

# Relapse Versus Reinfection: Recurrent *Clostridium difficile* Infection Following Treatment With Fidaxomicin or Vancomycin

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Our study sought to compare the strain types of *Clostridium difficile* causing initial and recurrent episodes of *C. difficile* infection (CDI) in adult patients with a first episode of CDI or 1 prior episode of CDI within the previous 90 days. Strains originated from patients who had been entered into two phase 3 randomized clinical trials of fidaxomicin versus vancomycin. Isolates of *C. difficile* from the initial and recurrent episodes within 28 ( $\pm$ 2) days of cure of CDI were compared using restriction endonuclease analysis (REA) typing. Paired isolates were available from 90 of 194 (46%) patients with recurrent CDI. Patients with isolates available were significantly younger ( $P = .008$ ) and more likely to be from Canadian sites ( $P = .0001$ ), compared with patients without isolates. In 75 of 90 subjects (83.3%), the identical REA type strain was identified at recurrence and the initial episode (putative relapse). Early recurrences (0–14 days after treatment completion) were relapses in 86.7% and a new strain (reinfection) in 13.3%. Later recurrences (15–31 days after treatment) were relapses in 76.7% and reinfections in 23.3%. Mean time ( $\pm$  standard deviation) to recurrence was 12.2 ( $\pm$ 6.4) days for relapses and 14.7 ( $\pm$ 6.8) days for reinfections ( $P = .177$ ). The most common BI/NAP1/027 group and the previous US epidemic REA group J/NAP2/001 had a significantly higher combined rate of recurrence with the same strain (relapse), compared with the other REA groups (39 of 42 [93%] vs 36 of 48 [75%], respectively;  $P = .023$ ). We found a higher than historic rate of recurrent CDI caused by the same isolate as the original episode, a finding that may be related to the relatively short observation period in this study and the high frequency of isolation of epidemic strains, such as groups BI and J, for which relapse rates may be higher than for other REA groups. Caution in generalizing these observations is required, because the patients studied were younger and more likely to be from Canadian sites than were patients with recurrence who did not provide isolates.

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Recurrence of symptoms after effective treatment of *Clostridium difficile* infection (CDI) is a very common and vexing clinical problem [1]. Historically, recurrent CDI occurs in 20%–25% of patients after the initial episode but may be higher since the appearance of the epidemic strain, BI/NAP1/027 [2]. Relapse with the

same strain and reinfection with a new strain have both been documented with recurrent CDI. Infection with a new strain has been reported to occur in 33%–56% of cases, but most of these studies are small or include convenience-based samples [3–7]. How often relapse and reinfection occur, the timing of the recurrence with relapse or reinfection, the relative frequency of epidemic strains, and the possibility of initial treatment influencing either outcome have not been well studied. Differentiating the nature of recurrence requires that infecting organisms be cultured and typed for both the initial and recurrent episodes of CDI. Therefore, we used data from a large, prospective, randomized, clinical treatment trial of fidaxomicin

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significantly younger and significantly more likely to be from Canadian study sites, compared with the patients with CDI recurrence who did not provide paired specimens.

## Notes

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