A400	Malnutrition-related diabetes mellitus wth neuro complicatns

## 10.8.2Multilex drug codes for

### Diabetes Mellitus

Drugcode	Generic name
86177998	INSULIN ISOPHANE BOVINE CARTRIDGE inj susp 100 units/ml
90683997	Biphasic isophane insulin product
92376997	Biphasic isophane insulin product
86249998	Insulin biphasic lispro disposable pen inj susp 25:75; 100 units/ml 3ml disposable pen(s) 5
96047998	INSULIN NEUTRAL HUMAN inj 100 units/ml
94322998	Insulin isophane human crb inj 100 iu/ml 3ml disposable pen(s) 5
97524998	INSULIN SOLUBLE BOVINE inj 100 units/ml
98227998	INSULIN SOLUBLE HUMAN VIAL inj soln 100 units/ml
98228998	INSULIN ISOPHANE HUMAN EMP inj 100 units/ml
91295998	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml
96053997	ISOPHANE INSULIN 100iu/mL 10m
86243998	Insulin glargine vial inj soln 100 units/ml 1 10ml vial(s)
86237998	Insulin glulisine vial inj soln 100 units/ml 1 10ml vial(s)
86303998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 30:70; 100 units/ml
92940994	INSULIN 1mL syrg+12mm(29G) ndl
90012998	Insulin lispro human prb inj 100 iu/ml 3ml disposable pen(s) 5
91777994	NovoPenClassic
97598992	Insulin isophane (nph) 40 i/u 0
98225998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 50:50; 100 units/ml
96283992	Insulin isophane (nph) 100 i/u inj 0
86269998	INSULIN ISOPHANE HUMAN DISPOSABLE PEN inj susp 100 units/ml
96292992	Insulin isophane (highly purified) 100 i/u inj 0
96076992	Insulin bovine protamine zinc 100 i/u inj 0
90681998	Biphasic isophane insulin product
86284998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp

	15:85; 100 units/ml
86254998	Insulin lispro disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)
91275998	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 10:90; 100 units/ml
97601992	Insulin zinc semilente susp bp 100 i/u inj 0
86308998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 20:80; 100 units/ml
97322997	INSULIN SOLUBLE HUMAN PYR inj 100 units/ml
96061998	Insulin zinc mixed bovine vial inj susp 100 units/ml 10ml vial(s) 1
89555998	Insulin biphasic aspart human pyr inj 30:70; 100 units/ml 3ml disposable pen(s) 5
86253998	INSULIN LISPRO VIAL inj soln 100 units/ml
91505998	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml
86250998	Insulin biphasic lispro cartridge inj susp 25:75; 100 units/ml 3ml cartridge(s) 5
94292998	INSULIN SOLUBLE HUMAN EMP inj 100 units/ml
91293997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 20:80; 100 units/ml
97854998	INSULIN ISOPHANE HUMAN CRB inj 100 iu/ml
88973994	Autopen Junior
94296998	INSULIN ISOPHANE HUMAN EMP inj 100 units/ml
96794992	Biphasic isophane insulin product
86186998	INSULIN BIPHASIC ISOPHANE PORCINE CARTRIDGE inj susp 30:70; 100 units/ml
86191998	INSULIN ISOPHANE PORCINE VIAL inj susp 100 units/ml
91276998	INSULIN ISOPHANE HUMAN PRB inj 100 iu/ml
90681996	Biphasic isophane insulin product
86266998	INSULIN ISOPHANE HUMAN DISPOSABLE PEN inj susp 100 units/ml
90817994	BD Ultra Pen
96291992	ISOPHANE INSULIN 100iu/mL 10m
84779998	INSULIN DETEMIR DISPOSABLE PEN inj soln 100 units/ml
91292997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
90697997	Biphasic isophane insulin product
91294997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 10:90; 100 units/ml
92376998	Biphasic isophane insulin product
96053996	Biphasic isophane insulin product
86288998	Biphasic isophane insulin product
96792992	Biphasic isophane insulin product
86256998	Insulin lispro vial inj soln 100 units/ml 1 10ml vial(s)
86189998	ISOPHANE INSULIN 100iu/mL 10m
86242998	Insulin glargine disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)
91292996	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
95162992	NEUTRAL INSULIN 100iu/mL 10mL
92908998	INSULIN BIPHASIC ISOPHANE

	HUMAN PYR inj 20:80; 100 units/ml
98239994	U100 insulin syringe 0.5ml syringe(s) 100
86260998	INSULIN BIPHASIC ASPART CARTRIDGE inj susp 30:70; 100 units/ml
86182998	INSULIN SOLUBLE PORCINE CARTRIDGE inj soln 100 units/ml
86193998	Insulin isophane porcine cartridge inj susp 100 units/ml 3ml cartridge(s) 5
86314998	INSULIN SOLUBLE HUMAN CARTRIDGE inj soln 100 units/ml
94319998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 10:90; 100 units/ml
90689998	Insulin soluble human prb inj 100 units/ml 5ml vial(s) 1
88210994	Autopen Special Edition
97527998	INSULIN ZINC MIXED BOVINE VIAL inj susp 100 units/ml
91274998	INSULIN SOLUBLE HUMAN DISPOSABLE PEN inj soln 100 units/ml
92906998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml
86274998	Insulin isophane human disposable pen inj susp 100 units/ml 5 3ml disposable pen(s)
95168992	Insulin zinc suspension amorphous product
98505998	INSULIN ZINC MIXED BOVINE VIAL inj susp 100 units/ml
99480998	INSULIN ZINC susp MIXED BOVINE & PORCINE inj 100 units/ml
86549998	INSULIN GLULISINE CARTRIDGE inj soln 100 units/ml
87415994	Humapen Ergoburgundy
88413998	INSULIN SOLUBLE PORCINE VIAL inj soln 100 units/ml
94298998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 25:75; 100 units/ml
85591998	INSULIN GLULISINE CARTRIDGE inj soln 100 units/ml
86305998	Biphasic isophane insulin product
97600992	Insulin bovine protamine zinc 40 i/u inj 0
86080998	INSULIN ISOPHANE HUMAN DISPOSABLE PEN inj susp 100 units/ml
90684997	Biphasic isophane insulin product
88995998	INSULIN ISOPHANE PORCINE inj 100 units/ml
96052998	Insulin isophane mixed human inj 100 units/ml 3ml cartridge(s) 5
86315998	INSULIN SOLUBLE HUMAN CARTRIDGE inj soln 100 units/ml
86313998	INSULIN SOLUBLE HUMAN DISPOSABLE PEN inj soln 100 units/ml
86185998	Insulin soluble porcine vial inj soln 100 units/ml 10ml vial(s) 1
86298998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 30:70; 100 units/ml
96045998	Isophane insulin inj 100 iu/ml 10ml vial(s) 1
88974994	Autopen Junior
90169998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 30:70; 100 units/ml
94299998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 50:50; 100 units/ml
86267998	INSULIN ISOPHANE HUMAN VIAL inj susp 100 units/ml
86282998	Biphasic isophane insulin product



99532998	INSULIN ISOPHANE PORCINE VIAL inj susp 100 units/ml		syringe(s)
86169998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 50:50; 100 units/ml	90682998	Biphasic isophane insulin product
94297998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 15:85; 100 units/ml	99401998	INSULIN ZINC susp MIXED PORCINE inj 100 units/ml
91273998	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 40:60; 100 units/ml	97323998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
96281992	Insulin soluble 320 i/u inj 0	97526998	INSULIN ISOPHANE BOVINE inj 100 units/ml
96284992	Isophane insulin product	89685994	U100 insulin syringe 0.5ml
86310998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 10:90; 100 units/ml	97639992	INSULIN/COMBINATION
98817998	INSULIN ZINC susp CRYSTALLINE HUMAN PRB - INTERMEDIATE ACTING inj 100 units/ml	91289998	INSULIN BIPHASIC ISOPHANE HUMAN CRB inj 15:85; 100 units/ml
88211994	Autopen Special Edition	90015998	INSULIN LISPRO HUMAN PRB inj 100 iu/ml
99356998	INSULIN SOLUBLE BOVINE inj 100 units/ml	98474990	INSULIN SOLUBLE BOVINE inj 100 units/ml
91293998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 20:80; 100 units/ml	96286992	NEUTRAL INSULIN 100iu/mL 10mL
86214998	Insulin glulisine disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)	86301998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 30:70; 100 units/ml
90690998	Insulin soluble human emp inj 100 units/ml 10ml vial(s) 1	86251998	INSULIN LISPRO DISPOSABLE PEN inj soln 100 units/ml
98238994	U100 pre-set insulin syringe 1ml sp.36 [2a] 1 syringe(s)	96050998	Neutral insulin bovine inj 100 iu/ml 3ml cartridge(s) 5
94477992	NEUTRAL INSULIN 100iu/mL 10mL	86241998	Insulin glargine cartridge inj soln 100 units/ml 5 3ml cartridge(s)
97322998	INSULIN SOLUBLE HUMAN PYR inj 100 units/ml	96688992	Insulin neutral (human) 100 i/u inj 0
86252998	INSULIN LISPRO CARTRIDGE inj soln 100 units/ml	86077998	Insulin biphasic lispro disposable pen inj susp 50:50; 100 units/ml 3ml disposable pen(s) 5
86179998	Insulin isophane bovine cartridge inj susp 100 units/ml 3ml cartridge(s) 5	88297994	One Touch Ultra
97244992	INSULIN/DEPOT	86265998	Insulin aspart vial inj soln 100 units/ml 1 10ml vial(s)
86278998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 25:75; 100 units/ml	96063998	Insulin neutral human inj 100 units/ml 10ml vial(s) 1
90697996	Biphasic isophane insulin product	86175998	Insulin soluble bovine cartridge inj soln 100 units/ml 3ml cartridge(s) 5
99359998	INSULIN ISOPHANE BOVINE inj 100 units/ml	90682996	Biphasic isophane insulin product
91758998	Insulin glargine inj 100 iu/ml 3ml cartridge(s) 5	89554998	INSULIN BIPHASIC ASPART HUMAN PYR inj 30:70; 100 units/ml
86271998	INSULIN ISOPHANE HUMAN VIAL inj susp 100 units/ml	87471998	INSULIN DETEMIR DISPOSABLE PEN inj soln 100 units/ml
96561992	INSULIN SYRINGE	93137992	Insulin isophane (human) 100 i/u inj 0
99976992	Insulin soluble 100 i/u inj 0	90682997	Biphasic isophane insulin product
86176998	Insulin soluble bovine vial inj soln 100 units/ml 10ml vial(s) 1	97053998	INSULIN ZINC susp MIXED HUMAN PRB inj 100 units/ml
86264998	Insulin aspart cartridge inj soln 100 units/ml 5 3ml cartridge(s)	86248998	INSULIN BIPHASIC LISPRO CARTRIDGE inj susp 25:75; 100 units/ml
96290992	Insulin neutral (purified) 100 i/u inj 0	86081998	INSULIN ISOPHANE HUMAN VIAL inj susp 100 units/ml
86180998	Insulin isophane bovine vial inj susp 100 units/ml 10ml vial(s) 1	96787992	Soluble neutral insulin product
83405998	INSULIN BIPHASIC LISPRO DISPOSABLE PEN inj susp 50:50; 100 units/ml	91509998	INSULIN ASPART DISPOSABLE PEN inj soln 100 units/ml
99556998	INSULIN ZINC susp MIXED HUMAN PYR inj 100 units/ml	86272998	INSULIN GLARGINE CARTRIDGE inj soln 100 units/ml
99048992	Syringe insulin (bs1619/1) 2ml 0	98198998	INSULIN ASPART CARTRIDGE inj soln 100 units/ml
83403998	INSULIN LISPRO DISPOSABLE PEN inj soln 100 units/ml	96294992	Insulin zinc bovine susp 100 i/u inj 0
89990998	Insulin biphasic lispro human prb inj 25:75; 100 units/ml 3ml disposable pen(s) 5	86281998	Biphasic isophane insulin product
86247998	INSULIN BIPHASIC LISPRO DISPOSABLE PEN inj susp 25:75; 100 units/ml	87967998	Biphasic isophane insulin product
97268994	U100 insulin syringe 1ml 100	86285998	Biphasic isophane insulin product
		92555998	INSULIN GLARGINE inj 100 iu/ml
		98480998	INSULIN SOLUBLE PORCINE inj 100 units/ml

92909998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 10:90; 100 units/ml	86240998	INSULIN GLARGINE VIAL inj soln 100 units/ml
86316998	INSULIN SOLUBLE HUMAN VIAL inj soln 100 units/ml	90688998	Insulin isophane human pyr inj 100 iu/ml 3ml pre-filled syringe 5
94337998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml	86255998	Insulin lispro cartridge inj soln 100 units/ml 5 3ml cartridge(s)
89888998	Biphasic isophane insulin product	91292998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
99553998	INSULIN SOLUBLE HUMAN PRB inj 100 units/ml	86268998	INSULIN ISOPHANE HUMAN CARTRIDGE inj susp 100 units/ml
90168998	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml	86168998	INSULIN ISOPHANE HUMAN CARTRIDGE inj susp 100 units/ml
90697998	Biphasic isophane insulin product	90508994	Novopen 3demi
93713998	Insulin disp 1ml syringe appliance(s) 1	91291998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 40:60; 100 units/ml
91294998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 10:90; 100 units/ml	86291998	Biphasic isophane insulin product
94413998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 40:60; 100 units/ml	98506998	INSULIN ISOPHANE BOVINE inj 100 units/ml
97052996	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 30:70; 100 units/ml	86246998	Insulin detemir cartridge inj soln 100 units/ml 5 3ml cartridge(s)
88978998	INSULIN BIPHASIC ISOPHANE PORCINE inj 30:70; 100 units/ml	96056998	INSULINISOPHANE BOVINE
92323998	INSULIN BIPHASIC LISPRO DISPOSABLE PEN inj susp 50:50; 100 units/ml	99196998	INSULIN BIPHASIC inj 100 units/ml
91291997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 40:60; 100 units/ml	96044992	Insulin bp 100 i/u 0
86044998	INSULIN HUMAN inhalation pwdr 3mg	94202992	Soluble neutral insulin product
96064992	Insulin zinc suspension amorphous product	86317998	Insulin soluble human cartridge inj soln 100 units/ml 5 3ml cartridge(s)
96057998	Insulin zinc susp crystalline human prb - intermediate acting inj 100 units/ml 10ml vial(s) 1	90829994	Novopen 3fun-red
91290996	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml	96049998	INSULIN SOLUBLE PORCINE inj 100 units/ml
96289992	Insulin zinc suspension crystalline product	86261998	Insulin biphasic aspart disposable pen inj susp 30:70; 100 units/ml 3ml disposable pen(s) 5
86295998	Biphasic isophane insulin product	86174998	INSULIN SOLUBLE BOVINE CARTRIDGE inj soln 100 units/ml
90828994	Novopen 3fun-blue	86215998	INSULIN GLULISINE DISPOSABLE PEN inj soln 100 units/ml
98507998	INSULIN SOLUBLE BOVINE inj 100 units/ml	92456994	Novofine
97602992	Insulin soluble 40 i/u inj 0	92907998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 40:60; 100 units/ml
92649994	Novofine	95150997	TOLAZAMIDE
97528998	INSULIN PROTAMINE ZINC BOVINE VIAL inj susp 100 units/ml	99415998	INSULIN BIPHASIC ISOPHANE PORCINE VIAL inj susp 30:70; 100 units/ml
98895998	INSULIN BIPHASIC LISPRO HUMAN PRB inj 25:75; 100 units/ml	91933994	NovoPen
90684998	Biphasic isophane insulin product	91612998	INSULIN ASPART HUMAN PYR inj 100 iu/ml
86553998	Insulin glulisine inj soln 100 units/ml 3ml disposable pen(s) 5	96295992	Soluble neutral insulin product
90685998	Insulin zinc susp mixed human prb inj 100 units/ml 10ml vial(s) 1	86551998	INSULIN GLULISINE VIAL inj soln 100 units/ml
97051997	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 50:50; 100 units/ml	96795992	Isophane insulin product
94328998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 20:80; 100 units/ml	93467992	Insulin soluble inj i/u^2 0
98982998	INSULIN SOLUBLE PORCINE inj 100 units/ml	99047992	Syringe pre-set insulin for blind 2ml 0
99402998	INSULIN ASPART VIAL inj soln 100 units/ml	86046998	Insulin human inhalation pwdr 3mg 90 blisters
94948998	Insulin soluble porcine inj 100 units/ml 3ml cartridge(s) 5	96046998	Insulin zinc lente bovine vial inj susp 100 units/ml 1 10ml vial(s)
99144998	INSULIN ZINC susp AMORPHOUS PORCINE inj 100 units/ml	87008994	Optipen Pro 1
86183998	INSULIN SOLUBLE PORCINE VIAL inj soln 100 units/ml	87967997	Biphasic isophane insulin product
91275996	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 30:70; 100 units/ml	96059998	Insulin zinc susp amorphous porcine inj 100 units/ml 10ml vial(s) 1
95165992	Biphasic isophane insulin product	99554998	INSULIN ISOPHANE HUMAN PRB inj 100 iu/ml
86275998	Insulin isophane human cartridge inj susp 100 units/ml 5 3ml cartridge(s)	86270998	INSULIN ISOPHANE HUMAN CARTRIDGE inj susp 100 units/ml
		90379998	Insulin aspart human pyr inj 100 iu/ml 3ml disposable pen(s) 5

96058998	Insulin zinc susp crystalline human pyr - long acting inj 100 units/ml 10ml vial(s) 1	91701998	INSULIN BIPHASIC ISOPHANE HUMAN CRB inj 25:75; 100 units/ml
98481997	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml	96046992	Biphasic isophane insulin product
96282992	Biphasic isophane insulin product	86245998	Insulin detemir disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)
96293992	Insulin zinc semilente susp 80 i/u inj 0	86262998	Insulin biphasic aspart cartridge inj susp 30:70; 100 units/ml 3ml cartridge(s) 5
86259998	INSULIN BIPHASIC ASPART DISPOSABLE PEN inj susp 30:70; 100 units/ml	92932998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 30:70; 100 units/ml
91700998	INSULIN BIPHASIC ISOPHANE HUMAN CRB inj 50:50; 100 units/ml	93714997	Insulin disp 0.5ml syringe appliance(s) 1
89990997	Insulin biphasic lispro human prb inj 50:50; 100 units/ml 3ml disposable pen(s) 5	86312998	INSULIN SOLUBLE HUMAN VIAL inj soln 100 units/ml
86318998	Biphasic isophane insulin product	86190998	INSULIN ISOPHANE PORCINE CARTRIDGE inj susp 100 units/ml
93714996	Insulin 1 ml syringe appliance(s) 1	86173998	INSULIN SOLUBLE BOVINE VIAL inj soln 100 units/ml
86029998	Insulin biphasic lispro cartridge inj susp 50:50; 100 units/ml 3ml cartridge(s) 5	89082994	Novopen Juniorgreen
98228997	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml	96053998	Biphasic isophane insulin product
93713997	Insulin 2 ml syringe appliance(s) 1	90684996	Biphasic isophane insulin product
98268998	INSULIN ZINC susp CRYSTALLINE HUMAN PYR - LONG ACTING inj 100 units/ml	88999998	INSULIN SOLUBLE PORCINE inj 100 units/ml
86194998	Insulin isophane porcine vial inj susp 100 units/ml 10ml vial(s) 1	99533998	INSULIN BIPHASIC ISOPHANE PORCINE inj 50:50; 100 units/ml
86188998	Biphasic isophane insulin product	86187998	INSULIN BIPHASIC ISOPHANE PORCINE VIAL inj susp 30:70; 100 units/ml
86306998	Biphasic isophane insulin product	86287998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 50:50; 100 units/ml
86286998	INSULIN BIPHASIC ISOPHANE HUMAN DISPOSABLE PEN inj susp 50:50; 100 units/ml	90686998	Insulin isophane human emp inj 100 units/ml 3ml cartridge(s) 5
93713996	Insulin pre-set 1 ml syringe appliance(s) 1	86283998	Biphasic isophane insulin product
96055998	Insulin isophane porcine inj 100 units/ml 10ml vial(s) 1	95163992	ISOPHANE INSULIN 100iu/mL 10m
99977992	Biphasic insulin product	90691998	Insulin soluble human pyr inj 100 units/ml 3ml cartridge(s) 5
86028998	INSULIN BIPHASIC LISPRO CARTRIDGE inj susp 50:50; 100 units/ml	88003998	Insulin soluble human crb inj 100 iu/ml 3ml disposable pen(s) 5
96065998	Human insulin 100u/mL inj cart	87416994	Humapen Ergoteal
86184998	Insulin soluble porcine cartridge inj soln 100 units/ml 3ml cartridge(s) 5	94436998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml
96287992	ISOPHANE INSULIN 100iu/mL 10m	99360998	INSULIN ZINC MIXED BOVINE VIAL inj susp 100 units/ml
95846992	ZINC BOVINE & PORCINE INSULIN SUSPENSION	91160998	Insulin zinc susp mixed porcine inj 100 units/ml 10ml vial(s) 1
89684994	U100 insulin syringe 1ml	98226998	INSULIN BIPHASIC ISOPHANE HUMAN EMP inj 30:70; 100 units/ml
84421998	INSULIN GLULISINE DISPOSABLE PEN inj soln 100 units/ml	86319998	Insulin soluble human vial inj soln 100 units/ml 1 10ml vial(s)
96054998	Insulin isophane human inj 100 iu/ml 3ml cartridge(s) 5	90681997	Biphasic isophane insulin product
91767994	NovoPenfun	83404998	INSULIN BIPHASIC LISPRO DISPOSABLE PEN inj susp 25:75; 100 units/ml
90698998	Insulin zinc susp mixed bovine & porcine inj 100 units/ml 10ml vial(s) 1	86078998	INSULIN BIPHASIC ISOPHANE HUMAN VIAL inj susp 30:70; 100 units/ml
86047998	Insulin human inhalation pwdr 1mg 90 blisters	86276998	Insulin isophane human vial inj susp 100 units/ml 1 5ml vial(s)
98525990	INSULIN ZINC MIXED BOVINE VIAL inj susp 100 units/ml	91275997	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 20:80; 100 units/ml
96060998	Insulin zinc susp mixed human pyr inj 100 units/ml 10ml vial(s) 1	89081994	Novopen Junioryellow
98228996	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml	96689992	Insulin zinc crystalline susp 100 i/u inj 0
96285992	Protamine zinc insulin product	96062998	Insulin biphasic inj 100 units/ml 10ml vial(s) 1
95158992	NEUTRAL INSULIN 100iu/mL 10mL	97599992	ISOPHANE INSULIN 100iu/mL 10m
88851998	INSULIN SOLUBLE HUMAN CRB inj 100 iu/ml	86239998	INSULIN GLARGINE DISPOSABLE PEN inj soln 100 units/ml
		90683998	Biphasic isophane insulin product

99978992	Insulin isophane (purified) 100 i/u inj 0	97026990	GLICLAZIDE tabs 80mg
90830994	Novopen 3classic	88449997	Glimepiride tabs 1mg 30 tablet(s)
98481998	INSULIN ISOPHANE HUMAN PYR inj 100 iu/ml	97146990.00	GLIPIZIDE tabs 5mg
86280998	INSULIN BIPHASIC ISOPHANE HUMAN VIAL inj susp 25:75; 100 units/ml	97537997	GLIBENCLAMIDE tabs 5mg
97051998	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 40:60; 100 units/ml	93781990	GLICLAZIDE tabs 80mg
92376996	Biphasic isophane insulin product	93542990	GLIMEPIRIDE tabs 4mg
95164992	INSULIN/BOVINE INSULIN ZINC SUSPN/PURE	93562990	GLIMEPIRIDE tabs 3mg
96048998	INSULIN NEUTRAL HUMAN inj 100 units/ml	95025990.00	GLICLAZIDE tabs 80mg
96064998	Insulin neutral bovine inj 100 units/ml 10ml vial(s) 1	97303998	GLICLAZIDE tabs 80mg
93714998	Insulin 0.5 ml syringe appliance(s) 1	96280998	GLIQUIDONE
91290997	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml	98643990	GLIBENCLAMIDE tabs 5mg
86238998	INSULIN GLARGINE CARTRIDGE inj soln 100 units/ml	91407998	GLICLAZIDE mr tab 30mg
97525998	INSULIN SOLUBLE BOVINE inj 100 units/ml	93372990	GLIMEPIRIDE tabs 2mg
84422998	INSULIN GLARGINE DISPOSABLE PEN inj soln 100 units/ml	98418989	GLIBENCLAMIDE tabs 5mg
91641994	Humapen	95403990	TOLBUTAMIDE tabs 500mg
96548992	Biphasic isophane insulin product	99349990	TOLBUTAMIDE tabs 500mg
93139992	Insulin isophane 100 i/u 0	83838998	GLIMEPIRIDE tabs 2mg
91273997	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 50:50; 100 units/ml	99754998	ACETOHEXAMIDE
97052998	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 10:90; 100 units/ml	98418990	GLIBENCLAMIDE tabs 2.5mg
96051998	Insulin protamine zinc bovine vial inj susp 100 units/ml 10ml vial(s) 1	93373990	GLIMEPIRIDE tabs 1mg
86178998.00	INSULIN ISOPHANE BOVINE VIAL inj susp 100 units/ml	96427990	GLICLAZIDE tabs 80mg
90687998	Insulin isophane human prb inj 100 iu/ml 5ml vial(s) 1	99582989	GLIBENCLAMIDE tabs 2.5mg
98048990	INSULIN ISOPHANE BOVINE inj 100 units/ml	93095990	GLIMEPIRIDE tabs 2mg
87472998	INSULIN DETEMIR CARTRIDGE inj soln 100 units/ml	83410998	GLICLAZIDE mr tab 30mg
86294998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 40:60; 100 units/ml	97590990	GLICLAZIDE tabs 80mg
86309998	Biphasic isophane insulin product	98664990	GLIBENCLAMIDE tabs 5mg
97052997	INSULIN BIPHASIC ISOPHANE HUMAN PRB inj 20:80; 100 units/ml	88447997	GLIMEPIRIDE tabs 1mg
86300998	INSULIN BIPHASIC ISOPHANE HUMAN VIAL inj susp 30:70; 100 units/ml	97202990	GLIPIZIDE tabs 5mg
86263998	Insulin aspart disposable pen inj soln 100 units/ml 5 3ml disposable pen(s)	88355998	Glimepiride tabs 4mg 30 tablet(s)
86279998	INSULIN BIPHASIC ISOPHANE HUMAN CARTRIDGE inj susp 25:75; 100 units/ml	93096990	GLIMEPIRIDE tabs 1mg
91290998	INSULIN BIPHASIC ISOPHANE HUMAN PYR inj 50:50; 100 units/ml	83916998	GLICLAZIDE mr tab 30mg
99557998	INSULIN SOLUBLE HUMAN PYR inj 100 units/ml	88528998	TROGLITAZONE
86236998	Insulin glulisine cartridge inj soln 100 units/ml 5 3ml cartridge(s)	97089998	TOLBUTAMIDE tabs 500mg
86311998	Biphasic isophane insulin product	99195998	TOLBUTAMIDE tabs 500mg
86304998	Biphasic isophane insulin product	83836998	GLIMEPIRIDE tabs 4mg
87473998	Insulin detemir inj soln 100 iu/ml 3ml disposable pen(s) 5	95672992	TOLBUTAMIDE
86045998	INSULIN HUMAN inhalation pwdr 1mg	97057998	GLIBENCLAMIDE tabs 5mg
97834990.00	GLIPIZIDE tabs 5mg	97775989	CHLORPROPAMIDE tabs 250mg
		99582990	GLIBENCLAMIDE tabs 5mg
		96495990	GLICLAZIDE tabs 80mg
		95898990	GLICLAZIDE tabs 80mg
		93322990	GLIMEPIRIDE tabs 3mg
		97751990	GLIBENCLAMIDE tabs 2.5mg
		95255992	CHLORPROPAMIDE

96687998	CHLORPROPAMIDE tabs 250mg	97109998	Tolbutamide tabs 500mg 28 tablet(s)
95288990	TOLBUTAMIDE tabs 500mg	97889990	GLICLAZIDE tabs 80mg
99246990	CHLORPROPAMIDE tabs 100mg	97938990	GLICLAZIDE tabs 80mg
96795990	GLIPIZIDE tabs 5mg	98188990	CHLORPROPAMIDE tabs 100mg
96893990	GLIPIZIDE tabs 5mg	96220990	GLIBENCLAMIDE tabs 5mg
93545990	GLIMEPIRIDE tabs 1mg	99348990	TOLBUTAMIDE tabs 500mg
96755997	Chlorpropamide tabs 250mg 28 tablet(s)	99668998	GLIBENCLAMIDE tabs 2.5mg
99764998	CHLORPROPAMIDE tabs 100mg	97775990	CHLORPROPAMIDE tabs 100mg
97537998	GLIBENCLAMIDE tabs 2.5mg	97538990	GLICLAZIDE tabs 80mg
96615989	CHLORPROPAMIDE tabs 250mg	99764997	CHLORPROPAMIDE tabs 250mg
97583997	GLIBENCLAMIDE tabs 5mg	93561990	GLIMEPIRIDE tabs 4mg
96559990	GLIBENCLAMIDE tabs 2.5mg	93118990	GLIMEPIRIDE tabs 4mg
86018998	GLICLAZIDE	93544990	GLIMEPIRIDE tabs 2mg
93323990	GLIMEPIRIDE tabs 2mg	93867990	TOLBUTAMIDE tabs 500mg
97097998	GLIBENCLAMIDE tabs 2.5mg	93370990	GLIMEPIRIDE tabs 4mg
88334998	GLIMEPIRIDE tabs 4mg	93128990	GLIMEPIRIDE tabs 1mg
96221990	GLIBENCLAMIDE tabs 2.5mg	99580990	GLIBENCLAMIDE tabs 5mg
93371990	GLIMEPIRIDE tabs 3mg	88449998	Glimepiride tabs 2mg 30 tablet(s)
84783998	Tolbutamide oral liq	97717998	GLICLAZIDE tabs 80mg
93126990	GLIMEPIRIDE tabs 3mg	99247989	CHLORPROPAMIDE tabs 250mg
93564990	GLIMEPIRIDE tabs 1mg	97158990	GLIPIZIDE tabs 5mg
97236992	GLIBENCLAMIDE	99347990	TOLBUTAMIDE tabs 500mg
99581989	GLIBENCLAMIDE tabs 5mg	93121990	GLIMEPIRIDE tabs 1mg
96282997.00	Glipizide tabs 5mg 60 tablet(s)	97127998	Glibenclamide tabs 2.5mg 28 tablet blister pack
88447996	GLIMEPIRIDE tabs 3mg	96707990	GLICLAZIDE tabs 80mg
99668997	GLIBENCLAMIDE tabs 5mg	95422990	TOLBUTAMIDE tabs 500mg
97097997	GLIBENCLAMIDE tabs 5mg	96699990	GLIPIZIDE tabs 5mg
96281998	GLIPIZIDE tabs 2.5mg	97127997	Glibenclamide tabs 5mg 28 tablet blister pack
83887998	Chlorpropamide oral liq	97751989	GLIBENCLAMIDE tabs 5mg
97552990	GLIBENCLAMIDE tabs 2.5mg	96615990	CHLORPROPAMIDE tabs 100mg
97166990	GLICLAZIDE tabs 80mg	85901998	GLIBENCLAMIDE
94333992	TOLBUTAMIDE I/V	97032990	GLICLAZIDE tabs 80mg
98643989	GLIBENCLAMIDE tabs 2.5mg	83837998	GLIMEPIRIDE tabs 3mg
99247990	CHLORPROPAMIDE tabs 100mg	93324990	GLIMEPIRIDE tabs 1mg
93119990	GLIMEPIRIDE tabs 3mg	93094990	GLIMEPIRIDE tabs 3mg
95446990	GLICLAZIDE tabs 80mg	99580989	GLIBENCLAMIDE tabs 2.5mg
95601990	GLIBENCLAMIDE tabs 5mg	96282998	Glipizide tabs 2.5mg 28 tablet(s)
98188989	CHLORPROPAMIDE tabs 250mg	99041990	TOLBUTAMIDE tabs 500mg
97133992	CHLORPROPAMIDE	99787998	GLIBENCLAMIDE tabs 5mg
85003998	Gliclazide oral liq	99230998	TOLBUTAMIDE tabs 500mg
99246989	CHLORPROPAMIDE tabs 250mg	99588998	GLIBORNURIDE
93901990	GLICLAZIDE tabs 80mg	96283997	Gliclazide mr tab 30mg 112 tablet(s)
93125990	GLIMEPIRIDE tabs 4mg	91247998	GLICLAZIDE tabs 80mg
88447998	GLIMEPIRIDE tabs 2mg	98133990	GLICLAZIDE tabs 80mg

99419998	GLIPIZIDE tabs 5mg	99514990	METFORMIN tabs 500mg
85265998	Glibenclamide oral liq	92983990	METFORMIN oral soln 500mg/5ml
84684998	Rosiglitazone + glimepiride (ipu) tabs 8mg + 4mg	97087998	Metformin tabs 500mg 30 tablet(s)
95149998	TOLAZAMIDE	95600990	METFORMIN tabs 500mg
98053990	TOLBUTAMIDE tabs 500mg	99590997	METFORMIN tabs 850mg
88135998	GLICLAZIDE tabs 80mg	95272992	METFORMIN
98548990	GLIBENCLAMIDE tabs 5mg	94246990	METFORMIN tabs 850mg
97154990	GLICLAZIDE tabs 80mg	87180998	ROSIGLITAZONE + METFORMIN tabs 2mg + 1000mg
99145998	GLIBENCLAMIDE tabs 2.5mg	96850990	METFORMIN tabs 500mg
93127990	GLIMEPIRIDE tabs 2mg	87773998	Rosiglitazone + metformin tabs 2mg + 500mg 112 tablet(s)
96755998	Chlorpropamide tabs 100mg 250 tablet(s)	98494990	METFORMIN tabs 500mg
84685998	Rosiglitazone + glimepiride (ipu) tabs 4mg + 4mg	91221997	METFORMIN tabs 850mg
99591998	GLIPIZIDE tabs 5mg	83733998	Metformin mr tab 750mg tablet(s) 28
97552989	GLIBENCLAMIDE tabs 5mg	98654989	METFORMIN tabs 500mg
95148998	TOLBUTAMIDE	91221998	METFORMIN tabs 500mg
97057997	GLIBENCLAMIDE tabs 2.5mg	99513989	METFORMIN tabs 850mg
99581990	GLIBENCLAMIDE tabs 2.5mg	87054998	Metformin mr tab 500mg 56 tablet(s)
88449996	Glimepiride tabs 3mg 30 tablet(s)	99149990	METFORMIN tabs 500mg
83949998	GLICLAZIDE mr tab 30mg	96296989	METFORMIN tabs 850mg
96981998	ACETOHEXAMIDE	98125989	METFORMIN tabs 850mg
92518997	GLIBENCLAMIDE tabs 5mg	84008998	VILDAGLIPTIN + METFORMIN tabs 50mg + 1000mg
96283998	Gliclazide tabs 80mg 120 tablet(s)	94280992	PHENFORMIN HYDROCHLORIDE S/R
99589998	GLIQUIDONE	87536998	Metformin oral susp 100mg/ml mls 150
98664989	GLIBENCLAMIDE tabs 2.5mg	97110990	METFORMIN tabs 500mg
83839998	GLIMEPIRIDE tabs 1mg	95381990	METFORMIN tabs 500mg
93120990	GLIMEPIRIDE tabs 2mg	87182998	Rosiglitazone + metformin tabs 2mg + 1000mg 56 tablet(s)
97583998	GLIBENCLAMIDE tabs 2.5mg	98493989	METFORMIN tabs 500mg
95150998	TOLAZAMIDE	85406998	Metformin (ipu) tabs 1000mg
93563990	GLIMEPIRIDE tabs 2mg	95239990	METFORMIN tabs 850mg
95256992	CHLORPROPAMIDE	99149989	METFORMIN tabs 850mg
94371992	TOLBUTAMIDE	87053998	METFORMIN mr tab 500mg
93093990	GLIMEPIRIDE tabs 4mg	95228990	METFORMIN tabs 500mg
95674992	TOLBUTAMIDE	97087997	Metformin tabs 850mg 28 tablet(s)
92518998	GLIBENCLAMIDE tabs 2.5mg	94978990	METFORMIN oral susp 100mg/ml
93543990	GLIMEPIRIDE tabs 3mg	87772998	Metformin + rosiglitazone tabs 500mg + 2mg 112 tablet(s)
92831990	GLICLAZIDE mr tab 30mg	95880997	METFORMIN tabs 850mg
96296990	METFORMIN tabs 500mg	93167990	METFORMIN oral soln 500mg/5ml
84009998	VILDAGLIPTIN + METFORMIN tabs 50mg + 850mg	87774998	Metformin + rosiglitazone tabs 500mg + 1mg 112 tablet(s)
85622998	PIOGLITAZONE + METFORMIN tabs 15mg + 850mg	94518990	METFORMIN tabs 850mg
99590998	METFORMIN tabs 500mg	85673998	METFORMIN oral soln 500mg/5ml
96270989	METFORMIN tabs 850mg	85554998	Metformin caps
94248990	METFORMIN tabs 500mg	95298990	METFORMIN tabs 850mg
84011998	Vildagliptin + metformin tabs 50mg + 850mg tablet(s) 60	87181998	Rosiglitazone + metformin tabs 4mg + 1000mg 56 tablet(s)
99514989	METFORMIN tabs 850mg		

83732998	METFORMIN mr tab 750mg	88131996	NATEGLINIDE tabs 180mg
95271992	Metformin hcl 850 mg tab 0	89763996	Rosiglitazone tabs 8mg 28 tablet(s)
85624998	Metformin + pioglitazone tabs 850mg + 15mg 56 tablet(s)	84694998	EXENATIDE inj 5 micrograms
99513990	METFORMIN tabs 500mg	84696998	Exenatide inj 10micrograms 1 pre-filled pen
94235992	Metformin hcl 500 mg tab 0	84693998	EXENATIDE inj 10micrograms
85625998	Pioglitazone + metformin tabs 15mg + 850mg tablet(s) 56	92237997	Pioglitazone tabs 30mg 28 tablet(s)
83401998	Sitagliptin + metformin (ipu) tabs 50mg + 1000mg	92238998	PIOGLITAZONE tabs 15mg
85555998	Metformin oral liq	89763997	Rosiglitazone tabs 4mg 56 tablet(s)
83619998	METFORMIN mr tab 500mg	98915998	Acarbose tabs 50mg 90 tablet(s)
87165998	Metformin + rosiglitazone tabs 1000mg + 4mg 56 tablet(s)	92237998	Pioglitazone tabs 15mg 28 tablet(s)
98654990	METFORMIN tabs 850mg	85267998	REPAGLINIDE tabs 1mg
95599990	METFORMIN tabs 850mg	85266998	REPAGLINIDE tabs 2mg
96270990	METFORMIN tabs 500mg	99587998	GLYMIDINE SODIUM
87770998	ROSIGLITAZONE + METFORMIN tabs 2mg + 500mg	88132997	Nateglinide tabs 120mg 84 tablet(s)
87166998	Metformin + rosiglitazone tabs 1000mg + 2mg 56 tablet(s)	88528996	TROGLITAZONE
95380990	METFORMIN tabs 850mg	90048998	ROSIGLITAZONE tabs 2mg
87775998	Rosiglitazone + metformin tabs 1mg + 500mg 112 tablet(s)	90048997	ROSIGLITAZONE tabs 4mg
98125990	METFORMIN tabs 500mg	88131998	NATEGLINIDE tabs 60mg
95270992	METFORMIN	91924997	Repaglinide tabs 1mg 90 tablet(s)
89155998	METFORMIN tabs 500mg	91924998	Repaglinide tabs 500 micrograms 90 tablet(s)
87882998	METFORMIN tabs 850mg	91923997	REPAGLINIDE tabs 1mg
95299990	METFORMIN tabs 500mg	89763998	ROSIGLITAZONE
89155997	METFORMIN tabs 850mg	97800994	Dextrostix
95880998	METFORMIN tabs 500mg	87884998	PIOGLITAZONE tabs 45mg
97110989	METFORMIN tabs 850mg	84697998	Exenatide inj 5 micrograms 1 pre-filled pen
87883998	METFORMIN tabs 500mg	91924996	Repaglinide tabs 2mg 90 tablet(s)
87771998	ROSIGLITAZONE + METFORMIN tabs 1mg + 500mg	88528997	TROGLITAZONE
94473990	METFORMIN tabs 850mg	98475997	ACARBOSE tabs 100mg
87179998	ROSIGLITAZONE + METFORMIN tabs 4mg + 1000mg	87885998	Pioglitazone tabs 45mg 28 tablet(s)
85674998	Metformin oral soln 500mg/5ml 150 mls	84639998	SITAGLIPTIN tabs 100mg
96850989	METFORMIN tabs 850mg	85268998	REPAGLINIDE tabs 500 micrograms
94519990	METFORMIN tabs 500mg	88523996	TROGLITAZONE
98493990	METFORMIN tabs 850mg	98475998	ACARBOSE tabs 50mg
94474990	METFORMIN tabs 500mg	83830998	Pioglitazone oral liq
83402998	Sitagliptin + metformin (ipu) tabs 50mg + 850mg	95752990	DEXTROSE INTRAVENOUSHUDDERSFIELD R.I.
84010998	Vildagliptin + metformin tabs 50mg + 1000mg tablet(s) 60	91923998	REPAGLINIDE tabs 500 micrograms
96110990	METFORMIN tabs 850mg	91559998	GLIBORNURIDE
96111990	METFORMIN tabs 500mg	84341998	Vildagliptin tabs 50mg tablet(s) 56
92238997	PIOGLITAZONE tabs 30mg	95149997	TOLAZAMIDE
88131997	NATEGLINIDE tabs 120mg	91923996	REPAGLINIDE tabs 2mg
84338998	VILDAGLIPTIN tabs 50mg	98333994	Clinitest
88132996	Nateglinide tabs 180mg 84 tablet(s)	88132998	Nateglinide tabs 60mg 84 tablet(s)
90048996	ROSIGLITAZONE tabs 8mg	98915997	Acarbose tabs 100mg 90 tablet(s)
		95130994	Glucotide

