Background and Objectives: Point prevalence studies have reported higher carriage rates of *C. difficile* in IBD patients compared with the general population, but longitudinal prospective data are lacking. The objectives of this observational study were to investigate and molecularly characterize isolates of *C. difficile*, collected prospectively on a monthly basis over a one-year period among IBD outpatients and healthy controls (HC).

Methods: At enrolment, recruited participants had established diagnoses of UC (n=16) and Crohn’s disease (n=6) and reported no recent hospitalization or exposure to antibiotics. PCR ribotype and toxin status (cytotoxigenic culture) were determined for all +ive stool cultures. All participants underwent a monthly telephone interview to identify potential risk factors for *C. difficile* acquisition (changes in medications, exposure to antibiotics, clinic attendances, hospitalization) and to assess for disease activity (Harvey-Bradshaw Index and Simple Clinical Activity Colitis Index).
Results: Two patients underwent physician-initiated laboratory testing of *C. difficile* during the sample collection phase, although no participants developed or were treated for *C. difficile* infection. *C. difficile* was cultured from 29/223 samples (13%) representing 16/22 patients and 1 of 5 HC with concurrent antibiotic exposure in 6/29 visits (20%). Of the toxin +ive isolates (n=25; 078, 005, 302 and 015), 72% (n=21) were PCR ribotype 078. Toxigenic negative ribotypes included 023, 026 and 656. Of those toxin +ive isolates, 9 samples (36%) were associated with relapsing IBD of which 7/9 were ribotype 078. Multiple stool specimens also tested +ive for different ribotypes in 3 patients with UC, all of whom were taking regular immunosuppressants. WGS studies of the 078 isolates revealed marked genetic similarity, with only 3 of the 21 isolates varying by 1 or more nucleotides when compared to the 078 reference genome, suggesting there may have been a common source for cross-transmission.

Conclusions: The high prevalence of PCR ribotype 078 in this IBD outpatient cohort is consistent with the recent emergence of this strain in the community. These results reinforce the importance of testing all in-and outpatients with an apparent flare or relapsing IBD for carriage of toxigenic *C. difficile* to inform optimal management strategies. Future research is needed to understand the predominance of 078 isolates in IBD, particularly in the context of clinical relapse.