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Re: Burden of *Clostridium difficile* Infection in the United States

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The Authors Reply:

Banaei and colleagues express concern that *Clostridium difficile* infection (CDI) may be over diagnosed using PCR given that in their study only a third of patients had clinically significant diarrhea defined as 3 or more unformed stools in a 24-hour period, and half of these patients had recent exposure to laxatives. (1) Because positive predictive value is influenced by the prevalence of true disease, care must be taken to assure the appropriate population is tested; this is especially true with nucleic acid amplification tests (NAATs) where a *C. difficile* prevalence closer to 20% has been associated with a more accurate CDI diagnosis. (2) We included in the supplementary material of our report an evaluation of the impact of different NAAT usage rates on the U.S. burden of CDI. (3)

Meanwhile, Bouwknecht and colleagues are concerned that CDI may be under diagnosed in outpatient settings because *C. difficile* is frequently detected in diarrheal stool samples submitted by general practitioners for other diagnostic tests. (4) Although it is possible there is a hidden burden of CDI in the United States due to a lack of clinical suspicion, non-infectious conditions and brief, self-limited infections often cause diarrhea, and testing of non-clinically significant diarrheal specimens may lead to detection of *C. difficile* colonization rather than infection (5).

As outlined by the letters of Banaei and Bouwknecht, there are several limitations to the diagnosis of CDI that can impact disease burden estimates and consequently limitations to any surveillance definition or approach that is employed.

References

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Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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