88523998	TROGLITAZONE	97281992	DIAGNOSTIC SOLUTION-TABLETS OF COPPER
96262989	GLUCOSE	90430994	U100single use
99261998	GLUCOSE	96253998	GUAR GUM
94470992	GLYMIDINE	96253997	GUAR GUM
84640998	Sitagliptin tabs 100mg 28 tablet(s)	91577994	Medi-Test Protein 2
96406998	Diazoxide tabs 50mg 100 tablet(s)	85888994	U100 SINGLE USE INS SYR+8MM NDLE30G 1ML
87537998	DIAZOXIDE	90434994	U100single use
85521998	Diazoxide oral liq	97778994	Albym Test
85412998	DIAZOXIDE	90282994	Labstix
94581998	Glucagon inj 1mg 1mg vial + pre-filled syringe 1	99648989	DEXTROSE
96406997	Diazoxide inj 300mg/20ml 5 ampoule(s)	95843990	GLUCOSE10% + KCL (HRI)
99670998	DIAZOXIDE tabs 50mg	97948996	GLUCOSE
93176990	DIAZOXIDE oral susp 50mg/5ml	85557994	MHI-500 3 MONTH CONSUMABLE KIT SIZE 7 NOZZLE
96638992	DIAZOXIDE	89897994	Unilet GType A
92061998	GLUCAGON inj 1mg	88219994	Medisense Soft-Sense
98896998	GLUCAGON inj 1mg	85560994	MHI-500 NEEDLE FREE STARTER KIT
94582998	GLUCAGON inj 1mg	90412994	Vitrex Softtype A
99669998	DIAZOXIDE inj 300mg/20ml	96686992	BLOOD GLUCOSE REAGENT STRIPS 1-22MMOL/L
94581997	Glucagon inj 10mg 1 10mg vial + diluent	93489994	Unilet Universal Comfortouchtype B
87184998	DIAZOXIDE BCM	86574994	U100single use
94582997	GLUCAGON inj 10mg	87512994	Medisense Optium Plus
85496994	U100 SINGLE USE INS SYR+12MM NDLE30G	90429994	U100single use
95414992	PHENFORMIN HYDROCHLORIDE S/R	94226994	Unilet Universal Comfortouchtype A&B
86862994	Ascensia Autodisc	88370994	Syringeord purp spec16[2A]
90168994	U100single use	98331994	Acetest
89909994	Advantage II	89661994	MicroletType A ster sgle use
93078992	BLOOD GLUCOSE TEST STRIPS	96252998	GUAR GUM
94064994	Cleanlet 25type A	88371994	Syringeord purp spec16[2A]
97723994	Monolet Extratype A	90148994	U100single use
90165994	U100single use	90274994	U100single use
87322994	mhi-500	92813994	Ascensia Glucodisc
88310994	Glucoflex-R	90818994	BD Ultra Pen
90411994	Vitrex Gentle	90169994	U100single use
90435994	U100single use	98332994	Clinistix
98877992	LANCET	97323994	Diabur Test 5000
98861992	INSULIN NEEDLES	88523997	TROGLITAZONE
98329994	Ketur Test	93543992	LANCETS
96262988	GLUCOSE	90109994	Glucotrendplus
87320994	mhi-500	98219994	U100single use
90147994	U100single use	98227994	Micro-Fine
90271994	U100single use	90098994	Autopen
94192994	Unilet Superlitetype B	89760994	U100single use
88473994	U100single use	85499994	Omnican 100 ins
89346998	GLUCOSE10% + KCL (HRI)	91179994	Pocket Scan



85546994	Medisense Optium Beta-Ketone test strips	86086994	Ascensia Microfill
90232994	GlucoTip (Fine)type A	93070992	BLOOD LANCETS
88218994	One Touch Ultrasofttype A	85498994	Omnican 50 ins
99336994	BM-Accutest	95377994	Monolettype A
87885994	U100single use	87909994	Unilet Comfortouchtype A&B
98189994	Syringeord purp spec16[2A]	87317994	Autopen 24
99268994	BM-Test 1-44	94063994	Cleanlet 25 XLtype B
99733994	Syringeord purp spec16[2A]	90820994	Autopen
93067992	URINE GLUCOSE TEST STRIPS	97322994	Glucostix
94201992	ZINC HUMAN INSULIN SUSPENSION	92627994	Glucotrend
98229994	Unilettype B	89842994	Prestige Smart System
94191994	Unilet G Superlitetype A	89800994	Unilet General Purposetype A
85889994	U100 SINGLE USE INS SYR+8MM NDLE29G 1ML	89759994	U100single use
95084992	GUAR GUM	95653992	REAGENT
98313994	GA	92924994	U100single use
87411994	mhi-5003 month	87412994	mhi-500needle free
90119994	GlucoMen Sensors	96251998	GUAR GUM
97899998	GUAR GUM	90431994	U100single use
88474994	U100single use	90166994	U100single use
95693994	Supreme	92948994	B-D U-100single use
92949994	B-D U-100single use	94190994	Unilet G Superlitetype A
85558994	MHI-500 3 MONTH CONSUMABLE KIT SIZE 6 NOZZLE	98312994	ExacTech
85497994	U100 SINGLE USE INS SYR+12MM NDL30G	96920992	REAGENT STRIPS
95186994	Medi-Test Glucose	96051992	GUAR GUM
92925994	U100single use	88227994	Freestyletype A
94225994	Unilet Universal Comfortouchtype A	90272994	U100single use
90163994	U100single use	98237994	Hypoguard U100click/count
86020994	Softclix XLtype C	96264998	GLYMIDINE SODIUM
87494994	GlucoMen (Fine)type A	99391994	U100single use
91326994	Fine Pointtype A	95305994	Diastix
90273994	U100single use	95413992	PHENFORMIN HYDROCHLORIDE
89799994	Unilet General Purposetype A	85559994	MHI-500
98334994	Albustix	88278994	Compact Colorimetric
90444994	U100single use	90167994	U100single use
93836998	DEXTROSE	90428994	U100single use
87321994	mhi-500	87410994	mhi-5003 month
98993990	DEXTROSE	85851994	TrueTrack Smart System biosensor strips
91943994	U100single use	95217994	Glucose VT
90819994	Autopen	90332994	Supreme Spectrum
90432994	U100single use	91778998	DEXTROSE INTRAVENOUSHUDDERSFIELD R.I.
90270994	U100single use	95124994	Unilet G Superlitetype A
95125994	Unilet G Superlitetype A	91942994	U100single use
90164994	U100single use	92950994	B-D U-100single use
98330994	Ketostix	89801994	Unilet General PurposeSuperlite type A

90433994	U100single use
99592994	One Touch
90622994	Unilet GPtype A
94193994	Unilet Superlitetype B
98218994	U100single use
90161994	Medisense Optium
98803998	GUAR GUM
93477994	Unilet Universal Comfortouchtype B
96253996	GUAR GUM
95185994	Medi-Test Glycaemie C
90821994	Autopen
89094994	Active
90146994	U100single use
95200994	Medisense G2
95194994	Micro-Fine Plustype A
87319994	Autopen 24

### 10.8.3AHD codes for Diabetes

#### Mellitus

Ahd code	Description
1009100000	Diabetes Annual Check

### 10.8.4Medical codes for

#### Hypertension

Medcode	Description
14A2.00	H/O: hypertension
2126100	Hypertension resolved
212K.00	Hypertension resolved
246M.00	White coat hypertension
6146200	Hypertension induced by oral contraceptive pill
662..12	Hypertension monitoring
6627	Good hypertension control
6628	Poor hypertension control
6629	Hypertension:follow-up default
662b.00	Moderate hypertension control
662c.00	Hypertension six month review
662d.00	Hypertension annual review
662F.00	Hypertension treatm. started
662H.00	Hypertension treatm.stopped
662O.00	On treatment for hypertension
662P.00	Hypertension monitoring

7Q01.00	High cost hypertension drugs
7Q01000	Primary pulmonary hypertension drugs band 1
7Q01100	Primary pulmonary hypertension drugs band 2
7Q01200	Primary pulmonary hypertension drugs band 3
7Q01300	Primary pulmonary hypertension drugs band 4
7Q01y00	Other specified high cost hypertension drugs
7Q01z00	High cost hypertension drugs NOS
8CR4.00	Hypertension clinical management plan
8HT5.00	Referral to hypertension clinic
8I3N.00	Hypertension treatment refused
9h3..00	Exception reporting: hypertension quality indicators
9h31.00	Excepted from hypertension qual indicators: Patient unsuit
9h32.00	Excepted from hypertension qual indicators: Informed dissent
9N03.00	Seen in hypertension clinic
9N1y200	Seen in hypertension clinic
9N4L.00	DNA - Did not attend hypertension clinic
9OD..00	Hypertension screen admin.
9ODZ.00	Hypertension screen admin. NOS
9OI..00	Hypertension monitoring admin.
9OI..11	Hypertension clinic admin.
9OI1.00	Attends hypertension monitor.
9OI2.00	Refuses hypertension monitor.
9OIA.00	Hypertension monitor.chkck done
9OIA.11	Hypertension monitored
F450400	Ocular hypertension
G20..00	Essential hypertension
G200.00	Malignant essential hypertension
G201.00	Benign essential hypertension
G202.00	Systolic hypertension
G203.00	Diastolic hypertension
G20z.00	Essential hypertension NOS
G20z.11	Hypertension NOS
G22z.11	Renal hypertension
G24..00	Secondary hypertension
G240.00	Secondary malignant hypertension
G240000	Secondary malignant renovascular hypertension
G240z00	Secondary malignant hypertension NOS
G241.00	Secondary benign hypertension
G241000	Secondary benign renovascular hypertension
G241z00	Secondary benign hypertension NOS
G244.00	Hypertension secondary to endocrine disorders
G24z.00	Secondary hypertension NOS
G24z000	Secondary renovascular hypertension NOS

G24z100	Hypertension secondary to drug
G24zz00	Secondary hypertension NOS
G410.00	Primary pulmonary hypertension
G41y000	Secondary pulmonary hypertension
G8y3.00	Chronic peripheral venous hypertension
Gyu2000	[X]Other secondary hypertension
Gyu2100	[X]Hypertension secondary to other renal disorders
J623.00	Portal hypertension
L12..00	Hypertension complicating pregnancy/childbirth/puerperium
L120.00	Benign essential hypertension in pregnancy/childbirth/puerp
L120000	Benign essential hypertension in preg/childb/puerp unspec
L120100	Benign essential hypertension in preg/childb/puerp - deliv
L120300	Benign essential hypertension in preg/childb/puerp-not deliv
L120400	Benign essential hypertension in preg/childb/puerp +p/n comp
L120z00	Benign essential hypertension in preg/childb/puerp NOS
L121.00	Renal hypertension in pregnancy/childbirth/puerperium
L121000	Renal hypertension in pregnancy/childbirth/puerp unspecified
L121100	Renal hypertension in pregnancy/childbirth/puerp - delivered
L121200	Renal hypertension in preg/childb/puerp -deliv with p/n comp
L121300	Renal hypertension in preg/childbirth/puerp - not delivered
L121400	Renal hypertension in preg/childb/puerp + p/n complication
L121z00	Renal hypertension in pregnancy/childbirth/puerperium NOS
L122.00	Other pre-existing hypertension in preg/childbirth/puerp
L122000	Other pre-existing hypertension in preg/childb/puerp unspec
L122100	Other pre-existing hypertension in preg/childb/puerp - deliv
L122300	Other pre-exist hypertension in preg/childb/puerp-not deliv
L122400	Other pre-exist hypertension in preg/childb/puerp + p/n comp
L122z00	Other pre-existing hypertension in preg/childb/puerp NOS
L123.00	Transient hypertension of pregnancy
L123000	Transient hypertension of pregnancy unspecified
L123100	Transient hypertension of pregnancy - delivered
L123200	Transient hypertension of pregnancy - deliv with p/n comp
L123300	Transient hypertension of pregnancy - not delivered
L123400	Transient hypertension of pregnancy + postnatal complication
L123500	Gestational hypertension
L123600	Transient hypertension of pregnancy
L123z00	Transient hypertension of pregnancy NOS
L127.00	Pre-eclampsia or eclampsia with pre-existing hypertension

L127000	Pre-eclampsia or eclampsia with hypertension unspecified
L127100	Pre-eclampsia or eclampsia with hypertension - delivered
L127200	Pre-eclampsia or eclampsia with hypertension - del+p/n comp
L127300	Pre-eclampsia or eclampsia with hypertension - not delivered
L127400	Pre-eclampsia or eclampsia with hypertension + p/n comp
L127z00	Pre-eclampsia or eclampsia + pre-existing hypertension NOS
L128.00	Pre-exist hypertension compl preg childbirth and puerperium
L12B.00	Proteinuric hypertension of pregnancy
L12z.00	Unspecified hypertension in pregnancy/childbirth/puerperium
L12z000	Unspecified hypertension in preg/childb/puerp unspecified
L12z100	Unspecified hypertension in preg/childb/puerp - delivered
L12z200	Unspecified hypertension in preg/childb/puerp -del +p/n comp
L12z300	Unspecified hypertension in preg/childb/puerp - not deliv
L12z400	Unspecified hypertension in preg/childb/puerp with p/n comp
L12zz00	Unspecified hypertension in preg/childb/puerp NOS

### 10.8.5AHD codes for hypertension

Ahdcode	Description
1005010500	Blood Pressure
1009315000	Target Blood pressure

### 10.8.6Medical Codes for BMI

Medcode	Description
22K1.00	Body Mass Index normal K/M2
22K2.00	Body Mass Index high K/M2
22K3.00	Body Mass Index low K/M2
22K4.00	Body mass index index 25-29 - overweight
22K5.00	Body mass index 30+ - obesity
22K6.00	Body mass index less than 20
22K7.00	Body mass index 40+ - severely obese
22K8.00	Body mass index 20-24 - normal

### 10.8.7AHD codes for BMI

1005010200	Weight
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### 10.8.8 Medical codes for asthma

Medcode	Description
14B4.00	H/O: asthma
173A.00	Exercise induced asthma
1780.00	Aspirin induced asthma
102..00	Asthma confirmed
2126200	Asthma resolved
663..11	Asthma monitoring
663N.00	Asthma disturbing sleep
663N000	Asthma causing night waking
663N100	Asthma disturbs sleep weekly
663N200	Asthma disturbs sleep frequently
663O.00	Asthma not disturbing sleep
663O000	Asthma never disturbs sleep
663P.00	Asthma limiting activities
663Q.00	Asthma not limiting activities
663U.00	Asthma management plan given
663V.00	Asthma severity
663V000	Occasional asthma
663V100	Mild asthma
663V200	Moderate asthma
663V300	Severe asthma
663W.00	Asthma prophylactic medication used
663d.00	Emergency asthma admission since last appointment
663e.00	Asthma restricts exercise
663e000	Asthma sometimes restricts exercise
663e100	Asthma severely restricts exercise
663f.00	Asthma never restricts exercise
663h.00	Asthma - currently dormant
663j.00	Asthma - currently active
663m.00	Asthma accident and emergency attendance since last visit
663n.00	Asthma treatment compliance satisfactory
663p.00	Asthma treatment compliance unsatisfactory
663q.00	Asthma daytime symptoms
663r.00	Asthma causes night symptoms 1 to 2 times per month
663s.00	Asthma never causes daytime symptoms
663t.00	Asthma causes daytime symptoms 1 to 2 times per month
663u.00	Asthma causes daytime symptoms 1 to 2 times per week
663v.00	Asthma causes daytime symptoms most days
663w.00	Asthma limits walking up hills or stairs
663x.00	Asthma limits walking on the flat
663y.00	Number of asthma exacerbations in past year
66Y5.00	Change in asthma management plan

66Y9.00	Step up change in asthma management plan
66YA.00	Step down change in asthma management plan
66YC.00	Absent from work or school due to asthma
66YE.00	Asthma monitoring due
66YJ.00	Asthma annual review
66YK.00	Asthma follow-up
66YP.00	Asthma night-time symptoms
66YQ.00	Asthma monitoring by nurse
66YR.00	Asthma monitoring by doctor
8791.00	Further asthma - drug prevent.
8793.00	Asthma control step 0
8794.00	Asthma control step 1
8795.00	Asthma control step 2
8796.00	Asthma control step 3
8797.00	Asthma control step 4
8798.00	Asthma control step 5
8B3j.00	Asthma medication review
8H2P.00	Emergency admission, asthma
90JA.11	Asthma monitored
H312000	Chronic asthmatic bronchitis
H33..00	Asthma
H33..11	Bronchial asthma
H330.00	Extrinsic (atopic) asthma
H330.11	Allergic asthma
H330.12	Childhood asthma
H330.13	Hay fever with asthma
H330.14	Pollen asthma
H330000	Extrinsic asthma without status asthmaticus
H330011	Hay fever with asthma
H330100	Extrinsic asthma with status asthmaticus
H330111	Extrinsic asthma with asthma attack
H330z00	Extrinsic asthma NOS
H331.00	Intrinsic asthma
H331.11	Late onset asthma
H331000	Intrinsic asthma without status asthmaticus
H331100	Intrinsic asthma with status asthmaticus
H331111	Intrinsic asthma with asthma attack
H331z00	Intrinsic asthma NOS
H332.00	Mixed asthma
H333.00	Acute exacerbation of asthma
H33z.00	Asthma unspecified
H33z000	Status asthmaticus NOS
H33z011	Severe asthma attack
H33z100	Asthma attack

H33z111	Asthma attack NOS
H33z200	Late-onset asthma
H33zz00	Asthma NOS
H33zz11	Exercise induced asthma
H33zz12	Allergic asthma NEC
H35y600	Sequoiosis (red-cedar asthma)
H35y700	Wood asthma
H47y000	Detergent asthma

## 10.8.9 Multilex drug codes for

### Asthma

MULTILEX EID	GENERIC NAME
87105998	IPRATROPIUM BROMIDE
87107998	IPRATROPIUM BROMIDE
87108998	IPRATROPIUM BROMIDE
87109998	IPRATROPIUM BROMIDE
87125998	IPRATROPIUM BROMIDE
87126998	IPRATROPIUM BROMIDE
87127998	IPRATROPIUM BROMIDE
87128998	IPRATROPIUM BROMIDE
87173998	BECLOMETASONE
87174998	BECLOMETASONE
87275998	SALBUTAMOL
87276998	SALBUTAMOL
87277998	SALBUTAMOL
87438998	BUDESONIDE
87439998	BUDESONIDE REFILLABLE
87513998	IPRATROPIUM BROMIDE
87514998	IPRATROPIUM BROMIDE
87597998	MONTELUKAST(AS SODIUM SALT)
87601998	MONTELUKAST(AS SODIUM SALT)
87704998	CORTISONE ACETATE
87878998	TERBUTALINE
87928998	THEOPHYLLINE
87929998	THEOPHYLLINE
87930998	THEOPHYLLINE
87950998	HYDROCORTISONE
87979998	SALMETEROL+ FLUTICASONE
87980996	SALMETEROL+ FLUTICASONE
87980997	SALMETEROL+ FLUTICASONE
87980998	SALMETEROL+ FLUTICASONE
87986997	BECLOMETASONEEXTRAFINE PARTICLE
87986998	BECLOMETASONEEXTRAFINE PARTICLE
87988997	BECLOMETASONEEXTRAFINE PARTICLE
87988998	BECLOMETASONEEXTRAFINE PARTICLE
87990997	BECLOMETASONEEXTRAFINE PARTICLE
87990998	BECLOMETASONEEXTRAFINE PARTICLE
87991997	BECLOMETASONEEXTRAFINE PARTICLE
87991998	BECLOMETASONEEXTRAFINE PARTICLE
88004998	SALBUTAMOL
88095998	ZAFIRLUKAST
88102998	ZAFIRLUKAST

88156998	BUDESONIDE	89235998	TIOTROPIUM
88262998	SALBUTAMOL	89275998	SALBUTAMOL
88273998	IPRATROPIUM BROMIDE	89276996	BECLOMETASONE
88299998	IPRATROPIUM BROMIDE	89276997	BECLOMETASONE
88305997	BUDESONIDEWITH FORMOTEROL	89276998	BECLOMETASONE
88305998	BUDESONIDEWITH FORMOTEROL	89286998	SODIUM CROMOGLICATE
88342998	MONTELUKAST(AS SODIUM SALT)	89347998	SALBUTAMOL
88351996	MONTELUKAST(AS SODIUM SALT)	89443996	DEFLAZACORT
88351997	MONTELUKAST(AS SODIUM SALT)	89443997	DEFLAZACORT
88351998	MONTELUKAST(AS SODIUM SALT)	89443998	DEFLAZACORT
88352997	MONTELUKAST(AS SODIUM SALT)	89446996	DEFLAZACORT
88352998	MONTELUKAST(AS SODIUM SALT)	89446997	DEFLAZACORT
88357998	SALBUTAMOL	89446998	DEFLAZACORT
88434996	BECLOMETASONE	89862996	BECLOMETASONE
88434997	BECLOMETASONE	89862997	BECLOMETASONE
88434998	BECLOMETASONE	89862998	BECLOMETASONE
88469996	BECLOMETASONE	90394997	BUDESONIDEWITH FORMOTEROL
88469997	BECLOMETASONE	90394998	BUDESONIDEWITH FORMOTEROL
88469998	BECLOMETASONE	90416996	BECLOMETASONE
88470998	SALBUTAMOL	90416997	BECLOMETASONE
88480997	SALBUTAMOL	90416998	BECLOMETASONE
88480998	SALBUTAMOL	90417996	BECLOMETASONE
88487998	FORMOTEROL FUMARATE	90417997	BECLOMETASONE
88488998	FORMOTEROL FUMARATE	90417998	BECLOMETASONE
88490997	FORMOTEROL FUMARATE	90418998	SALBUTAMOL
88490998	FORMOTEROL FUMARATE	90419998	SALBUTAMOL
88522998	SALMETEROL+ FLUTICASONE	90587998	SALBUTAMOL
88524996	FLUTICASONE+ SALMETEROL	90588998	BECLOMETASONE
88524997	FLUTICASONE+ SALMETEROL	90680998	SALBUTAMOL+ IPRATROPIUM BR
88524998	FLUTICASONE+ SALMETEROL	90758998	MOMETASONE FUROATE
88525996	SALMETEROL+ FLUTICASONE	90927998	THEOPHYLLINE+GUAIFEN &EPHEDRINE
88525997	SALMETEROL+ FLUTICASONE	90929998	THEOPHYLLINE+GUAIFEN &EPHEDRINE
88525998	SALMETEROL+ FLUTICASONE	90942998	FORMOTEROL FUMARATE
88706997	EPHEDRINE	90943998	FORMOTEROL FUMARATE
88706998	EPHEDRINE	90968998	MOMETASONE FUROATE
88727998	MOMETASONE FUROATE	91078998	FENOTEROL+ IPRATROPIUM BR
88832998	BECLOMETASONE	91088996	BECLOMETASONE
88833997	BECLOMETASONE	91088997	BECLOMETASONE
88833998	BECLOMETASONE	91088998	BECLOMETASONE
88834998	SALBUTAMOL	91107998	SALBUTAMOL+ IPRATROPIUM BR
89060998	SALBUTAMOL	91272998	SALBUTAMOL
89121998	BUDESONIDE	91284997	SALBUTAMOL
89178998	SALBUTAMOL	91284998	SALBUTAMOL
89229998	MOMETASONE FUROATE	91285998	AMINOPHYLLINE

91310998	IPRATROPIUM BROMIDE+ SALBUTAMOL	92842997	FLUTICASON
91311998	IPRATROPIUM BROMIDE+ SALBUTAMOL	92842998	FLUTICASON
91320998	SALBUTAMOL	92843998	FLUTICASON
91322997	FLUTICASON	92844998	FLUTICASON
91322998	FLUTICASON	92845996	FLUTICASON
91334997	FLUTICASON	92845997	FLUTICASON
91334998	FLUTICASON	92845998	FLUTICASON
91335998	SALBUTAMOL	92861998	BETAMETHASONE SODIUM PHOSPHATE
91345998	SALBUTAMOL	92894998	FENOTEROL+ IPRATROPIUM BR
91348998	SALMETEROL+ FLUTICASON	92895998	IPRATROPIUM BROMIDE
91363996	BECLOMETASONE	92899996	FLUTICASON
91363997	BECLOMETASONE	92899997	FLUTICASON
91363998	BECLOMETASONE	92899998	FLUTICASON
91387998	BECLOMETASONE	92900996	FLUTICASON
91390997	AMINOPHYLLINE	92900997	FLUTICASON
91390998	AMINOPHYLLINE	92900998	FLUTICASON
91397998	SALBUTAMOL	93017992	SODIUM CROMOGLYCATE
91403996	BECLOMETASONE	93035992	SODIUM CROMOGLYCATE NEBULISER SOLUTION
91403997	BECLOMETASONE	93056996	FLUTICASON
91403998	BECLOMETASONE	93056997	FLUTICASON
91417998	SALBUTAMOL	93056998	FLUTICASON
91493998	BUDESONIDEWITH FORMOTEROL	93057996	FLUTICASON
91547998	SALMETEROL+ FLUTICASON	93057997	FLUTICASON
91570997	SALBUTAMOL	93057998	FLUTICASON
91570998	SALBUTAMOL	93065998	SODIUM CROMOGLICATE
91619996	FLUTICASON	93066996	BECLOMETASONE
91619997	FLUTICASON	93066997	BECLOMETASONE
91619998	FLUTICASON	93066998	BECLOMETASONE
91646998	DEXAMETHASONE	93075998	PREDNISOLONE SODIUM PHOSPHATE
92199998	SALMETEROL+ FLUTICASON	93083997	BAMBUTEROL
92285996	BECLOMETASONE	93083998	BAMBUTEROL
92285997	BECLOMETASONE	93084997	BAMBUTEROL
92285998	BECLOMETASONE	93084998	BAMBUTEROL
92411998	BUDESONIDEWITH FORMOTEROL	93086992	SALBUTAMOL (ALBUTEROL)
92412998	HYDROCORTISONE	93123992	SALBUTAMOL (ALBUTEROL) SULPHATE
92473996	FLUTICASON	93154998	TERBUTALINE
92473997	FLUTICASON	93181996	SALMETEROL
92473998	FLUTICASON	93181997	SALMETEROL
92665998	IPRATROPIUM BROMIDE	93181998	SALMETEROL
92755998	IPRATROPIUM BROMIDE+ SALBUTAMOL	93182996	SALMETEROL
92756998	IPRATROPIUM BROMIDE+ SALBUTAMOL	93182997	SALMETEROL
92810997	DEXAMETHASONE	93182998	SALMETEROL
92810998	DEXAMETHASONE	93264998	THEOPHYLLINE+ EPHEDRINE
92842996	FLUTICASON	93302996	BUDESONIDE

93302997	BUDESONIDE	94024997	EPHEDRINE HYDROCHLORIDE
93302998	BUDESONIDE	94024998	EPHEDRINE HYDROCHLORIDE
93303996	BUDESONIDE	94027992	EPHEDRINE HCL/THEOPHYLLINE
93303997	BUDESONIDE	94041997	AMINOPHYLLINE
93303998	BUDESONIDE	94041998	AMINOPHYLLINE
93326992	BECLOMETHASONE/SALBUTAMOL(ALBU T)100/400	94063992	AMINOPHYLLINE
93350998	THEOPHYLLINE+ EPHEDRINE	94066992	AMINOPHYLLINE
93411992	AMINOPHYLLINE	94134992	DEXAMETHASONE
93439998	TERBUTALINE	94199998	SALBUTAMOL
93440998	TERBUTALINE	94251994	Salbutamol Cyclohalertype 5
93457998	TIOTROPIUM	94259998	SALBUTAMOL
93584998	THEOPHYLLINE	94260996	SALBUTAMOL
93588998	HYDROCORTISONE NA SUCCINATE	94260997	SALBUTAMOL
93620992	BECLOMETHASONE DIPROPIONATE CARTRIDGE	94260998	SALBUTAMOL
93621992	BECLOMETHASONE DIPROPIONATE CARTRIDGE	94324992	BUDESONIDE REFILL
93643992	BETAMETHASONE VALERATE	94334992	CHOLINE THEOPHYLLINATE
93645992	BETAMETHASONE	94343992	SODIUM CROMOGLYCATE
93646992	BETAMETHASONE	94373992	TRIAMCINOLONE
93647992	BETAMETHASONE	94383996	SALBUTAMOL
93650992	BETAMETHASONE VALERATE	94383997	SALBUTAMOL
93684997	IPRATROPIUM BROMIDE	94383998	SALBUTAMOL
93684998	IPRATROPIUM BROMIDE	94405992	AMINOPHYLLINE
93685997	IPRATROPIUM BROMIDE	94406992	AMINOPHYLLINE
93685998	IPRATROPIUM BROMIDE	94407997	SALBUTAMOL
93697997	ORCIPRENALINE	94407998	SALBUTAMOL
93697998	ORCIPRENALINE	94435998	AMINOPHYLLINE
93731997	SODIUM CROMOGLICATE+ SALBUTAMOL	94442992	CORTISONE ACETATE
93731998	SODIUM CROMOGLICATE+ SALBUTAMOL	94442996	SALBUTAMOL
93732997	SODIUM CROMOGLICATE+ SALBUTAMOL	94442997	SALBUTAMOL
93732998	SODIUM CROMOGLICATE+ SALBUTAMOL	94442998	SALBUTAMOL
93754992	AMINOPHYLLINE	94455997	SALBUTAMOL
93783998	EPHEDRINE	94455998	SALBUTAMOL
93912996	PREDNISOLONE	94456996	BECLOMETASONE
93912997	PREDNISOLONE	94456997	BECLOMETASONE
93912998	PREDNISOLONE	94456998	BECLOMETASONE
93941996	TERBUTALINE	94491997	IPRATROPIUM BROMIDE
93941997	TERBUTALINE	94491998	IPRATROPIUM BROMIDE
93941998	TERBUTALINE	94492997	IPRATROPIUM BROMIDE
93983996	FLUTICASONE+ SALMETEROL	94492998	IPRATROPIUM BROMIDE
93983997	FLUTICASONE+ SALMETEROL	94529998	SALBUTAMOL
93983998	FLUTICASONE+ SALMETEROL	94532996	SALBUTAMOL
94002992	TERBUTALINE SULPHATE NEBULE	94532997	SALBUTAMOL
94023998	EPHEDRINE HYDROCHLORIDE	94532998	SALBUTAMOL
94024996	EPHEDRINE HYDROCHLORIDE	94533996	SALBUTAMOL



94533997	SALBUTAMOL	94861997	SALBUTAMOL
94533998	SALBUTAMOL	94861998	SALBUTAMOL
94534998	SALBUTAMOLRONGO	94862998	SALBUTAMOL
94544992	SALBUTAMOL (ALBUTEROL) INHALER	94870992	CORTISONE ACETATE
94557996	BECLOMETASONE	94908992	DEXAMETHASONE
94557997	BECLOMETASONE	94909992	DEXAMETHASONE
94557998	BECLOMETASONE	94941996	SALBUTAMOL+BECLOMETASONE
94558996	BECLOMETASONE	94941997	SALBUTAMOL+BECLOMETASONE
94558997	BECLOMETASONE	94941998	SALBUTAMOL+BECLOMETASONE
94558998	BECLOMETASONE	94943996	SALBUTAMOL
94559996	BECLOMETASONE	94943997	SALBUTAMOL
94559997	BECLOMETASONE	94943998	SALBUTAMOL
94559998	BECLOMETASONE	94944997	SALBUTAMOL
94585990	IPRATROPIUM BROMIDE	94944998	SALBUTAMOL
94586990	IPRATROPIUM BROMIDE	94963992	EPHEDRINE HCL 24MG/THEOPHYLLINE 120MG
94587990	IPRATROPIUM BROMIDE	94969992	EPHEDRINE HCL/THEOPHYLLINE 48/180MG S/R
94587992	SALBUTAMOL (ALBUTEROL) REFILL	95036992	EPHEDRINE/THEOPHYLLINE
94588990	IPRATROPIUM BROMIDE	95062998	AMINOPHYLLINE+DRIED AL HYDROX GEL
94597992	SALBUTAMOL (ALBUTEROL)	95063997	AMINOPHYLLINE
94624992	ORCIPRENALINE SULPHATE	95063998	AMINOPHYLLINE
94624998	THEOPHYLLINE+ LYSINE	95111998	BECLOMETASONE
94625998	SALMETEROL+ FLUTICASONE	95124992	HYDROCORTISONE
94627997	THEOPHYLLINE+ EPHEDRINE HCL	95139997	TRIAMCINOLONE
94627998	THEOPHYLLINE+ EPHEDRINE HCL	95139998	TRIAMCINOLONE
94628992	AMINOPHYLLINE/EPHEDRINE/AMYLOBA RBITONE	95140990	CORTISONE ACETATE
94628998	THEOPHYLLINE+ LYSINE	95162990	BECLOMETASONE
94630992	AMINOPHYLLINE	95163990	BECLOMETASONE
94632992	AMINOPHYLLINE	95164990	BECLOMETASONE
94633992	AMINOPHYLLINE	95179998	THEOPHYLLINE
94634992	AMINOPHYLLINE	95180998	THEOPHYLLINE+PHENOBARB &GUAIFEN
94635992	AMINOPHYLLINE	95181998	THEOPHYLLINE+ EPHEDRINE SULPHATE
94658992	EPHEDRINE RESINATE/THEOPHYLLINE	95182998	THEOPHYLLINE+ EPHEDRINE HCL
94736992	TERBUTALINE SULPHATE/GUAPHENESIN	95183998	THEOPHYLLINE
94833998	SALBUTAMOL	95184996	THEOPHYLLINE
94840997	SALBUTAMOL	95184997	THEOPHYLLINE
94840998	SALBUTAMOL	95184998	THEOPHYLLINE
94846997	SALBUTAMOL	95185996	THEOPHYLLINE
94846998	SALBUTAMOL	95185997	THEOPHYLLINE
94847996	BECLOMETASONE	95185998	THEOPHYLLINE
94847997	BECLOMETASONE	95186996	THEOPHYLLINE
94847998	BECLOMETASONE	95186997	THEOPHYLLINE
94849997	SALBUTAMOL+BECLOMETASONE	95186998	THEOPHYLLINE
94849998	SALBUTAMOL+BECLOMETASONE	95187996	THEOPHYLLINE
94853992	SALBUTAMOL (ALBUTEROL)	95187997	THEOPHYLLINE

95187998	THEOPHYLLINE	95812992	SODIUM CROMOGLYCATE
95188998	THEOPHYLLINE	95847996	METHYLPREDNISOLONE
95195992	THEOPHYLLINE/ LYSINE	95847997	METHYLPREDNISOLONE
95210998	TERBUTALINE	95847998	METHYLPREDNISOLONE
95211997	TERBUTALINE+ GUAIFENESIN	95851996	METHYLPREDNISOLONE
95211998	TERBUTALINE+ GUAIFENESIN	95851997	METHYLPREDNISOLONE
95212997	TERBUTALINE	95851998	METHYLPREDNISOLONE
95212998	TERBUTALINE	95912990	PREDNISOLONE
95213997	TERBUTALINE	95913990	CORTISONE ACETATE
95213998	TERBUTALINE	95938996	BUDESONIDE
95214996	TERBUTALINE	95938997	BUDESONIDE
95214997	TERBUTALINE	95938998	BUDESONIDE
95214998	TERBUTALINE	95967998	BETAMETHASONE
95243990	SALBUTAMOL	95982990	BUDESONIDE
95306998	SALBUTAMOL	95983990	BUDESONIDE
95357992	DEXAMETHASONE	95983996	BECLOMETASONE+ SALBUTAMOL
95416998	PREDNISOLONESTEAGLATE	95983997	BECLOMETASONE+ SALBUTAMOL
95417996	PREDNISOLONE	95983998	BECLOMETASONE+ SALBUTAMOL
95417997	PREDNISOLONE	95998992	SODIUM CROMOGLYCATE COMPLETE UNIT
95417998	PREDNISOLONE	96025990	SALBUTAMOL
95441992	AMINOPHYLLINE	96026990	SALBUTAMOL
95484992	PREDNISOLONE E/C	96027990	BECLOMETASONE
95487992	PREDNISOLONE	96028990	BECLOMETASONE
95492992	PREDNISOLONE	96029990	BECLOMETASONE
95492997	BUDESONIDE	96041992	FLUTICASONE PROPIONATE DISCS
95492998	BUDESONIDE	96089992	SALBUTAMOL (ALBUTEROL)
95493992	PREDNISOLONE	96089998	ISOPRENALINE SULPHATE+SODIUM CROMOGLICATE
95493997	BUDESONIDE	96101992	EPHEDRINE HYDROCHLORIDE S/F
95493998	BUDESONIDE	96102990	SALBUTAMOL
95526992	BUDESONIDE	96108992	AMINOPHYLLINE
95527992	BUDESONIDE REFILL	96110997	IPRATROPIUM BROMIDE+FENOTEROL HYDROBROM
95528992	BUDESONIDE	96110998	IPRATROPIUM BROMIDE+FENOTEROL HYDROBROM
95536990	BECLOMETASONE	96111996	IPRATROPIUM BROMIDE
95571990	IPRATROPIUM BROMIDE	96111997	IPRATROPIUM BROMIDE
95593990	PREDNISOLONE	96111998	IPRATROPIUM BROMIDE
95594990	PREDNISOLONE	96112998	IPRATROPIUM BROMIDE
95651992	EPHEDRINE HC/THEOPHYLLINE/PHENOBARBITONE	96113997	IPRATROPIUM BROMIDE
95652992	EPHEDRINE HYDROCHLORIDE/THEOPHYLLINE	96113998	IPRATROPIUM BROMIDE
95658992	TERBUTALINE SULPHATE/GUAIPHENESIN	96130990	BECLOMETASONE
95676998	ORCIPRENALINE	96131990	BECLOMETASONE
95677997	ORCIPRENALINE	96132990	BECLOMETASONE
95677998	ORCIPRENALINE	96143997	HYDROCORTISONE
95722992	SALBUTAMOL (ALBUTEROL) S/R	96143998	HYDROCORTISONE
95750998	NEDOCROMIL SODIUM	96146990	TERBUTALINE

96165990	SALBUTAMOL	96629992	PREDNISOLONE
96177992	PREDNISONE	96631992	PREDNISONE
96181992	DEXAMETHASONE	96642989	AMINOPHYLLINE
96182992	DEXAMETHASONE	96642990	AMINOPHYLLINE
96219992	EPHEDRINE	96675998	CHOLINE THEOPHYLLINATE
96222992	EPHEDRINE 15MG/THEOPHYLLINE 120MG	96676998	CHOLINE THEOPHYLLINATE
96223992	EPHEDRINE HCL/AMINOPHYLLINE 25/130/MG	96677996	CHOLINE THEOPHYLLINATE
96224992	EPHEDRINE	96677997	CHOLINE THEOPHYLLINATE
96226992	EPHEDRINE HCL 50MG/THEOPHYLLINE 65MG	96677998	CHOLINE THEOPHYLLINATE
96269992	HYDROCORTISONE PELLETS	96692990	SALBUTAMOL
96361989	PREDNISOLONE	96733996	SODIUM CROMOGLICATE
96361990	PREDNISOLONE	96733997	SODIUM CROMOGLICATE
96372992	ORCIPRENALINE SULPHATE	96733998	SODIUM CROMOGLICATE
96402990	PREDNISOLONE	96734996	SODIUM CROMOGLICATE
96403997	AMINOPHYLLINE	96734997	SODIUM CROMOGLICATE
96403998	AMINOPHYLLINE	96734998	SODIUM CROMOGLICATE
96409992	PREDNISOLONE	96735998	SODIUM CROMOGLICATE+ ISOPRENALINE
96410992	PREDNISONE	96736998	SODIUM CROMOGLICATE
96411992	PREDNISOLONE	96743992	PREDNISONE
96425990	SALBUTAMOL	96744992	PREDNISOLONE
96431997	DEXAMETHASONE	96765990	IPRATROPIUM BROMIDE
96431998	DEXAMETHASONE	96766992	SODIUM CROMOGLYCAT E INSUF CARTRIDGES
96488992	THEOPHYLLINE	96792990	SALBUTAMOL
96489992	THEOPHYLLINE	96798992	CHOLINE THEOPHYLLINATE
96490992	THEOPHYLLINE	96804992	TERBUTALINE RESPULES FOR NEBULISATION
96506992	SALBUTAMOL (ALBUTEROL)	96835988	SALBUTAMOL
96507992	SALBUTAMOL (ALBUTEROL)	96835989	SALBUTAMOL
96553997	FENOTEROL+ IPRATROPIUM BR	96835990	SALBUTAMOL
96553998	FENOTEROL+ IPRATROPIUM BR	96842992	SALBUTAMOL (ALBUTEROL) SULPHATE/NEB SOLN
96554996	FENOTEROL	96884992	FLUTICASONE PROPIONATE DISCS
96554997	FENOTEROL	96885990	IPRATROPIUM BROMIDE
96554998	FENOTEROL	96885992	FLUTICASONE PROPIONATE DISCS
96557992	SALBUTAMOL (ALBUTEROL)	96888992	SALBUTAMOL (ALBUTEROL)
96564990	SALBUTAMOL	96926992	SODIUM CROMOGLYCAT E/SPACER
96577990	PREDNISOLONE SODIUM PHOSPHATE	96935988	BECLOMETASONE
96578992	TRIAMCINOLONE ACETONIDE	96935989	BECLOMETASONE
96580992	AMINOPHYLLINE	96935990	BECLOMETASONE
96581992	AMINOPHYLLINE	96938990	AMINOPHYLLINE
96603997	CORTISONE ACETATE	96940992	AMINOPHYLLINE
96603998	CORTISONE ACETATE	96988992	TERBUTALINE SULPHATE
96626988	BECLOMETASONE	96989992	TERBUTALINE SULPHATE RESPULES 5MG/2ML
96626989	BECLOMETASONE	97006988	BECLOMETASONE
96626990	BECLOMETASONE	97006989	BECLOMETASONE
96628990	SALBUTAMOL	97006990	BECLOMETASONE

97013992	CAFFEINE/EPHEDRINE	97358992	EPHEDRINE HCL/AMINOPHYLLINE E/C
97085997	SALBUTAMOL	97359992	EPHEDRINE
97085998	SALBUTAMOL	97391997	THEOPHYLLINE+ EPHEDRINE HCL
97088998	EPHEDRINE	97391998	THEOPHYLLINE+ EPHEDRINE HCL
97098989	SALBUTAMOL	97418992	FENOTEROL HYDROBROMIDE
97098990	SALBUTAMOL	97419992	FENOTEROL HYDROBROMIDE COMPLETE UNIT
97101989	PREDNISOLONE	97436998	PREDNISOLONE
97101990	PREDNISOLONE	97463998	SALBUTAMOL
97121997	SALBUTAMOL	97484998	SALBUTAMOL
97121998	SALBUTAMOL	97485997	SALBUTAMOL
97137992	CHOLINE THEOPHYLLINATE	97485998	SALBUTAMOL
97147998	PREDNISOLONE	97492997	HYDROCORTISONE
97148997	PREDNISOLONE	97492998	HYDROCORTISONE
97148998	PREDNISOLONE	97502998	DEXAMETHASONE
97149997	PREDNISONE	97517997	BECLOMETASONE
97149998	PREDNISONE	97517998	BECLOMETASONE
97155997	PREDNISOLONE	97583992	HYDROCORTISONE
97155998	PREDNISOLONE	97585998	SALBUTAMOL
97156997	PREDNISONE	97586997	SALBUTAMOL
97156998	PREDNISONE	97586998	SALBUTAMOL
97163997	AMINOPHYLLINE	97672997	FLUTICASONE
97163998	AMINOPHYLLINE	97672998	FLUTICASONE
97164997	AMINOPHYLLINE	97680997	FLUTICASONE
97164998	AMINOPHYLLINE	97680998	FLUTICASONE
97172996	NEDOCROMIL SODIUM	97698998	BECLOMETASONE
97172997	NEDOCROMIL SODIUM	97726990	PREDNISOLONE
97172998	NEDOCROMIL SODIUM	97740992	METHYLPREDNISOLONE
97177990	TERBUTALINE	97758997	SALBUTAMOL
97203992	CORTISONE ACETATE	97758998	SALBUTAMOL
97237992	PREDNISOLONE ACETATE	97778997	SALBUTAMOL
97238992	PREDNISOLONE ACETATE	97778998	SALBUTAMOL
97240992	PREDNISOLONE	97779998	SODIUM CROMOGLICATE
97242998	TERBUTALINE	97791990	AMINOPHYLLINE
97243992	DEXAMETHASONE	97822990	IPRATROPIUM BROMIDE
97253996	THEOPHYLLINE	97829998	METHYLPREDNISOLONE
97253997	THEOPHYLLINE	97832998	METHYLPREDNISOLONE
97253998	THEOPHYLLINE	97862998	SODIUM CROMOGLICATE
97255988	BECLOMETASONE	97872996	BECLOMETASONE
97255989	BECLOMETASONE	97872997	BECLOMETASONE
97255990	BECLOMETASONE	97872998	BECLOMETASONE
97334998	IPRATROPIUM BROMIDE	97929990	PREDNISOLONE
97354992	EPHEDRINE HCL/BUTETHAMATE CITRATE	97933990	TERBUTALINE
97356992	EPHEDRINE 11MG/THEOPHYLLINE 120MG	97942992	PREDNISONE
97357992	EPHEDRINE/GUAIPHEN/PHENOBAR/THE OPHYLLINE	97943992	PREDNISONE

97950998	SODIUM CROMOGLICATE	98456990	PREDNISOLONE
97967989	SALBUTAMOL	98514997	PREDNISOLONE
97967990	SALBUTAMOL	98514998	PREDNISOLONE
98046990	SALBUTAMOL	98561990	EPHEDRINE
98057996	EPHEDRINE	98562997	PREDNISOLONE
98057997	EPHEDRINE	98562998	PREDNISOLONE
98057998	EPHEDRINE	98580998	SALBUTAMOL+BECLOMETASONE
98072990	DEXAMETHASONE	98586998	SALBUTAMOL
98100990	THEOPHYLLINE	98588998	BECLOMETASONE
98101996	AMINOPHYLLINE	98590996	BECLOMETASONE
98101997	AMINOPHYLLINE	98590997	BECLOMETASONE
98101998	AMINOPHYLLINE	98590998	BECLOMETASONE
98107990	PREDNISOLONE	98595997	BUDESONIDE
98167988	SALBUTAMOL	98595998	BUDESONIDE
98167989	SALBUTAMOL	98596997	BUDESONIDE
98167990	SALBUTAMOL	98596998	BUDESONIDE
98169992	THEOPHYLLINE/NOSCAPINE	98601998	TERBUTALINE+ GUAIFENESIN
98170992	THEOPHYLLINE 100MG/LYSINE 74MG	98602998	TERBUTALINE
98171992	THEOPHYLLINE	98615998	THEOPHYLLINE
98172992	THEOPHYLLINE	98623998	THEOPHYLLINE
98208990	AMINOPHYLLINE	98644989	DEXAMETHASONE
98219990	AMINOPHYLLINE	98644990	DEXAMETHASONE
98223996	SODIUM CROMOGLICATE	98659996	SALBUTAMOL
98223997	SODIUM CROMOGLICATE	98659997	SALBUTAMOL
98223998	SODIUM CROMOGLICATE	98659998	SALBUTAMOL
98277998	IPRATROPIUM BROMIDE	98718998	SODIUM CROMOGLICATE+ ISOPRENALINE
98288998	BECLOMETASONE	98724997	DEXAMETHASONE
98326997	TRIAMCINOLONE	98724998	DEXAMETHASONE
98326998	TRIAMCINOLONE	98804998	SALBUTAMOL
98332996	BECLOMETASONE	98805998	SALBUTAMOL
98332997	BECLOMETASONE	98806996	SALBUTAMOL
98332998	BECLOMETASONE	98806997	SALBUTAMOL
98333990	AMINOPHYLLINE	98806998	SALBUTAMOL
98394998	BETAMETHASONE SODIUM PHOSPHATE	98808998	THEOPHYLLINE
98438990	SALBUTAMOL	98809998	THEOPHYLLINE
98439990	SALBUTAMOL	98810998	THEOPHYLLINE
98440990	SALBUTAMOL	98887996	BUDESONIDE
98441988	SALBUTAMOL	98887997	BUDESONIDE
98441989	SALBUTAMOL	98887998	BUDESONIDE
98441990	SALBUTAMOL	98934998	THEOPHYLLINE+ EPHEDRINE HCL
98442990	SALBUTAMOL	98975997	SALBUTAMOL
98455990	PREDNISOLONE	98975998	SALBUTAMOL
98456988	PREDNISOLONE	98976998	SALBUTAMOL
98456989	PREDNISOLONE	98977996	SALBUTAMOL

98977997	SALBUTAMOL	99393990	SALBUTAMOL
98977998	SALBUTAMOL	99394988	SALBUTAMOL
98978997	SALBUTAMOL	99394989	SALBUTAMOL
98978998	SALBUTAMOL	99394990	SALBUTAMOL
98979996	SALBUTAMOL	99395988	SALBUTAMOL
98979997	SALBUTAMOL	99395989	SALBUTAMOL
98979998	SALBUTAMOL	99395990	SALBUTAMOL
98981996	SALBUTAMOL	99396988	SALBUTAMOL
98981997	SALBUTAMOL	99396989	SALBUTAMOL
98981998	SALBUTAMOL	99396990	SALBUTAMOL
99003996	THEOPHYLLINE	99397988	SALBUTAMOL
99003997	THEOPHYLLINE	99397989	SALBUTAMOL
99003998	THEOPHYLLINE	99397990	SALBUTAMOL
99013992	SALBUTAMOL (ALBUTEROL)	99423988	PREDNISOLONE
99050997	THEOPHYLLINE	99423989	PREDNISOLONE
99050998	THEOPHYLLINE	99423990	PREDNISOLONE
99051998	AMINOPHYLLINE+DRIED AL HYDROX GEL	99424989	PREDNISOLONE
99060989	PREDNISONE	99424990	PREDNISOLONE
99060990	PREDNISONE	99425988	PREDNISOLONE
99061989	PREDNISONE	99425989	PREDNISOLONE
99061990	PREDNISONE	99425990	PREDNISOLONE
99062990	PREDNISONE	99531998	SODIUM CROMOGLICATE
99098989	PREDNISONE	99550998	HYDROCORTISONE
99098990	PREDNISONE	99609988	EPHEDRINE
99099988	PREDNISOLONE	99609989	EPHEDRINE
99099989	PREDNISOLONE	99609990	EPHEDRINE
99099990	PREDNISOLONE	99624998	THEOPHYLLINE+PHENOBARB &GUAIFEN
99100989	PREDNISOLONE	99626998	THEOPHYLLINE+ EPHEDRINE SULPHATE
99100990	PREDNISOLONE	99718998	FENOTEROL+ IPRATROPIUM BR
99134996	THEOPHYLLINE	99781998	PREDNISONE
99134997	THEOPHYLLINE	99802998	CORTISONE ACETATE
99134998	THEOPHYLLINE	99803997	CORTISONE ACETATE
99137998	PREDNISOLONESTEAGLATE	99803998	CORTISONE ACETATE
99163998	AMINOPHYLLINE	99804998	CORTISONE ACETATE
99214990	EPHEDRINE	99806998	HYDROCORTISONE
99226998	PREDNISOLONE SODIUM PHOSPHATE	99817992	AMINOPHYLLINE
99228997	PREDNISOLONE	99818992	AMINOPHYLLINE
99228998	PREDNISOLONE	99827992	AMINOPHYLLINE/ALUMINIUM HYDROXIDE DRIED
99254998	IPRATROPIUM BROMIDE+FENOTEROL HYDROBROM	99828992	AMINOPHYLLINE
99256998	IPRATROPIUM BROMIDE+FENOTEROL HYDROBROM	99829992	AMINOPHYLLINE
99326992	SODIUM CROMOGLYCATE	99830992	AMINOPHYLLINE INTRAMUSCULAR
99336998	THEOPHYLLINE	99831992	AMINOPHYLLINE PAEDIATRIC
99393988	SALBUTAMOL	99833996	CHOLINE THEOPHYLLINATE
99393989	SALBUTAMOL	99833997	CHOLINE THEOPHYLLINATE

99833998	CHOLINE THEOPHYLLINATE	1B1N.00	Poor self esteem
99859998	EPHEDRINE	1B1U.00	Symptoms of depression
99873989	AMINOPHYLLINE	1B1U.11	Depressive symptoms
99873990	AMINOPHYLLINE	1B1V.00	C/O - panic attack
99876998	TERBUTALINE+ GUAIFENESIN	1BH..00	Delusions
99877997	TERBUTALINE	1BH..11	Delusion
99877998	TERBUTALINE	1BI..00	Blunted affect
99878996	TERBUTALINE	1BO..00	Mood swings
99878997	TERBUTALINE	1BP..00	Loss of interest
99878998	TERBUTALINE	1BQ..00	Loss of capacity for enjoyment
99879997	TERBUTALINE	1BT..00	Depressed mood
99879998	TERBUTALINE	1BT..11	Low mood
99890998	BETAMETHASONE	1BU..00	Loss of hope for the future
99893996	FENOTEROL	1BY..00	Elevated mood
99893997	FENOTEROL	1Ba0.00	Obsessional thoughts
99893998	FENOTEROL	1P01.00	Psychomotor retardation
99896992	HYDROCORTISONE SODIUM PHOSPHATE	2254.00	O/E - apathetic
99910998	BECLOMETASONE	2257.00	O/E - depressed
99914997	BECLOMETASONE	2258.00	O/E - anxious
99914998	BECLOMETASONE	225C.00	O/E - elated
99922990	AMINOPHYLLINE	62T1.00	Puerperal depression
99930998	IPRATROPIUM BROMIDE	6G00.00	Postnatal depression counselling
99965997	BECLOMETASONE	8BK0.00	Depression management programme
99965998	BECLOMETASONE	8G94.00	Anxiety management training
99966998	ORCIPRENALINE	9HA0.00	On depression register
99967996	ORCIPRENALINE	E10..00	Schizophrenic disorders
99967997	ORCIPRENALINE	E100.00	Simple schizophrenia
99967998	ORCIPRENALINE	E100000	Unspecified schizophrenia

### 10.8.10 Medical codes for mental illnesses combined

Medcode	Description
13Y3.00	Manic-depression association member
1464.00	H/O: schizophrenia
1465.00	H/O: depression
1466.00	H/O: anxiety state
146D.00	H/O: manic depressive disorder
1B13.00	Anxiousness
1B13.11	Anxiousness - symptom
1B17.00	Depressed
1B17.11	C/O - feeling depressed
1B17.12	C/O - feeling unhappy
1B1E.00	Hallucinations

E100200	Chronic schizophrenic
E100400	Acute exacerbation of chronic schizophrenia
E100500	Schizophrenia in remission
E100z00	Simple schizophrenia NOS
E101.00	Hebephrenic schizophrenia
E101z00	Hebephrenic schizophrenia NOS
E102.00	Catatonic schizophrenia
E103.00	Paranoid schizophrenia
E103000	Unspecified paranoid schizophrenia
E103200	Chronic paranoid schizophrenia
E103300	Acute exacerbation of subchronic paranoid schizophrenia
E103400	Acute exacerbation of chronic paranoid schizophrenia
E103500	Paranoid schizophrenia in remission
E103z00	Paranoid schizophrenia NOS
E104.00	Acute schizophrenic episode
E106.00	Residual schizophrenia

E107.00	Schizo-affective schizophrenia		unspecified
E107000	Unspecified schizo-affective schizophrenia	E113100	Recurrent major depressive episodes, mild
E107100	Subchronic schizo-affective schizophrenia	E113200	Recurrent major depressive episodes, moderate
E107200	Chronic schizo-affective schizophrenia	E113300	Recurrent major depressive episodes, severe, no psychosis
E107300	Acute exacerbation subchronic schizo-affective schizophrenia	E113400	Recurrent major depressive episodes, severe, with psychosis
E107400	Acute exacerbation of chronic schizo-affective schizophrenia	E113500	Recurrent major depressive episodes, partial/unspec remission
E107z00	Schizo-affective schizophrenia NOS	E113600	Recurrent major depressive episodes, in full remission
E10y000	Atypical schizophrenia	E113700	Recurrent depression
E10yz00	Other schizophrenia NOS	E113z00	Recurrent major depressive episode NOS
E10z.00	Schizophrenia NOS	E114.00	Bipolar affective disorder, currently manic
E11..12	Depressive psychoses	E114.11	Manic-depressive - now manic
E110.00	Manic disorder, single episode	E114000	Bipolar affective disorder, currently manic, unspecified
E110.11	Hypomanic psychoses	E114100	Bipolar affective disorder, currently manic, mild
E110000	Single manic episode, unspecified	E114200	Bipolar affective disorder, currently manic, moderate
E110100	Single manic episode, mild	E114300	Bipolar affect disord, currently manic, severe, no psychosis
E110200	Single manic episode, moderate	E114400	Bipolar affect disord, currently manic, severe with psychosis
E110300	Single manic episode, severe without mention of psychosis	E115.00	Bipolar affective disorder, currently depressed
E110400	Single manic episode, severe, with psychosis	E115.11	Manic-depressive - now depressed
E110z00	Manic disorder, single episode NOS	E115000	Bipolar affective disorder, currently depressed, unspecified
E111.00	Recurrent manic episodes	E115100	Bipolar affective disorder, currently depressed, mild
E111000	Recurrent manic episodes, unspecified	E115200	Bipolar affective disorder, currently depressed, moderate
E111100	Recurrent manic episodes, mild	E115300	Bipolar affect disord, now depressed, severe, no psychosis
E111200	Recurrent manic episodes, moderate	E115500	Bipolar affect disord, now depressed, part/unspec remission
E111300	Recurrent manic episodes, severe without mention psychosis	E116.00	Mixed bipolar affective disorder
E111400	Recurrent manic episodes, severe, with psychosis	E116000	Mixed bipolar affective disorder, unspecified
E111600	Recurrent manic episodes, in full remission	E116200	Mixed bipolar affective disorder, moderate
E111z00	Recurrent manic episode NOS	E116300	Mixed bipolar affective disorder, severe, without psychosis
E112.00	Single major depressive episode	E116400	Mixed bipolar affective disorder, severe, with psychosis
E112.11	Agitated depression	E116500	Mixed bipolar affective disorder, partial/unspec remission
E112.12	Endogenous depression first episode	E116600	Mixed bipolar affective disorder, in full remission
E112.13	Endogenous depression first episode	E116z00	Mixed bipolar affective disorder, NOS
E112.14	Endogenous depression	E117.00	Unspecified bipolar affective disorder
E112000	Single major depressive episode, unspecified	E117000	Unspecified bipolar affective disorder, unspecified
E112100	Single major depressive episode, mild	E117100	Unspecified bipolar affective disorder, mild
E112200	Single major depressive episode, moderate	E117200	Unspecified bipolar affective disorder, moderate
E112300	Single major depressive episode, severe, without psychosis	E117400	Unspecified bipolar affective disorder, severe with psychosis
E112400	Single major depressive episode, severe, with psychosis	E117500	Unspecified bipolar affect disord, partial/unspec remission
E112500	Single major depressive episode, partial or unspec remission	E117600	Unspecified bipolar affective disorder, in full remission
E112600	Single major depressive episode, in full remission	E117z00	Unspecified bipolar affective disorder, NOS
E112z00	Single major depressive episode NOS	E118.00	Seasonal affective disorder
E113.00	Recurrent major depressive episode		
E113.11	Endogenous depression - recurrent		
E113000	Recurrent major depressive episodes,		



E11y.00	Other and unspecified manic-depressive psychoses	E203100	Obsessional neurosis
E11y000	Unspecified manic-depressive psychoses	E203z00	Obsessive-compulsive disorder NOS
E11y200	Atypical depressive disorder	E204.00	Neurotic depression reactive type
E11yz00	Other and unspecified manic-depressive psychoses NOS	E204.11	Postnatal depression
E11z.00	Other and unspecified affective psychoses	E211100	Hypomanic personality disorder
E11z000	Unspecified affective psychoses NOS	E211200	Depressive personality disorder
E11z100	Rebound mood swings	E211300	Cyclothymic personality disorder
E11z200	Masked depression	E214.00	Compulsive personality disorders
E11zz00	Other affective psychosis NOS	E214.11	Anancastic personality
E12..00	Paranoid states	E275111	Compulsive eating disorder
E120.00	Simple paranoid state	E275711	Compulsive water drinking
E121.00	Chronic paranoid psychosis	E290.00	Brief depressive reaction
E122.00	Paraphrenia	E290z00	Brief depressive reaction NOS
E123.11	Folie a deux	E291.00	Prolonged depressive reaction
E12y.00	Other paranoid states	E2B..00	Depressive disorder NEC
E12yz00	Other paranoid states NOS	E2B0.00	Postviral depression
E12z.00	Paranoid psychosis NOS	E2B1.00	Chronic depression
E13..00	Other nonorganic psychoses	E2D0.00	Disturbance of anxiety and fearfulness childhood/adolescent
E13..11	Reactive psychoses	E2D0000	Childhood and adolescent overanxiousness disturbance
E130.00	Reactive depressive psychosis	E2D0100	Childhood and adolescent fearfulness disturbance
E130.11	Psychotic reactive depression	E2D0z00	Disturbance anxiety and fearfulness childhood/adolescent NOS
E131.00	Acute hysterical psychosis	Eu2..00	[X]Schizophrenia, schizotypal and delusional disorders
E132.00	Reactive confusion	Eu20.00	[X]Schizophrenia
E133.00	Acute paranoid reaction	Eu20000	[X]Paranoid schizophrenia
E134.00	Psychogenic paranoid psychosis	Eu20100	[X]Hebephrenic schizophrenia
E135.00	Agitated depression	Eu20211	[X]Catatonic stupor
E13y.00	Other reactive psychoses	Eu20213	[X]Schizophrenic catatonia
E13y000	Psychogenic stupor	Eu20214	[X]Schizophrenic flexibilatis cerea
E13y100	Brief reactive psychosis	Eu20400	[X]Post-schizophrenic depression
E13yz00	Other reactive psychoses NOS	Eu20511	[X]Chronic undifferentiated schizophrenia
E13z.00	Nonorganic psychosis NOS	Eu20600	[X]Simple schizophrenia
E13z.11	Psychotic episode NOS	Eu20y13	[X]Schizophreniform psychos NOS
E1y..00	Other specified non-organic psychoses	Eu20z00	[X]Schizophrenia, unspecified
E200.00	Anxiety states	Eu21.00	[X]Schizotypal disorder
E200000	Anxiety state unspecified	Eu21.12	[X]Borderline schizophrenia
E200100	Panic disorder	Eu21.18	[X]Schizotypal personality disorder
E200111	Panic attack	Eu22.00	[X]Persistent delusional disorders
E200200	Generalised anxiety disorder	Eu22000	[X]Delusional disorder
E200300	Anxiety with depression	Eu22011	[X]Paranoid psychosis
E200400	Chronic anxiety	Eu22012	[X]Paranoid state
E200500	Recurrent anxiety	Eu22015	[X]Paranoia
E200z00	Anxiety state NOS	Eu22y11	[X]Delusional dysmorphophobia
E203.00	Obsessive-compulsive disorders	Eu23.00	[X]Acute and transient psychotic disorders
E203000	Compulsive neurosis	Eu23000	[X]Acute polymorphic psychot disord

	without symp of schizop	Eu31200	[X]Bipolar affect disorder cur epi manic with psychotic symp
Eu23012	[X]Cycloid psychosis	Eu31300	[X]Bipolar affect disorder cur epi mild or moderate depressn
Eu23100	[X]Acute polymorphic psychot disord with symp of schizopren	Eu31400	[X]Bipol aff disord, curr epis sev depress, no psychot symp
Eu23112	[X]Cycloid psychosis with symptoms of schizophrenia	Eu31500	[X]Bipolar affect dis cur epi severe depres with psyc symp
Eu23200	[X]Acute schizophrenia-like psychotic disorder	Eu31600	[X]Bipolar affective disorder, current episode mixed
Eu23300	[X]Other acute predominantly delusional psychotic disorders	Eu31700	[X]Bipolar affective disorder, currently in remission
Eu23312	[X]Psychogenic paranoid psychosis	Eu31y00	[X]Other bipolar affective disorders
Eu23y00	[X]Other acute and transient psychotic disorders	Eu31z00	[X]Bipolar affective disorder, unspecified
Eu23z00	[X]Acute and transient psychotic disorder, unspecified	Eu32.00	[X]Depressive episode
Eu23z11	[X]Brief reactive psychosis NOS	Eu32.11	[X]Single episode of depressive reaction
Eu23z12	[X]Reactive psychosis	Eu32.12	[X]Single episode of psychogenic depression
Eu24.00	[X]Induced delusional disorder	Eu32.13	[X]Single episode of reactive depression
Eu24.12	[X]Induced paranoid disorder	Eu32000	[X]Mild depressive episode
Eu24.13	[X]Induced psychotic disorder	Eu32100	[X]Moderate depressive episode
Eu25.00	[X]Schizoaffective disorders	Eu32200	[X]Severe depressive episode without psychotic symptoms
Eu25000	[X]Schizoaffective disorder, manic type	Eu32211	[X]Single episode agitated depressn w/out psychotic symptoms
Eu25011	[X]Schizoaffective psychosis, manic type	Eu32212	[X]Single episode major depression w/out psychotic symptoms
Eu25012	[X]Schizophreniform psychosis, manic type	Eu32300	[X]Severe depressive episode with psychotic symptoms
Eu25100	[X]Schizoaffective disorder, depressive type	Eu32311	[X]Single episode of major depression and psychotic symptoms
Eu25111	[X]Schizoaffective psychosis, depressive type	Eu32312	[X]Single episode of psychogenic depressive psychosis
Eu25112	[X]Schizophreniform psychosis, depressive type	Eu32313	[X]Single episode of psychotic depression
Eu25200	[X]Schizoaffective disorder, mixed type	Eu32314	[X]Single episode of reactive depressive psychosis
Eu25212	[X]Mixed schizophrenic and affective psychosis	Eu32400	[X]Mild depression
Eu25z00	[X]Schizoaffective disorder, unspecified	Eu32y00	[X]Other depressive episodes
Eu25z11	[X]Schizoaffective psychosis NOS	Eu32y11	[X]Atypical depression
Eu2y.00	[X]Other nonorganic psychotic disorders	Eu32z00	[X]Depressive episode, unspecified
Eu2y.11	[X]Chronic hallucinatory psychosis	Eu32z11	[X]Depression NOS
Eu2z.00	[X]Unspecified nonorganic psychosis	Eu32z12	[X]Depressive disorder NOS
Eu2z.11	[X]Psychosis NOS	Eu32z13	[X]Prolonged single episode of reactive depression
Eu30.00	[X]Manic episode	Eu32z14	[X] Reactive depression NOS
Eu30.11	[X]Bipolar disorder, single manic episode	Eu33.00	[X]Recurrent depressive disorder
Eu30000	[X]Hypomania	Eu33.11	[X]Recurrent episodes of depressive reaction
Eu30100	[X]Mania without psychotic symptoms	Eu33.12	[X]Recurrent episodes of psychogenic depression
Eu30200	[X]Mania with psychotic symptoms	Eu33.13	[X]Recurrent episodes of reactive depression
Eu30212	[X]Mania with mood-incongruent psychotic symptoms	Eu33.14	[X]Seasonal depressive disorder
Eu30y00	[X]Other manic episodes	Eu33.15	[X]SAD - Seasonal affective disorder
Eu30z11	[X]Mania NOS	Eu33000	[X]Recurrent depressive disorder, current episode mild
Eu31.00	[X]Bipolar affective disorder	Eu33100	[X]Recurrent depressive disorder, current episode moderate
Eu31.11	[X]Manic-depressive illness	Eu33200	[X]Recurr depress disorder cur epi severe without psyc sympt
Eu31.12	[X]Manic-depressive psychosis	Eu33211	[X]Endogenous depression without psychotic symptoms
Eu31.13	[X]Manic-depressive reaction	Eu33212	[X]Major depression, recurrent without psychotic symptoms
Eu31000	[X]Bipolar affective disorder, current episode hypomanic		
Eu31100	[X]Bipolar affect disorder cur epi manic wout psychotic symp		

Eu33213	[X]Manic-depress psychosis,depressd,no psychotic symptoms	Eu53011	[X]Postnatal depression NOS
Eu33300	[X]Recurrent depress disorder cur epi severe with psyc symp	Eu53012	[X]Postpartum depression NOS
Eu33311	[X]Endogenous depression with psychotic symptoms	Eu53111	[X]Puerperal psychosis NOS
Eu33312	[X]Manic-depress psychosis,depressed type+psychotic symptoms	Eu60500	[X]Anankastic personality disorder
Eu33313	[X]Recurr severe episodes/major depression+psychotic symptom	Eu60511	[X]Compulsive personality disorder
Eu33314	[X]Recurr severe episodes/psychogenic depressive psychosis	Eu60512	[X]Obsessional personality disorder
Eu33315	[X]Recurrent severe episodes of psychotic depression	Eu60513	[X]Obsessive-compulsive personality disorder
Eu33316	[X]Recurrent severe episodes/reactive depressive psychosis	Eu92000	[X]Depressive conduct disorder
Eu33400	[X]Recurrent depressive disorder, currently in remission	R001.00	[D]Hallucinations
Eu33y00	[X]Other recurrent depressive disorders	R001000	[D]Hallucinations, auditory
Eu33z00	[X]Recurrent depressive disorder, unspecified	R001100	[D]Hallucinations, gustatory
Eu33z11	[X]Monopolar depression NOS	R001200	[D]Hallucinations, olfactory
Eu34000	[X]Cyclothymia	R001300	[D]Hallucinations, tactile
Eu34012	[X]Cycloid personality	R001400	[D]Visual hallucinations
Eu34013	[X]Cyclothymic personality	R001z00	[D]Hallucinations NOS
Eu34100	[X]Dysthymia	R007z13	[D]Postoperative depression
Eu34111	[X]Depressive neurosis	R00z600	[D]Unhappiness
Eu34112	[X]Depressive personality disorder	Z4I7.00	Acknowledging anxiety
Eu34113	[X]Neurotic depression	Z4I7200	Alleviating anxiety
Eu34114	[X]Persistant anxiety depression	Z4I7211	Reducing anxiety
Eu3y011	[X]Mixed affective episode	Z4L1.00	Anxiety counselling
Eu3y111	[X]Recurrent brief depressive episodes	ZV11000	[V]Personal history of schizophrenia
Eu40012	[X]Panic disorder with agoraphobia	ZV11100	[V]Personal history of affective disorder
Eu41.00	[X]Other anxiety disorders	ZV11111	[V]Personal history of manic-depressive psychosis
Eu41000	[X]Panic disorder [episodic paroxysmal anxiety]	ZV11112	[V]Personal history of manic-depressive psychosis
Eu41011	[X]Panic attack		
Eu41012	[X]Panic state		
Eu41100	[X]Generalized anxiety disorder		
Eu41111	[X]Anxiety neurosis		
Eu41112	[X]Anxiety reaction		
Eu41113	[X]Anxiety state		
Eu41200	[X]Mixed anxiety and depressive disorder		
Eu41211	[X]Mild anxiety depression		
Eu41300	[X]Other mixed anxiety disorders		
Eu41z00	[X]Anxiety disorder, unspecified		
Eu41z11	[X]Anxiety NOS		
Eu42.00	[X]Obsessive - compulsive disorder		
Eu42.12	[X]Obsessive-compulsive neurosis		
Eu42000	[X]Predominantly obsessional thoughts or ruminations		
Eu42100	[X]Predominantly compulsive acts [obsessional rituals]		
Eu42200	[X]Mixed obsessional thoughts and acts		
Eu42z00	[X]Obsessive-compulsive disorder, unspecified		
Eu51511	[X]Dream anxiety disorder		

### 10.8.11 Medical codes for epilepsy

Medcode	Description
R003100	[D]Convulsions, infantile
R003z00	[D]Convulsion NOS
F256000	Hypsarrhythmia
Q480.11	Fits in newborn
Q480.00	Convulsions in newborn
F258.00	Post-ictal state
1B64.00	Had a convulsion
R003.00	[D]Convulsions
282..11	O/E - a convulsion
2825.00	O/E - psychomotor fit
2824.11	O/E - Jacksonian fit
R003y00	[D]Other specified convulsion
6676.00	Last fit
282..00	O/E - fit/convulsion
282..12	O/E - a fit
R003200	[D]Fit
2822.00	O/E - grand mal fit
F252.00	Petit mal status
2824.12	O/E - focal fit
Ryu7100	[X]Other and unspecified convulsions
F253.00	Grand mal status
282Z.00	O/E - fit/convulsion NOS
1B63.11	Fit - had one, symptom
6675.00	Fit frequency
1B64.11	Convulsion - symptom
2824.00	O/E - focal (Jacksonian) fit
1B63.00	Had a fit
2823.00	O/E - petit mal fit
F25y500	Panayiotopoulos syndrome
667N.00	Epilepsy severity
667D.00	Epilepsy control poor
667Z.00	Epilepsy monitoring NOS
ZS82.00	Acquired epileptic aphasia
F250100	Pykno-epilepsy
F251.00	Generalised convulsive epilepsy
F250000	Petit mal (minor) epilepsy
667V.00	Many seizures a day
667G.00	Epilepsy restricts employment
F255600	Simple partial epileptic seizure
F255500	Unilateral epilepsy

667W.00	Emergency epilepsy treatment since last appointment
F132z12	Myoclonic seizure
667S.00	1 to 7 seizures a week
F250011	Epileptic absences
F25A.00	Juvenile myoclonic epilepsy
F250z00	Generalised nonconvulsive epilepsy NOS
F25y200	Locl-rlt(foc)(part)idiop epilep&epilptic syn seiz locl onset
6678.00	Epilepsy treatment changed
F25z.00	Epilepsy NOS
667R.00	2 to 4 seizures a month
Q480.12	Seizures in newborn
282..13	O/E - a seizure
667A.00	Epilepsy treatment stopped
F254000	Temporal lobe epilepsy
F250y00	Other specified generalised nonconvulsive epilepsy
F256.12	West syndrome
F255z00	Partial epilepsy without impairment of consciousness NOS
90f4.00	Epilepsy monitoring telephone invite
F255200	Somatosensory epilepsy
F256.00	Infantile spasms
667K.00	Epilepsy limits activities
F250500	Lennox-Gastaut syndrome
1030.00	Epilepsy confirmed
667P.00	No seizures on treatment
2126000	Epilepsy resolved
667C.00	Epilepsy control good
6672.00	Follow-up epilepsy assessment
667X.00	No epilepsy drug side effects
F251z00	Generalised convulsive epilepsy NOS
667J.00	Epilepsy impairs education
F256.11	Lightning spasms
6677.00	Epilepsy drug side effects
Fyu5000	[X]Other generalized epilepsy and epileptic syndromes
667L.00	Epilepsy does not limit activities
F253.11	Status epilepticus
2828.00	Absence seizure
8BIF.00	Epilepsy medication review
667Q.00	1 to 12 seizures a year
F255000	Jacksonian, focal or motor epilepsy
212J.00	Epilepsy resolved
F254100	Psychomotor epilepsy
1B1W.00	Transient epileptic amnesia
R003400	[D]Nocturnal seizure
F254500	Complex partial epileptic seizure

F25X.00	Status epilepticus, unspecified	667F.00	Seizure free >12 months
F255012	Motor epilepsy	F250.00	Generalised nonconvulsive epilepsy
F254400	Epileptic automatism	Fyu5200	[X]Other status epilepticus
F25y100	Gelastictic epilepsy	F255011	Focal epilepsy
90F3.00	Epilepsy monitoring verbal invite	F251111	Otoharara syndrome
F251000	Grand mal (major) epilepsy	F250300	Epileptic seizures - akinetic
F132100	Progressive myoclonic epilepsy	F25y.00	Other forms of epilepsy
6671.00	Initial epilepsy assessment	F25E.00	Stress-induced epilepsy
F251500	Tonic-clonic epilepsy	F25z.11	Fit (in known epileptic) NOS
6679.00	Epilepsy treatment started	Fyu5100	[X]Other epilepsy
667H.00	Epilepsy prevents employment	F251y00	Other specified generalised convulsive epilepsy
F254.00	Partial epilepsy with impairment of consciousness	8CE7.00	Epilepsy leaflet given
F251400	Epileptic seizures - tonic	F254300	Limbic system epilepsy
F257.00	Kojevnikov's epilepsy	F251100	Neonatal myoclonic epilepsy
F255311	Partial epilepsy with autonomic symptoms	F250400	Juvenile absence epilepsy
F251300	Epileptic seizures - myoclonic	F254200	Psychosensory epilepsy
R003z11	[D]Seizure NOS	F255y00	Partial epilepsy without impairment of consciousness OS
F25y000	Cursive (running) epilepsy	F250200	Epileptic seizures - atonic
F132200	Myoclonic encephalopathy	F25yz00	Other forms of epilepsy NOS
F256100	Salaam attacks	Fyu5900	[X>Status epilepticus, unspecified
F251011	Tonic-clonic epilepsy		
F251200	Epileptic seizures - clonic		
1473.00	H/O: epilepsy		
F25F.00	Photosensitive epilepsy		
F255.00	Partial epilepsy without impairment of consciousness		
F25y400	Benign Rolandic epilepsy		
F25C.00	Drug-induced epilepsy		
F25B.00	Alcohol-induced epilepsy		
667M.00	Epilepsy management plan given		
F259.11	Ohtahara syndrome		
F259.00	Early infant epileptic encephalopathy with suppression bursts		
667..00	Epilepsy monitoring		
F256z00	Infantile spasms NOS		
F25..00	Epilepsy		
F255100	Sensory induced epilepsy		
SC20000	Traumatic epilepsy		
667B.00	Nocturnal epilepsy		
F25D.00	Menstrual epilepsy		
F254z00	Partial epilepsy with impairment of consciousness NOS		
6674.00	Epilepsy associated problems		
667T.00	Daily seizures		
F255400	Visual reflex epilepsy		
F251600	Grand mal seizure		
F255300	Visceral reflex epilepsy		

## 10.8.12 Drug codes for epilepsy

Multilexe id	Genericname
99332998	BECLAMIDE tabs 500mg
96914998	BECLAMIDE tabs 500mg
93771990	LAMOTRIGINE disp tab 25mg
95532997	PHENYTOIN susp 30mg/5ml
92200990	TOPIRAMATE tabs 25mg
93016996	VALPROIC ACID ec soft gelatin ca 10mg
95186990	GABAPENTIN tabs 800mg
96339990	PARALDEHYDE inj
92332990	TOPIRAMATE tabs 50mg
92735998	CARBAMAZEPINE supp 125mg
92734997	CARBAMAZEPINE supp 250mg
93934990	LAMOTRIGINE disp tab 25mg
94409997	SODIUM VALPROATE ec tab 500mg
94834996	GABAPENTIN caps 400mg
94090990	LAMOTRIGINE tabs 200mg
83946998	OXCARBAZEPINE oral liq
87401998	PREGABALIN caps 25mg
95409992	PHENOBARBITONE 10 MG PUL
86843998	ZONISAMIDE caps 25mg
92131997	CARBAMAZEPINE mr tab 400mg
92969990	GABAPENTIN caps 100mg
97955992	PRIMIDONE/PHENYTOIN SODIUM TAB
91051997	TOPIRAMATE tabs 100mg
96479992	TEGRETOL liq 100 MG/5ML LIQ
94285992	PHENOBARBITONE 50 MG CAP
84667998	SODIUM VALPROATE mr cap 150mg
95216990	SODIUM VALPROATE + VALPROIC ACID r tab 500mg
94119990	LAMOTRIGINE tabs 50mg
95417992	PHENOBARBITONE 5 MG ELI
96446990	CARBAMAZEPINE mr tab 200mg
94520992	PHENOBARBITONE 75 MG SUP
96697990	CARBAMAZEPINE tabs 400mg
98315996	PHENYTOIN SODIUM caps 100mg
94116990	GABAPENTIN caps 300mg
94282992	PHENOBARBITONE 15 MG CAP
97884992	PHENOBARBITONE & PHENYTOIN 60 5 CAP
92291990	TOPIRAMATE caps 50mg
96885998	CARBAMAZEPINE liq 100mg/5ml
94049990	LAMOTRIGINE tabs 25mg
94834997	GABAPENTIN caps 300mg

94835996	GABAPENTIN caps 400mg
99751990	CARBAMAZEPINE tabs 100mg
99752988	CARBAMAZEPINE tabs 400mg
92197990	TOPIRAMATE tabs 200mg
91625997	OXCARBAZEPINE tabs 300mg
94121990	GABAPENTIN caps 400mg
94092990	LAMOTRIGINE tabs 50mg
93806990	LAMOTRIGINE tabs 200mg
94606997	SODIUM VALPROATE ec tab 500mg
93939990	LAMOTRIGINE tabs 25mg
94568997	SODIUM VALPROATE sf liq 200mg/5ml
94010990	LAMOTRIGINE tabs 200mg
93808990	LAMOTRIGINE tabs 50mg
92700996	LAMOTRIGINE disp tab 100mg
95187990	GABAPENTIN tabs 600mg
94013990	LAMOTRIGINE tabs 25mg
94428992	CANTIL + PHENOBARB TAB
98049990	PHENOBARBITAL tabs 15mg
92388990	OXCARBAZEPINE tabs 300mg
99124989	PHENOBARBITAL tabs 30mg
94166990	GABAPENTIN caps 300mg
91596998	LAMOTRIGINE tabs 200mg
94165990	GABAPENTIN caps 400mg
92284990	TOPIRAMATE caps 25mg
92297990	TOPIRAMATE tabs 50mg
83511998	LACOSAMIDE tabs 150mg
94283992	PHENOBARBITONE 15 MG SUP
83518998	LACOSAMIDE soln for inf 200mg/20ml
92734998	CARBAMAZEPINE supp 125mg
92917997	SODIUM VALPROATE + VALPROIC ACID r tab 300mg
93769997	VIGABATRIN sf powdr 500mg
94409996	SODIUM VALPROATE crushable tab 10mg
99459989	PHENOBARBITAL tabs 30mg
99176997	CLONAZEPAM tabs 2mg
96676990	SODIUM VALPROATE crushable tab 10mg
97203997	PHENOBARBITAL tabs 30mg
95444998	LAMOTRIGINE tabs 50mg
97140990	PHENYTOIN SODIUM tabs 50mg
94068998	VALPROIC ACID (AS SEMISODIUM ALT) ec tab 250mg
98049989	PHENOBARBITAL tabs 30mg
94093990	LAMOTRIGINE tabs 25mg
83707998	SODIUM VALPROATE MR granules 10mg
95553998	PHENOBARBITAL SODIUM inj 10mg/1ml
84095998	STIRIPENTOL sach 500mg

94105990	LAMOTRIGINE tabs 25mg
93493990	LAMOTRIGINE tabs 25mg
99454990	PHENYTOIN SODIUM tabs 50mg
95361992	OSPOLOT 50 MG TAB
92802996	SODIUM VALPROATE sf liq 200mg/5ml
83705998	SODIUM VALPROATE MR granules 100mg
93876990	LAMOTRIGINE disp tab 100mg
93769998	VIGABATRIN tabs 500mg
98111990	PHENOBARBITAL SODIUM inj 100mg/1ml
93460992	LAMICTAL NON-VALPROATE ADD-ON ART PACK TAB 25 mg
98658998	PHENYTOIN susp 30mg/5ml
94120990	LAMOTRIGINE tabs 25mg
82857998	SODIUM VALPROATE MR granules 100mg
83790998	SODIUM VALPROATE + VALPROIC ACID MR granules 1000mg
95161990	GABAPENTIN caps 100mg
96916990	CARBAMAZEPINE tabs 100mg
96536990	CARBAMAZEPINE mr tab 200mg
92918997	SODIUM VALPROATE mr tab 300mg
92389990	OXCARBAZEPINE tabs 150mg
84097998	STIRIPENTOL caps 500mg
97514997	PHENYTOIN paed tab 50mg
98338988	CARBAMAZEPINE tabs 400mg
96128990	CARBAMAZEPINE mr tab 200mg
96159990	SODIUM VALPROATE sf liq 200mg/5ml
84668998	SODIUM VALPROATE MR granules 100mg
96195992	DIAZEPAM 10 MG INJ
95444996	LAMOTRIGINE tabs 25mg
92331990	TOPIRAMATE tabs 100mg
93882990	LAMOTRIGINE tabs 25mg
93769990	LAMOTRIGINE disp tab 5mg
96407998	DIAZEPAM rectal tubes 5mg
89210996	LEVETIRACETAM tabs 1000mg
93530998	CARBAMAZEPINE chewable tab 100mg
89408998	TIAGABINE tabs 5mg
88868997	TOPIRAMATE caps 25mg
93935990	LAMOTRIGINE disp tab 5mg
98385989	SODIUM VALPROATE ec tab 500mg
96536989	CARBAMAZEPINE mr tab 400mg
94087990	LAMOTRIGINE disp tab 100mg
86604998	CLONAZEPAM sf soln 10micrograms/5ml
93768992	PHENOBARBITONE 100 MG SPA
96648997	CLOBAZAM tabs 10mg
90776998	PHENYTOIN SODIUM caps 300mg
87400998	PREGABALIN caps 50mg

95852998	METHYLPHENOBARBITAL tabs 30mg
96978990	PHENYTOIN SODIUM tabs 100mg
95189990	GABAPENTIN caps 300mg
93404992	PHENOBARBITONE 10 MG TAB
96407997	DIAZEPAM rectal tubes 10mg
83896998	PHENYTOIN SODIUM oral liq
94047990	LAMOTRIGINE tabs 100mg
92701990	PHENYTOIN SODIUM inj 250mg/5ml
91050997	TOPIRAMATE tabs 100mg
99110990	PHENOBARBITAL tabs 100mg
99751989	CARBAMAZEPINE tabs 200mg
87193998	LEVETIRACETAM oral soln 100mg/ml
96767998	ETHOSUXIMIDE caps 250mg
93443990	SODIUM VALPROATE ec tab 500mg
93511990	LAMOTRIGINE disp tab 25mg
93530997	CARBAMAZEPINE chewable tab 200mg
97736997	PHENYTOIN SODIUM tabs 100mg
83708998	SODIUM VALPROATE MR granules 100mg
91839998	OXCARBAZEPINE sf oral susp 60mg/ml
87398998	PREGABALIN caps 100mg

## 10.9 DETAILED DESCRIPTION OF SURVEYS AND STUDIES CONDUCTED IN THE UK ON SMOKING DURING PREGNANCY

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
	<p><b>Background:</b> The first infant feeding survey took place in 1975 as a result of recommendation from the Committee on Medical Aspects of Food and Nutrition Policy (COMA) working party to establish basic information about infant feeding practices. Information on smoking during pregnancy was asked for the first time in 1985. All infant feeding surveys were postal surveys, with three stages of each survey.</p> <p>Stage 1: when babies were approx. 6-8 weeks</p> <p>Stage 2: when babies were approx. 4-5 months</p> <p>Stage 3: when babies were approx. 8-10 months</p> <p>59,62,138,139,315,316</p>	<p><b>Background:</b> Health education authority commissioned these surveys of pregnant women to monitor the effectiveness of its smoking and pregnancy campaign targeted at women aged 15-24 years in the social grade C2DE. The 1992 survey was to provide the HEA with some baseline figures. All 9 tracks of HEA survey were conducted in England, based on quota sampling techniques, where door-step screening was used to sample pregnant women, who were home-interviewed after press advertising aimed at reducing smoking during pregnancy each year. 63,64</p>	<p>Smoking behaviour in pregnancy is collected at a woman's first antenatal booking appointment which usually takes place within the first three months of pregnancy. These booking appointments take place either at hospital or in the community and are recorded on the Scottish Woman Held Maternity Record, with data being subsequently transcribed onto the Scottish Morbidity Record (SMR02). Estimates are based on financial year so each year ends on March 31<sup>st</sup>.</p>	
1984				<p>This study was performed between 1<sup>st</sup> October 1982 and 31 March 1984 on patients attending the antenatal clinics at the Stobhill General Hospital , Glasgow. Total sample obtained: 2,765.</p> <p><i>Results</i></p> <p>34.5% of pregnant women smoked</p>



Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
				during pregnancy <sup>317</sup>
1985	<p><b>Sample:</b> Babies born between August to September 1985 in Great Britain, chosen through systematic random sampling of births in a sample of 100 registration sub-districts in England and Wales and birth registrations in Scotland. Social class V was oversampled.</p> <p><b>Sample size, response rate at each stage</b>  Stage 1: initial sample 8,154, response rate (90%), sample obtained 7,396  Stage 2: response rate (81%), sample obtained 5,969  Stage 3: response rate (83%) , sample obtained 4,946</p> <p><b>Results:</b>  39% of women smoked before pregnancy  30% of women smoked during pregnancy  24% gave up smoking during pregnancy<sup>62</sup></p>			
1986				<p>Self-administered questionnaires given to 3882 pregnant women attending antenatal clinics at the Nottingham City Hospital and University Hospital Nottingham between July to August 1986 for six weeks. Response rate 90%, final study sample 3,483.</p> <p><i>Results</i>  31% of women smoked in pregnancy.  36% never smoked, 26% stopped before getting pregnant, 7% stopped</p>

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
				on hearing about pregnancy, 21% reduced their smoking consumption while 2% increased their smoking. 41% of women aged 14-20 smoked during pregnancy compared to 30% aged 21-30 and 22% aged 31 and over. <sup>318</sup>
1987				
1988				
1989				
1990	<p><b>Sample:</b> Babies born between August to October 1990, in the UK. Sampling methodology and frame same as the 1985 survey except for the inclusion of births from Northern Ireland chosen randomly from birth registrations.</p> <p><b>Sample size, response rate at each stage</b>  Stage 1: initial sample 11,105, response rate (88%), sample obtained 9,778  Stage 2: response rate (90%), sample obtained 8,793  Stage 3: response rate (81%) , sample obtained 7,083</p> <p><b>Results:</b>  28% of women smoked before pregnancy  30% of women smoked during pregnancy  27% of women gave up smoking during pregnancy<sup>316</sup></p>			

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
1992		<p><b>Track 1:</b> Baseline measures – January 1992. Sampled 625 pregnant women.</p> <p><b>Results:</b>  40% of the women in the sample were smoking in the 12 months before pregnancy  27% were smoking during pregnancy  44% women had never smoked  36% in C2DE class smoked compared to 14% in ABC1. <sup>64</sup></p> <p><b>Track 2:</b> March 1992 after the launch of HEA campaign, sampled 606 women.</p> <p><b>Results:</b>  39% of the women in the sample were smoking in the 12 months before pregnancy  26% were smoking during pregnancy  45% women had never smoked  34% in C2DE class smoked compared to 14% in ABC1. <sup>64</sup></p>		<p>A systematic random sample of 3200 adults aged over 18 from each of the 19 districts within the North Western Region of UK was taken from the Family Health Services Authority registers. The total sample was 60,800 out of which 38,014 replied, in which 513 women were pregnant.</p> <p><i>Results</i>  29% of pregnant women stated that they smoked and 8.4% smoked more than 15 cigarettes a day. Pregnant smokers were more likely to be under 25 years of age, tenants, and less likely to be engaged in any formal work or education. <sup>319</sup></p>
1993		<p><b>Track 3:</b> March 1993. Sample size = 526 pregnant women.</p>		

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies
		<b>Results:</b> 37% of the women in the sample were smoking in the 12 months before pregnancy 27% were smoking during pregnancy 44% women had never smoked 36% in C2DE class smoked compared to 11% in ABC1. <sup>64</sup>		
1994		<b>Track 4:</b> March 1994. Sample size = 1,039  <b>Results:</b> 41% of the women in the sample were smoking in the 12 months before pregnancy 26% were smoking during pregnancy 43% women had never smoked 35% in C2DE class smoked compared to 14% in ABC1 <sup>64</sup>		
1995	<b>Sample:</b> Babies born between August to October 1995 in the UK chosen randomly from birth registers compiled by the General Register Offices in the UK. Social class V was oversampled.  <b>Sample size, response rate at each stage</b> Initial sample 12,314, response rate (74%) sample obtained 9,130.	<b>Track 5:</b> March 1995. Sample size = 1,002  <b>Results:</b> 39% of the women in the sample were smoking in the 12 months before pregnancy 27% were smoking during	Total women:59,862 Current smokers : 29.0% Former smokers: 7.9% Never smokers: 58.1% Not known: 5.0% <sup>320</sup>	

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies																												
	<p><b>Results:</b></p> <p>35% of women smoked before pregnancy</p> <p>23% of women smoked during pregnancy</p> <p>33% gave up smoking during pregnancy <sup>315</sup></p> <p><i>Smoking in pregnancy by social class</i></p> <table><tr><td>social class</td><td>Before pregnancy</td><td>During pregnancy</td><td>Gave up smoking</td></tr><tr><td>I</td><td>14%</td><td>7%</td><td>50%</td></tr><tr><td>II</td><td>22%</td><td>12%</td><td>44%</td></tr><tr><td>IIINM</td><td>27%</td><td>14%</td><td>47%</td></tr><tr><td>IIIM</td><td>35%</td><td>23%</td><td>33%</td></tr><tr><td>IV</td><td>40%</td><td>28%</td><td>31%</td></tr><tr><td>V</td><td>52%</td><td>37%</td><td>29%</td></tr></table>	social class	Before pregnancy	During pregnancy	Gave up smoking	I	14%	7%	50%	II	22%	12%	44%	IIINM	27%	14%	47%	IIIM	35%	23%	33%	IV	40%	28%	31%	V	52%	37%	29%	<p>pregnancy</p> <p>46% women had never smoked</p> <p>41% in C2DE class smoked compared to</p> <p>11% in ABC1 <sup>64</sup></p>		
social class	Before pregnancy	During pregnancy	Gave up smoking																													
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1996		<p><b>Track 6:</b> March 1996. Sample size = 1,004</p> <p><b>Results:</b></p> <p>41% of the women in the sample were smoking in the 12 months before pregnancy</p> <p>28% were smoking during pregnancy</p> <p>46% women had never smoked</p> <p>39% in C2DE class smoked compared to 15% in ABC1 <sup>64</sup></p>	<p>Total women: 58,478</p> <p>Current smokers: 28.8%</p> <p>Former smokers: 7.9%</p> <p>Never smokers: 58.2%</p> <p>Not known: 5.1% <sup>320</sup></p>																													
1997		<p><b>Track 7:</b> March 1997. Sample size = 1,018</p>	<p>Total women:57,500</p> <p>Current smokers: 29.4%</p>																													

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		<b>Results:</b> 38% of the women in the sample were smoking in the 12 months before pregnancy 26% were smoking during pregnancy 47% women had never smoked 37% in C2DE class smoked compared to 13% in ABC1 64	Former smokers: 8.0% Never smokers: 54.2% Not known: 8.5% <sup>320</sup>																																									
1998		<b>Track 8:</b> March 1998. Sample size = 1,019  <b>Results:</b> 38% of the women in the sample were smoking in the 12 months before pregnancy 22% were smoking during pregnancy 46% women had never smoked 32% in C2DE class smoked compared to 10% in ABC1 <sup>64</sup>	Total women: 57,560 Current smokers: 28.7% Former smokers: 8.2% Never smokers: 56.5% Not known: 6.6% <sup>320</sup>  Smoking by SES <table border="1"> <tr> <th>SES</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr> <tr> <td>SIMD1</td><td>47.8%</td><td>8.1%</td><td>40.0%</td><td>4.2%</td></tr> <tr> <td>SIMD2</td><td>34.3%</td><td>8.3%</td><td>51.3%</td><td>6.0%</td></tr> <tr> <td>SIMD3</td><td>24.5%</td><td>8.4%</td><td>58.5%</td><td>8.5%</td></tr> <tr> <td>SIMD4</td><td>17.1%</td><td>8.9%</td><td>66.7%</td><td>7.4%</td></tr> <tr> <td>SIMD5</td><td>9.8%</td><td>7.3%</td><td>74.9%</td><td>7.9%</td></tr> <tr> <td>NK</td><td>17.9%</td><td>6.0%</td><td>61.5%</td><td>14.7%</td></tr> </table> Smoking by age <table border="1"> <tr> <th>Age</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr> </table>	SES	Current	Former	Never	NK	SIMD1	47.8%	8.1%	40.0%	4.2%	SIMD2	34.3%	8.3%	51.3%	6.0%	SIMD3	24.5%	8.4%	58.5%	8.5%	SIMD4	17.1%	8.9%	66.7%	7.4%	SIMD5	9.8%	7.3%	74.9%	7.9%	NK	17.9%	6.0%	61.5%	14.7%	Age	Current	Former	Never	NK	
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1999		<p><b>Track 9:</b> March 1999. Sample size = 999</p> <p><b>Results:</b>  45% of the women in the sample were smoking in the 12 months before pregnancy  30% were smoking during pregnancy  42% women had never smoked  43% in C2DE class smoked compared to 15% in ABC1 <sup>64</sup></p>	<p>Total women: 55,776  Current smokers: 27.6%  Former smokers: 8.2%  Never smokers: 57.0%  Not known: 7.1% <sup>320</sup></p> <p>Smoking by SES</p> <table> <tr><th>SES</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr> <tr><td>SIMD1</td><td>45.9%</td><td>8.6%</td><td>40.6%</td><td>4.9%</td></tr> <tr><td>SIMD2</td><td>32.5%</td><td>9.0%</td><td>51.7%</td><td>6.7%</td></tr> <tr><td>SIMD3</td><td>24.9%</td><td>8.2%</td><td>57.9%</td><td>9.0%</td></tr> <tr><td>SIMD4</td><td>17.2%</td><td>7.8%</td><td>66.3%</td><td>8.6%</td></tr> <tr><td>SIMD5</td><td>9.1%</td><td>7.3%</td><td>76.7%</td><td>7.0%</td></tr> <tr><td>NK</td><td>18.5%</td><td>8.7%</td><td>54.4%</td><td>18.5%</td></tr> </table> <p>Smoking by age</p> <table> <tr><th>Age</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr> <tr><td>&lt;20</td><td>45.5%</td><td>11.5%</td><td>36.0%</td><td>7.0%</td></tr> <tr><td>20-24</td><td>39.9%</td><td>9.7%</td><td>43.6%</td><td>6.8%</td></tr> <tr><td>25-29</td><td>26.7%</td><td>8.5%</td><td>57.9%</td><td>7.0%</td></tr> <tr><td>30-34</td><td>19.8%</td><td>7.2%</td><td>66.0%</td><td>7.1%</td></tr> </table>	SES	Current	Former	Never	NK	SIMD1	45.9%	8.6%	40.6%	4.9%	SIMD2	32.5%	9.0%	51.7%	6.7%	SIMD3	24.9%	8.2%	57.9%	9.0%	SIMD4	17.2%	7.8%	66.3%	8.6%	SIMD5	9.1%	7.3%	76.7%	7.0%	NK	18.5%	8.7%	54.4%	18.5%	Age	Current	Former	Never	NK	<20	45.5%	11.5%	36.0%	7.0%	20-24	39.9%	9.7%	43.6%	6.8%	25-29	26.7%	8.5%	57.9%	7.0%	30-34	19.8%	7.2%	66.0%	7.1%	
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2000	<p><b>Sample:</b> Babies born between August to October 2000 in the UK chosen randomly from birth registers compiled by the General Register Offices in the UK. In England and Wales a clustered sample within 100 registration districts was selected and Scotland and NI sample was chosen from all registration districts. Social class V was oversampled.</p> <p><b>Sample size, response rate at each stage</b></p> <p>Stage 1: initial sample 13,112, response rate (72%), sample obtained 9,492</p> <p>Stage 2: response rate (87%), sample obtained 8,299</p> <p>Stage 3: response rate (88%) , sample obtained 7,267</p> <p><b>Results:</b></p> <p>35% of women smoked before or during pregnancy</p> <p>20% of women smoked throughout pregnancy</p> <p>44% gave up smoking during or before pregnancy <sup>138</sup></p> <p><i>Smoking in pregnancy by social class</i></p> <table><tr><td>NS-SEC</td><td>Before/during pregnancy</td><td>Throughout pregnancy</td><td>Gave up smoking</td></tr><tr><td>Higher</td><td>22%</td><td>8%</td><td>63%</td></tr><tr><td>Intermediate</td><td>29%</td><td>13%</td><td>55%</td></tr><tr><td>Lower</td><td>46%</td><td>29%</td><td>38%</td></tr><tr><td>Never</td><td>50%</td><td>36%</td><td>29%</td></tr></table>	NS-SEC	Before/during pregnancy	Throughout pregnancy	Gave up smoking	Higher	22%	8%	63%	Intermediate	29%	13%	55%	Lower	46%	29%	38%	Never	50%	36%	29%		<p>Total women: 53,355</p> <p>Current smokers: 26.6%</p> <p>Former smokers: 8.2%</p> <p>Never smokers: 57.3%</p> <p>Not known: 7.9% <sup>320</sup></p> <p>Smoking by SES</p> <table><tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>SIMD1</td><td>44.7%</td><td>8.5%</td><td>40.6%</td><td>6.1%</td></tr><tr><td>SIMD2</td><td>31.7%</td><td>8.8%</td><td>52.0%</td><td>7.4%</td></tr><tr><td>SIMD3</td><td>23.4%</td><td>8.4%</td><td>59.5%</td><td>8.7%</td></tr><tr><td>SIMD4</td><td>16.2%</td><td>8.0%</td><td>66.9%</td><td>8.8%</td></tr><tr><td>SIMD5</td><td>9.5%</td><td>7.1%</td><td>74.4%</td><td>9.0%</td></tr><tr><td>NK</td><td>16.1%</td><td>4.0%</td><td>60.3%</td><td>19.6%</td></tr></table> <p>Smoking by age</p> <table><tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>&lt;20</td><td>44.5%</td><td>10.5%</td><td>37.0%</td><td>8.0%</td></tr><tr><td>20-24</td><td>38.8%</td><td>10.5%</td><td>43.5%</td><td>7.2%</td></tr><tr><td>25-29</td><td>25.8%</td><td>8.1%</td><td>58.4%</td><td>7.6%</td></tr><tr><td>30-34</td><td>19.0%</td><td>7.1%</td><td>66.1%</td><td>7.8%</td></tr><tr><td>35.39</td><td>19.0%</td><td>6.5%</td><td>65.3%</td><td>9.2%</td></tr><tr><td>40+</td><td>17.7%</td><td>6.6%</td><td>64.0%</td><td>11.7%</td></tr></table>	SES	Current	Former	Never	NK	SIMD1	44.7%	8.5%	40.6%	6.1%	SIMD2	31.7%	8.8%	52.0%	7.4%	SIMD3	23.4%	8.4%	59.5%	8.7%	SIMD4	16.2%	8.0%	66.9%	8.8%	SIMD5	9.5%	7.1%	74.4%	9.0%	NK	16.1%	4.0%	60.3%	19.6%	Age	Current	Former	Never	NK	<20	44.5%	10.5%	37.0%	8.0%	20-24	38.8%	10.5%	43.5%	7.2%	25-29	25.8%	8.1%	58.4%	7.6%	30-34	19.0%	7.1%	66.1%	7.8%	35.39	19.0%	6.5%	65.3%	9.2%	40+	17.7%	6.6%	64.0%	11.7%	
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2005	<p><b>Sample:</b> A completely unclustered sample of 19,848 births selected from all births registered in the period August to October 2005. No oversampling of mothers from lower social class groups. Births with no partner oversampled.</p> <p><b>Sample size, response rate at each stage</b></p> <p>Stage 1: initial sample 19,848, response rate (62%), sample obtained 12,290</p> <p>Stage 2: response rate (88%), sample obtained 10,814</p> <p>Stage 3: response rate (87%) , sample obtained 9,416</p> <p><b>Results:</b></p> <p>33% of women smoked before or during pregnancy</p> <p>17% of women smoked throughout pregnancy</p> <p>48% gave up smoking during or before pregnancy <sup>139</sup></p> <p><i>Smoking in pregnancy by social class</i></p> <table><tr><td>NS-SEC</td><td>Before/during pregnancy</td><td>Throughout pregnancy</td><td>Gave up smoking</td></tr><tr><td>Manag/prof.</td><td>22%</td><td>8%</td><td>63%</td></tr><tr><td>Intermediate</td><td>29%</td><td>13%</td><td>55%</td></tr></table>	NS-SEC	Before/during pregnancy	Throughout pregnancy	Gave up smoking	Manag/prof.	22%	8%	63%	Intermediate	29%	13%	55%		<p>Total women:52,646</p> <p>Current smokers: 22.5%</p> <p>Former smokers: 9.3%</p> <p>Never smokers: 60.9%</p> <p>Not known: 7.3% <sup>320</sup></p> <p>Smoking by SES</p> <table><tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>SIMD1</td><td>38.5%</td><td>8.8%</td><td>44.1%</td><td>8.6%</td></tr><tr><td>SIMD2</td><td>27.1%</td><td>10.6%</td><td>55.5%</td><td>6.7%</td></tr><tr><td>SIMD3</td><td>19.8%</td><td>10.7%</td><td>61.9%</td><td>7.5%</td></tr><tr><td>SIMD4</td><td>13.6%</td><td>9.2%</td><td>69.6%</td><td>7.6%</td></tr><tr><td>SIMD5</td><td>7.1%</td><td>7.1%</td><td>80.4%</td><td>5.4%</td></tr><tr><td>NK</td><td>18.0%</td><td>7.9%</td><td>64.0%</td><td>10.1%</td></tr></table> <p>Smoking by age</p> <table><tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>&lt;20</td><td>41.8%</td><td>10.3%</td><td>39.5%</td><td>8.3%</td></tr><tr><td>20-24</td><td>34.3%</td><td>10.9%</td><td>47.5%</td><td>7.2%</td></tr><tr><td>25-29</td><td>22.0%</td><td>10.6%</td><td>60.3%</td><td>7.2%</td></tr><tr><td>30-34</td><td>15.4%</td><td>8.2%</td><td>69.4%</td><td>7.0%</td></tr></table>	SES	Current	Former	Never	NK	SIMD1	38.5%	8.8%	44.1%	8.6%	SIMD2	27.1%	10.6%	55.5%	6.7%	SIMD3	19.8%	10.7%	61.9%	7.5%	SIMD4	13.6%	9.2%	69.6%	7.6%	SIMD5	7.1%	7.1%	80.4%	5.4%	NK	18.0%	7.9%	64.0%	10.1%	Age	Current	Former	Never	NK	<20	41.8%	10.3%	39.5%	8.3%	20-24	34.3%	10.9%	47.5%	7.2%	25-29	22.0%	10.6%	60.3%	7.2%	30-34	15.4%	8.2%	69.4%	7.0%	<p><b>Smoking status at time of delivery, England</b></p> <p>Data for this year didn’t pass the data quality checks hence percentage not given <sup>322</sup></p>
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2006						Total women:52,261 Current smokers: 21.7% Former smokers: 8.5% Never smokers: 60.4% Not known: 9.4% <sup>320</sup>  Smoking by SES <table><tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>SIMD1</td><td>35.7%</td><td>8.2%</td><td>43.9%</td><td>12.2%</td></tr><tr><td>SIMD2</td><td>25.9%</td><td>10.1%</td><td>55.3%</td><td>8.7%</td></tr><tr><td>SIMD3</td><td>19.3%</td><td>9.6%</td><td>62.7%</td><td>8.5%</td></tr><tr><td>SIMD4</td><td>13.4%</td><td>8.1%</td><td>69.1%</td><td>9.4%</td></tr><tr><td>SIMD5</td><td>7.6%</td><td>6.5%</td><td>78.9%</td><td>6.9%</td></tr><tr><td>NK</td><td>15.1%</td><td>9.2%</td><td>61.6%</td><td>14.1%</td></tr></table> Smoking by age					SES	Current	Former	Never	NK	SIMD1	35.7%	8.2%	43.9%	12.2%	SIMD2	25.9%	10.1%	55.3%	8.7%	SIMD3	19.3%	9.6%	62.7%	8.5%	SIMD4	13.4%	8.1%	69.1%	9.4%	SIMD5	7.6%	6.5%	78.9%	6.9%	NK	15.1%	9.2%	61.6%	14.1%	Smoking status at the time of delivery  15.1% maternities smoking out of total 601,262 maternities (95% CI 15.0-15.2%) 2006-07 <sup>322</sup>
SES	Current	Former	Never	NK																																										
SIMD1	35.7%	8.2%	43.9%	12.2%																																										
SIMD2	25.9%	10.1%	55.3%	8.7%																																										
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Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data					Other studies																																																																	
			Age	Current	Former	Never	NK																																																																		
			<20	39.8%	10.0%	40.2%	10.1%																																																																		
			20-24	32.2%	10.2%	47.8%	9.8%																																																																		
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			35-39	14.8%	6.5%	69.2%	9.5%																																																																		
			40+	15.0%	5.2%	70.9%	8.9%																																																																		
2007			Total women:54,197 Current smokers: 20.8% Former smokers: 9.4% Never smokers: 57.8% Not known: 12.0% <sup>320</sup>  Smoking by SES <table><tr><td>SES</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>SIMD1</td><td>33.3%</td><td>8.3%</td><td>40.8%</td><td>17.7%</td></tr><tr><td>SIMD2</td><td>26.1%</td><td>11.1%</td><td>51.6%</td><td>11.2%</td></tr><tr><td>SIMD3</td><td>18.5%</td><td>10.6%</td><td>60.4%</td><td>10.5%</td></tr><tr><td>SIMD4</td><td>12.7%</td><td>9.3%</td><td>67.7%</td><td>10.3%</td></tr><tr><td>SIMD5</td><td>7.6%</td><td>7.6%</td><td>76.8%</td><td>8.0%</td></tr><tr><td>NK</td><td>13.7%</td><td>7.3%</td><td>62.0%</td><td>17.1%</td></tr></table>  Smoking by age <table><tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>&lt;20</td><td>40.4%</td><td>9.9%</td><td>36.2%</td><td>13.4%</td></tr><tr><td>20-24</td><td>31.8%</td><td>10.8%</td><td>44.7%</td><td>12.8%</td></tr><tr><td>25-29</td><td>20.3%</td><td>10.1%</td><td>57.4%</td><td>12.2%</td></tr><tr><td>30-34</td><td>13.8%</td><td>8.9%</td><td>66.2%</td><td>11.1%</td></tr><tr><td>35-39</td><td>13.6%</td><td>7.4%</td><td>67.1%</td><td>11.9%</td></tr></table>					SES	Current	Former	Never	NK	SIMD1	33.3%	8.3%	40.8%	17.7%	SIMD2	26.1%	11.1%	51.6%	11.2%	SIMD3	18.5%	10.6%	60.4%	10.5%	SIMD4	12.7%	9.3%	67.7%	10.3%	SIMD5	7.6%	7.6%	76.8%	8.0%	NK	13.7%	7.3%	62.0%	17.1%	Age	Current	Former	Never	NK	<20	40.4%	9.9%	36.2%	13.4%	20-24	31.8%	10.8%	44.7%	12.8%	25-29	20.3%	10.1%	57.4%	12.2%	30-34	13.8%	8.9%	66.2%	11.1%	35-39	13.6%	7.4%	67.1%	11.9%	<b>Smoking status at time of delivery, England</b>  14.4% (95% CI 14.4%-14.5%) maternities smoking out of total 634,035 maternities - 2007-08 <sup>322</sup>
SES	Current	Former	Never	NK																																																																					
SIMD1	33.3%	8.3%	40.8%	17.7%																																																																					
SIMD2	26.1%	11.1%	51.6%	11.2%																																																																					
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			<table> <tr> <td>40+</td><td>13.6%</td><td>7.7%</td><td>67.6%</td><td>11.2%</td></tr> </table>	40+	13.6%	7.7%	67.6%	11.2%																																																																		
40+	13.6%	7.7%	67.6%	11.2%																																																																						
2008			<p>Total women: 56,927</p> <p>Current smokers: 19.1%</p> <p>Former smokers: 9.0%</p> <p>Never smokers: 57.7%</p> <p>Not known: 14.2% <sup>320</sup></p> <p>Smoking by SES</p> <table> <tr> <th>SES</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr> <tr> <td>SIMD1</td><td>30.1%</td><td>8.2%</td><td>41.1%</td><td>20.6%</td></tr> <tr> <td>SIMD2</td><td>24.2%</td><td>9.7%</td><td>52.8%</td><td>13.3%</td></tr> <tr> <td>SIMD3</td><td>16.9%</td><td>10.7%</td><td>60.2%</td><td>12.1%</td></tr> <tr> <td>SIMD4</td><td>11.8%</td><td>8.9%</td><td>67.5%</td><td>11.8%</td></tr> <tr> <td>SIMD5</td><td>6.5%</td><td>7.6%</td><td>75.7%</td><td>10.2%</td></tr> <tr> <td>NK</td><td>16.3%</td><td>6.4%</td><td>58.7%</td><td>18.6%</td></tr> </table> <p>Smoking by age</p> <table> <tr> <th>Age</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr> <tr> <td>&lt;20</td><td>37.9%</td><td>10.7%</td><td>36.1%</td><td>15.4%</td></tr> <tr> <td>20-24</td><td>29.2%</td><td>10.5%</td><td>45.5%</td><td>14.7%</td></tr> <tr> <td>25-29</td><td>18.7%</td><td>9.7%</td><td>57.2%</td><td>14.4%</td></tr> <tr> <td>30-34</td><td>12.4%</td><td>8.1%</td><td>65.7%</td><td>13.9%</td></tr> <tr> <td>35-39</td><td>12.2%</td><td>7.4%</td><td>66.8%</td><td>13.6%</td></tr> <tr> <td>40+</td><td>13.4%</td><td>6.1%</td><td>67.9%</td><td>12.6%</td></tr> </table>	SES	Current	Former	Never	NK	SIMD1	30.1%	8.2%	41.1%	20.6%	SIMD2	24.2%	9.7%	52.8%	13.3%	SIMD3	16.9%	10.7%	60.2%	12.1%	SIMD4	11.8%	8.9%	67.5%	11.8%	SIMD5	6.5%	7.6%	75.7%	10.2%	NK	16.3%	6.4%	58.7%	18.6%	Age	Current	Former	Never	NK	<20	37.9%	10.7%	36.1%	15.4%	20-24	29.2%	10.5%	45.5%	14.7%	25-29	18.7%	9.7%	57.2%	14.4%	30-34	12.4%	8.1%	65.7%	13.9%	35-39	12.2%	7.4%	66.8%	13.6%	40+	13.4%	6.1%	67.9%	12.6%	<p><b>Smoking status at time of delivery, England</b></p> <p>14.4% (95% CI 14.3%-14.5%)</p> <p>maternities smoking out of a total 640,681 maternities – 2008-09 <sup>322</sup></p>
SES	Current	Former	Never	NK																																																																						
SIMD1	30.1%	8.2%	41.1%	20.6%																																																																						
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40+	13.4%	6.1%	67.9%	12.6%																																																																						
2009			<p>Total women: 57,338</p> <p>Current smokers: 18.1%</p> <p>Former smokers: 8.8%</p>	<p><b>Smoking status at time of delivery, England</b></p>																																																																						



Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data	Other studies																																																																						
			<p>Never smokers: 58.9%</p> <p>Not known: 14.3% <sup>323</sup></p> <p>Smoking by SES</p> <table border="1"> <tr> <th>SES</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr> <tr> <td>SIMD1</td><td>29.4%</td><td>7.6%</td><td>44.2%</td><td>18.8%</td></tr> <tr> <td>SIMD2</td><td>22.1%</td><td>9.8%</td><td>54.8%</td><td>13.3%</td></tr> <tr> <td>SIMD3</td><td>15.9%</td><td>9.8%</td><td>62.4%</td><td>11.9%</td></tr> <tr> <td>SIMD4</td><td>10.9%</td><td>9.5%</td><td>67.6%</td><td>12.0%</td></tr> <tr> <td>SIMD5</td><td>5.8%</td><td>7.4%</td><td>73.6%</td><td>13.2%</td></tr> <tr> <td>NK</td><td>8.9%</td><td>7.0%</td><td>51.4%</td><td>32.7%</td></tr> </table> <p>Smoking by age</p> <table border="1"> <tr> <th>Age</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr> <tr> <td>&lt;20</td><td>36.8%</td><td>11.2%</td><td>38.1%</td><td>13.9%</td></tr> <tr> <td>20-24</td><td>27.8%</td><td>10.7%</td><td>47.0%</td><td>14.4%</td></tr> <tr> <td>25-29</td><td>17.2%</td><td>9.4%</td><td>59.4%</td><td>13.9%</td></tr> <tr> <td>30-34</td><td>11.7%</td><td>7.6%</td><td>66.3%</td><td>14.4%</td></tr> <tr> <td>35-39</td><td>11.1%</td><td>6.8%</td><td>67.6%</td><td>14.5%</td></tr> <tr> <td>40+</td><td>13.4%</td><td>6.2%</td><td>65.8%</td><td>14.7%</td></tr> </table>	SES	Current	Former	Never	NK	SIMD1	29.4%	7.6%	44.2%	18.8%	SIMD2	22.1%	9.8%	54.8%	13.3%	SIMD3	15.9%	9.8%	62.4%	11.9%	SIMD4	10.9%	9.5%	67.6%	12.0%	SIMD5	5.8%	7.4%	73.6%	13.2%	NK	8.9%	7.0%	51.4%	32.7%	Age	Current	Former	Never	NK	<20	36.8%	11.2%	38.1%	13.9%	20-24	27.8%	10.7%	47.0%	14.4%	25-29	17.2%	9.4%	59.4%	13.9%	30-34	11.7%	7.6%	66.3%	14.4%	35-39	11.1%	6.8%	67.6%	14.5%	40+	13.4%	6.2%	65.8%	14.7%	<p>14.1% (14.0%-14.2%) maternities smoking out of a total 647,505 maternities – 2009-10 <sup>322</sup></p>
SES	Current	Former	Never	NK																																																																						
SIMD1	29.4%	7.6%	44.2%	18.8%																																																																						
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2010	<p><b>Sample:</b> A sample of 22,400 births selected from all births registered in the period August to November 2010. All births in Wales and Northern Ireland were sampled and over-sampling of deprived mothers was done in England and Scotland.</p> <p><b>Sample size, response rate at each stage</b>  Stage 1: initial sample 22,400, response rate (52%), further 7,788 questionnaires sent</p>		<p>Total women: 57,398</p> <p>Current smokers: 18.8%</p> <p>Former smokers: 10%</p> <p>Never smokers: 60.6%</p> <p>Not known: 10.7% <sup>203</sup></p> <p>Smoking by SES</p> <table border="1"> <tr> <th>SES</th><th>Current</th><th>Former</th><th>Never</th><th>NK</th></tr> <tr> <td>SIMD1</td><td>30.6%</td><td>8.9%</td><td>50.7%</td><td>9.9%</td></tr> </table>	SES	Current	Former	Never	NK	SIMD1	30.6%	8.9%	50.7%	9.9%	<p><b>Smoking status at time of delivery, England <sup>322</sup></b></p> <p>13.5% (95% CI 13.4%-13.6%) maternities smoking out of a total 659,763 maternities – 2010-11</p>																																																												
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SIMD1	30.6%	8.9%	50.7%	9.9%																																																																						

Year	Infant Feeding Survey	HEA/HDA survey*	Scottish Morbidity Record Data					Other studies																																																																																																								
	<p><b>Results:</b></p> <p>26% of women smoked before or during pregnancy</p> <p>12% of women smoked throughout pregnancy</p> <p>54% gave up smoking during or before pregnancy <sup>59</sup></p> <p><i>Smoking in pregnancy by social class</i></p> <table><tr><td>NS-SEC</td><td>Before/during pregnancy</td><td>Throughout pregnancy</td><td>Gave up smoking</td></tr><tr><td>Manag/prof.</td><td>14%</td><td>4%</td><td>72%</td></tr><tr><td>Intermediate</td><td>26%</td><td>10%</td><td>61%</td></tr><tr><td>Rout./manual</td><td>40%</td><td>20%</td><td>50%</td></tr><tr><td>Never worked</td><td>30%</td><td>21%</td><td>29%</td></tr><tr><td>Unclassified</td><td>29%</td><td>14%</td><td>53%</td></tr></table> <p><i>Smoking in pregnancy by mother's age</i></p> <table><tr><td>age</td><td>Before/during pregnancy</td><td>Throughout pregnancy</td><td>Gave up smoking</td></tr><tr><td>&lt; 20</td><td>57%</td><td>35%</td><td>38%</td></tr><tr><td>20-24</td><td>44%</td><td>22%</td><td>50%</td></tr><tr><td>25-29</td><td>26%</td><td>11%</td><td>58%</td></tr><tr><td>30-34</td><td>17%</td><td>7%</td><td>62%</td></tr><tr><td>35+</td><td>15%</td><td>9%</td><td>58%</td></tr></table>	NS-SEC	Before/during pregnancy	Throughout pregnancy	Gave up smoking	Manag/prof.	14%	4%	72%	Intermediate	26%	10%	61%	Rout./manual	40%	20%	50%	Never worked	30%	21%	29%	Unclassified	29%	14%	53%	age	Before/during pregnancy	Throughout pregnancy	Gave up smoking	< 20	57%	35%	38%	20-24	44%	22%	50%	25-29	26%	11%	58%	30-34	17%	7%	62%	35+	15%	9%	58%		<table><tr><td>SIMD2</td><td>22.0%</td><td>10.6%</td><td>56.8%</td><td>10.6%</td></tr><tr><td>SIMD3</td><td>16.9%</td><td>11.0%</td><td>62.2%</td><td>9.9%</td></tr><tr><td>SIMD4</td><td>11.3%</td><td>10.1%</td><td>69.3%</td><td>9.2%</td></tr><tr><td>SIMD5</td><td>6.1%</td><td>9.6%</td><td>70.3%</td><td>14.0%</td></tr><tr><td>NK</td><td>12.1%</td><td>6.9%</td><td>53.4%</td><td>27.6%</td></tr></table> <p>Smoking by age</p> <table><tr><td>Age</td><td>Current</td><td>Former</td><td>Never</td><td>NK</td></tr><tr><td>&lt;20</td><td>38.2%</td><td>12.0%</td><td>40.0%</td><td>9.8%</td></tr><tr><td>20-24</td><td>29.7%</td><td>10.8%</td><td>50.0%</td><td>9.5%</td></tr><tr><td>25-29</td><td>17.9%</td><td>10.0%</td><td>61.8%</td><td>10.3%</td></tr><tr><td>30-34</td><td>12.2%</td><td>9.6%</td><td>67.0%</td><td>11.2%</td></tr><tr><td>35.39</td><td>11.5%</td><td>9.0%</td><td>67.5%</td><td>12.0%</td></tr><tr><td>40+</td><td>12.8%</td><td>8.6%</td><td>67.8%</td><td>10.8%</td></tr></table>	SIMD2	22.0%	10.6%	56.8%	10.6%	SIMD3	16.9%	11.0%	62.2%	9.9%	SIMD4	11.3%	10.1%	69.3%	9.2%	SIMD5	6.1%	9.6%	70.3%	14.0%	NK	12.1%	6.9%	53.4%	27.6%	Age	Current	Former	Never	NK	<20	38.2%	12.0%	40.0%	9.8%	20-24	29.7%	10.8%	50.0%	9.5%	25-29	17.9%	10.0%	61.8%	10.3%	30-34	12.2%	9.6%	67.0%	11.2%	35.39	11.5%	9.0%	67.5%	12.0%	40+	12.8%	8.6%	67.8%	10.8%	
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< 20	57%	35%	38%																																																																																																													
20-24	44%	22%	50%																																																																																																													
25-29	26%	11%	58%																																																																																																													
30-34	17%	7%	62%																																																																																																													
35+	15%	9%	58%																																																																																																													
SIMD2	22.0%	10.6%	56.8%	10.6%																																																																																																												
SIMD3	16.9%	11.0%	62.2%	9.9%																																																																																																												
SIMD4	11.3%	10.1%	69.3%	9.2%																																																																																																												
SIMD5	6.1%	9.6%	70.3%	14.0%																																																																																																												
NK	12.1%	6.9%	53.4%	27.6%																																																																																																												
Age	Current	Former	Never	NK																																																																																																												
<20	38.2%	12.0%	40.0%	9.8%																																																																																																												
20-24	29.7%	10.8%	50.0%	9.5%																																																																																																												
25-29	17.9%	10.0%	61.8%	10.3%																																																																																																												
30-34	12.2%	9.6%	67.0%	11.2%																																																																																																												
35.39	11.5%	9.0%	67.5%	12.0%																																																																																																												
40+	12.8%	8.6%	67.8%	10.8%																																																																																																												

## 10.10 MEDICAL READ CODES FOR CONGENITAL ANOMALIES

Med codes	Description
14H..00	H/O: congenital anomaly
14H1.00	H/O: cardiac anomaly
14H1.11	H/O: heart anomaly
14H2.00	H/O: cleft palate
14H3.00	H/O: cleft lip
14H4.00	H/O: urinary anomaly
14H5.00	H/O: cong. dislocation - hip
14HZ.00	H/O: congenital anomaly NOS
66g..00	Congenital heart condition monitoring
7010111	Insertion of Halber valve for spina bifida
7031000	Repair of meningoencephalocele
7043.00	Repair of spina bifida
7043000	Freeing of spinal tether
7043100	Closure of spinal myelomeningocele
7043200	Closure of spinal meningocele
7043y00	Other specified repair of spina bifida
7043z00	Repair of spina bifida NOS
7406200	Correction of congenital atresia of choana
7409.00	Correction of cleft lip nasal deformity
7409000	Primary correction of cleft lip nasal deformity
7409011	Primary correction of alar cartilage
7409012	McComb primary correction of cleft nose
7409013	Pigott alar leap-frog correction
7409100	Secondary correction of cleft lip nasal deformity
7409111	Secondary correction of alar slump
7409112	Kernahan correction of alar slump
7409113	Skoog correction of alar slump
7409114	Dibbell correction of alar slump
7409200	Correction of cleft lip nasal tip deformity
7409211	Alar base advancement
7409212	Kilner inroll
7409300	Columella lengthening procedure unspecified
7409400	Unilateral columella lengthening operation
7409411	Tajima unilateral columella lengthening operation
7409500	Rhinoplasty for cleft lip nasal deformity
7409600	Septorhinoplasty for cleft lip nasal deformity
7409700	Septoplasty for cleft lip nasal deformity
7409800	Correction of nostril stenosis
7409z00	Correction of nasal deformity NOS
7502.00	Correction of deformity of lip

7502.11	Repair of cleft lip operations
7502000	Primary closure of cleft lip, unspecified
7502011	Lemesurier cleft lip repair
7502012	Millard cleft lip correction
7502013	Randall cleft lip repair
7502014	Tenison cleft lip repair
7502100	Revision of primary closure of cleft lip
7502200	Adjustment to vermilion border of lip NEC
7502300	Unilateral lip adhesion
7502400	Bilateral lip adhesion
7502500	Repair of unilateral cleft lip using straight line technique
7502511	Kilner repair unilateral cleft lip
7502600	Repair unilat cleft lip - rotation advancement flp technique
7502611	Millard repair unilateral cleft lip
7502700	Repair of unilateral cleft lip with triangular flap
7502711	Randall repair unilateral cleft lip
7502712	Skoog repair unilateral cleft lip
7502713	Tennyson repair unilateral cleft lip
7502800	Repair unilateral cleft lip with quadrilateral flap
7502811	Repair unilateral cleft lip with quadrilateral flap
7502900	Repair of unilateral cleft lip unspecified
7502A00	Repair bilateral cleft lip - rotation advancement flap tech
7502A11	Rep bilat cleft lip Millard
7502B00	Repair of bilateral cleft lip with quadrilateral flap
7502B11	Barsky repair bilateral cleft lip
7502C00	Repair of bilateral cleft lip using straight line technique
7502C11	Manchester bilateral cleft lip repair
7502C12	Veau type III bilateral cleft lip repair
7502D00	Repair of bilateral cleft lip unspecified
7502E00	Synchronous bilateral cleft lip repair
7502F00	Asynchronous bilateral cleft lip repair
7502y00	Other specified correction of deformity of lip
7502z00	Correction of deformity of lip NOS
7525.00	Correction of deformity of palate
7525.11	Repair of deformity of palate
7525.12	Repair of cleft palate
7525000	Primary repair of cleft palate, unspecified
7525011	Kilner repair of cleft palate
7525012	Langenbeck repair of cleft palate
7525013	Wardill repair of cleft palate
7525100	Revision of repair of cleft palate
7525200	Repair cleft hard palate post based axial transposition flap
7525211	Repair cleft hard palate post based axial transposition flap

7525212	Wardill repair cleft palate	7905z00	Correction total anomalous pulmonary venous connection NOS
7525213	Veau flap repair cleft palate	7906.00	Closure of defect of atrioventricular septum
7525300	Repair of cleft hard palate with bipedicle flaps	7906000	Close defect atrioventric septum using dual prosthetic patch
7525311	Langenbeck repair cleft palate	7906100	Close defect atrioventric septum using prosthetic patch NEC
7525400	Repair of cleft soft palate with Z-plasty	7906200	Closure defect atrioventricular septum using tissue graft
7525411	Furlow repair cleft palate	7906300	Closure of persistent ostium primum
7525500	Repair of anterior cleft palate with local flap	7906400	Primary closure of defect of atrioventricular septum NEC
7525600	Repair of anterior cleft palate with vomerine flap	7906500	Revision of closure of defect of atrioventricular septum
7525700	Repair of cleft soft palate with intra-velar veloplasty	7906y00	Other specified closure of defect of atrioventricular septum
7525711	Rep anterior cleft palate local flap	7906z00	Closure of defect of atrioventricular septum NOS
7525712	Plastic repair palate mucosal graft	7907.00	Closure of defect of interatrial septum
7525800	Repair cleft soft palate with other musculature correction	7907000	Closure defect of interatrial septum using prosthetic patch
7525y00	Other specified correction of deformity of palate	7907100	Closure defect of interatrial septum using pericardial patch
7525z00	Correction of deformity of palate NOS	7907200	Closure defect of interatrial septum using tissue graft NEC
7606000	Closure of tracheoesophageal fistula	7907300	Primary closure of defect of interatrial septum NEC
7606011	Excision of tracheoesophageal fistula	7907400	Revision of closure of defect of interatrial septum
7606200	Correction of congenital atresia of oesophagus	7907y00	Other specified closure of defect of interatrial septum
761B100	Repair of congenital atresia of pylorus	7907z00	Closure of defect of interatrial septum NOS
7902.00	Correction of tetralogy of Fallot	7908.00	Closure of defect of interventricular septum
7902000	Correct Fallot tetralogy- valved right ventr outflow conduit	7908000	Close defect interventricular septum using prosthetic patch
7902100	Correct Fallot tetralogy- right ventric outflow conduit NEC	7908100	Close defect interventricular septum using pericardial patch
7902200	Correct Fallot tetralogy- right ventricular outflow patch	7908200	Close defect interventricular septum using tissue graft NEC
7902300	Revision of correction of tetralogy of Fallot	7908300	Primary closure of defect of interventricular septum NEC
7902y00	Other specified correction of tetralogy of Fallot	7908400	Revision of closure of defect of interventricular septum
7902z00	Correction of tetralogy of Fallot NOS	7908y00	Other specified closure of defect of interventricular septum
7903.00	Atrial inversion ops for transposition of great vessels	7908z00	Closure of defect of interventricular septum NOS
7903.11	Mustard interatrial tr venous return	7909.00	Closure of defect of unspecified septum of heart
7903.12	Senning correction for transposition of great vessels	7909000	Closure of defect of heart septum using prosthetic patch NEC
7903000	Atrium reconstruction atrial patch for transpos great vessel	7909100	Closure defect of heart septum using pericardial patch NEC
7903100	Atrium reconstruction atrial wall for transpos great vessels	7909200	Closure of defect of septum of heart using tissue graft NEC
7903y00	Atrial inversion op for transposition of great vessels OS	7909300	Primary closure of defect of septum of heart NEC
7903z00	Atrial inversion op for transposition of great vessels NOS	7909400	Revision of closure of septum of heart NEC
7904.00	Other correction of transposition of great vessels	7909y00	Other specified closure of defect unspecified heart septum
7904000	Repositioning of transposed great vessels	7909z00	Closure of defect of unspecified septum of heart NOS
7904y00	Other correction of transposition of great vessels OS	7A00.00	Open operations for combined abnormality of great vessels
7904z00	Other correction of transposition of great vessels NOS	7A00000	Correction of persistent truncus arteriosus
7905.00	Correction of total anomalous pulmonary venous connection	7A00100	Application of band to persistent truncus arteriosus
7905000	Correct total anomal pulm venous connect to supracard vessel	7A00200	Repair of hemitruncus arteriosus
7905100	Correct total anomal pulm venous connect to coronary sinus	7A00300	Closure of aortopulmonary window
7905200	Correct total anomal pulm venous connect to infradiaph vess	7A00y00	Open operation for combined abnormality of great vessels OS
7905y00	Correction of total anomalous pulmonary venous connection OS		

7A00z00	Open operation for combined abnormality of great vessels NOS	7L0F200	Correction of syndactyly of fingers using skin graft
7A01.00	Open correction of patent ductus arteriosus	7L0F300	Correction of syndactyly of fingers using skin expander
7A01.11	Open correction of patent ductus arteriosus (PDA)	7L0F400	Amputation of duplicate thumb
7A01000	Division of patent ductus arteriosus	7L0F500	Amputation of supernumerary finger NEC
7A01100	Ligation of patent ductus arteriosus	7L0F600	Stabilisation of hypoplastic thumb
7A01200	Closure of patent ductus arteriosus NEC	7L0F700	Repositioning of thumb for cleft hand
7A01300	Revision of correction of patent ductus arteriosus	7L0F800	Correction of cleft hand
7A01y00	Other specified open correction of patent ductus arteriosus	7L0F900	Release of thumb-in-palm deformity
7A01z00	Open correction of patent ductus arteriosus NOS	7L0FA00	Realignment of congenital ulnar drift
7A02.00	Transluminal operations on abnormality of great vessel	7L0FB00	Correction of camtodactyly
7A02000	Percut transluminal prosth occlusion patent ductus arterios	7L0FC00	Correction of clinodactyly with osteotomy and bone graft
7A02011	Percut translum prosth occlus patent ductus arteriosus (PDA)	7L0FD00	Correction of clinodactyly with closing wedge osteotomy
7A02y00	Transluminal operation on abnormality of great vessel OS	7L0FE00	Correction of clinodactyly with reversed wedge osteotomy
7A02z00	Transluminal operation on abnormality of great vessel NOS	7L0FF00	Correction of radial polydactyly
7B41000	Other hypospadias repair	7L0FG00	Excision of radial digit & skeletal repair for polydactyly
7B41011	Byars hypospadias repair	7L0FH00	Excision of ulnar digit and skeletal repair for polydactyly
7B41012	Cecil reconstruction of urethra	7L0FJ00	Correction of macrodactyly
7B41013	Denis - Browne hypospadias repair	7L0Fy00	Other specified correction of congenital deformity of hand
7B41014	Ombredanne hypospadias repair	7L0Fz00	Correction of congenital deformity of hand NOS
7B41015	Van der Meulen hypospadias repair	7L0G.00	Correction of congenital deformity of hip
7B41016	Young hypospadias repair	7L0G000	Open reduction of congenital dislocation of hip
7B41017	First stage hypospadias repair	7L0G011	Ferguson open reduction of congenital deformity of hip
7B41018	Second stage hypospadias repair	7L0G012	Ludloff open reduction of congenital deformity of hip
7B41100	Epispadias repair	7L0G100	Primary osteotomy pelvis correction congenital deformity hip
7B41111	Browne-Denis epispadias repair	7L0G111	Albee osteotomy of pelvis
7B41112	Denis-Browne epispadias repair	7L0G112	Bosworth osteotomy of pelvis
7B41113	Young-Dees epispadias repair	7L0G113	Chiari osteotomy of pelvis
7B41700	MAGPI hypospadias repair	7L0G114	Dial osteotomy of pelvis
7B41800	Duckett hypospadias repair	7L0G115	Gill osteotomy of pelvis
7C04200	Excision of cyst of male hydatid of Morgagni	7L0G116	Pemberton osteotomy of ilium
7C09700	Excision of appendix of testis	7L0G117	Salter osteotomy of pelvis
7C09711	Excision of male hydatid of Morgagni	7L0G118	Shelf procedure for stabilisation of hip joint
7F1A300	Drainage of hydrocephalus of fetus to facilitate delivery	7L0G119	Steez osteotomy of pelvis
7H01000	Correction of pectus deformity of chest wall	7L0G11A	Sutherland osteotomy of pelvis
7H01011	Correction of pectus carinatum	7L0G200	Secndry arthroplasty hip for correctn congenital deformity
7H01012	Correction of pectus excavatum	7L0G211	Colonna arthroplasty of hip
7H0D300	Repair of congenital diaphragmatic hernia	7L0G300	Intraartic soft tiss proced correct congenital deformity hip
7L0D.00	Correction of congenital deformity of shoulder or upper arm	7L0G400	Extraarticular proced correction congenital deformity of hip
7L0E.00	Correction of congenital deformity of forearm	7L0G500	Osteotomy of ilium correction of congenital deformity of hip
7L0F.00	Correction of congenital deformity of hand	7L0G600	Femoral osteotomy for correction congenital deformity of hip
7L0F000	Reduction of gigantism of hand	7L0G700	Pelvic osteotomy for congenital deformity of hip
7L0F100	Correction of mirror hand	7L0G800	Salter osteotomy for congenital deformity of hip

7L0G900	Pemberton osteotomy for congenital deformity of hip	7L0Jz00	Primary correction of congenital deformity of foot NOS
7L0GA00	Chiari osteotomy for congenital deformity of hip	7L0K.00	Other correction of congenital deformity of foot
7L0GB00	Colonna osteotomy for congenital deformity of hip	7L0K.11	Other operations for club foot
7L0GC00	Shelf procedure for correction congenital deformity of hip	7L0K.12	Other correction of talipes
7L0Gy00	Other specified correction of congenital deformity of hip	7L0K000	Osteotomy of body of os calcis
7L0Gz00	Correction of congenital deformity of hip NOS	7L0K011	Baker osteotomy of body of os calcis
7L0Gz11	Adams correction of congenital dislocation of hip	7L0K012	Dwyer osteotomy of body of os calcis
7L0H.00	Correction of congenital deformity of leg	7L0K100	Wedge tarsectomy for correction congenital deformity of foot
7L0H000	Open reduction of congenital dislocation of knee	7L0K111	Elmslie wedge tarsectomy
7L0H100	Correction of pseudarthrosis of tibia	7L0K200	Reduction of gigantism of foot
7L0H111	Boyd bone graft pseudarthrosis of tibia	7L0K300	Separation of tarsal coalition
7L0H112	McFarland bone graft pseudoarthrosis of tibia	7L0K400	Triple arthrodesis for correction of congenital deformity
7L0H200	Excision of anlage of fibula	7L0K500	Dilwyn Evans proc for correction of congenital deformity
7L0H300	Excision of anlage of tibia	7L0K600	Metatarsal osteotomy for correction of congenital deformity
7L0H400	Centralisation tarsus correction congenital deformity of leg	7L0K700	Closure of cleft foot
7L0H500	Reversal rotation plasty ankle correct congenital deform leg	7L0Ky00	Other correction of congenital deformity of foot OS
7L0H511	Van Nes rotationplasty for congenital deformity	7L0Kz00	Other correction of congenital deformity of foot NOS
7L0H600	Coventry tibial osteotomy	7L0L.00	Correction of minor congenital deformity of foot
7L0H700	Gruca tibial bifurcation procedure	7L0L000	Release of Streeter(constriction) band
7L0H800	Open reduction congenital dislocation of patella	7L0L100	Release of syndactyly of toes
7L0H900	Tibiofibular synostosis for congenital deformity	7L0L200	Amputation of supernumerary toe
7L0Hy00	Other specified correction of congenital deformity of leg	7L0L300	Correction of curly fifth toe
7L0Hz00	Correction of congenital deformity of leg NOS	7L0L311	Lapidus transplantation of tendon of fifth toe
7L0J.00	Primary correction of congenital deformity of foot	7L0L400	Correction of congenital crossed toes
7L0J.11	Primary correction of club foot	7L0L500	Reduction of macrodactyly of toe
7L0J.12	Primary correction of talipes	7L0Ly00	Correction of minor congenital deformity of foot OS
7L0J000	Release pantalar joints correction congenital deformity foot	7L0Lz00	Correction of minor congenital deformity of foot NOS
7L0J011	Turco soft tissue release for club foot	7L0N.00	Correction of complex craniofacial deformity
7L0J100	Post release foot joints for correction congenital deformity	7L0N000	Cranio-orbital remodelling for plagiocephaly
7L0J200	Medial release foot joints- correction congenital deformity	7L0N100	Cranio-orbital remodelling for trigonocephaly
7L0J211	Dillwyn operation for club foot	7L0N200	Cranio-orbital remodelling, unspecified
7L0J212	Evans operation for club foot	7L0N400	Frontal advancement - fixed
7L0J213	Medial release of joints of foot for correction of club foot	7L0N500	Correction of oblique facial cleft
7L0J214	Perkins operation for club foot	7L0Nz00	Correction of complex craniofacial deformity NOS
7L0J300	Anterior release foot joints correction congenital deformity	9RD0.00	Transfer of care from paediatric congenital heart service
7L0J400	Posteromedial release of clubfoot	A560200	Rubella deafness
7L0J500	Combined posteromedial + posterolateral release of clubfoot	AD00.00	Toxoplasma meningoencephalitis
7L0J600	Lateral release for congenital deformity of foot	F030700	Encephalitis due to cytomegalovirus
7L0J700	Correction of congenital vertical talus	F030711	Cytomegaloviral encephalitis
7L0J800	Complete subtalar release of clubfoot	F033400	Encephalitis due to toxoplasmosis
7L0Jy00	Primary correction of congenital deformity of foot OS	F033411	Toxoplasmosis encephalitis
		F113000	Normal pressure hydrocephalus

F113011	Low pressure hydrocephalus	P101200	Chiari malformation type III
F115.00	Hydrocephalus	P101300	Chiari malformation type IV
F11x300	Cerebral degeneration due to congenital hydrocephalus	P102.00	Spina bifida with hydrocephalus - open
F23y511	Congenital suprabulbar paresis	P102.11	Fissured spine with hydrocephalus
F427J00	Leber's congenital amaurosis	P102.12	Hydromyelocele with hydrocephalus
F480011	Congenital amblyopia	P102.13	Myelocele with hydrocephalus
F486300	Congenital night blindness NOS	P102.14	Rachischisis with hydrocephalus
F4Gy011	Encephalocele of orbit	P102000	Unspecified spina bifida with hydrocephalus - open
F4K5100	Congenital nystagmus	P102100	Cervical spina bifida with hydrocephalus - open
F591800	Congenital prelingual deafness	P102200	Thoracic spina bifida with hydrocephalus - open
L236.00	Hydrocephalic disproportion	P102300	Lumbar spina bifida with hydrocephalus - open
L236000	Hydrocephalic disproportion unspecified	P102400	Sacral spina bifida with hydrocephalus - open
L236200	Hydrocephalic disproportion with antenatal problem	P102z00	Spina bifida with hydrocephalus - open NOS
L236z00	Hydrocephalic disproportion NOS	P103.00	Spina bifida with hydrocephalus - closed
L253.11	Fetus with suspected rubella damage via mother	P103000	Unspecified spina bifida with hydrocephalus - closed
L254.12	Suspect fetal damage from maternal toxoplasmosis	P103100	Cervical spina bifida with hydrocephalus - closed
P0...00	Anencephalus and similar anomalies	P103200	Thoracic spina bifida with hydrocephalus - closed
P00..00	Anencephalus	P103300	Lumbar spina bifida with hydrocephalus - closed
P00..11	Congenital absence of brain	P103400	Sacral spina bifida with hydrocephalus - closed
P000.00	Acrania	P103z00	Spina bifida with hydrocephalus - closed NOS
P001.00	Amyelencephalus	P103z11	Thoracolumbar spina bifida with hydrocephalus - closed
P002.00	Hemicephaly	P104.00	Spina bifida with hydrocephalus of late onset
P002.11	Hemianencephaly	P105.00	Spina bifida with stenosis of aqueduct of Sylvius
P00y.00	Other specified anencephalus	P10y.00	Other specified spina bifida with hydrocephalus
P00z.00	Anencephalus NOS	P10y000	Dandy - Walker syndrome with spina bifida
P01..00	Craniorachischisis	P10yz00	Other spina bifida with hydrocephalus NOS
P02..00	Iniencephaly	P10z.00	Spina bifida with hydrocephalus NOS
P020.00	Iniencephaly - closed	P11..00	Spina bifida without mention of hydrocephalus
P021.00	Open iniencephaly	P110.00	Spina bifida without mention of hydrocephalus, unspecified
P02z.00	Iniencephaly NOS	P110.11	Split notochord syndrome
P0z..00	Anencephalus and similar anomalies NOS	P110000	Spina bifida without hydrocephalus, site unspecified
P1...00	Spina bifida	P110100	Cervical spina bifida without mention of hydrocephalus
P10..00	Spina bifida with hydrocephalus	P110200	Thoracic spina bifida without mention of hydrocephalus
P10..11	Arnold - Chiari syndrome	P110300	Lumbar spina bifida without mention of hydrocephalus
P100.00	Unspecified spina bifida with hydrocephalus	P110z00	Unspecified spina bifida without hydrocephalus NOS
P100000	Spina bifida with hydrocephalus, unspecified	P111.00	Spinal hydromeningocele
P100100	Cervical spina bifida with hydrocephalus	P111000	Spinal hydromeningocele, unspecified
P100200	Thoracic spina bifida with hydrocephalus	P111100	Cervical spinal hydromeningocele
P100300	Lumbar spina bifida with hydrocephalus	P111200	Thoracic spinal hydromeningocele
P100z00	Spina bifida with hydrocephalus NOS	P111z00	Spinal hydromeningocele NOS
P101.00	Arnold - Chiari syndrome	P112.00	Hydromyelocele
P101.11	Closed spina bifida with Arnold-Chiari malformation		
P101000	Chiari malformation type I		
P101100	Chiari malformation type II		

P112000	Hydromyelocele of unspecified site	P118400	Sacral spina bifida without hydrocephalus - closed
P112100	Cervical hydromyelocele	P118z00	Spina bifida without hydrocephalus - closed NOS
P112200	Thoracic hydromyelocele	P118z11	Thoracolumbar spina bifida without hydrocephalus - closed
P112300	Lumbar hydromyelocele	P11y.00	Other specified spina bifida without hydrocephalus
P112z00	Hydromyelocele NOS	P11y.11	Syringomyelocele
P113.00	Spinal meningocele	P11z.00	Spina bifida without mention of hydrocephalus NOS
P113000	Spinal meningocele of unspecified site	P11z.11	Rachischisis
P113100	Cervical spinal meningocele	P11z.12	Syringomyelocele
P113200	Thoracic spinal meningocele	P11z.13	Billroth's disease
P113300	Lumbar spinal meningocele	P11z.14	Congenital hernia of dura mater
P113z00	Spinal meningocele NOS	P1z.00	Spina bifida NOS
P114.00	Meningomyelocele	P2...00	Other nervous system congenital anomalies
P114000	Meningomyelocele of unspecified site	P20..00	Encephalocele
P114100	Cervical meningomyelocele	P20..11	Hydroencephalocele
P114200	Thoracic meningomyelocele	P20..12	Cephalocele
P114300	Lumbar meningomyelocele	P20..13	Congenital cerebral hernia
P114z00	Meningomyelocele NOS	P20..14	Congenital endaural hernia
P115.00	Myelocele	P20..15	Sinus pericranii
P115000	Myelocele of unspecified site	P20..16	Congenital cerebral hernia
P115100	Cervical myelocele	P200.00	Encephalocystocele
P115200	Thoracic myelocele	P201.00	Encephalomyelocele
P115300	Lumbar myelocele	P202.00	Hydromeningocele - cranial
P115z00	Myelocele NOS	P203.00	Meningocele - cerebral
P116.00	Myelocystocele	P203.11	Meningocele - cranial
P116000	Myelocystocele of unspecified site	P204.00	Meningoencephalocele
P116100	Cervical myelocystocele	P205.00	Frontal encephalocele
P116200	Thoracic myelocystocele	P206.00	Nasofrontal encephalocele
P116300	Lumbar myelocystocele	P20z.00	Encephalocele NOS
P116z00	Myelocystocele NOS	P20z000	Occipital encephalocele
P117.00	Spina bifida without hydrocephalus - open	P20z100	Encephalocele of other specified site
P117.11	Fissured spine	P20z111	Absence of roof of orbit
P117.12	Rachischisis	P21..00	Microcephalus
P117000	Unspecified spina bifida without hydrocephalus - open	P210.00	Hydromicrocephaly
P117100	Cervical spina bifida without hydrocephalus - open	P211.00	Micrencephaly
P117200	Thoracic spina bifida without hydrocephalus - open	P21z.00	Microcephalus NOS
P117300	Lumbar spina bifida without hydrocephalus - open	P22..00	Reduction deformities of brain
P117400	Sacral spina bifida without hydrocephalus - open	P220.00	Agenesis of brain, part unspecified
P117z00	Spina bifida without hydrocephalus - open NOS	P221.00	Aplasia of brain, part unspecified
P118.00	Spina bifida without hydrocephalus - closed	P222.00	Hypoplasia of brain, part unspecified
P118000	Unspecified spina bifida without hydrocephalus - closed	P223.00	Agyria
P118100	Cervical spina bifida without hydrocephalus - closed	P223.11	Lissencephaly
P118200	Thoracic spina bifida without hydrocephalus - closed	P224.00	Arhinencephaly
P118300	Lumbar spina bifida without hydrocephalus - closed	P225.00	Holoprosencephaly
		P226.00	Microgyria



P226.11	Hypoplasia of brain gyri	P233.11	Dandy - Walker syndrome
P226000	Congenital bilateral perisylvian syndrome	P233.12	Hydrocephalus with atresia of foramina of Magendie+Luschka
P227.00	Anomalies of cerebrum	P234.00	Hydranencephaly
P227000	Agenesis of cerebrum	P23y.00	Other specified congenital hydrocephalus
P227100	Congenital hypoplasia of cerebrum	P23z.00	Congenital hydrocephalus NOS
P227z00	Anomaly of cerebrum NOS	P24..00	Other specified brain anomalies
P228.00	Anomalies of corpus callosum	P240.00	Congenital cerebral cyst
P228000	Congenital absence of corpus callosum	P240.11	Congenital intracerebral cyst
P228011	Agenesis of corpus callosum	P240000	Single congenital cerebral cyst
P228100	Hypoplasia of corpus callosum	P240100	Multiple congenital cerebral cysts
P228200	Aplasia of corpus callosum	P240200	Schizencephaly
P228300	Aicardi syndrome	P240z00	Congenital cerebral cyst NOS
P228z00	Anomaly of corpus callosum NOS	P241.00	Macroencephaly
P229.00	Anomalies of hypothalamus	P241.11	Megalencephaly
P22A.00	Anomalies of cerebellum	P241.12	Enlarged brain
P22A000	Congenital absence of cerebellum	P241.13	Macrocephaly
P22A011	Agenesis of cerebellum	P242.00	Macrogyria
P22A100	Hypoplasia of cerebellum	P243.00	Porencephaly
P22A200	Aplasia of cerebellum	P244.00	Ulegyria
P22Az00	Anomaly of cerebellum NOS	P245.00	Congenital adhesions of cerebral meninges
P22y.00	Other specified reduction deformities of brain	P246.00	Septo-optic dysplasia
P22y000	Cebocephaly	P247.00	Dysplasia of cerebral cortex
P22y100	Familial aplasia of the vermis	P248.00	Congenital dilated lateral ventricles of brain
P22y111	Joubert syndrome	P249.00	Megalencephaly
P22y200	Gillespie syndrome	P24A.00	Hemimegalencephaly
P22y300	Partial absence of septum pellucidum	P24x.00	Multiple brain anomalies
P22yz00	Other reduction deformity of brain NOS	P24z.00	Other specified brain anomalies NOS
P22z.00	Reduction deformities of brain NOS	P25..00	Other specified spinal cord anomalies
P22z.11	Cerebellar hypoplasia	P250.00	Diastematomyelia
P22z.12	Agenesis of part of brain NEC	P251.00	Hydromyelia
P22z.13	Hypoplasia of part of brain NEC	P251.11	Hydrorachis
P22z.14	Aplasia of part of brain NEC	P252.00	Congenital tethering of spinal cord
P23..00	Congenital hydrocephalus	P25y.00	Other specified anomalies of spinal cord
P230.00	Aqueduct of Sylvius anomaly	P25y.11	Neuroenteric cyst
P230.11	Hydrocephalus with anomaly of aqueduct of Sylvius	P25y000	Amyelia
P230.12	Stenosis of aqueduct of Sylvius	P25y100	Atelomyelia
P230000	Aqueduct of Sylvius obstruction	P25y111	Myelatelasia
P230011	Aqueduct of Sylvius septum NEC	P25y112	Myelodysplasia of spinal cord
P230100	Aqueduct of Sylvius stenosis	P25y200	Congenital anomaly of spinal meninges
P230200	Atresia of aqueduct of Sylvius NEC	P25y300	Defective development of the cauda equina
P230z00	Aqueduct of Sylvius anomaly NOS	P25y400	Spinal cord hypoplasia
P231.00	Foramen of Magendie atresia	P25yz00	Other specified spinal cord anomalies NOS
P232.00	Foramen of Luschka atresia	P25z.00	Spinal cord anomalies NOS
P233.00	Atresia of foramina of Magendie and Luschka	P2x..00	Other specified nervous system anomalies

P2x0.00	Agenesis of nerve, unspecified	P321.11	Enlarged eye NOS
P2x1.00	Brachial plexus displacement	P322.00	Buphthalmos with other eye anomaly
P2x2.00	Familial dysautonomia	P322000	Congenital keratoglobus
P2x3.00	Jaw-winking syndrome	P322100	Congenital megalocornea
P2x4.00	Marcus - Gunn syndrome	P322111	Enlarged cornea
P2x5.00	Riley - Day syndrome	P322112	Congenital macrocornea
P2x6.00	Chiari malformation type I	P322z00	Buphthalmos with other eye anomaly NOS
P2x7.00	Congenital facial nerve palsy	P32z.00	Buphthalmos NOS
P2x8.00	Structural central nervous system abnormality	P33..00	Congenital cataract and lens anomalies
P2xz.00	Other specified nervous system anomalies NOS	P33..11	Congenital lens anomaly
P2xz000	Agenesis of nerve NEC	P330.00	Congenital cataract, unspecified
P2xz100	Congenital optic atrophy	P331.00	Capsular and subcapsular cataract
P2y..00	Unspec nervous system anomaly of brain/cord/nervous system	P331000	Capsular cataract
P2y0.00	Congenital brain anomaly	P331100	Subcapsular cataract
P2y1.00	Congenital spinal cord anomaly	P331z00	Capsular or subcapsular cataract NOS
P2yz.00	Unspecified nervous system anomaly NOS	P332.00	Cortical and zonular cataract
P2z..00	Nervous system anomalies NOS	P332000	Cortical cataract - congenital
P3...00	Congenital eye anomalies	P332100	Zonular cataract
P30..00	Anophthalmos	P332z00	Cortical or zonular cataract NOS
P300.00	Clinical anophthalmos, unspecified	P333.00	Nuclear cataract - congenital
P300100	Agenesis of eye	P334.00	Total and subtotal congenital cataract
P300200	Congenital absence of eye	P334000	Total congenital cataract
P300z00	Anophthalmos NOS	P334100	Subtotal congenital cataract
P301.00	Congenital cystic eyeball	P334z00	Total or subtotal congenital cataract NOS
P302.00	Cryptophthalmos syndrome	P335.00	Congenital aphakia
P303.00	Congenital absence of eyes	P335.11	Congenital absence of lens
P30z.00	Anophthalmos NOS	P335.12	Agenesis of lens
P31..00	Microphthalmos	P336.00	Anomalies of lens shape
P310.00	Microphthalmos, unspecified	P336000	Microphakia
P310000	Dysplasia of eye	P336100	Spherophakia
P310100	Hypoplasia of eye	P336111	Spherical lens
P310200	Rudimentary eye	P336200	Coloboma of lens
P310z00	Unspecified microphthalmos NOS	P336z00	Anomalies of lens shape NOS
P311.00	Simple microphthalmos	P337.00	Congenital ectopic lens
P312.00	Microphthalmos with other eye anomaly	P337.11	Congenital displaced lens
P313.00	Lenz microphthalmia syndrome	P337.12	Congenital dislocation of lens
P31z.00	Microphthalmos NOS	P33y.00	Other specified congenital cataract or lens anomaly
P32..00	Buphthalmos	P33y000	Blue dot cataract
P320.00	Buphthalmos, unspecified	P33y100	Congenital membranous cataract
P320000	Congenital glaucoma	P33yz00	Other congenital cataract or lens anomaly NOS
P320011	Newborn glaucoma	P33z.00	Congenital cataract or lens anomaly NOS
P320100	Hydrophthalmos	P34..00	Anterior chamber anomalies
P320z00	Unspecified buphthalmos NOS	P340.00	Corneal size and shape anomalies
P321.00	Simple buphthalmos	P340000	Microcornea

P340100	Congenital keratoconus	P355.00	Other congenital retinal changes
P340200	Cornea plana	P355000	Coloboma of retina
P340z00	Corneal size or shape anomalies NOS	P355100	Congenital retinal fold
P341.00	Congenital corneal opacities	P355200	Congenital hypertrophy of retinal pigment epithelium
P341.11	Arcus juvenilis	P355z00	Other congenital retinal changes NOS
P341000	Congenital corneal opacity with visual deficit	P356.00	Specified optic disc anomalies
P341100	Congenital corneal opacity without visual deficit	P356.11	Optic disc congenital anomalies
P341z00	Congenital corneal opacities NOS	P356000	Congenital optic disc coloboma
P342.00	Specified anterior chamber anomalies	P356z00	Specified optic disc anomaly NOS
P342000	Axenfield's anomaly	P357.00	Posterior chamber vascular anomalies
P342100	Peter's anomaly	P357000	Congenital retinal aneurysm
P342200	Rieger's anomaly	P357100	Congenital arteriovenous malformation of retina
P342z00	Specified anterior chamber anomalies NOS	P357200	Congenital stricture of retinal artery
P343.00	Aniridia	P357z00	Posterior chamber vascular anomalies NOS
P343.11	Congenital absence of iris	P358.00	Specified anomalies of choroid
P343.12	Agenesis of iris	P358000	Coloboma of choroid
P344.00	Other iris and ciliary body anomalies	P358z00	Specified anomaly of choroid NOS
P344.11	Goniodysgenesis	P35y.00	Other specified congenital anomalies of posterior chamber
P344000	Congenital anisocoria	P35z.00	Congenital anomalies of posterior chamber NOS
P344100	Atresia of pupil	P36..00	Congenital anomalies of eyelid, lacrimal system and orbit
P344200	Coloboma of iris	P360.00	Congenital ptosis
P344300	Corectopia	P360.11	Blepharoptosis
P344311	Ectopic pupil	P361.00	Congenital eyelid deformity
P344400	Polycoria	P361000	Ablepharon -absent eyelids
P344500	Hypoplasia of iris	P361100	Accessory eyelid
P344600	Aplasia of iris	P361200	Congenital entropion
P344z00	Other iris or ciliary body anomalies NOS	P361300	Congenital ectropion
P345.00	Specified anomalies of sclera	P361400	Congenital blepharophimosis
P345000	Blue sclera	P361500	Coloboma of eyelids
P345z00	Specified anomaly of sclera NOS	P361z00	Congenital eyelid deformity NOS
P346.00	Multiple anterior segment anomalies	P362.00	Other specified congenital eyelid anomalies
P34y.00	Other specified anterior segment anomalies	P362000	Agenesis of cilia
P34z.00	Anterior segment anomalies NOS	P362100	Agenesis of eyelid
P35..00	Posterior chamber congenital anomalies	P362200	Fused eyelids
P350.00	Vitreous anomalies	P362300	Hypoplasia of eyelid
P350000	Congenital vitreous opacity	P362z00	Other specified congenital eyelid anomalies NOS
P350z00	Vitreous anomalies NOS	P363.00	Congenital lacrimal gland anomalies
P351.00	Fundus coloboma	P364.00	Congenital lacrimal passage anomalies
P352.00	Congenital chorioretinal degeneration	P364.11	Congenital blocked tear duct
P353.00	Congenital folds and cysts of the posterior segment	P364000	Agenesis of lacrimal apparatus
P353000	Congenital folds of the posterior segment	P364011	Congenital absence of lacrimal apparatus
P353100	Congenital cysts of the posterior segment	P364100	Agenesis of punctum lacrimale
P353z00	Congenital folds or cysts of the posterior segment NOS	P364111	Congenital absence of punctum lacrimale
P354.00	Congenital macular changes		

P364200	Accessory lacrimal canal	P40z.00	Other and unspecified ear anomaly with hearing impaired
P364300	Stenosis or stricture of lacrimal duct	P40z.11	Deafness due to congenital anomaly NEC
P364400	Congenital blocked tear duct	P40z000	Congenital absence of ear NOS
P364y00	Other specified congenital anomaly of lacrimal passages	P40zz00	Ear anomaly with hearing impaired NOS
P364z00	Congenital anomaly of lacrimal passages NOS	P41..00	Accessory ear auricle
P365.00	Congenital orbit anomalies	P41..11	Polyotia
P36z.00	Other/unspecified anomalies of eyelid/lacrimal system/orbit	P410.00	Supernumerary ear
P36z000	Accessory eye muscles	P411.00	Accessory tragus
P36z100	Hypoplasia of eye muscle	P412.00	Supernumerary ear lobule
P36zz00	Eyelid, lacrimal system and orbit congenital anomalies NOS	P413.00	Preauricular appendage, tag or lobule
P37..00	Macrophthalmos	P413.11	Preauricular appendage
P3y..00	Other specified eye anomalies	P413.12	Preauricular tag
P3y0.00	Ocular albinism	P413.13	Preauricular lobule
P3yz.00	Other eye anomalies NOS	P414.00	Other ear appendage or tag
P3z..00	Congenital eye anomalies NOS	P414.11	Other ear appendage
P4...00	Ear, face and neck congenital anomalies	P414.12	Other ear tag
P40..00	Ear anomalies with hearing impairment	P41z.00	Accessory ear auricle NOS
P400.00	Ear anomalies with hearing impaired, unspecified	P42..00	Other specified ear anomalies
P401.00	Congenital absence of external ear	P420.00	Congenital ear lobe absence
P401000	Congenital absence of external ear, unspecified	P421.00	Macrotia - abnormally big ears
P401011	Absence of ear NOS	P421.11	Congenital big ears
P401100	Absence of external auditory canal	P422.00	Microtia - abnormally small ears
P401200	Ear auricle and external auditory canal absent	P422.11	Congenital small ears
P401211	Congenital absence ear auricle	P423.00	Eustachian tube anomalies
P401300	Congenital absence of auricle	P423000	Congenital absence of eustachian tube
P401z00	Absence of external ear NOS	P423100	Congenital stenosis of eustachian tube
P402.00	Other external ear anomaly with hearing impairment	P423z00	Eustachian tube anomalies NOS
P402000	Atresia of external auditory canal	P42z.00	Other specified ear anomalies NOS
P402100	Stenosis of external auditory canal	P42z000	Congenital Bat ear
P402111	Congenital stricture of external auditory canal	P42z100	Darwin's tubercle
P402112	Congenital stricture of osseous meatus	P42z200	Congenital pointed ear
P402z00	Other external ear anomaly with hearing impairment NOS	P42z300	Congenital prominent auricle
P403.00	Middle ear anomaly, excluding ossicles	P42z400	Congenital ridge ear
P403000	Ear osseous meatus atresia	P42z500	Other mis-shapen ear
P403100	Ear osseous meatus stricture	P42z511	Aztec ear
P403z00	Middle ear anomaly NEC NOS	P42z512	Cat ear
P404.00	Anomaly of ossicles	P42z513	Vulcan ear
P404000	Congenital fusion of ear ossicles	P42z600	Misplaced ears
P404z00	Anomaly of ossicles NOS	P42z611	Low-set ears
P405.00	Inner ear anomalies	P42zz00	Other ear anomalies NOS
P405000	Congenital anomaly of the membranous labyrinth	P43..00	Congenital ear anomaly NOS
P405100	Congenital anomaly of the organ of Corti	P44..00	Branchial cleft, cyst or fistula; preauricular sinus
P405z00	Inner ear anomalies NOS	P440.00	Branchial cleft sinus and fistula
		P440.11	Branchial cleft

P440.12	Branchial cleft sinus	P500.11	Persistent truncus arteriosus
P440000	Branchial cleft vestige, unspecified	P500.12	Truncus arteriosus
P440100	Branchial cleft external sinus	P501.00	Aortic septal defect
P440200	Branchial cleft internal sinus	P501.11	Aortopulmonary window
P440300	Branchial cleft fistula	P501.12	Aorticopulmonary septal defect
P440z00	Branchial cleft vestige NOS	P502.00	Persistent truncus arteriosus
P441.00	Branchial cleft cyst	P502.11	Truncus arteriosus
P442.00	Cervical auricle	P50z.00	Common aorto-pulmonary trunk NOS
P443.00	Preauricular sinus and fistula	P51..00	Transposition of great vessels
P443000	Preauricular sinus	P510.00	Total great vessel transposition
P443100	Preauricular fistula	P511.00	Double outlet right ventricle
P443z00	Preauricular sinus or fistula NOS	P511000	Double outlet right ventricle, unspecified
P444.00	Preauricular cyst	P511100	Dextratransposition of aorta
P44y.00	Other branchial cleft anomalies	P511200	Incomplete great vessel transposition
P44z.00	Branchial cleft,cyst,or fistula preauricular anomaly OS/NOS	P511300	Taussig-Bing syndrome
P44z000	Fistula of congenital auricle	P511z00	Double outlet right ventricle NOS
P44z100	Cervicoaural fistula	P512.00	Corrected great vessel transposition
P44zz00	Branchial cleft, cyst or fistula preauricular anomaly NOS	P51y.00	Other specified transposition of great vessels
P45..00	Congenital webbing of neck	P51y.11	Transposition of aorta
P450.00	Congenital neck webbing, unspecified	P51z.00	Great vessel transposition NOS
P451.00	Pterygium colli	P51z.11	Transposition of arterial trunk NEC
P45z.00	Congenital webbing of neck NOS	P52..00	Tetralogy of Fallot
P4y..00	Other specified face and neck anomalies	P520.00	Tetralogy of Fallot, unspecified
P4y0.00	Macrocheilia	P520.11	Ventricular septal defect in Fallot's tetralogy
P4y0.11	Lip hypertrophy	P520.12	Dextraposition of aorta in Fallot's tetralogy
P4y1.00	Microcheilia	P521.00	Pentalogy of Fallot
P4y2.00	Macrostomia	P52z.00	Tetralogy of Fallot NOS
P4y2.11	Congenital hypertrophy of lip	P53..00	Common ventricle
P4y3.00	Microstomia	P54..00	Ventricular septal defect
P4y4.00	Congenital absence of chin	P540.00	Ventricular septal defect, unspecified
P4y5.00	Mid-facial hypoplasia	P541.00	Interventricular septal defect
P4yz.00	Other specified face and neck anomalies NOS	P542.00	Left ventricle to right atrial communication
P4z..00	Congenital face or neck anomaly NOS	P543.00	Eisenmenger's complex
P4z0.00	Congenital anomaly of neck NOS	P544.00	Gerbode's defect
P4z1.00	Congenital anomaly of face NOS	P545.00	Roger's disease
P5...00	Bulbus cordis and cardiac septal closure anomalies	P54y.00	Other specified ventricular septal defect
P5...11	Cardiac septal defects	P54z.00	Ventricular septal defect NOS
P5...12	Congenital heart disease, septal and bulbar anomalies	P55..00	Ostium secundum atrial septal defect
P5...13	Heart septal defects	P550.00	Atrial septal defect NOS
P50..00	Common aorto-pulmonary trunk	P550.11	Auricular septal defect NOS
P50..11	Aortic septal defect	P550.12	Interatrial septal defect NEC
P50..12	Common truncus	P550.13	Interauricular septal defect
P50..13	Persistent truncus arteriosus	P551.00	Patent foramen ovale
P500.00	Absent septum between aorta and pulmonary artery	P552.00	Persistent ostium secundum

P552.11	Patent ostium secundum	P61z.00	Congenital tricuspid atresia or stenosis NOS
P553.00	Lutembacher's syndrome	P62..00	Ebstein's anomaly
P55y.00	Other specified ostium secundum atrial septal defect	P63..00	Congenital aortic valve stenosis
P55y.11	Other specified atrial septal defect	P64..00	Congenital aortic valve insufficiency
P55z.00	Ostium secundum atrial septal defect NOS	P640.00	Congenital aortic valve insufficiency, unspecified
P56..00	Endocardial cushion defects	P641.00	Bicuspid aortic valve
P560.00	Endocardial cushion defects, unspecified	P64z.00	Congenital aortic valve insufficiency NOS
P561.00	Ostium primum defect	P65..00	Congenital mitral stenosis
P561.11	Persistent ostium primum	P65..11	Duroziez's disease
P561.12	Ostium primum type interauricular septal defect	P650.00	Congenital mitral stenosis, unspecified
P56y.00	Other specified endocardial cushion defects	P651.00	Fused commissure of the mitral valve
P56z.00	Endocardial cushion defects NOS	P652.00	Parachute deformity of the mitral valve
P56z000	Common atrium	P653.00	Supernumerary cusps of the mitral valve
P56z011	Cor triloculare biventriculare	P65z.00	Congenital mitral stenosis NOS
P56z100	Common atrioventricular canal	P66..00	Congenital mitral insufficiency
P56z200	Common atrioventricular-type ventricular septal defect	P67..00	Hypoplastic left heart syndrome
P56zz00	Endocardial cushion defects NOS	P68..00	Congenital heart disease
P57..00	Cor biloculare	P6W..00	Congenital malformation of aortic and mitral valves unsp
P58..00	Double outlet left ventricle	P6X..00	Congenital malformation of tricuspid valve, unspecified
P59..00	Isomerism of atrial appendages	P6y..00	Other specified heart anomalies
P5X..00	Congenital malforms of cardiac chambers+connections unsp	P6y0.00	Subaortic stenosis
P5y..00	Other heart bulb and septal closure defect	P6y1.00	Cor triatriatum
P5z..00	Heart bulb or septal closure defects NOS	P6y2.00	Pulmonary infundibular stenosis
P6...00	Other congenital heart anomalies	P6y3.00	Obstructive heart anomaly NEC
P60..00	Pulmonary valve anomalies	P6y3000	Uhl's disease
P600.00	Pulmonary valve anomaly, unspecified	P6y3z00	Obstructive heart anomaly NEC NOS
P601.00	Congenital atresia of the pulmonary valve	P6y4.00	Coronary artery anomaly
P601000	Hypoplasia of pulmonary valve	P6y4000	Congenital absence of coronary artery
P601z00	Congenital atresia of pulmonary valve NOS	P6y4100	Single coronary artery
P602.00	Congenital pulmonary stenosis	P6y4200	Coronary artery from aorta
P602000	Congenital fusion of pulmonic cusps	P6y4300	Coronary artery from pulmonary trunk
P602100	Congenital fusion of pulmonary valve segment	P6y4400	Anomalous coronary artery communication
P602z00	Congenital pulmonary stenosis NOS	P6y4411	Congenital coronary arterio-venous fistula
P603.00	Right hypoplastic heart syndrome	P6y4500	Congenital coronary aneurysm
P603.11	Pseudotruncus arteriosus	P6y4600	Congenital stricture of coronary artery
P60z.00	Other pulmonary valve anomalies	P6y4z00	Coronary artery anomaly NOS
P60z000	Congenital insufficiency of the pulmonary valve	P6y5.00	Congenital heart block
P60z100	Fallot's trilogy	P6y5000	Congenital heart block, unspecified
P60z200	Supernumerary pulmonary valve cusps	P6y5100	Congenital complete atrio-ventricular heart block
P60zz00	Other pulmonary valve anomaly NOS	P6y5200	Congenital incomplete atrio-ventricular heart block
P61..00	Congenital tricuspid atresia and stenosis	P6y5z00	Congenital heart block NOS
P610.00	Congenital tricuspid atresia	P6y6.00	Heart and cardiac apex malposition
P611.00	Congenital tricuspid stenosis	P6y6.11	Ectopic heart
		P6y6000	Dextrocardia

P6y6100	Levocardia	P710.00	Hypoplasia of aortic arch, unspecified
P6y6111	Laevocardia	P711.00	Preductal coarctation of aorta
P6y6200	Mesocardia	P711.11	Preductal hypoplasia of aorta
P6y6300	Ectopia cordis	P711.12	Preductal interruption of aorta
P6y6400	Abdominal heart	P711.13	Preductal aortic stenosis
P6y6z00	Heart or cardiac apex malposition NOS	P712.00	Postductal coarctation of aorta
P6y7.00	Myocardial bridge of coronary artery	P712.11	Postductal hypoplasia of aorta
P6y8.00	Congenital dextroposition of heart	P712.12	Postductal interruption of aorta
P6yy.00	Other specified heart anomalies	P712.13	Postductal aortic stenosis
P6yy.11	Hypoplastic aortic orifice or valve	P713.00	Interruption of aortic arch
P6yy.12	Hypoplasia of heart NOS	P713.11	Stenosis of aortic arch
P6yy.13	Congenital insufficiency of heart valve NEC	P71z.00	Coarctation of aorta NOS
P6yy000	Atresia of cardiac vein	P72..00	Other anomalies of aorta
P6yy100	Hypoplasia of cardiac vein	P72..11	Anomalies of the aorta excluding coarction
P6yy200	Congenital cardiomegaly	P720.00	Anomaly of aorta, unspecified
P6yy300	Congenital left ventricular diverticulum	P721.00	Aortic arch anomalies
P6yy400	Congenital pericardial defect	P721000	Anomalous origin of the aortic arch
P6yy411	Congenital absence of pericardium	P721100	Dextraposition of aorta
P6yy500	Congenital anomaly of myocardium	P721111	Overriding aorta
P6yy600	Congenital aneurysm of heart	P721200	Double aortic arch
P6yy700	Atresia of heart valve NEC	P721211	Vascular ring
P6yy800	Cor triloculare	P721300	Kommerell's diverticulum
P6yy900	Congenital epicardial cyst	P721400	Persistent aortic arch convolutions
P6yyA00	Hemicardia	P721500	Persistent right aortic arch
P6yyB00	Supernumerary heart valve cusps NEC	P721600	Vascular ring, aorta
P6yyC00	Fusion of mitral valve cusps	P721700	Overriding aorta
P6yyD00	Fusion of heart valve cusps NEC	P721z00	Aortic arch anomalies NOS
P6yyD11	Fusion of tricuspid valve cusps NEC	P722.00	Atresia and stenosis of aorta
P6yyz00	Other specified heart anomalies NOS	P722000	Congenital absence of aorta
P6z..00	Congenital heart anomaly NOS	P722100	Aplasia of aorta
P6z..11	Chiari's malformation	P722200	Hypoplasia of aorta
P6z0.00	Unspecified anomaly of heart valve	P722211	Tubular hypoplasia of aorta
P6z1.00	Anomalous bands of heart	P722300	Stricture of aorta
P6z1000	Anomalous atrial bands	P722400	Supra-valvular aortic stenosis
P6z1100	Anomalous ventricular bands	P722411	Congenital stenosis of ascending aorta
P6z1z00	Anomalous bands of heart NOS	P722500	Atresia of aorta
P6z2.00	Acyanotic congenital heart disease NOS	P722z00	Atresia or stenosis of aorta NOS
P6z3.00	Cyanotic congenital heart disease NOS	P72z.00	Other anomalies of aorta NOS
P6z3.11	Blue baby	P72z000	Aneurysm of sinus of Valsalva
P6zz.00	Congenital heart anomaly NOS	P72z100	Congenital aneurysm of aorta
P7...00	Other congenital circulatory system anomalies	P72z111	Congenital dilatation of aorta
P70..00	Patent ductus arteriosus	P72zz00	Other anomaly of aorta NOS
P70..11	Botalli's patent ductus	P73..00	Pulmonary artery anomalies
P71..00	Coarctation of aorta	P730.00	Pulmonary artery anomaly, unspecified

P731.00	Pulmonary artery agenesis	P752.00	Single umbilical artery
P731.11	Congenital absence of pulmonary artery	P753.00	Two umbilical vessels
P732.00	Pulmonary artery atresia	P75z.00	Absence or hypoplasia of the umbilical artery NOS
P733.00	Coarctation of the pulmonary artery	P76..00	Other peripheral vascular system anomalies
P734.00	Hypoplasia of the pulmonary artery	P76..11	Other congenital anomalies of peripheral arteries
P735.00	Stenosis of pulmonary artery	P76..12	Other congenital anomalies of peripheral veins
P735.11	Congenital stricture of pulmonary artery	P760.00	Absence of artery NEC
P736.00	Pulmonary arterio-venous aneurysm	P761.00	Anomaly of artery NEC
P736.11	Pulmonary arterio-venous fistula	P762.00	Atresia of artery NEC
P736.12	Pulmonary arterio-venous malformation	P763.00	Absence of vein NEC
P737.00	Pulmonary artery aneurysm	P764.00	Anomaly of vein NEC
P737.11	Dilatation of pulmonary artery	P765.00	Atresia of vein NEC
P738.00	Atresia of pulmonary artery with septal defect	P766.00	Peripheral arterio-venous aneurysm
P73y.00	Other specified anomaly of pulmonary artery	P766.11	Peripheral arterio-venous malformation
P73z.00	Pulmonary artery anomaly NOS	P767.00	Congenital peripheral aneurysm
P74..00	Anomalies of great veins	P767.11	Cirroid aneurysm
P740.00	Anomaly of great veins, unspecified	P768.00	Congenital phlebectasia
P740000	Anomaly of the pulmonary veins, unspecified	P769.00	Congenital arterial stricture
P740100	Anomaly of the vena cava, unspecified	P769000	Renal artery stenosis
P740z00	Unspecified anomaly of the great veins, NOS	P76A.00	Congenital varix
P741.00	Total anomalous pulmonary venous return - TAPVR	P76B.00	Multiple renal arteries
P741000	Subdiaphragmatic total anomalous pulmonary venous return	P76B.11	Accessory renal artery
P741100	Supradiaphragmatic total anomalous pulmonary venous return	P76C.00	Anomalies of renal artery NEC
P741z00	Total anomalous pulmonary venous return NOS	P76C000	Aberrant main renal artery
P742.00	Partial anomalous pulmonary venous return	P76Cz00	Anomaly of renal artery NEC NOS
P742.11	Anomalous termination of right pulmonary vein	P76D.00	Arteriovenous malformation
P743.00	Anomalous portal vein termination	P76E.00	Aber retro-oesophag subclavian artery causing dysphag lusori
P744.00	Portal vein - hepatic artery fistula	P76y.00	Congenital anomaly of peripheral vascular system OS
P74z.00	Other great vein anomalies	P76y000	Hypoplasia of spinal vessel
P74z.11	Persistent left posterior cardinal vein	P76y100	Four vessels in umbilical cord
P74z000	Absence of inferior vena cava	P76yz00	Other congenital anomaly of peripheral vascular system NOS
P74z100	Absence of superior vena cava	P76z.00	Peripheral vascular system anomaly NOS
P74z200	Stenosis of inferior vena cava	P77..00	Arteriovenous malformation of precerebral vessels
P74z300	Stenosis of superior vena cava	P7W..00	Congenital malformation of circulatory system, unspecif
P74z400	Persistent left posterior cardinal vein	P7X..00	Congenital malformation of great arteries, unspecified
P74z500	Persistent left superior vena cava	P7y..00	Other specified circulatory system anomalies
P74z600	Scimitar syndrome	P7y0.00	Cerebrovascular system anomalies
P74z700	Transposition of pulmonary veins	P7y0000	Congenital anomaly of cerebral vessel, unspecified
P74z800	Atresia of pulmonary vein	P7y0100	Congenital cerebral arteriovenous aneurysm
P74zz00	Other great vein anomaly NOS	P7y0111	Congenital arteriovenous fistula of brain
P75..00	Absence or hypoplasia of the umbilical artery	P7y0112	Congenital cerebral arteriovenous malformation
P750.00	Congenital absence of umbilical artery, unspecified	P7y0200	Congenital brain aneurysm NEC
P751.00	Umbilical artery hypoplasia, unspecified	P7y0300	Congenital stricture of cerebral artery



P7y0400	Vein of Galen malformation	P830200	Agenesis of trachea
P7y0y00	Other specified cerebrovascular anomaly	P830211	Congenital absence of trachea
P7y0z00	Cerebrovascular system anomaly NOS	P830z00	Agenesis of larynx, trachea or bronchus NOS
P7yz..00	Other cardiovascular system anomaly NOS	P831..00	Anomaly of laryngeal and tracheal cartilage
P7yz000	Congenital aneurysm NEC	P831000	Anomaly of cricoid cartilage
P7yz100	Congenital chylothorax	P831100	Anomaly of epiglottis
P7yzz00	Other cardiovascular system anomaly NOS	P831200	Anomaly of thyroid cartilage
P7z..00	Circulatory system anomaly NOS	P831300	Anomaly of tracheal cartilage
P7z..11	Fetal circulation	P831400	Tracheomalacia
P8...00	Respiratory system congenital anomalies	P831500	Laryngeal hypoplasia
P80..00	Choanal atresia	P831600	Laryngomalacia
P800.00	Choanal atresia, unspecified	P831z00	Anomaly of laryngeal or tracheal cartilage NOS
P801.00	Atresia of the anterior nares	P832..00	Atresia of larynx and trachea
P802.00	Atresia of the posterior nares	P832000	Atresia of epiglottis
P803.00	Congenital stenosis of the anterior nares	P832100	Atresia of glottis
P804.00	Congenital stenosis of the posterior nares	P832200	Atresia of larynx
P80z.00	Choanal atresia NOS	P832300	Atresia of trachea
P81..00	Other anomalies of nose	P832z00	Atresia of larynx or trachea NOS
P810.00	Congenital nose deformity, unspecified	P833..00	Congenital stenosis of larynx, trachea and bronchus
P811.00	Absent nose	P833000	Congenital stenosis of larynx
P811.11	Agenesis of nose	P833100	Congenital stenosis of trachea
P811000	Agenesis of nose	P833200	Congenital stenosis of bronchus
P811100	Underdevelopment of nose	P833300	Congenital subglottic stenosis
P811z00	Absent nose NOS	P833400	Congenital supraglottic stenosis
P812.00	Accessory nose	P833z00	Congenital stenosis of larynx or trachea NOS
P813.00	Congenital cleft nose	P83y..00	Other anomaly of larynx, trachea and bronchus
P814.00	Deformity of nasal sinus wall	P83y000	Congenital cleft thyroid cartilage
P815.00	Congenital notching of tip of nose	P83y100	Congenital dilatation of trachea
P816.00	Congenital perforation of the nasal sinus wall	P83y200	Congenital tracheocele
P817.00	Perforated nasal septum	P83y300	Congenital laryngocele
P818.00	Congenital fissure of nose	P83y400	Congenital diverticulum of bronchus
P819.00	Congenital hypoplastic nose	P83y500	Congenital diverticulum of trachea
P81z.00	Other anomalies of nose NOS	P83y600	Congenital fissure of epiglottis
P81z.11	Single nostril	P83y700	Congenital cleft of posterior cricoid cartilage
P82..00	Congenital web of larynx	P83y800	Rudimentary tracheal bronchus
P820.00	Congenital web of larynx, unspecified	P83y900	Congenital laryngeal stridor
P821.00	Congenital glottic web of larynx	P83yA00	Congenital fissure of larynx
P822.00	Congenital subglottic web of larynx	P83yB00	Congenital bronchomalacia
P82z.00	Congenital web of larynx NOS	P83yX00	Congenital malformation of larynx, unspecified
P83..00	Other anomalies of larynx, trachea and bronchus	P83yw00	Other anomaly of larynx
P830.00	Agenesis of larynx, trachea and bronchus	P83yx00	Other anomaly of trachea
P830000	Agenesis of bronchus	P83yy00	Other anomaly of bronchus
P830100	Agenesis of larynx	P83yz00	Other anomaly of larynx, trachea or bronchus NOS
P830111	Congenital absence of larynx		

P83z.00	Other anomalies of larynx, trachea or bronchus NOS	P8yz.00	Other specified respiratory system anomaly NOS
P84..00	Congenital cystic lung	P8z..00	Respiratory system anomaly NOS
P840.00	Congenital cystic lung disease, unspecified	P9...00	Cleft palate and lip
P841.00	Congenital polycystic lung	P90..00	Cleft palate
P841.11	Multiple lung cysts	P900.00	Cleft palate, unspecified
P841.12	Multiple congenital bronchogenic cysts	P900.11	Palatoschisis
P842.00	Congenital honeycomb lung	P901.00	Unilateral complete cleft palate
P843.00	Single lung cyst	P901.11	Cleft hard palate, unilateral
P843.11	Lung cyst	P902.00	Unilateral incomplete cleft palate
P843.12	Congenital bronchogenic cyst	P902.11	Cleft uvula
P844.00	Congenital cystic adenomatoid malformation of the lung	P902.12	Cleft soft palate, unilateral
P84y.00	Other specified congenital cystic lung	P903.00	Bilateral complete cleft palate
P84z.00	Congenital cystic lung NOS	P903.11	Cleft hard palate, bilateral
P85..00	Lung agenesis, hypoplasia and dysplasia	P904.00	Bilateral incomplete cleft palate
P850.00	Aplasia of lung	P904.11	Cleft soft palate, bilateral
P851.00	Hypoplasia of lung	P905.00	Central complete cleft palate
P852.00	Sequestration of lung	P905.11	Cleft hard palate, central
P853.00	Agenesis of lung	P906.00	Central incomplete cleft palate
P853.11	Congenital absence of lung	P906.11	Cleft soft palate, central
P853000	Congenital absence of lung fissures	P907.00	Complete cleft palate NOS
P853100	Congenital absence of lobe of lung	P907.11	Cleft hard palate NOS
P853z00	Agenesis of lung NOS	P908.00	Incomplete cleft palate NOS
P85y.00	Other specified lung agenesis, hypoplasia or dysplasia	P908.11	Cleft soft palate NOS
P85y000	Fusion of lobes of lung	P909.00	Cleft uvula
P85yz00	Other lung agenesis, hypoplasia or dysplasia NOS	P90A.00	Cleft soft palate, bilateral
P85z.00	Lung agenesis, hypoplasia or dysplasia NOS	P90B.00	Cleft hard palate, bilateral
P86..00	Other lung anomalies	P90C.00	Cleft hard palate, unilateral
P860.00	Anomaly of lung, unspecified	P90z.00	Cleft palate NOS
P861.00	Congenital bronchiectasis	P91..00	Cleft lip (harelip)
P86y.00	Other lung anomaly	P91..11	Cheiloschisis
P86y000	Accessory lung	P91..12	Congenital fissure of lip
P86y100	Azygos lobe of lung	P910.00	Cleft lip, unspecified
P86y200	Accessory lobe of lung	P911.00	Unilateral complete cleft lip
P86y300	Ectopic tissues in lung	P912.00	Unilateral incomplete cleft lip
P86y311	Ectopic bone and cartilage in lung	P913.00	Bilateral complete cleft lip
P86yz00	Other lung anomaly NOS	P914.00	Bilateral incomplete cleft lip
P86z.00	Lung anomaly NOS	P915.00	Central cleft lip
P8y..00	Other specified respiratory system anomalies	P91z.00	Cleft lip NOS
P8y0.00	Abnormal pericardio-pleural communication	P92..00	Cleft palate with cleft lip
P8y1.00	Anomaly, pleural folds	P92..11	Cheilopalatoschisis
P8y2.00	Atresia of nasopharynx	P920.00	Cleft palate with cleft lip, unspecified
P8y3.00	Congenital cyst of mediastinum	P921.00	Unilateral complete cleft palate with cleft lip
P8y4.00	Congenital pulmonary lymphangiectasis	P922.00	Unilateral incomplete cleft palate with cleft lip
		P923.00	Bilateral complete cleft palate with cleft lip

P924.00	Bilateral incomplete cleft palate with cleft lip	PA25y11	Flat palate
P925.00	Central complete cleft palate with cleft lip	PA25z00	Other mouth anomalies NOS
P926.00	Central incomplete cleft palate with cleft lip	PA26.00	Diverticulum of pharynx
P927.00	Cleft hard palate with cleft soft palate, bilateral	PA26.11	Pharyngeal pouch
P928.00	Cleft hard palate with cleft soft palate, unilateral	PA27.00	Other pharynx anomalies
P92A.00	Cleft hard palate with cleft lip, bilateral	PA27000	Imperforate pharynx
P92B.00	Cleft hard palate with cleft lip, unilateral	PA27100	Congenital pharyngeal polyp
P92z.00	Cleft palate with cleft lip NOS	PA27z00	Other pharynx anomalies NOS
P9z..00	Cleft palate or cleft lip NOS	PA28.00	Ranula, congenital
PA...00	Other congenital upper alimentary tract anomalies	PA29.00	Other anomalies of salivary glands or ducts
PA0..00	Tongue tie - ankyloglossia	PA29.11	Displacement of Wharton's duct
PA0..11	Ankyloglossia	PA2A.00	Other anomalies of lip
PA0..12	Tongue tie	PA2A000	Congenital ectropion of lip
PA1..00	Other tongue anomalies	PA2Az00	Other anomaly of lip NOS
PA10.00	Anomaly of tongue, unspecified	PA2z.00	Other mouth and pharynx anomalies NOS
PA11.00	Aglossia	PA3..00	Oesophageal atresia, stenosis and fistula
PA11.11	Congenital absence of tongue	PA3..11	Congenital oesophageal ring
PA12.00	Congenital adhesions of tongue	PA30.00	Atresia of oesophagus
PA13.00	Fissure of tongue	PA31.00	Congenital oesophageal stricture
PA13.11	Bifid tongue	PA31.11	Congenital oesophageal stenosis
PA13.12	Double tongue	PA32.00	Congenital oesophageal fistula
PA14.00	Macroglossia	PA32000	Oesophagobronchial fistula
PA14.11	Congenital tongue hypertrophy	PA32100	Oesophagotracheal fistula
PA15.00	Microglossia	PA32111	Congenital tracheo-oesophageal fistula
PA15.11	Hypoplasia of tongue	PA32z00	Congenital oesophageal fistula NOS
PA15.12	Short tongue	PA33.00	Imperforate oesophagus
PA16.00	Dislocation of tongue	PA34.00	Webbed oesophagus
PA16.11	Displacement of tongue	PA35.00	Congenital absence of oesophagus
PA17.00	Cleft tongue	PA36.00	Cong.absence of oesophagus with tracheo-oesophageal fistula
PA17.11	Whiteman's syndrome	PA37.00	Atresia of oesophagus with tracheo-oesophageal fistula
PA18.00	Congenital plicated tongue	PA3y.00	Other specified oesophageal atresia, stenosis or fistula
PA1z.00	Other tongue anomalies NOS	PA3z.00	Oesophageal atresia, stenosis or fistula NOS
PA2..00	Other specified mouth and pharynx anomalies	PA4..00	Other specified oesophageal anomalies
PA20.00	Congenital absence of salivary gland	PA40.00	Congenital dilatation of oesophagus
PA21.00	Accessory salivary gland	PA41.00	Congenital displacement of oesophagus
PA22.00	Atresia, salivary duct	PA42.00	Congenital diverticulum of oesophagus
PA23.00	Congenital salivary gland fistula	PA43.00	Congenital duplication of oesophagus
PA24.00	Congenital fistula of lip	PA44.00	Giant oesophagus
PA24.11	Congenital pits of lip	PA45.00	Congenital oesophageal pouch
PA25.00	Other mouth anomalies	PA4z.00	Other specified oesophageal anomaly NOS
PA25.11	Fordyce's disease of mouth	PA5..00	Congenital hypertrophic pyloric stenosis
PA25000	Congenital absence of uvula	PA50.00	Congenital pyloric hypertrophy
PA25100	High arched palate	PA51.00	Congenital pyloric spasm
PA25y00	Other congenital anomaly of palate	PA51.11	Congenital pylorospasm

PA52.00	Congenital pyloric stenosis	PB11100	Congenital absence of jejunum
PA52.11	Congenital pyloric stricture	PB11200	Congenital absence of ileum
PA5y.00	Other specified congenital pyloric obstruction	PB12.00	Congenital obstruction of small intestine
PA5z.00	Congenital pyloric obstruction NOS	PB13.00	Congenital stenosis of small intestine
PA6..00	Congenital hiatus hernia	PB13000	Congenital stenosis of duodenum
PA7..00	Other specified stomach anomalies	PB13100	Congenital stenosis of jejunum
PA70.00	Congenital cardiospasm	PB13200	Congenital stenosis of ileum
PA70.11	Congenital achalasia of cardia	PB13z00	Congenital stenosis of small intestine NOS
PA71.00	Congenital hourglass stomach	PB13z11	Congenital stricture of small intestine
PA72.00	Congenital stomach displacement	PB14.00	Imperforate jejunum
PA73.00	Congenital stomach diverticulum	PB15.00	Imperforate small intestine NEC
PA74.00	Duplication of stomach	PB1z.00	Small intestine atresia or stenosis NOS
PA75.00	Megalogastria	PB2..00	Atresia and stenosis of large intestine/rectum/anal canal
PA76.00	Microgastria	PB2..11	Atresia large intestine
PA77.00	Transposition of stomach	PB2..12	Stenosis large intestine
PA78.00	Ectopic gastric mucosa	PB20.00	Congenital absence of large intestine
PA7z.00	Other specified stomach anomaly NOS	PB20000	Congenital absence of anus
PA7z.11	Congenital displacement of gastric mucosa	PB20100	Congenital absence of appendix
PAy..00	Other specified upper alimentary tract anomaly	PB20200	Congenital absence of rectum
PAz..00	Upper alimentary tract anomalies NOS	PB20211	Agenesis of rectum
PAz0.00	Unspecified anomalies of mouth and pharynx	PB20300	Congenital absence of anus with fistula
PAz1.00	Unspecified anomalies of oesophagus	PB20400	Congenital absence of rectum with fistula
PAz2.00	Unspecified anomalies of stomach	PB20411	Agenesis of rectum with fistula
PAzz.00	Anomalies of upper alimentary tract NOS	PB20z00	Congenital absence of large intestine NOS
PAzz.11	Malformation of throat	PB21.00	Atresia of large intestine
PB...00	Other congenital digestive system anomaly	PB21000	Atresia of anus
PB0..00	Meckel's diverticulum	PB21100	Atresia of colon
PB0..11	Persistent omphalomesenteric duct	PB21200	Atresia of rectum
PB0..12	Persistent vitelline duct	PB21300	Atresia of appendix
PB00.00	Meckel's diverticulum, unspecified	PB21400	Atresia of anus with fistula
PB01.00	Displaced Meckel's diverticulum	PB21500	Atresia of rectum with fistula
PB02.00	Hypertrophic Meckel's diverticulum	PB21z00	Atresia of large intestine NOS
PB03.00	Persistent omphalomesenteric duct	PB22.00	Congenital obstruction of large intestine
PB03.11	Persistent vitelline duct	PB22.11	Congenital stenosis of large intestine
PB0z.00	Meckel's diverticulum NOS	PB22.12	Congenital stenosis of appendix
PB1..00	Small intestine atresia and stenosis	PB23.00	Congenital occlusion of anus
PB10.00	Atresia of small intestine	PB23.11	Anal septum
PB10000	Atresia of small intestine, unspecified	PB23000	Congenital occlusion of anus with fistula
PB10100	Atresia of duodenum	PB23z00	Congenital occlusion of anus NOS
PB10200	Atresia of ileum	PB24.00	Congenital stricture of anus
PB10300	Atresia of jejunum	PB24.11	Congenital anal stricture
PB10z00	Small intestine atresia NOS	PB24000	Congenital stricture of anus with fistula
PB11.00	Congenital absence of small intestine	PB24011	Congenital stenosis of anus with fistula
PB11000	Congenital absence of duodenum	PB24100	Congenital stricture of anus without mention of fistula

PB24111	Congenital stenosis of anus without mention of fistula	PB43.00	Other anomalies of mesentery
PB24z00	Congenital stricture of anus NOS	PB4y.00	Other specified intestinal fixation anomaly
PB25.00	Congenital stricture of rectum	PB4z.00	Intestinal fixation anomaly NOS
PB25.11	Congenital rectal stricture	PB4z.11	Malfixation of gut NEC
PB25000	Congenital stricture of rectum with fistula	PB4z.12	Malrotation of gut
PB25011	Congenital stenosis of rectum with fistula	PB4z.13	Malrotation of intestine
PB25100	Congenital stricture of rectum without mention of fistula	PB5..00	Other anomalies of intestine
PB25111	Congenital stenosis of rectum without mention of fistula	PB50.00	Congenital diverticulum of colon
PB25z00	Congenital stricture of rectum NOS	PB51.00	Dolichocolon
PB26.00	Imperforate anus	PB52.00	Duplication of intestine
PB26000	Imperforate anus with fistula	PB52000	Duplication of intestine, unspecified
PB26z00	Imperforate anus NOS	PB52100	Duplication of anus
PB27.00	Imperforate rectum	PB52200	Duplication of appendix
PB27000	Imperforate rectum with fistula	PB52300	Duplication of caecum
PB27z00	Imperforate rectum NOS	PB52z00	Duplication of intestine NOS
PB28.00	Imperforate large intestine	PB52z11	Congenital redundant rectal mucosa
PB2z.00	Atresia and stenosis of large intestine/rectum/anus NOS	PB52z12	Congenital redundant colon
PB3..00	Hirschsprung's disease and allied congenital conditions	PB53.00	Transposition of intestine
PB3..11	Aganglionosis	PB53000	Transposition of intestine, unspecified
PB3..12	Congenital dilatation colon	PB53100	Transposition of appendix
PB30.00	Hirschsprung's disease	PB53200	Transposition of caecum
PB30000	Long segment Hirschsprung's disease	PB53300	Transposition of colon
PB30100	Short segment Hirschsprung's disease	PB53z00	Transposition of intestine NOS
PB30z00	Hirschsprung's disease NOS	PB54.00	Ectopic anus
PB31.00	Idiopathic congenital megacolon	PB55.00	Megaloappendix
PB31.11	Congenital giant colon NEC	PB56.00	Megaloduodenum
PB32.00	Macrocolon	PB57.00	Microcolon
PB33.00	Total intestinal aganglionosis	PB58.00	Persistent cloaca
PB33.11	Aganglionic macrocolon	PB58.11	Anal fusion
PB33.12	Congenital aganglionic megacolon	PB58.12	Anal and urogenital canal fusion
PB3z.00	Hirschsprung's disease and allied congenital conditions NOS	PB59.00	Congenital anal fistula
PB4..00	Intestinal fixation anomalies	PB5A.00	Enterogenous cyst
PB40.00	Congenital intestinal adhesions	PB5B.00	Dysplasia of colon
PB40000	Congenital omental adhesions	PB5X.00	Congenital malformation of intestine, unspecified
PB40011	Congenital omental bands	PB5z.00	Other intestine anomalies NOS
PB40100	Jackson's membrane	PB5z.11	Congenital volvulus
PB40200	Congenital peritoneal adhesions	PB5z.12	Short bowel syndrome
PB40211	Congenital peritoneal bands	PB5z000	Congenital faecal fistula
PB40z00	Congenital intestinal adhesions NOS	PB6..00	Liver and biliary system anomalies
PB41.00	Malrotation of colon and caecum	PB6..11	Bile duct anomalies
PB41000	Malrotation of colon	PB6..12	Biliary anomalies
PB41100	Malrotation of caecum	PB6..13	Gallbladder anomalies
PB41z00	Malrotation of colon or caecum NOS	PB6..14	Liver anomalies
PB42.00	Universal mesentery	PB60.00	Liver and biliary system anomalies, unspecified

PB60000	Liver anomaly, unspecified	PB6y000	Congenital choledochal cyst
PB60100	Gallbladder anomaly, unspecified	PB6y100	Congenital hepatomegaly
PB60200	Bile duct anomaly, unspecified	PB6y200	Congenital floating gallbladder
PB60z00	Unspecified liver and biliary system anomaly NOS	PB6y300	Congenital floating liver
PB61.00	Biliary atresia	PB6y400	Intrahepatic gallbladder
PB61.11	Bile duct atresia	PB6y500	Hypoplasia of gallbladder
PB61000	Congenital absence of bile duct	PB6y600	Atrophy of left lobe of liver
PB61011	Agenesis of bile duct	PB6y700	Congenital dilation of bile duct
PB61100	Congenital hypoplasia of bile duct	PB6y800	Congenital diverticulum of bile duct
PB61200	Congenital obstruction of bile duct	PB6y900	Liver hyperplasia
PB61300	Congenital stricture of bile duct	PB6yw00	Other congenital anomaly of liver
PB61311	Congenital stricture of common bile duct	PB6yw11	Liver hamartoma
PB61400	Atresia of bile duct	PB6yw12	Abnormal liver lobulation
PB61411	Intrahepatic atresia of bile duct	PB6yw13	Trilobular liver
PB61412	Extrahepatic atresia of bile duct	PB6yx00	Other congenital anomaly of gallbladder
PB61500	Congenital absence of hepatic ducts	PB6yy00	Other congenital anomaly of hepatic or bile ducts
PB61511	Agenesis of hepatic ducts	PB6yy11	Congenital kink of cystic duct
PB61600	Atresia of hepatic ducts	PB6yz00	Other liver or biliary system anomalies NOS
PB61z00	Biliary atresia NOS	PB6z.00	Liver or biliary system anomalies NOS
PB62.00	Congenital cystic liver disease	PB7..00	Anomalies of pancreas
PB62.11	Congenital hepatic cyst	PB70.00	Congenital absence of pancreas
PB62000	Congenital polycystic liver disease	PB71.00	Agenesis of pancreas
PB62100	Fibrocystic liver disease	PB72.00	Hypoplasia of pancreas
PB62z00	Congenital cystic liver disease NOS	PB73.00	Accessory pancreas
PB63.00	Congenital absence of liver and gallbladder	PB74.00	Annular pancreas
PB63000	Congenital absence of gallbladder	PB75.00	Ectopic pancreas
PB63011	Agenesis of gallbladder	PB76.00	Pancreatic heterotopia
PB63100	Congenital absence of liver lobe	PB77.00	Pancreatic cyst, congenital
PB63111	Congenital agenesis of liver lobe	PB7y.00	Other specified anomalies of pancreas
PB63200	Congenital small left lobe of liver	PB7z.00	Anomalies of pancreas NOS
PB63300	Riedel's lobe liver	PBy..00	Other specified digestive system anomalies
PB63400	Congenital absence of liver,total	PBy0.00	Congenital absence of digestive system NOS
PB63411	Congenital agenesis liver,total	PBy0000	Complete absence of alimentary tract NOS
PB63500	Alagille syndrome	PBy0100	Partial absence of alimentary tract NOS
PB63z00	Absence of liver or gallbladder NOS	PBy0z00	Absence of digestive system NOS
PB64.00	Liver and biliary duplication	PBy1.00	Duplication of digestive system NOS
PB64000	Duplication of biliary duct	PBy2.00	Congenital malposition of digestive system NOS
PB64100	Duplication of cystic duct	PBy2.11	Ectopic digestive organs NOS
PB64200	Duplication of gallbladder	PByz.00	Other specified digestive system anomalies NOS
PB64300	Duplication of liver	PBz..00	Digestive system anomalies NOS
PB64311	Accessory liver	PC...00	Congenital genital organ anomalies
PB64400	Accessory hepatic ducts	PC0..00	Anomalies of ovaries
PB64z00	Liver or biliary duplication NOS	PC00.00	Congenital absence of ovary
PB6y.00	Other liver and biliary anomalies	PC00.11	Agenesis of ovary

PC01.00	Accessory ovary	PC36100	Uterovesical fistula, congenital
PC02.00	Ectopic ovary	PC36z00	Fistula involving uterus with digestive or urinary tract NOS
PC03.00	Streak ovary	PC3y.00	Other specified anomalies of uterus
PC04.00	Developmental ovarian cyst	PC3z.00	Anomalies of uterus NOS
PC05.00	Congenital torsion of ovary	PC4..00	Cervical, vaginal and external female genital anomalies
PC0y.00	Other specified congenital anomalies of ovaries	PC40.00	Cervical/vaginal/external female genital anomalies, unspec
PC0y.11	Congenital ovarian dysplasia	PC41.00	Embryonic cyst of cervix/vagina/external female genitalia
PC0z.00	Congenital anomalies of ovaries NOS	PC41000	Congenital cyst of canal of Nuck
PC1..00	Fallopian tube and broad ligament anomalies	PC41011	Patent canal of Nuck
PC10.00	Fallopian tube and broad ligament anomalies, unspecified	PC41100	Embryonal cyst of vagina
PC11.00	Embryonic cyst of fallopian tube and broad ligament	PC41200	Congenital cyst of vulva
PC11.11	Cyst of mesenteric remnant	PC41300	Embryonic cyst of cervix
PC11000	Epoophoron cyst	PC41z00	Embryonic cyst cervix/vagina/external female genitalia NOS
PC11100	Fimbrial cyst	PC42.00	Imperforate hymen
PC11200	Gartner's duct cyst	PC43.00	Rectovaginal fistula, congenital
PC11211	Persistent Gartner's duct	PC4y.00	Other cervical, vaginal and external female genital anomaly
PC11300	Parovarian cyst	PC4y000	Congenital absence of cervix
PC11z00	Embryonic cyst of fallopian tube or broad ligament NOS	PC4y100	Agenesis of cervix
PC1y.00	Other fallopian tube and broad ligament anomalies	PC4y200	Congenital absence of clitoris
PC1y000	Congenital absence of fallopian tube	PC4y300	Agenesis of clitoris
PC1y011	Congenital absence of oviduct	PC4y400	Congenital absence of vagina
PC1y100	Accessory fallopian tube	PC4y411	Rudimentary vagina
PC1y200	Atresia of fallopian tube	PC4y500	Agenesis of vagina
PC1y300	Absent broad ligament	PC4y600	Congenital absence of vulva
PC1y400	Accessory broad ligament	PC4y611	Congenital absence of labium major
PC1y500	Atresia of broad ligament	PC4y612	Congenital absence of labium minor
PC1yz00	Other fallopian tube or broad ligament anomalies NOS	PC4y700	Agenesis of vulva
PC1z.00	Fallopian tube or broad ligament anomalies NOS	PC4y800	Congenital stenosis of cervical canal
PC2..00	Doubling of uterus	PC4y900	Congenital stenosis of vagina
PC20.00	Doubling of uterus, unspecified	PC4y911	Congenital stricture of vagina
PC21.00	Didelphic uterus	PC4yA00	Atresia of cervix
PC22.00	Doubling of uterus, including cervix and vagina	PC4yB00	Atresia of vagina
PC2z.00	Doubling of uterus NOS	PC4yB11	Imperforate vagina
PC3..00	Other anomalies of uterus	PC4yC00	Congenital vaginal cyst NEC
PC30.00	Congenital absence of uterus	PC4yD00	Fusion of vulva
PC31.00	Agenesis of uterus	PC4yD11	Fusion of labia
PC32.00	Aplasia of uterus	PC4yE00	Congenital labial adhesions
PC33.00	Bicornuate uterus	PC4yv00	Other congenital anomaly of cervix
PC34.00	Uterus unicornis	PC4yw00	Other congenital anomaly of vagina
PC35.00	Displaced uterus	PC4yw11	Vaginal septum
PC35.11	Congenital prolapse of uterus	PC4yx00	Other congenital anomaly of vulva
PC36.00	Fistulae involving uterus with digestive or urinary tract	PC4yy00	Other congenital anomaly of clitoris
PC36000	Uterointestinal fistula, congenital	PC4yy11	Hooded clitoris
		PC4yy12	Hypertrophy of clitoris

PC4yz00	Other cervical/vaginal/external female genital anomaly NOS	PCy0000	Congenital absence of penis
PC4z.00	Cervical, vaginal and external female genital anomaly NOS	PCy0100	Congenital absence of prostate
PC5..00	Undescended testicle	PCy0200	Congenital absence of spermatic cord
PC50.00	Cryptorchidism	PCy0300	Congenital absence of vas deferens
PC50000	Cryptorchidism, unilateral	PCy0311	Congenital absence of seminal tract
PC50100	Cryptorchidism, bilateral	PCy0z00	Genital organ absence NEC NOS
PC50z00	Cryptorchidism NOS	PCy1.00	Congenital aplasia of genital organ NEC
PC51.00	Ectopic testis	PCy1000	Congenital aplasia of prostate
PC5z.00	Undescended testicle NOS	PCy1100	Congenital aplasia of round ligament
PC5z.11	Retractile testis	PCy1200	Congenital aplasia of testicle
PC5z.12	Maldescent of testicle	PCy1300	Congenital aplasia of scrotum
PC5z000	Undescended testis, unilateral	PCy1400	Aplasia of penis
PC5z011	Maldescent of testis, unilateral	PCy1z00	Congenital aplasia of genital organ NEC NOS
PC5z100	Undescended testis, bilateral	PCy2.00	Hypoplasia of genital organ NEC
PC5z111	Maldescent of testis, bilateral	PCy2000	Hypoplasia of penis
PC6..00	Hypospadias and epispadias	PCy2100	Hypoplasia of testis
PC60.00	Hypospadias	PCy2200	Hypoplasia of scrotum
PC60.11	Anaspadias	PCy2z00	Hypoplasia of genital organ NEC NOS
PC60000	Hypospadias, penile	PCy3.00	Atresia of genital organ NEC
PC60100	Hypospadias, penoscrotal	PCy3000	Atresia of ejaculatory duct
PC60200	Hypospadias, perineal	PCy3100	Atresia of vas deferens
PC60300	Hypospadias, balanic	PCy3z00	Atresia of genital organ NEC NOS
PC60311	Hypospadias, glanular	PCy4.00	Anorchism
PC60312	Hypospadias, glandular	PCy4.11	Congenital absence of both testes
PC61.00	Epispadias	PCy4.12	Testicular agenesis, bilateral
PC61.11	Anaspadias	PCy5.00	Monorchism
PC62.00	Congenital chordee	PCy5.11	Congenital absence of testis, unilateral
PC6z.00	Hypospadias or epispadias NOS	PCy5.12	Testicular agenesis, unilateral
PC7..00	Indeterminate sex and pseudohermaphroditism	PCy6.00	Polyorchism
PC7..11	Gynandris	PCy7.00	Congenital lateral curvature of penis
PC70.00	True hermaphroditism	PCy8.00	Fusion of testes
PC70.11	Ovotestis	PCy9.00	Paraspadias
PC71.00	Male pseudohermaphroditism	PCyA.00	Cysts of embryonic remnants NEC
PC72.00	Female pseudohermaphroditism	PCyA000	Hydatid cyst of Morgagni
PC73.00	Pure gonadal dysgenesis	PCyA100	Wolffian duct cyst
PC7z.00	Indeterminate sex or pseudohermaphroditism NOS	PCyA200	Hydatid cyst of Morgagni - male
PC7z000	Indeterminate sex NOS	PCyA300	Hydatid cyst of Morgagni - female
PC7z011	Intersex NEC	PCyA400	Wolffian duct cyst - male
PC7z100	Pseudohermaphrodite NOS	PCyA500	Wolffian duct cyst - female
PC7z111	False hermaphrodite	PCyA600	Cyst of embryonic remnant - male
PC8..00	Congenital anomaly of male genital system	PCyA700	Cyst of embryonic remnant - female
PC80.00	Other specified congenital anomaly of male genital system	PCyAz00	Cyst of embryonic remnant NEC NOS
PCy..00	Other specified genital organ anomaly	PCyB.00	Doubling of vagina
PCy0.00	Absence of genital organ NEC	PCyW.00	Other congenital anomaly of testis or scrotum



PCyx.00	Other congenital anomaly of vas deferens or prostate	PD12111	Medullary sponge kidney
PCyy.00	Other congenital anomaly of penis	PD12y00	Medullary cystic disease OS
PCyy000	Hooded penis	PD12z00	Medullary cystic disease NOS
PCyy100	Webbed penis	PD13.00	Multicystic renal dysplasia
PCyyz00	Other congenital anomaly of penis NOS	PD13.11	Multicystic kidney
PCyz.00	Other specified genital organ anomaly NOS	PD1y.00	Other specified congenital cystic kidney disease
PCz..00	Genital organ anomaly NOS	PD1y000	Fibrocystic kidney disease
PD...00	Urinary system congenital anomalies	PD1y011	Fibrocystic renal degeneration
PD0..00	Renal agenesis and dysgenesis	PD1yz00	Other congenital cystic kidney disease NOS
PD00.00	Renal agenesis, unspecified	PD1z.00	Congenital cystic kidney disease NOS
PD00000	Bilateral renal agenesis	PD2..00	Renal pelvis and ureter obstructive defects
PD00100	Unilateral renal agenesis	PD20.00	Atresia of ureter
PD00z00	Renal agenesis, unspecified NOS	PD21.00	Occlusion of ureter
PD01.00	Congenital renal atrophy	PD21.11	Congenital ureteric valves
PD02.00	Congenital absence of kidney	PD22.00	Congenital stricture of ureter
PD02000	Bilateral congenital absence of kidneys	PD22.11	Congenital stenosis of ureter
PD02100	Unilateral congenital absence of kidney	PD22000	Congenital stricture of ureter, unspecified
PD02z00	Congenital absence of kidney NOS	PD22100	Congenital stricture of ureteropelvic junction
PD03.00	Hypoplasia of kidney	PD22200	Congenital stricture of ureterovesical orifice
PD03000	Bilateral renal hypoplasia	PD22z00	Congenital stricture of ureter NOS
PD03011	Potter's syndrome	PD23.00	Congenital hydronephrosis
PD03100	Unilateral renal hypoplasia	PD23.11	Congenital dilated renal pelvis
PD04.00	Dysplasia of kidney	PD24.00	Congenital dilatation of ureter
PD04000	Bilateral renal dysplasia	PD25.00	Hydroureter - congenital
PD04011	Bilateral renal dysgenesis	PD26.00	Megaloureter - congenital
PD04100	Unilateral renal dysplasia	PD27.00	Ureterocele - congenital
PD04111	Unilateral renal dysgenesis	PD28.00	Impervious ureter
PD04z00	Dysplasia of kidney NOS	PD2y.00	Other specified obstructive defect of renal pelvis or ureter
PD0z.00	Renal agenesis or dysgenesis NOS	PD2z.00	Obstructive defect of renal pelvis or ureter NOS
PD1..00	Congenital cystic kidney disease	PD3..00	Other specified renal anomaly
PD1..11	Congenital cystic renal disease	PD30.00	Accessory kidney
PD1..12	Fibrocystic kidney	PD30.11	Duplication of kidney
PD1..13	Polycystic kidney	PD30.12	Renal duplication NEC
PD1..14	Sponge kidney	PD30.13	Supernumerary kidney
PD10.00	Congenital renal cyst, single	PD31.00	Congenital calculus of kidney
PD11.00	Polycystic kidney disease	PD32.00	Congenital displaced kidney
PD11000	Polycystic kidneys, infantile type	PD33.00	Discoid kidney
PD11100	Polycystic kidneys, adult type	PD34.00	Double kidney with double pelvis
PD11z00	Polycystic kidney disease NOS	PD34.11	Duplex kidneys
PD11z11	Cystic kidney disease NEC	PD34.12	Pyelon duplex
PD12.00	Medullary cystic disease	PD35.00	Ectopic kidney
PD12000	Medullary cystic disease, juvenile type	PD35.11	Pelvic kidney
PD12011	Nephronophthisis	PD36.00	Fusion of kidneys
PD12100	Medullary cystic disease, adult type	PD37.00	Giant kidney

PD38.00	Horseshoe kidney	PD63.12	Congenital pinhole urinary meatus
PD39.00	Hyperplasia of kidney	PD63000	Atresia of urinary meatus
PD3A.00	Lobulation of kidney	PD63100	Stenosis of urinary meatus
PD3A.11	Ren arcuatus	PD63z00	Congenital urinary meatus stricture NOS
PD3A.12	Ren unguiformis	PD64.00	Congenital vesicourethral orifice stricture
PD3B.00	Malrotation of kidney	PD65.00	Imperforate urinary meatus
PD3C.00	Triple kidney with triple pelvis	PD66.00	Impervious urethra
PD3C.11	Trifid kidney	PD67.00	Congenital posterior urethral valves
PD3C.12	Pyelon triplex	PD6y.00	Other specified urethra or bladder neck atresia or stenosis
PD3D.00	Enlarged kidney	PD6z.00	Urethra or bladder neck atresia or stenosis NOS
PD3z.00	Other specified renal anomaly NOS	PD7..00	Anomalies of urachus
PD4..00	Other specified ureter anomalies	PD70.00	Cyst of urachus
PD40.00	Absent ureter	PD71.00	Fistula of urachus
PD41.00	Accessory ureter	PD72.00	Patent urachus
PD42.00	Deviation of ureter	PD72.11	Persistent urachus
PD43.00	Displaced ureteric orifice	PD73.00	Persistent umbilical sinus
PD44.00	Double ureter	PD7y.00	Other specified anomalies of urachus
PD44.11	Duplication of ureter	PD7z.00	Anomalies of urachus NOS
PD45.00	Ectopic ureter	PDy..00	Other specified bladder and urethral anomalies
PD45.11	Congenital displacement of opening of ureter	PDy0.00	Congenital absence of bladder
PD45.12	Ectopic insertion of ureter	PDy1.00	Congenital absence of urethra
PD46.00	Anomalous ureter implantation	PDy2.00	Accessory bladder
PD47.00	Congenital vesico-uretero-renal reflux	PDy3.00	Accessory urethra
PD4z.00	Other specified ureter anomaly NOS	PDy4.00	Congenital bladder diverticulum
PD5..00	Exstrophy of urinary bladder	PDy5.00	Congenital bladder hernia
PD5..11	Ectopia vesicae	PDy6.00	Congenital urethrectal fistula
PD5..12	Ectopic bladder	PDy7.00	Congenital prolapse of bladder mucosa
PD50.00	Ectopic bladder	PDy8.00	Congenital prolapse of urethra
PD50.11	Ectopia vesicae	PDy9.00	Double urethra
PD5z.00	Exstrophy of urinary bladder NOS	PDyA.00	Double urinary meatus
PD6..00	Urethra and bladder neck atresia and stenosis	PDyB.00	Congenital hourglass bladder
PD60.00	Congenital bladder neck obstruction	PDyz.00	Other bladder or urethral anomaly NOS
PD60000	Atresia of bladder neck	PDyz000	Epispadias, female
PD60100	Stenosis of bladder neck	PDyz100	Hypospadias, female
PD60z00	Congenital bladder neck obstruction NOS	PDz..00	Urinary system anomalies NOS
PD61.00	Congenital obstruction of urethra	PDz0.00	Unspecified anomaly of kidney
PD61000	Atresia of anterior urethra	PDz1.00	Unspecified anomaly of ureter
PD61100	Stenosis of anterior urethra	PDz2.00	Unspecified anomaly of bladder
PD61z00	Congenital obstruction of urethra NOS	PDz3.00	Unspecified anomaly of urethra
PD62.00	Congenital urethral valvular stricture	PE...00	Certain congenital musculoskeletal deformities
PD62.11	Congenital posterior urethral valves	PE...11	Congenital musculoskeletal deformities
PD62.12	Congenital urethral posterior valvular stricture	PE0..00	Skull, face and jaw congenital deformities
PD63.00	Congenital urinary meatus stricture	PE0..11	Face congenital deformities
PD63.11	Congenital urinary meatus obstruction	PE0..12	Jaw congenital deformities

PE0..13	Skull congenital deformities	PE35100	Bilateral unstable hip
PE00.00	Asymmetry of face	PE3z.00	Congenital dislocation of hip NOS
PE00000	Hemifacial microsomia	PE4..00	Genu recurvatum and long leg bone bowing
PE00100	Asymmetrical crying face syndrome	PE4..11	Congenital leg bone bowing
PE01.00	Compression facies	PE40.00	Congenital genu recurvatum
PE02.00	Potter's facies	PE41.00	Congenital dislocation of knee
PE03.00	Depressions in skull	PE41000	Congenital dislocation of knee grade I
PE04.00	Dolichocephaly	PE41100	Congenital dislocation of knee grade II
PE05.00	Plagiocephaly	PE41200	Congenital dislocation of knee grade III
PE05.11	Asymmetric head	PE41300	Congenital dislocation of patella
PE06.00	Congenital nasal septum deviation	PE42.00	Congenital bowing of femur
PE07.00	Congenital bent or squashed nose	PE43.00	Congenital bowing of tibia and fibula
PE0z.00	Skull, face or jaw congenital deformities NOS	PE43000	Congenital bowing of tibia
PE1..00	Congenital sternomastoid torticollis	PE43100	Congenital bowing of fibula
PE1..11	Congenital wry neck	PE44.00	Congenital bowing of long leg bone, unspecified
PE1..12	Sternomastoid tumour	PE44.11	Bow legs NOS
PE2..00	Congenital spine deformity	PE4z.00	Genu recurvatum and long leg bone bowing NOS
PE20.00	Congenital spine deformity, unspecified	PE5..00	Varus deformities of feet
PE21.00	Congenital postural lordosis	PE50.00	Congenital talipes varus
PE22.00	Congenital postural scoliosis	PE50.11	Pes varus
PE23.00	Congenital scoliosis due to congenital bony malformation	PE50.12	Congenital clubfoot - varus
PE2z.00	Congenital spine deformity NOS	PE51.00	Congenital talipes equinovarus
PE2z.11	Congenital postural curvature of spine NOS	PE52.00	Metatarsus primus varus
PE3..00	Congenital dislocation and subluxation of the hip	PE53.00	Congenital metatarsus varus
PE30.00	Congenital dislocation of hip	PE54.00	Congenital metatarsus adductus
PE30000	Unilateral congenital dislocation of hip	PE5x.00	Complex varus foot deformities
PE30100	Bilateral congenital dislocation of hip	PE5y.00	Other specified varus feet deformity
PE30z00	Congenital dislocation of hip NOS	PE5y000	Congenital talipes calcaneovarus
PE31.00	Congenital subluxation of hip	PE5yz00	Other specified varus foot deformity NOS
PE31000	Unilateral congenital subluxation of hip	PE5z.00	Varus foot deformity NOS
PE31011	Unstable hip	PE6..00	Valgus deformities of feet
PE31012	Preluxation of hip	PE60.00	Congenital talipes valgus
PE31013	Predislocation status of hip at birth	PE60.11	Congenital clubfoot - valgus
PE31014	Congenital instability of hip joint	PE61.00	Congenital pes planus
PE31100	Bilateral congenital subluxation of hip	PE61.11	Congenital flat foot
PE31z00	Congenital subluxation of hip NOS	PE61.13	Rigid flat foot
PE32.00	Congenital dislocation one hip with subluxation other hip	PE61.14	Spastic flat foot
PE33.00	Congenital clicking hip	PE61000	Congenital vertical talus
PE33.11	Clicky hips - congenital	PE62.00	Congenital talipes calcaneovalgus
PE34.00	Dysplastic hip	PE6y.00	Other valgus foot deformities
PE34000	Unilateral dysplastic hip	PE6y000	Congenital talipes equinovalgus
PE34100	Bilateral dysplastic hip	PE6y100	Congenital planovalgus
PE35.00	Unstable hip	PE6yz00	Other valgus foot deformity NOS
PE35000	Unilateral unstable hip	PE6z.00	Valgus foot deformity NOS

PE6z.11	Congenital metatarsus valgus	PF...00	Other congenital limb anomalies
PE7..00	Other deformities of feet	PF0..00	Polydactyly - supernumerary digits
PE70.00	Talipes, unspecified	PF00.00	Supernumerary digits, unspecified
PE70.11	Clubfoot NOS	PF01.00	Accessory fingers
PE71.00	Talipes cavus	PF01000	Radial polydactyly Wassel 1
PE71.11	Congenital claw toe	PF01100	Radial polydactyly Wassel 2
PE71.12	Pes cavus	PF01200	Radial polydactyly Wassel 3
PE72.00	Congenital pes cavus	PF01300	Radial polydactyly Wassel 4
PE73.00	Congenital claw foot	PF01400	Radial polydactyly Wassel 5
PE74.00	Short Achilles tendon, congenital	PF01500	Radial polydactyly Wassel 6
PE7y.00	Other specified foot deformity	PF01600	Radial polydactyly Wassel 7
PE7y000	Asymmetric talipes	PF01700	Central polydactyly
PE7y100	Congenital talipes calcaneus	PF01800	Ulnar polydactyly
PE7y200	Congenital talipes equinus	PF02.00	Accessory toes
PE7y300	Congenital positional talipes	PF02000	Accessory hallux
PE7yz00	Other specified foot deformity NOS	PF02100	Accessory little toe
PE7z.00	Feet deformities NOS	PF02200	Other accessory toe
PE8..00	Other specified nonteratogenic anomalies	PF03.00	Accessory thumbs
PE80.00	Pectus excavatum, congenital	PF0z.00	Polydactyly NOS
PE80.11	Congenital funnel chest	PF1..00	Syndactyly - webbing of digits
PE81.00	Pectus carinatum, congenital	PF10.00	Syndactyly of multiple digits, unspecified
PE81.11	Congenital pigeon chest	PF11.00	Syndactyly of fingers without bone fusion
PE8y.00	Other nonteratogenic anomalies OS	PF11.11	Webbed fingers
PE8y000	Congenital club hand	PF11000	Simple syndactyly - 1st web
PE8y011	Congenital club fingers	PF11100	Simple syndactyly - 2nd to 4th web
PE8y100	Congenital chest wall deformity NEC	PF12.00	Syndactyly of fingers with bone fusion
PE8y111	Congenital thoracic wall deformity NEC	PF12.11	Fused fingers
PE8y200	Congenital dislocation of elbow	PF12.12	Osseous syndactyly of fingers
PE8y300	Congenital flexion contractures of leg	PF12000	Osseous syndactyly - 1st web
PE8y400	Congenital spade-like hand	PF12100	Osseous syndactyly - 2nd to 4th web
PE8y500	Guerin - Stern syndrome	PF13.00	Syndactyly of toes without bone fusion
PE8y600	Congenital flexion contracture of hip	PF13.11	Webbed toes
PE8y700	Congenital abduction contracture of hip	PF13000	Simple syndactyly of toes 1st web space
PE8y800	Congenital flexion contracture of knee	PF13100	Simple syndactyly lesser toes
PE8y900	Congenital short quadriceps	PF14.00	Syndactyly of toes with bone fusion
PE8yA00	Congenital dislocation of radial head	PF14.11	Fused toes
PE8yB00	Discoid meniscus - congenital	PF14.12	Conjoined toes
PE8yz00	Other nonteratogenic anomaly NOS	PF14.13	Syndactyly of toes with bone fusion
PE8yz11	Specified intrauterine postural deformity NEC	PF14000	Osseous syndactyly of toes 1st web space
PE8yz12	Multiple congenital articular rigidities	PF14100	Osseous syndactyly lesser toes
PE8z.00	Nonteratogenic anomalies NOS	PF15.00	Polysyndactyly
PE9..00	Other musc skeletal deformity	PF1z.00	Syndactyly NOS
PE9..11	Other congenital musculoskeletal deformity	PF1z.11	Polysyndactyly
PEz..00	Congenital musculoskeletal deformity NOS	PF1z.12	Symphalangism

PF2..00	Reduction deformity of upper limb	PF26800	Hypoplastic thumb-Blauth 5
PF2..11	Arm reduction deformity	PF27.00	Agenesis of ulna
PF20.00	Congenital shortening of arm, unspecified	PF27000	Partial defect of ulna
PF20.11	Brachymelia of arm	PF27100	Total absence of ulna
PF20100	Ectromelia of upper limb NOS	PF27200	Ulnar and humeroulnar synostosis
PF20200	Hemimelia of upper limb NOS	PF28.00	Agenesis of carpals and metacarpals
PF20z00	Unspecified congenital shortening of arm NOS	PF28.11	Transverse arrest of carpals and metacarpals
PF21.00	Transverse deficiency of arm	PF28000	Transverse arrest carpal level
PF21.11	Congenital absence part of arm	PF28100	Transverse arrest metacarpal 1st ray
PF21000	Transverse deficiency of arm, unspecified	PF28200	Transverse arrest metacarpal other
PF21100	Transverse deficiency of arm, phalangeal level, all fingers	PF29.00	Congenital absence of finger
PF21200	Transverse deficiency of arm, forearm level	PF29.11	Ectrodactyly of finger
PF21300	Transverse deficiency of arm, shoulder level(amelia)	PF29.12	Transverse arrest of phalanges
PF21400	Congenital amputation of upper limb	PF29000	Transverse arrest phalangeal level 1st ray
PF21500	Transverse deficiency of arm, elbow level(hemimelia)	PF29100	Transverse arrest phalangeal level 2nd ray
PF21600	Transverse deficiency of arm, wrist level(hemimelia)	PF29200	Transverse arrest phalangeal level 3rd ray
PF21611	Acheiria	PF29300	Transverse arrest phalangeal level 4th ray
PF21612	Rudimentary hand	PF29400	Transverse arrest phalangeal level 5th ray
PF21613	Congenital absence of hand	PF29z00	Congenital absence finger NOS
PF21700	Transverse deficiency of arm, upper arm level-short	PF2y.00	Other specified reduction deformities of upper limb
PF21800	Transverse deficiency of arm, upper arm level-long	PF2z.00	Reduction deformity of upper limb NOS
PF21z00	Transverse deficiency of arm NOS	PF2z.11	Hypoplasia of upper limb
PF21z11	Agenesis of hand	PF3..00	Reduction deformity of lower limb
PF22.00	Longitudinal deficiency of arm NEC	PF3..11	Leg reduction deformity
PF22000	Phocomelia of upper limb NOS	PF30.00	Congenital shortening of leg, unspecified
PF22100	Rudimentary arm	PF30.11	Brachymelia of leg
PF22z00	Longitudinal deficiency of arm NEC NOS	PF30000	Ectromelia of lower limb NOS
PF23.00	Congenital absence upper arm and forearm with hand present	PF30100	Hemimelia of lower limb NOS
PF23.11	Complete phocomelia of upper limb	PF30z00	Unspecified congenital leg shortening NOS
PF24.00	Congenital absence of upper arm only	PF31.00	Transverse deficiency of leg
PF24.11	Proximal phocomelia of upper limb	PF31000	Transverse deficiency lower limb - unspecified
PF25.00	Congenital absence of forearm only	PF31100	Transverse deficiency lower limb - ankle level
PF25.11	Distal phocomelia of upper limb	PF31111	Apodia
PF26.00	Agenesis of radial ray	PF31112	Hemimelia - ankle level
PF26.11	Congenital absence of radius	PF31200	Congenital absence of leg and foot
PF26000	Hypoplasia of radius	PF31300	Transverse deficiency lower limb - hip level
PF26100	Partial radial absence	PF31311	Amelia - lower limb
PF26200	Total radial absence	PF31400	Transverse deficiency lower limb - metatarsal level
PF26300	Absent thumb	PF31500	Transverse deficiency lower limb - knee level
PF26400	Hypoplastic thumb-Blauth 1	PF31511	Hemimelia - knee level
PF26500	Hypoplastic thumb-Blauth 2	PF31600	Transverse deficiency lower limb - through femur
PF26600	Hypoplastic thumb-Blauth 3	PF31700	Transverse deficiency lower limb - through tibia/fibula
PF26700	Hypoplastic thumb-Blauth 4	PF31800	Absent pelvis and lower limb

PF31z00	Transverse deficiency of leg NOS	PF44.00	Phocomelia of unspecified limb
PF32.00	Longitudinal reduction deformity of lower limb NEC	PF45.00	Congenital amputation of unspecified limb
PF32.11	Phocomelia of lower limb NOS	PF46.00	Longitudinal reduction deformity of unspecified limb
PF33.00	Congenital absence of thigh and lower leg with foot present	PF47.00	Congenital absence of digits NOS
PF33.11	Complete phocomelia of lower limb	PF47.11	Adactyly
PF34.00	Congenital absence of thigh only	PF4y.00	Other specified reduction deformities of unspecified limb
PF34.11	Proximal phocomelia of lower limb	PF4y000	Brachymelia NOS
PF34000	Proximal femoral focal deficiency	PF4yz00	Other reduction deformity of unspecified limb NOS
PF34100	Congenital short femur	PF4z.00	Reduction deformity of unspecified limb NOS
PF35.00	Congenital absence of lower leg only	PF4z.11	Brachydactyly NOS
PF35.11	Distal phocomelia of lower limb	PF4z.12	Withered limb
PF36.00	Agenesis of tibia	PF4z.13	Hypoplasia of limb NOS
PF36000	Congenital tibial deficiency type I	PF5..00	Other upper limb and shoulder anomaly
PF36100	Congenital tibial deficiency type II	PF50.00	Upper limb anomaly, unspecified
PF36200	Congenital tibial deficiency type III	PF51.00	Congenital deformity of clavicle
PF37.00	Agenesis of fibula	PF51.11	Clavicle agenesis
PF37000	Congenital fibular deficiency type I	PF52.00	Congenital elevation of scapula
PF37100	Congenital fibular deficiency type II	PF52.11	Sprengel's deformity
PF37200	Congenital fibular deficiency type III	PF52000	Undescended shoulder
PF38.00	Agenesis of tarsals and metatarsals	PF53.00	Radio-ulnar synostosis
PF38000	Agenesis of talus	PF53000	Proximal radioulnar synostosis
PF38100	Agenesis of calcaneum	PF53100	Radioulnar synostosis and dislocation of radial head
PF38200	Agenesis of other tarsal bone	PF53200	Distal radioulnar synostosis
PF38300	Agenesis of multiple tarsal bones	PF54.00	Madelung's deformity
PF38400	Agenesis of 1st metatarsal	PF55.00	Acrocephalosyndactyly
PF38500	Agenesis of 5th metatarsal	PF55.11	Apert's syndrome
PF38600	Agenesis of other metatarsal	PF55.12	Acrocephalopolysyndactyly
PF38700	Agenesis of 4th and 5th metatarsals	PF55000	Acrocephalosyndactyly (Apert)
PF38800	Agenesis of other multiple metatarsal	PF55100	Acrocephalosyndactyly (Pfeiffer)
PF39.00	Congenital absence of toe	PF55200	Acrocephalopolysyndactyly
PF39000	Congenital absence of great toe	PF55300	Saethre-Chotzen syndrome
PF39100	Congenital absence of 5th toe	PF56.00	Accessory carpal bones
PF39200	Congenital absence of other lesser toe	PF57.00	Macroductyilia (fingers)
PF39300	Congenital absence of 4th and 5th toes	PF57000	Macroductyly - simple
PF39400	Congenital absence of other multiple toes	PF57100	Macroductyly - fatty nerve tumor
PF3A.00	Split foot	PF58.00	Congenital cleft hand
PF3y.00	Other specified reduction deformities of lower limb	PF58.11	Lobster-claw hand
PF3z.00	Reduction deformity of lower limb NOS	PF58000	Cleft hand - first cleft
PF3z.11	Hypoplasia of lower limb	PF58100	Cleft hand - central
PF4..00	Reduction deformity of unspecified limb	PF58200	Cleft hand with syndactyly
PF40.00	Congenital absence of limb NOS	PF58300	Cleft hand with polydactyly
PF41.00	Amelia of unspecified limb	PF59.00	Other failure of differentiation of soft tissue of arm
PF42.00	Ectromelia of unspecified limb	PF59000	Windblown hand
PF43.00	Hemimelia of unspecified limb	PF59100	Aberrant forearm flexor muscle

PF59200	Aberrant forearm extensor muscle	PF5r500	Brachydactyly-all 3 phalanges
PF59300	Aberrant intrinsic muscles	PF5r600	Brachydactyly-missing phalanx
PF59400	Poland's syndrome	PF5r700	Symbrachydactyly
PF59500	Thumb in palm deformity	PF5r800	Camptodactyly-little finger
PF59600	Congenital trigger thumb	PF5r900	Camptodactyly-other or multiple
PF5A.00	Other failure of differentiation, skeletal tissues of arm	PF5rA00	Clinodactyly with delta phalanx
PF5A000	Lunate-triquetrum synostosis	PF5rB00	Clinodactyly, no delta phalanx
PF5A100	Capitate-hamate synostosis	PF5rC00	Brachymesophalangia
PF5A200	Scaphoid-lunate synostosis	PF5rD00	Congenital malformation of thumb
PF5A300	Other carpal synostosis	PF5rz00	Other anomaly of fingers NOS
PF5A400	PIP joint symphalangism	PF5s.00	Other congenital anomalies of hand
PF5A500	DIP joint symphalangism	PF5t.00	Other congenital anomalies of wrist
PF5Az00	Other failure of differentiation skeletal tissues of arm NOS	PF5u.00	Other congenital anomalies of forearm
PF5B.00	Other duplication of limb	PF5u000	Radio-ulnar dysostosis
PF5B000	Duplication of whole limb	PF5uz00	Other congenital anomaly forearm NOS
PF5B100	Duplication of humerus	PF5v.00	Congenital anomalies of elbow and upper arm
PF5B200	Duplication of radius	PF5v.11	Cubitus NOS
PF5B300	Duplication of ulnar ray	PF5w.00	Other congenital anomalies of shoulder
PF5B400	Duplication ulnar ray - mirror hand	PF5w.11	Congenital deformity of scapula NEC
PF5B500	Duplication of whole hand	PF5x.00	Other congenital anomalies of whole arm
PF5Bz00	Duplication of limb NOS	PF5y.00	Other upper limb and shoulder anomaly OS
PF5C.00	Other overgrowth of upper limb	PF5y000	Cleidocranial dysostosis
PF5C000	Overgrowth of whole upper limb	PF5y011	Cleidocranial dysplasia
PF5C100	Overgrowth of partial upper limb	PF5y100	Congenital cubitus valgus
PF5Cz00	Other overgrowth of limb NOS	PF5y200	Congenital cubitus varus
PF5D.00	Other undergrowth of limb	PF5y300	Congenital humeral varus
PF5D000	Undergrowth of whole limb	PF5y400	Humeroradial synostosis
PF5D100	Undergrowth of whole hand	PF5y500	Humeroulnar synostosis
PF5D200	Brachymetacarpia	PF5y600	Total elbow synostosis
PF5Dz00	Other undergrowth of limb NOS	PF5yz00	Other upper limb and shoulder anomaly NOS
PF5E.00	Constriction ring syndrome of upper limb	PF5z.00	Upper limb or shoulder anomaly NOS
PF5E000	Constriction ring	PF6..00	Other lower limb and pelvic girdle anomalies
PF5E100	Constriction ring with lymphoedema	PF60.00	Lower limb anomaly, unspecified
PF5E200	Acrosyndactyly	PF61.00	Congenital coxa valga
PF5E300	Intra-uterine amputation	PF62.00	Congenital coxa vara
PF5E400	Constriction ring with acrosyndactyly and amputation	PF63.00	Other congenital hip joint deformity
PF5F.00	Congenital absence of both forearm and hand	PF63000	Congenital anteversion of femoral neck
PF5G.00	Congenital complete absence of upper limb(s)	PF63100	Congenital hip dysplasia
PF5r.00	Other congenital anomalies of fingers	PF63111	Developmental dysplasia of the hip
PF5r000	Triphalangeal thumb	PF63200	Congenital acetabular dysplasia
PF5r100	Brachydactyly of fingers, unspecified	PF63X00	Congenital deformity of hip, unspecified
PF5r200	Camptodactyly	PF63z00	Other congenital hip joint deformity NOS
PF5r300	Clinodactyly	PF64.00	Congenital knee joint deformity
PF5r400	Flexion deformity of fingers	PF64000	Congenital absence of patella

PF64100	Congenital genu valgum - knock-knee	PF6B100	Congenital overgrowth of distal lower limb
PF64200	Congenital genu varum - bowleg	PF6B200	Congenital overgrowth of foot
PF64300	Rudimentary patella	PF6B300	Congen overgrowth of whole lower limb
PF64400	Congenital dislocation of patella	PF6C.00	Congenital undergrowth of lower limb
PF64500	Bipartite patella	PF6C000	Congenital undergrowth of proximal part of limb
PF64z00	Congenital knee joint deformity NOS	PF6C100	Congenital undergrowth of distal part of limb
PF65.00	Macroductylia of toes	PF6C200	Congenital undergrowth of foot
PF65000	Macroductyl of toes - simple	PF6C300	Brachymetapodia of 1st metatarsal
PF65100	Macroductyl of toes - fatty nerve tumor	PF6C400	Brachymetapodia of 4th metatarsal
PF66.00	Other congenital anomalies of toe	PF6C500	Brachymetapodia of other metatarsal
PF66000	Congenital hallux valgus	PF6C600	Congen undergrowth of whole lower limb
PF66100	Congenital hallux varus	PF6D.00	Constriction ring syndrome of lower limb
PF66200	Congenital hammer toe	PF6D000	Constriction ring of lower limb
PF66300	Brachyductyl of toes	PF6D100	Constriction ring of lower limb with lymphoedema
PF66400	Congenital crossed toes	PF6D200	Intrauterine amputation of lower limb
PF66411	Congenital overlapping toes	PF6D300	Constriction ring syndrome of lower limb with amputation
PF66500	Congenital curly toes	PF6E.00	Congenital absence of thigh and lower leg with foot present
PF66600	Brachyphalangia of little toe	PF6v.00	Other congenital anomalies of lower leg
PF66700	Brachyphalangia of other toes	PF6w.00	Other congenital anomalies of upper leg
PF66800	Perodactylia of great toe	PF6x.00	Other congenital anomalies of pelvis
PF66900	Perodactylia of lesser toe	PF6x000	Congenital absence of pubis NEC
PF66A00	Perodactylia of multiple toes	PF6xz00	Other congenital anomalies of pelvis NOS
PF66B00	Triphalangeal great toe	PF6y.00	Other lower limb anomalies
PF66z00	Other toe anomalies NOS	PF6y000	Congenital angulation of tibia
PF67.00	Congenital anomalies of foot NEC	PF6y100	Congenital deformity of ankle joint
PF67000	Astragaloscaphoid synostosis	PF6y200	Congenital deformity of sacroiliac joint
PF67100	Calcaneonavicular bar	PF6y300	Congenital fusion of sacroiliac joint
PF67200	Coalition of calcaneous	PF6y400	Congenital varus ankle
PF67300	Talonavicular synostosis	PF6y500	Congenital valgus ankle
PF67400	Tarsal coalitions	PF6y600	Congenital pseudarthrosis of tibia
PF67500	Lobster claw foot	PF6y700	Congenital ball-and-socket ankle
PF67600	Rocker bottom foot	PF6yz00	Other lower limb and pelvic girdle anomaly NOS
PF67700	Accessory tarsal bones	PFy..00	Other specified anomalies of unspecified limb
PF67800	Talocalcaneal bar	PFy0.00	Arthrogryposis multiplex congenita
PF67900	Naviculocuneiform bar	PFy1.00	Larsen's syndrome
PF67A00	Complex tarsal coalition	PFy2.00	Arthrogryposis, unspecified
PF67z00	Anomalies of foot NEC NOS	PFy3.00	Distal arthrogryposis syndrome
PF68.00	Failure of soft tissue differentiation of lower limb	PFy4.00	Other arthrogryposis syndromes
PF68000	Aberrant muscle of lower limb	PFyz.00	Other anomaly of unspecified limb NOS
PF69.00	Failure of differentiation of skeletal tissues of lower limb	PFz..00	Congenital anomaly of unspecified limb NOS
PF69000	Congenital synostosis of lower limb bones	PG...00	Other congenital musculoskeletal anomalies
PF6A.00	Duplication of lower limb bone	PG0..00	Skull and face bone anomalies
PF6B.00	Congenital overgrowth of lower limb	PG0..11	Face bone anomalies
PF6B000	Congenital overgrowth of proximal lower limb		



PG0..12	Skull and face bone anomalies	PG13100	Congenital absence of thoracic vertebra
PG00.00	Congenital absence of skull bones	PG13200	Congenital absence of lumbar vertebra
PG01.00	Acrocephaly	PG13300	Congenital absence of sacrum
PG02.00	Congenital forehead deformity	PG13311	Sacral agenesis
PG03.00	Craniosynostosis	PG13z00	Congenital absence of vertebra NOS
PG03.11	Scaphocephaly	PG14.00	Hemivertebra
PG03000	Muenke syndrome	PG14000	Cervical hemivertebra
PG04.00	Craniofacial dysostosis	PG14100	Thoracic hemivertebra
PG04.11	Crouzon's disease	PG14200	Lumbar hemivertebra
PG04.12	Triglorhinophalangeal dysplasia	PG14300	Cervical hemivertebra- balanced
PG05.00	Hypertelorism	PG14400	Cervical hemivertebra - unbalanced
PG06.00	Imperfect fusion of skull	PG14500	Thoracic hemivertebra- balanced
PG07.00	Oxycephaly	PG14600	Thoracic hemivertebra - unbalanced
PG08.00	Platybasia	PG14700	Lumbar hemivertebra - balanced
PG09.00	Premature cranial suture closure	PG14800	Lumbar hemivertebra - unbalanced
PG0A.00	Tower skull	PG14z00	Hemivertebra NOS
PG0B.00	Trigonocephaly	PG15.00	Congenital fusion of spine
PG0C.00	Pierre - Robin syndrome	PG15.11	Congenital lumbosacral fusion
PG0D.00	Mandibulofacial dysostosis	PG15000	Congenital complete fusion of spine
PG0D.11	Franceschetti syndrome	PG15100	Congenital partial fusion of spine - balanced
PG0D.12	Treacher - Collins syndrome	PG15200	Congenital partial fusion of spine - unbalanced
PG0E.00	Oculomandibular dysostosis	PG15300	Congenital partial fusion spine with hemivertebra, balanced
PG0E.11	Hallerman - Streif syndrome	PG15400	Congenital partial fusion spine with hemivertebra, unbalanced
PG0E.12	Oculomandibulofacial syndrome	PG16.00	Klippel-Feil syndrome
PG0F.00	Goldenhar's syndrome	PG16000	Wilderwanck's syndrome
PG0G.00	Localised skull defects	PG16z00	Klippel - Feil syndrome NOS
PG0G.11	Craniolacunia	PG17.00	Spina bifida occulta
PG0G.12	Lacunar skull	PG18.00	Congenital kyphosis
PG0G.13	Parietal foramina	PG18.11	Congenital kyphoscoliosis
PG0H.00	Macrocephaly	PG1u.00	Congenital anomalies of cervical vertebrae NEC
PG0J.00	Pierre Robin association	PG1u000	Supernumerary cervical vertebra
PG0y.00	Other specified skull or face bone anomaly	PG1uz00	Congenital anomaly of cervical vertebrae NEC NOS
PG0y.11	Defect of skull ossification	PG1v.00	Congenital anomalies of thoracic vertebrae NEC
PG0y.12	Cranial dysostosis NEC	PG1v000	Supernumerary thoracic vertebra
PG0y000	Brachycephaly	PG1vz00	Congenital anomaly of thoracic vertebrae NEC NOS
PG0yz00	Other anomaly of skull or face bone NOS	PG1w.00	Congenital anomalies of lumbar vertebrae NEC
PG0z.00	Skull or face bone anomaly NOS	PG1w000	Supernumerary lumbar vertebra
PG0z.11	Dysmorphic features	PG1wz00	Congenital anomaly of lumbar vertebra NEC NOS
PG1..00	Anomalies of spine	PG1x.00	Congenital sacrococcygeal anomalies NEC
PG10.00	Anomaly of spine, unspecified	PG1x000	Congenital absence of coccyx
PG11.00	Congenital lumbosacral spondylolysis	PG1x100	Congenital absence of sacrum
PG12.00	Congenital spondylolisthesis	PG1xz00	Congenital sacrococcygeal anomaly NOS
PG13.00	Congenital absence of vertebra	PG1y.00	Other anomaly of spine
PG13000	Congenital absence of cervical vertebra		

PG1y.11	Congenital deformity of lumbosacral joint	PG42100	Myotonic chondrodysplasia
PG1y.12	Congenital deformity of lumbosacral region	PG42111	Catel-Schwartz-Jampel syndrome
PG1y000	Platyspondylia	PG42z00	Dyschondroplasia NOS
PG1y100	Supernumerary vertebra	PG43.00	Asphyxiating thoracic dysplasia
PG1y200	Congenital absence of spine NEC	PG43.11	Jeune's syndrome
PG1y300	Defect of vertebral segmentation	PG44.00	Other specified dwarfing syndromes
PG1y400	Hypoplasia of spine	PG44000	Diastrophic dwarfism
PG1yz00	Other anomaly of spine NOS	PG44011	Diastrophic dysplasia
PG1z.00	Anomalies of spine NOS	PG44100	Metatropic dwarfism
PG2..00	Cervical rib	PG44111	Metatropic dysplasia
PG3..00	Other rib and sternum anomalies	PG44200	Thanatophoric dwarfism
PG30.00	Congenital absence of rib	PG44211	Thanatophoric dysplasia
PG31.00	Congenital absence of sternum	PG44300	Mesomelic dysplasia
PG32.00	Congenital fissure of sternum	PG44400	Acromesomelic dysplasia
PG33.00	Congenital fusion of ribs	PG44500	Kniest dysplasia
PG34.00	Sternum bifidum	PG44600	Pseudoachondroplasia
PG35.00	Mis-shapen ribs	PG44z00	Other dwarfing syndromes NOS
PG36.00	Extra ribs	PG45.00	Metaphyseal dysostosis
PG36.11	Supernumerary ribs	PG45.11	Jansen's metaphyseal dysostosis
PG37.00	Mis-shapen sternum	PG45.12	Schmid's metaphyseal dysostosis
PG3x.00	Other congenital anomalies of ribs	PG45.13	Craniometaphyseal dysostosis
PG3y.00	Other congenital anomalies of sternum	PG45.14	Frontometaphyseal dysostosis
PG3z.00	Other rib or sternum anomaly NOS	PG45.15	Metaphyseal dysplasia
PG3z.11	Anomalies of thoracic cage unspecified	PG46.00	Spondyloepiphyseal dysplasia
PG4..00	Chondrodysplasia	PG46.11	Pseudoachondroplasia
PG40.00	Chondrodysplasia, unspecified	PG46000	Spondyloepiphyseal dysplasia congenita
PG41.00	Achondroplasia	PG46100	Spondyloepiphyseal dysplasia tarda
PG41.11	Dwarfism	PG47.00	Congenital exostosis
PG41.12	Achondrogenesis	PG47.11	Multiple congenital exostosis
PG41.13	Achondroplastic dwarf	PG48.00	Diaphyseal aclasis
PG41000	Hypochondroplasia	PG49.00	Dysplasia epiphysealis hemimelica
PG42.00	Multiple enchondromata	PG4A.00	Metachondromatosis
PG42.11	Enchondromatosis	PG4B.00	Lethal retarded ossification syndromes
PG42.12	Ollier's disease	PG4B000	Achondrogenesis
PG42.13	Chondrodysplasia	PG4B100	Hypochondrogenesis
PG42.14	Chondrodystrophy NEC	PG4B200	Fibrochondrogenesis
PG42.15	Hypochondroplasia	PG4B300	Short-rib/polydactyly syndrome
PG42.16	Osteopathia striata	PG4B400	Camptomelia dysplasia
PG42.17	Pseudoachondroplasia	PG4By00	Other lethal retarded ossification syndromes
PG42.18	Dyschondroplasia	PG4C.00	Chondrodysplasia punctata
PG42000	Multiple enchondromata with haemangioma	PG4D.00	Metaphyseal chondrodysplasia
PG42011	Kast's syndrome	PG4E.00	Spondylometaphyseal dysplasia
PG42012	Maffucci's syndrome	PG4F.00	Lei-Weill dyschondrosteosis
PG42013	Chondrodysplasia with haemangioma	PG4y.00	Chondrodysplasia OS

PG4z.00	Chondrodysplasia NOS	PG5C.00	Craniometaphyseal dysplasia
PG5..00	Osteodysplasia	PG5D.00	Craniodiaphyseal dysplasia
PG5..11	Osteodystrophy	PG5E.00	Frontometaphyseal dysplasia
PG50.00	Osteodysplasia, unspecified	PG5y.00	Other specified osteodysplasia
PG51.00	Osteogenesis imperfecta	PG5y.11	Dyschondrosteosis
PG51.11	Vrolik's disease	PG5y.12	Furst-Ostrum syndrome
PG51.12	Eddowe's syndrome	PG5y000	Albright-Sternberg syndrome
PG51.13	Adair-Dighton syndrome	PG5y011	Albright-McCune-Sternberg syndrome
PG51.14	Lobstein's syndrome	PG5y012	Albright's polyostotic dysplasia
PG51.15	Van der Hoeve's syndrome	PG5yz00	Other osteodysplasia NOS
PG51.16	Brittle bone disease	PG5z.00	Osteodysplasia NOS
PG51000	Fragilitas ossium	PG5z.11	Osteochondrodysplasia
PG51100	Osteopsathyrosis	PG6..00	Anomalies of diaphragm
PG51200	Osteogenesis imperfecta - unclassifiable	PG60.00	Congenital absence of diaphragm
PG51300	Osteogenesis imperfecta type I	PG61.00	Congenital diaphragmatic hernia
PG51400	Osteogenesis imperfecta type II	PG61.11	Congenital defect of diaphragmatic NEC
PG51500	Osteogenesis imperfecta type III	PG62.00	Congenital foramen Morgagni hernia
PG51600	Osteogenesis imperfecta type IV	PG63.00	Eventration of diaphragm
PG51z00	Osteogenesis imperfecta NOS	PG6y.00	Other specified anomalies of diaphragm
PG52.00	Osteopetrosis	PG6z.00	Diaphragm anomalies NOS
PG52.11	Albers - Schonberg syndrome	PG7..00	Abdominal wall anomalies
PG52.12	Marble bones	PG70.00	Exomphalos
PG52000	Osteopetrosis - unclassified	PG71.00	Gastroschisis
PG52100	Osteopetrosis - congenita type	PG72.00	Prune belly syndrome
PG52200	Osteopetrosis - tarda type	PG7y.00	Other specified anomaly of abdominal wall
PG53.00	Osteopoikilosis	PG7z.00	Abdominal wall anomaly NOS
PG53.11	Buschke-Ollendorff syndrome	PG8..00	Congenital inguinal hernia
PG54.00	Polyostotic fibrous dysplasia	PGW..00	Osteochondrodyspl with defct growth tub bone spine unspec
PG55.00	Chondroectodermal dysplasia	PGX..00	Congenital malformation of bony thorax, unspecified
PG55.11	Ellis - Van Creveld syndrome	PGy..00	Other specified muscle, tendon and fascia anomaly
PG56.00	Multiple epiphyseal dysplasia	PGy0.00	Congenital absence of muscle and tendon
PG56000	Chondrodysplasia calcificans congenita	PGy0000	Absent tendon
PG56011	Chondrodysplasia calcificans congenita	PGy0100	Poland's syndrome
PG56012	Conradi - Hunermann syndrome	PGy0200	Other absent muscle
PG56z00	Multiple epiphyseal dysplasia NOS	PGy0211	Muscle agenesis
PG57.00	Infantile cortical hyperostosis	PGy0212	Orbinsky syndrome
PG57.11	Caffey's syndrome	PGy0z00	Absent muscle or tendon NOS
PG58.00	Progressive diaphyseal dysplasia	PGy1.00	Accessory muscle
PG58.11	Engelmann's syndrome	PGy2.00	Ehlers-Danlos syndrome
PG58.12	Camurati-Engelmann disease	PGy2000	Ehlers-Danlos syndrome type I
PG59.00	Pyknodysostosis	PGy2100	Ehlers-Danlos syndrome type II
PG59.11	Pycnodysostosis	PGy2200	Ehlers-Danlos syndrome type III
PG5A.00	Diaphyseal dysplasia	PGy2300	Ehlers-Danlos syndrome type IV
PG5B.00	Multiple synostosis syndrome	PGy2400	Ehlers-Danlos syndrome type V

PGy2500	Ehlers-Danlos syndrome type VI	PH1z.12	Alligator skin
PGy2600	Ehlers-Danlos syndrome type VII	PH2..00	Dermatoglyphic anomalies
PGy2700	Ehlers-Danlos syndrome type VIII	PH20.00	Abnormal palmar creases
PGy3.00	Nail-patella syndrome	PH2z.00	Dermatoglyphic anomalies NOS
PGy3.11	Osteo-onychodysostosis	PH3..00	Other specified skin anomalies
PGy3.12	Onycho-osteodysplasia	PH30.00	Congenital ectodermal dysplasia
PGy4.00	Fibrodysplasia ossificans congenita	PH31.00	Vascular hamartomas
PGyy.00	Other specified other anomalies of muscle, tendon and fascia	PH31.11	Vascular naevus
PGyy.11	Ayala's disease	PH31.12	Naevus flammeus
PGyy000	Amyotrophica congenita	PH31000	Birth mark, unspecified
PGyy100	Congenital shortening of tendon	PH31100	Port wine stain
PGyy200	Hypoplasia of muscle	PH31200	Strawberry naevus
PGyy300	Popliteal web syndrome	PH31300	Angiomatosis
PGyy400	Aplasia of muscle	PH31z00	Vascular hamartoma NOS
PGyyz00	Other anomaly of tendon, fascia or muscle NOS	PH32.00	Congenital pigmentary skin anomalies
PGyz.00	Other muscle, tendon or fascia anomalies NOS	PH32000	Congenital poikiloderma
PGz..00	Congenital musculoskeletal anomalies NOS	PH32100	Urticaria pigmentosa
PGz..11	Congenital deformity of musculoskeletal system NEC	PH32111	Mast cell disease
PGz0.00	Unspecified anomaly of muscle	PH32112	Mastocytosis
PGz1.00	Unspecified anomaly of tendon	PH32113	Nettleship's syndrome
PGz2.00	Unspecified anomaly of bones	PH32200	Xeroderma pigmentosum
PGz3.00	Unspecified anomaly of cartilage	PH32211	Kaposi's xeroderma pigmentosum
PGz4.00	Unspecified anomaly of connective tissue	PH32300	Incontinentia pigmenti
PH...00	Congenital integument anomalies	PH32311	Bloch - Sulzberger syndrome
PH...11	Congenital skin anomalies	PH32z00	Congenital pigmentary skin anomaly NOS
PH0..00	Hereditary oedema of legs	PH33.00	Specified syndromes NEC involving skin anomalies
PH00.00	Congenital lymphoedema	PH33000	Brugsch's syndrome
PH01.00	Hereditary trophoedema	PH33011	Acropachyderma
PH02.00	Milroy's disease	PH33100	Hailey-Hailey disease
PH02.11	Meige's disease	PH33111	Benign familial chronic pemphigus
PH03.00	Congenital elephantiasis	PH33200	Mibelli's disease
PH0z.00	Hereditary oedema of legs NOS	PH33300	Rothmund-Thomson syndrome
PH1..00	Ichthyosis congenita	PH33311	Atrophic heredofamilial dermatosis
PH10.00	Congenital ichthyosis, unspecified	PH33312	Thomson's disease
PH11.00	Harlequin fetus	PH33400	Focal dermal hypoplasia
PH12.00	Ichthyosiform erythroderma	PH33500	Pseudoxanthoma elasticum
PH12.11	Sjogren - Larsson syndrome	PH33511	Darier's disease - pseudoxanthoma elasticum
PH13.00	Collodion baby	PH33600	Siemen's syndrome
PH14.00	Ichthyosis vulgaris	PH33z00	Specified syndromes involving skin anomalies NEC NOS
PH15.00	X-linked ichthyosis	PH34.00	Other specified birthmark
PH1y.00	Other specified ichthyosis congenita	PH34.11	Naevus NEC
PH1y000	Nethertons syndrome"	PH34000	Naevus sebaceous
PH1z.00	Ichthyosis congenita NOS	PH35.00	Mongolian blue spot
PH1z.11	Congenital ichthyosiform erythroderma	PH3y.00	Other congenital skin anomalies

PH3y.11	Keratosis palmaris	PH54.11	Enlarged nails
PH3y000	Congenital accessory skin tags	PH55.00	Congenital pachyonychia
PH3y100	Congenital scar	PH55.11	Hypertrophic nails
PH3y200	Epidermolysis bullosa	PH5z.00	Specified nail anomalies NOS
PH3y211	Goldscheider's disease	PH6..00	Specified anomalies of breast
PH3y212	Koebner's disease	PH60.00	Absent breast
PH3y213	Bullous eruption of hand	PH61.00	Absent nipple
PH3y300	Congenital keratoderma	PH62.00	Accessory breast
PH3y400	Congenital keratosis follicularis	PH63.00	Accessory nipple
PH3y411	Darier's disease - keratosis follicularis	PH64.00	Supernumerary breast
PH3y500	Acanthosis nigricans, congenital	PH65.00	Supernumerary nipple
PH3y600	Keratosis palmaris et plantaris	PH66.00	Hypoplasia of breast
PH3y611	Tylosis palmaris et plantaris	PH67.00	Small nipple
PH3y700	Epidermolysis bullosa simplex	PH67.11	Hypoplasia of nipple
PH3y800	Epidermolysis bullosa letalis	PH68.00	Ectopic breast tissue
PH3y900	Epidermolysis bullosa dystrophica	PH6X.00	Congenital malformation of breast, unspecified
PH3yA00	Bloom syndrome	PH6z.00	Specified breast anomalies NOS
PH3yz00	Other congenital skin anomaly NOS	PH7..00	Cutis marmorata telangiectasia congenita
PH3yz11	Lichen spinulosus	PHy..00	Other specified integument anomaly
PH3z.00	Integument anomalies NOS	PHz..00	Integument anomalies NOS
PH4..00	Specified hair anomalies	PHz..11	Congenital ectodermal defect
PH40.00	Congenital alopecia	PHz0.00	Unspecified congenital anomalies of skin
PH40.11	Congenital atrichosis	PHz0.11	Congenital dermal defect
PH40000	Congenital alopecia, unspecified	PHz1.00	Unspecified congenital anomalies of hair
PH40100	Congenital localised alopecia	PHz2.00	Unspecified congenital anomalies of nail
PH40200	Congenital generalised alopecia	PHz2.11	Congenital deformity of nail
PH40211	Atrichosis	PJ...00	Chromosomal anomalies
PH40z00	Congenital alopecia NOS	PJ0..00	Down's syndrome - trisomy 21
PH41.00	Congenital monilethrix	PJ0..11	Mongolism
PH41.11	Beaded hair	PJ0..12	Trisomy 21
PH42.00	Congenital hypertrichosis	PJ0..13	Trisomy 22
PH43.00	Persistent lanugo	PJ00.00	Trisomy 21, meiotic nondisjunction
PH43.11	Hypertrichosis lanuginosa	PJ01.00	Trisomy 21, mosaicism
PH44.00	Twisted hair	PJ01.11	Trisomy 21, mitotic nondisjunction
PH44.11	Pili torti	PJ02.00	Trisomy 21, translocation
PH45.00	Taenzer's hair	PJ02.11	Partial trisomy 21 in Down's syndrome
PH4z.00	Specified hair anomalies NOS	PJ0z.00	Down's syndrome NOS
PH5..00	Specified anomalies of nails	PJ0z.11	Trisomy 21 NOS
PH50.00	Anonychia	PJ1..00	Patau's syndrome - trisomy 13
PH50.11	Congenital absence of nails	PJ10.00	Trisomy 13, meiotic nondisjunction
PH51.00	Congenital clubnail	PJ11.00	Trisomy 13, mosaicism
PH52.00	Congenital koilonychia	PJ11.11	Trisomy 13, mitotic nondisjunction
PH53.00	Congenital leukonychia	PJ12.00	Trisomy 13, translocation
PH54.00	Congenital onychauxis	PJ12.11	Partial trisomy 13 in Patau's syndrome

PJ1z.00	Patau's syndrome NOS	PJ50.00	Whole chromosome trisomy syndromes
PJ1z.11	Trisomy 13 NOS	PJ50000	Trisomy 6
PJ2..00	Edward's syndrome - trisomy 18	PJ50100	Trisomy 7
PJ20.00	Trisomy 18, meiotic nondisjunction	PJ50200	Trisomy 8
PJ21.00	Trisomy 18, mosaicism	PJ50300	Trisomy 9
PJ21.11	Trisomy 18, mitotic nondisjunction	PJ50400	Trisomy 10
PJ22.00	Trisomy 18, translocation	PJ50500	Trisomy 11
PJ22.11	Partial trisomy 18 in Edward's syndrome	PJ50600	Trisomy 12
PJ2z.00	Edward's syndrome NOS	PJ50700	Other trisomy C syndromes
PJ2z.11	TRISOMY 18 NOS	PJ50800	Trisomy 22
PJ3..00	Monosomies and deletions from the autosomes	PJ50w00	Whole chromosome trisomy, meiotic nondisjunction
PJ30.00	Antimongolism syndrome	PJ50x00	Whole chromosome trisomy, mosaicism
PJ30.11	Deletion of long arm of chromosome 21	PJ50x11	Whole chromosome trisomy, mitotic nondisjunction
PJ31.00	Cri-du-chat syndrome	PJ50y00	Other specified whole chromosome trisomy syndrome
PJ31.11	Deletion of short arm of chromosome 5	PJ50z00	Whole chromosome trisomy syndrome NOS
PJ32.00	Deletion of short arm of chromosome 4	PJ51.00	Partial trisomy syndromes
PJ32.11	Wolff - Hirschorn syndrome	PJ51000	Major partial trisomy
PJ33.00	Other deletions of part of a chromosome	PJ51100	Minor partial trisomy
PJ33000	Deletion of long arm of chromosome 13	PJ51z00	Partial trisomy syndrome NOS
PJ33100	Deletion of long arm of chromosome 18	PJ52.00	Trisomies of autosomes NEC
PJ33111	18p- syndrome	PJ52000	Duplications seen only at prometaphase
PJ33200	Deletion of short arm of chromosome 18	PJ52100	Duplications with other complex rearrangements
PJ33211	18q- syndrome	PJ52200	Extra marker chromosomes
PJ33300	Smith-Magenis syndrome	PJ52300	Triploidy
PJ33400	Jacobsen syndrome	PJ52400	Polyploidy
PJ33z00	Other deletion of part of a chromosome NOS	PJ52z00	Trisomy of autosomes NEC NOS
PJ34.00	Deletions seen only at prometaphase	PJ53.00	Balanced rearrangements and structural markers NEC
PJ35.00	Deletions with other complex rearrangements	PJ53.11	Balanced translocations
PJ36.00	Whole chromosome monosomy, meiotic nondisjunction	PJ53000	Chromosome inversion in normal individual
PJ37.00	Whole chromosome monosomy, mosaicism	PJ53100	Balanced autosomal rearrangement in abnormal individual
PJ37.11	Whole chromosome monosomy, mitotic nondisjunction	PJ53200	Balanced sex/autosomal rearrangement in abnormal individual
PJ37.12	Autosomal deletion - mosaicism	PJ53300	Individual with marker heterochromatin
PJ37000	Monosomy 21, mosaicism	PJ53400	Individual with autosomal fragile site
PJ37z00	Whole chromosome monosomy, mosaicism NOS	PJ53500	Shwachman-Diamond syndrome
PJ38.00	Chromosome replaced with ring or dicentric	PJ53z00	Balanced rearrangement or structural marker NEC NOS
PJ38.11	Chromosome replaced with dicentric	PJ5y.00	Other specified conditions due to autosomal anomalies
PJ38.12	Chromosome replaced with ring	PJ5z.00	Unspecified conditions due to autosomal anomalies
PJ3y.00	Other deletions from the autosomes	PJ5z.11	Aneuploidy NEC
PJ3y000	Shprintzen syndrome	PJ6..00	Gonadal dysgenesis
PJ3y011	Velocardiofacial syndrome	PJ60.00	Mixed gonadal dysgenesis
PJ3z.00	Monosomies and deletions from the autosomes NOS	PJ62.00	Ovarian dysgenesis
PJ4..00	Balanced autosomal translocation	PJ63.00	Turner's syndrome
PJ5..00	Other condition due to autosomal anomaly	PJ63000	Turner's phenotype, karyotype normal

PJ63100	Turner's phenotype, karyotype 45X	PJyy.11	Absence of sex chromosome
PJ63200	Turner's phenotype, karyotype 46X iso (Xq)	PJyy000	Chimera 46XX/46XY
PJ63300	Turner's, karyotype 46X + abnorm. sex chromosome, not iso(Xq)	PJyy011	Chimera 46XX/46XY, true hermaphrodite
PJ63400	Turner's phenotype, mosaicism 45X/46XX or 45X/46XY	PJyy100	46XX true hermaphrodite
PJ63500	Turner's, mosaic, 45X/other cell line with abn.sex chromosome	PJyy200	Fragile X chromosome
PJ63600	Turner's phenotype, other variant karyotypes	PJyy300	Karyotype 47, XYY
PJ63611	Turner's phenotype, ring chromosome karyotype	PJyy400	Fragile X syndrome
PJ63612	Turner's phenotype, partial X deletion karyotype	PJyyz00	Other sex chromosome abnormality NOS
PJ63z00	Turner's syndrome NOS	PJyz.00	Sex chromosome anomaly NOS
PJ63z11	Bonnevie-Ullrich syndrome NOS	PJz..00	Chromosomal anomalies NOS
PJ63z12	Ovarian dwarfism NEC	PJz0.00	Mosaicism NOS
PJ64.00	Other gonadal dysgenesis phenotype	PJz1.00	Additional chromosome NOS
PJ64000	XY, female phenotype	PJz2.00	Deletion of chromosome NOS
PJ64z00	Other gonadal dysgenesis phenotype NOS	PJz3.00	Duplication of chromosome
PJ6z.00	Gonadal dysgenesis NOS	PJzz.00	Conditions due to anomaly of unspecified chromosome NOS
PJ7..00	Klinefelter's syndrome	PK...00	Other and unspecified congenital anomalies
PJ70.00	Klinefelter's phenotype, karyotype 47XXY	PK0..00	Anomalies of spleen
PJ71.00	Klinefelter's syndrome, male with more than two X chromosomes	PK00.00	Aberrant spleen
PJ71.11	Klinefelter's syndrome, XXXY	PK01.00	Absent spleen
PJ71.12	Klinefelter's syndrome, XXXXY	PK01.11	Asplenia
PJ72.00	Klinefelter's syndrome, male with 46XX karyotype	PK02.00	Accessory spleen
PJ73.00	Klinefelter's syndrome, XXYY	PK03.00	Congenital splenomegaly
PJ74.00	Klinefelter's syndrome, XY/XXY mosaic	PK03.11	Hyperplasia of spleen
PJ7z.00	Klinefelter's syndrome NOS	PK04.00	Ectopic spleen
PJ8..00	Balanced translocation and insertion in normal individual	PK05.00	Congenital lobulation of spleen
PJ9..00	Mowat-Wilson syndrome	PK06.00	Hypoplasia of spleen
PJX..00	Sex chromosome abnormality, male phenotype, unspecified	PK07.00	Mis-shapen spleen
PJy..00	Other sex chromosome anomaly	PK0y.00	Other specified anomalies of spleen
PJy0.00	Additional sex chromosome	PK0z.00	Anomalies of spleen NOS
PJy1.00	Sex chromosome mosaicism	PK1..00	Anomalies of adrenal gland
PJy1000	Mosaic XO/XY	PK10.00	Aberrant adrenal gland
PJy1100	Mosaic XO/XX	PK11.00	Absent adrenal gland
PJy1200	Mosaic XY/XXY	PK12.00	Accessory adrenal gland
PJy1300	Mosaic including XXXXY	PK13.00	Hypoplasia of adrenal gland
PJy1z00	Sex chromosome mosaicism NOS	PK14.00	Ectopic adrenal gland
PJy2.00	XXX syndrome	PK15.00	Aplasia of adrenal gland
PJy2.11	Triple X female	PK1y.00	Other specified anomalies of adrenal gland
PJy2.12	Karyotype 47, XXX	PK1y000	Congenital cyst of adrenal gland
PJy3.00	XXY syndrome	PK1yz00	Other congenital anomaly of adrenal gland NOS
PJy4.00	Female with more than three X chromosomes	PK1z.00	Anomalies of adrenal gland NOS
PJy5.00	Mosaicism, lines with various numbers of X chromosomes	PK2..00	Other endocrine gland anomalies
PJy6.00	Male with structurally abnormal sex chromosome	PK20.00	Absent parathyroid gland
PJyy.00	Other specified sex chromosome anomaly	PK21.00	Accessory thyroid gland
		PK22.00	Persistent thyroglossal duct

PK22.11	Persistent thyrolingual duct	PK41.11	Conjoined twins with two heads
PK23.00	Thyroglossal duct cyst	PK42.00	Pygopagus
PK24.00	Anomalies of pituitary gland	PK42.11	Buttock-joined twins
PK24000	Aberrant pituitary gland	PK43.00	Thoracopagus
PK24100	Congenital absence of pituitary gland	PK43.11	Thorax-joined twins
PK24200	Accessory pituitary gland	PK44.00	Xiphopagus
PK24z00	Anomaly of pituitary gland NOS	PK44.11	Xiphoid- and pelvis-joined twins
PK25.00	Anomalies of thyroid gland NEC	PK45.00	Di axial (double) monster
PK25000	Aberrant thyroid gland	PK4y.00	Other specified conjoined twins
PK25011	Retrosternal thyroid gland	PK4z.00	Conjoined twins NOS
PK25100	Congenital absence of thyroid gland	PK5..00	Tuberous sclerosis
PK25z00	Anomaly of thyroid gland NEC NOS	PK5..11	Bourneville's disease
PK26.00	Anomalies of thyroglossal duct NEC	PK5..12	Epiloia
PK27.00	Anomalies of parathyroid gland NEC	PK6..00	Other hamartoses NEC
PK27000	Aberrant parathyroid gland	PK60.00	Peutz - Jegher's syndrome
PK27100	Accessory parathyroid gland	PK61.00	Sturge-Weber syndrome
PK27z00	Anomaly of parathyroid gland NEC NOS	PK61.11	Kalischer's disease
PK28.00	Anomalies of thymus	PK61.12	Encephalocutaneous angiomas
PK28000	Aberrant thymus gland	PK62.00	Von Hippel-Lindau syndrome
PK28100	Congenital absence of thymus	PK62.11	Lindau's disease
PK28200	Accessory thymus gland	PK63.00	Gardner's syndrome
PK28z00	Anomaly of thymus gland NOS	PK64.00	Proteus syndrome
PK2y.00	Other specified endocrine gland anomaly	PK6y.00	Other specified hamartoses NEC
PK2z.00	Endocrine gland anomaly NOS	PK6z.00	Hamartoses NOS
PK3..00	Situs inversus	PK7..00	Multiple congenital anomalies NOS
PK30.00	Situs inversus, unspecified	PK70.00	Monster NOS
PK30.11	Transposition of viscera unspecified	PK7z.00	Multiple congenital anomalies NOS
PK31.00	Situs inversus abdominalis	PK8..00	Congenital malformation syndromes due to known exogen causes
PK31.11	Transposition of abdominal viscera	PK80.00	Fetal alcohol syndrome
PK32.00	Situs inversus thoracis	PK81.00	Fetal hydantoin syndrome
PK32.11	Transposition of thoracic viscera	PK82.00	Dysmorphism due to warfarin
PK33.00	Complete situs inversus with dextrocardia	PK83.00	Fetus and newborn affected by maternal use of alcohol
PK34.00	Situs inversus with levocardia	PK84.00	Fetal valproate syndrome
PK35.00	Kartagener's syndrome	PKy..00	Other specified anomalies
PK3z.00	Situs inversus NOS	PKy0.00	Multiple system congenital anomalies NEC
PK4..00	Conjoined twins	PKy0.11	Prader-Willi Syndrome
PK40.00	Craniopagus	PKy0.12	Prader-Willi syndrome
PK40.11	Head-joined twins	PKy0.13	Noonan's syndrome
PK40000	Craniopagus frontalis	PKy0000	Bannayan-Riley-Ruvalcaba syndrome
PK40100	Craniopagus occipitalis	PKy0100	Currarino triad
PK40200	Craniopagus parietalis	PKy0200	Adams-Oliver syndrome
PK40300	Craniopagus parasiticus	PKy0300	Weaver syndrome
PK40z00	Craniopagus NOS	PKy1.00	Laurence-Moon-Biedl syndrome
PK41.00	Dicephalus	PKy1.11	Biedl-Bardet syndrome



PKy2.00	Marfan's syndrome	PKy7200	Klippel - Trenaunay - Weber syndrome
PKy3.00	Single monster, specified type	PKy7300	Rubenstein - Tayi syndrome
PKy4.00	William syndrome	PKy7400	Sirenomelia
PKy5.00	Congenital malformation syndromes affecting facial appearance	PKy7411	Symphus
PKy5000	Oral - facial - digital syndrome	PKy7412	Mermaid sirenomelia
PKy5011	Papillon-Leage-Psaume syndrome	PKy7500	Arachnodactyly
PKy5100	Mohr's syndrome	PKy7600	Aglossia - adactyly syndrome
PKy5200	Cyclops	PKy7611	Hanhart syndrome
PKy5300	Whistling face syndrome	PKy7700	Caudal dysplasia sequence
PKy5311	Freeman Sheldon syndrome	PKy7800	Multiple pterygium syndrome
PKy5400	Waardenburg's syndrome	PKy7900	Popliteal pterygium syndrome
PKy5500	Gorlin-Chaudhry-Moss syndrome	PKy7A00	Congenital contractural arachnodactyly
PKy5600	Marchesani syndrome	PKy7A11	Beals syndrome
PKy5611	Weill-Marchesani syndrome	PKy7B00	Stickler syndrome
PKy5612	Spherophakia-brachymorphia syndrome	PKy7z00	Congenital malformation syndrome involving limbs NOS
PKy5700	Otopalatodigital syndrome	PKy8.00	Congenital malformation syndromes with other skeletal change
PKy5800	Usher's syndrome	PKy8000	Noonan's syndrome
PKy5900	Oculo-palato-digital syndrome	PKy8z00	Congenital malformation syndrome+other skeletal changes NOS
PKy5A00	Trichorhinophalangeal syndrome	PKy9.00	Congenital malformation syndromes with metabolic disturbance
PKy5B00	Costello syndrome	PKy9000	Alport's syndrome
PKy5C00	Treacher Collins syndrome	PKy9100	Beckwith's syndrome
PKy5D00	Kabuki make-up syndrome	PKy9111	Wiedemann - Beckwith syndrome
PKy5E00	Branchio-otorenal dysplasia	PKy9200	Menke's syndrome
PKy5F00	Coffin-Lowry syndrome	PKy9211	Kinky hair syndrome
PKy5G00	Carey Fineman Ziter syndrome	PKy9212	Congenital kinking hair
PKy5H00	Simpson-Golabi-Behmel syndrome	PKy9300	Prader - Willi syndrome
PKy5z00	Congenital malform syndrome affecting facial appearance NOS	PKy9400	Zellweger's syndrome
PKy6.00	Congenital malformation syndromes with short stature	PKy9500	Biamond's syndrome
PKy6000	Amsterdam dwarf	PKy9600	VATER association
PKy6011	Cornelia de Lange syndrome	PKy9z00	Congenital malformation syndrome + metabolic disturbance NOS
PKy6012	Bruck-de Lange syndrome	PKyA.00	Cloacal exstrophy
PKy6013	Degenerative amsterodamensis typus	PKyB.00	CHARGE association
PKy6100	Cockayne syndrome	PKyC.00	Pena-Shokeir syndrome type I
PKy6200	Russell - Silver syndrome	PKyD.00	Nicolaides-Baraitser syndrome
PKy6300	Smith - Lemli - Opitz syndrome	PKyE.00	Barber-Say syndrome
PKy6400	Seckel syndrome	PKyF.00	Alstrom syndrome
PKy6500	Aarskog syndrome	PKyG.00	Men ret congen heart dis blepharophim blepharop hypopl teeth
PKy6600	Dubowitz syndrome	PKyG.11	Ohdo blepharophimosis syndrome
PKy6700	Robinow syndrome	PKyH.00	Moulded baby syndrome
PKy6800	Floating-Harbor syndrome	PKyJ.00	Lujan-Fryns syndrome
PKy6z00	Congenital malformation syndrome with short stature NOS	PKyK.00	Loeys-Dietz syndrome
PKy7.00	Congenital malformation syndromes involving limbs	PKyz.00	Other specified anomalies NOS
PKy7000	Carpenter's syndrome	PKyz.11	Cockayne's syndrome
PKy7100	Holt - Oram syndrome	PKyz.12	Local gigantism NEC

PKyz000	Ullrich - Feichtiger syndrome, chimaera	Pyu2000	[X]Other cong malformatn of cardiac chambers & connections
PKyz100	Acardia	Pyu2100	[X]Other congenital malformations of cardiac septa
PKyz200	Acephalobrachius	Pyu2200	[X]Other congenital malformations of pulmonary valve
PKyz300	Acephalogaster	Pyu2300	[X]Other congenital malformations of tricuspid valve
PKyz400	Acephalothorax	Pyu2400	[X]Other congenital malformations of aortic & mitral valves
PKyz500	Happy puppet syndrome	Pyu2500	[X]Other specified congenital malformations of the heart
PKyz511	Angelman syndrome	Pyu2600	[X]Other congenital malformations of aorta
PKyz600	Congenital hemihypertrophy	Pyu2700	[X]Other congenital malformations of pulmonary artery
PKyz700	Angelman's syndrome	Pyu2800	[X]Other congenital malformations of great arteries
PKyz711	Angelman syndrome	Pyu2900	[X]Other congenital malformations of great veins
PKyz800	DOOR - Deafness, triphalangeal thumbs, onychodystrophy	Pyu2A00	[X]Other congenital malformations of renal artery
PKz..00	Other anomalies NOS	Pyu2B00	[X]Oth specified cong malform of peripheral vascular system
PKz0.00	Anomalies of umbilicus	Pyu2C00	[X]Other malformations of precerebral vessels
PKz1.00	Embropathia NEC	Pyu2D00	[X]Other malformations of cerebral vessels
PKzz.00	Congenital anomaly NOS	Pyu2E00	[X]Other specified cong malformations of circulatory system
Pyu0.00	[X]Congenital malformations of the nervous system	Pyu2F00	[X]Congenital malforms of cardiac chambers+connections unsp
Pyu0000	[X]Encephalocele of other sites	Pyu2G00	[X]Congenital malformation of tricuspid valve, unspecified
Pyu0100	[X]Other congenital hydrocephalus	Pyu2H00	[X]Congenital malformation of aortic and mitral valves unsp
Pyu0200	[X]Other reduction deformities of brain	Pyu2J00	[X]Congenital malformation of great arteries, unspecified
Pyu0300	[X]Other specified congenital malformations of brain	Pyu2K00	[X]Congenital malformation of circulatory system, unspecif
Pyu0400	[X]Unspecified spina bifida with hydrocephalus	Pyu3.00	[X]Congenital malformations of the respiratory system
Pyu0500	[X]Other congenital cauda equina malformations	Pyu3000	[X]Other congenital malformations of nose
Pyu0600	[X]Other specified congenital malformations of spinal cord	Pyu3100	[X]Other congenital malformations of larynx
Pyu0700	[X]Other specif congenital malformations of nervous system	Pyu3200	[X]Other congenital malformations of trachea
Pyu1.00	[X]Congenital malformations of eye, ear, face and neck	Pyu3300	[X]Other congenital malformations of bronchus
Pyu1000	[X]Other congenital malformations of eyelid	Pyu3400	[X]Other congenital malformations of lung
Pyu1100	[X]Other congenital malformations of lacrimal apparatus	Pyu3500	[X]Other specified congen malformation respiratory system
Pyu1200	[X]Other anophthalmos	Pyu3600	[X]Congenital malformation of larynx, unspecified
Pyu1300	[X]Other congenital lens malformations	Pyu4.00	[X]Cleft lip and cleft palate
Pyu1400	[X]Other congenital malformations of iris	Pyu4000	[X]Cleft palate, unspecified, bilateral
Pyu1500	[X]Other congenital corneal malformations	Pyu4100	[X]Unspecified cleft palate with cleft lip, bilateral
Pyu1600	[X]Other congenital malforms of anterior segment of eye	Pyu5.00	[X]Other congenital malformations of the digestive system
Pyu1700	[X]Other cong malformations of posterior segment of eye	Pyu5000	[X]Other congenital malformations of tongue
Pyu1800	[X]Other specified congenital malformations of eye	Pyu5100	[X]Congenital malformations of palate, NEC
Pyu1900	[X]Other congenital malformations of middle ear	Pyu5200	[X]Other congenital malformations of mouth
Pyu1A00	[X]Congenital malformation of inner ear	Pyu5300	[X]Other congenital malformations of pharynx
Pyu1B00	[X]Malformation of ear with impairment of hearing, unsp	Pyu5400	[X]Other congenital malformations of oesophagus
Pyu1C00	[X]Other misshapen ear	Pyu5500	[X]Other specified congenital malformations of stomach
Pyu1D00	[X]Other specified congenital malformations of ear	Pyu5600	[X]Other specif congen malformations upper alimentary tract
Pyu1E00	[X]Other branchial cleft malformations	Pyu5700	[X]Cong absence/atresia/stenos oth spec parts small intest
Pyu1F00	[X]Other specified congenital malformations of face & neck		
Pyu2.00	[X]Congenital malformations of the circulatory system		

Pyu5800	[X]Cong absence/atresia/stenos of other parts large intest	Pyu8800	[X]Other reduction defects of lower limb(s)
Pyu5900	[X]Cong abs, atresia & stenosis of large intest, part unsp	Pyu8900	[X]Other reduction defects of unspecified limb(s)
Pyu5A00	[X]Other congenital functional disorders of colon	Pyu8A00	[X]Other congen malform upper limb(s), incl shoulder girdle
Pyu5B00	[X]Other specified congenital malformations of intestine	Pyu8B00	[X]Other congen malform lower limb(s), includ pelvic girdle
Pyu5C00	[X]Other congenital malformations of gallbladder	Pyu8C00	[X]Other specified congenital malformations of limb(s)
Pyu5D00	[X]Other congenital malformations of bile ducts	Pyu8D00	[X]Other specified congenit malformation skull & face bones
Pyu5E00	[X]Other congenital malformations of liver	Pyu8E00	[X]Other congen malform of spine, not assoc with scoliosis
Pyu5F00	[X]Other congen malformation of pancreas & pancreatic duct	Pyu8F00	[X]Other congenital malformations of ribs
Pyu5G00	[X]Other specified congen malformation of digestive system	Pyu8G00	[X]Other congenital malformations of bony thorax
Pyu5H00	[X]Congenital malformation of intestine, unspecified	Pyu8H00	[X]Oth osteochondrodyspl with def growth tub bones & spine
Pyu6.00	[X]Congenital malformations of genital organs	Pyu8J00	[X]Other specified osteochondrodysplasias
Pyu6000	[X]Other congenital malformations of ovary	Pyu8K00	[X]Other congenital malformations of diaphragm
Pyu6100	[X]Other congen malform of fallopian tube & broad ligament	Pyu8L00	[X]Other congenital malformations of abdominal wall
Pyu6200	[X]Other doubling of uterus	Pyu8M00	[X]Other congenital malforms of the musculoskeletal system
Pyu6300	[X]Other congenital malformations of uterus and cervix	Pyu8N00	[X]Congenital deformity of hip, unspecified
Pyu6400	[X]Other congenital malformations of vagina	Pyu8P00	[X]Congenital malformation of bony thorax, unspecified
Pyu6500	[X]Other congenital malformations of vulva	Pyu8Q00	[X]Osteochondrodyspl with defct growth tub bone spine unspc
Pyu6600	[X]Other specified congenital malform of female genitalia	Pyu9.00	[X]Other congenital malformations
Pyu6700	[X]Other specified hypospadias	Pyu9000	[X]Other congenital ichthyosis
Pyu6800	[X]Other congenital malformations of testis and scrotum	Pyu9100	[X]Other epidermolysis bullosa
Pyu6900	[X]Oth cong malform vas def/epidid/semin vesicles/prostate	Pyu9200	[X]Other specified congenital malformations of skin
Pyu6A00	[X]Other congenital malformations of penis	Pyu9300	[X]Other congenital malformations of breast
Pyu6B00	[X]Other specified congenit malform of male genital organs	Pyu9400	[X]Other congenital malformations of hair
Pyu7.00	[X]Congenital malformations of the urinary system	Pyu9500	[X]Other congenital malformations of nails
Pyu7000	[X]Other cystic kidney diseases	Pyu9600	[X]Other specified congenital malformations of integument
Pyu7100	[X]Other obstructive defects of renal pelvis and ureter	Pyu9700	[X]Other phakomatoses, not elsewhere classified
Pyu7200	[X]Other congenital malformations of ureter	Pyu9800	[X]Other cong malformat syndr due to known exogenous causes
Pyu7300	[X]Other specified congenital malformations of kidney	Pyu9900	[X]Other congen malform syndromes with other skelet changes
Pyu7400	[X]Other atresia and stenosis of urethra and bladder neck	Pyu9A00	[X]Other specified congenital malformation syndromes, NEC
Pyu7500	[X]Other congenital malformations of bladder and urethra	Pyu9B00	[X]Other specified congenital malformations
Pyu7600	[X]Other specified congenital malform of urinary system	Pyu9C00	[X]Congenital malformation of breast, unspecified
Pyu8.00	[X]Congenital malformations+deformations musculoskeletal sys	Pyu9D00	[X]Primary ciliary dyskinesia
Pyu8000	[X]Other congenital deformities of hip	PyuA.00	[X]Chromosomal abnormalities, not elsewhere classified
Pyu8100	[X]Other congenital varus deformities of feet	PyuA000	[X]Oth specif trisomies & partial trisomies of autosomes
Pyu8200	[X]Other congenital valgus deformities of feet	PyuA100	[X]Other deletions of part of a chromosome
Pyu8300	[X]Other congenital deformities of feet	PyuA200	[X]Other deletions from the autosomes
Pyu8400	[X]Other congenital deformities of skull, face and jaw	PyuA300	[X]Other balanced rearrangements and structural markers
Pyu8500	[X]Other congenital deformities of chest	PyuA400	[X]Balanced rearrangement & structural marker, unspecified
Pyu8600	[X]Other specified congenital musculoskeletal deformities	PyuA500	[X]Other variants of Turner's syndrome
Pyu8700	[X]Other reduction defects of upper limb(s)	PyuA600	[X]Other specif sex chromosome abnormalit, female phenotype

PyuA700	[X]Other male with 46,XX karyotype
PyuA800	[X]Other specif sex chromosome abnormalit, male phenotype
PyuA900	[X]Other specified chromosome abnormalities
PyuAA00	[X]Sex chromosome abnormality, male phenotype, unspecified
PyuAB00	[X]Pallister-Killian syndrome
PyuAC00	[X]Townes-Brocks syndrome
Pz...00	Congenital anomaly NOS
Q400.00	Congenital rubella
Q400.11	Extended rubella syndrome
Q48y500	Megalencephaly
ZV13600	[V]Personal history of congenital malformations

### 10.11 DETAILED DESCRIPTION OF MATERNAL NRT USE AND CORRESPONDING ANOMALIES IN EACH MOTHER-CHILD PAIR

	<b>NRT FORM</b>	<b>TIME</b>	<b>TOT PRSC. WEEKS</b>	<b>CONGENITAL ANOMALY</b>
1	inhalation cartridge 10mg	month 2	1 day	congenital dislocation of hip
2	sublingual tablet 2mg	month 2	2 days	congenital dilated renal pelvis enlarged kidney
3	nicotine patch 21mg	month 1	4 weeks	Unilateral congenital dislocation of hip
	nicotine patch 21mg	month 2	2 weeks	
4	nicotine patch 5mg	month 3	2 weeks	thyroglossal duct cyst
5	nicotine patch 5mg	month 1	2 weeks	patent ductus arteriosus
6	nicotine patch 21mg	month 1	2 weeks	polycystic kidneys, infantile type
	nicotine patch 21mg	at sp	2 weeks	
	nicotine patch 7mg	month 2	4 weeks	
	nicotine patch 14mg	month 1	4 weeks	
7	nicotine patch 15mg	month 2	8 weeks	ankyloglossia
8	nicotine patch 15mg	month 1	1 week	ventricular septal defect
	nicotine patch 21mg	month 2	1 week	
	nicotine patch 15mg	month 1	1 week	
	nicotine patch 21mg	month 1	1 week	
	nicotine patch 21mg	month 2	1 week	
	nicotine patch 7mg	month 2	2 weeks	
	nicotine patch 10mg	month 2	1 week	
	nicotine patch 15mg	month 2	1 week	
	nicotine patch 7mg	month 2	2 weeks	
9	nicotine chewing gum 2mg	month 3	1 week	patent ductus arteriosus
10	inhalation cartridge 10mg	month 3	1 week	atrial septal defect NOS
11	nicotine patch 21mg	14 days before	6 weeks	talipes, unspecified
	nicotine patch 14mg	month 3	2 weeks	congenital absence of toe
12	nicotine patch 14mg	first week preg		ventricular septal defect
	nicotine patch 7mg	month 1		
	nicotine patch 14mg	21 days before		

	<b>NRT FORM</b>	<b>TIME</b>	<b>TOT PRSC. WEEKS</b>	<b>CONGENITAL ANOMALY</b>
13	nicotine patch 21mg nicotine patch 21mg nicotine chewing gum 2mg nicotine patch 21mg nicotine patch 21mg	month 1 month 1 month 2 month 2 month 1	2 weeks 2 weeks 1 week 2 weeks 1 week	hypospadias
14	nicotine ptch 14mg	month 2	2 weeks	undescended testicle hirschprung's disease
15	inhalation cartridge 10mg	month 1	1 day	congenital dilated renal pelvis
16	nicotine patch 15mg	month 3	2 weeks	other lung anomaly NOS
17	nicotine patch 10mg	month 1	2 weeks	congenital bowing of long leg bone, unspecified hypospadias
18	nicotine lozenges 2mg	month 3	2 days	patent ductus arteriosis
19	nicotine patch 21mg nicotine patch 14mg inhalation cartridge 10mg	month 3 month 3 month 2	2 weeks 2 weeks 4 days	dandy-Walker syndrome coloboma of retina cleft palate and lip other musculoskeletal deformity coloboma of iris
20	nicotine patch 15mg	month 3	2 weeks	hirschprung's disease
21	nicotine patch 10mg	month 1	2 weeks	other lung anomalies
22	nicotine patch 15mg nicotine patch 15mg nicotine patch 15mg	first week preg month 1 month 1	1 week 1 week 4 weeks	balanced translocations
23	nicotine patch 21mg nicotine patch 14mg	25 days before month 1	3 weeks 2 weeks	congenital dislocation and subluxation of the hip
24	nicotine patch 15mg	month 3	1 week	fragile X chromosome
25	nicotine patch 15mg	month 2	4 weeks	congenital cystic adenomatoid malformation of the lung bow legs NOS
26	nicotine patch 21mg	month 3	1 week	multicystic kidney
27	nicotine patch 15mg	at sp	2 weeks	hypospadias, glandular
28	nicotine patch 10mg	month 3	2 weeks	supernumerary finger NEC

	<b>NRT FORM</b>	<b>TIME</b>	<b>TOT PRSC. WEEKS</b>	<b>CONGENITAL ANOMALY</b>
	nicotine patch 10mg	month 3	2 weeks	
29	nicotine lozenges 2mg	month 3	4 days	stenosis of pulmonary atrety pulmonary artery anomalies
30	nicotine patch 10mg	month 3	2 weeks	Poland's syndrome
31	nicotine patch 7mg	month 2	1 week	ventricular septal defect hypospadias
32	nicotine patch 21mg	month 3	4 weeks	patent ductus arteriosis
33	inhalation cartridge 10mg	month 3	1 day	craniosynostosis undescended testis, bilateral plagiocephaly
34	nicotine patch 21mg	month 2	2 weeks	pulmonary infundibular stenosis
	nicotine patch 21mg	month 3	2 weeks	
35	nicotine chewing gum 2mg	month 1	2 days	undescended testes
	nicotine chewing gum 2mg	month 3	2 days	congenital dislocation and subluxation of the hip
36	nicotine lozenges 2mg	month 3	2 days	congenital hypertrophic pyloric stenosis ventricular septal defect
37	nicotine patch 14mg	month 2	2 weeks	congenital posterior urethral valves
38	nicotine nasal spray 10mg/ml	at sp	1 day	choanal atresia
	nicotine patch 21mg	month 1	4 weeks	hypoplasia of upper limb aplasia of muscle congenial club hand
39	nicotine sublingual tab 2mg	month 1	1 week	congenital dislocation and subluxation of the hip primary ciliary dyskinesia
	nicotine patch 10mg		2 weeks	
40	nicotine patch 21mg	month 2	2 weeks	Lissencephaly
	nicotine patch 21mg	month 3	2 weeks	
	nicotine patch 14mg	month 3	2 weeks	
41	nicotine patch 21mg	28 days before	2 weeks	undescended testes, unilateral congenital posterior urethral valves

	<b>NRT FORM</b>	<b>TIME</b>	<b>TOT PRSC. WEEKS</b>	<b>CONGENITAL ANOMALY</b>
42	nicotine lozenges 2mg nicotine chewing gum 2mg	month 3 month 3	5 days 6 days	congenital bronchomalacia laryngeomalacia
43	nicotine patch 21mg	month 1	3 weeks	congenital cleft nose cleft lip
44	nicotine patch 5mg nicotine patch 5mg	month 3 month 3	2 weeks 4 weeks	plagiocephaly craniosynostosis
45	inhalation cartridge 10mg inhalation cartridge 10mg	month 3 month 3	4 days 1 day	congenital laryngeal stridor
46	nicotine patch 15mg nicotine patch 10mg	month 3 month 3	1 week 1 week	hypospadias
47	nicotine patch 7mg nicotine patch 21mg	month 3 month 3	2 weeks 2 weeks	congenital laryngeal stridor
48	nicotine patch 7mg nicotine patch 14mg nicotine patch 21mg	month 1 month 1 month 2	2 weeks 2 weeks 2 weeks	patent ductus arteriosus patent foramen ovale
49	nicotine patch 10mg nicotine patch 5mg	month 2 month 3	2 weeks 2 weeks	hypospadias
50	nicotine patch 21mg	month 3	2 weeks	undescended testes, bilateral congenital talipes varus Down's syndrome
51	nicotine patch 15mg	month 2	2 weeks	ankyloglossia
52	nicotine patch 15mg	month 2	2 weeks	microcephalus
53	inhalation cartridge 10mg inhalation cartridge 10mg nicotine patch 15mg	month 1 month 2 month 2	4 days 1 day 2 weeks	hypospadias
54	nicotine patch 14mg	month 1	4 weeks	patent ductus arteriosus



	<b>NRT FORM</b>	<b>TIME</b>	<b>TOT PRSC. WEEKS</b>	<b>CONGENITAL ANOMALY</b>
55	nicotine chewing gum 2mg	month 2	3 days	ventricular septal defect
56	nicotine patch 21mg	month 3	1 week	multicystic kidney
57	nicotine patch 21mg	month 2	2 weeks	ventricular septal defect patent ductus arteriosis
58	nicotine patch 10mg	month 1	2 weeks	other lung anomalies

\* Prescription days not recorded in more than 95% of the prescriptions, therefore the duration of prescription was recalculated by approximating the average daily dose according to the British National Formulary and then dividing the total dose prescribed by the average daily dose.