Clostridium difficile is mainly known as a hospital-acquired, nosocomial infection. The hospital environment is considered an ideal place for C. difficile to persist, infect susceptible elderly patients and spread among vulnerable patients. However, there are several reports of C. difficile infection acquired in the community. This is not surprising, since C. difficile has been cultured from the stool of 3% of healthy adults and up to 80% of healthy newborns and infants. In addition, the emergence of new strains of C. difficile that cause large outbreaks in hospitals and nursing homes will promote the carriage and circulation of such strains in the general population. This will first and foremost affect admitted patients, not all of whom will have symptoms of C. difficile-associated diarrhea during their hospital stay. Eventually, such carriage, even if transient, will increase the incidence and spread of C. difficile infection outside well-known risk groups that currently share the characteristic of prior hospital admission.

Host factors and the normal colonic flora are assumed to be of specific importance in containing C. difficile colonization. Risk factors associated with C. difficile infection are increased age, recent hospital admission, previous use of antibiotics and conditions that may affect the colonic flora. In this issue of CMAJ, Dial and colleagues report from their matched, nested case-control study that about half of the patients admitted to hospital because of community-acquired C. difficile infection had no recent antibiotic exposure. Clearly, this observation is of interest. However, the authors restricted the study population to patients 65 years of age and older who had severe C. difficile infection and at least 1 prior hospital stay during the 8-year study period. The question remains whether community-acquired C. difficile infection occurs among younger individuals without any predisposing condition or hospital stay.

When studying C. difficile infection with an apparent onset in the community, it is important to have a consensus on an appropriate definition. This is especially relevant when one wants to determine whether community-acquired C. difficile infection is associated with use of a health care facility. The European Centre for Disease Prevention and Control and the US Centers for Disease Control and Prevention have proposed similar definitions for community-acquired C. difficile infection: the onset of symptoms occurred while the patient was outside a health care facility and the patient had not been discharged from a health care facility within 12 weeks before symptom onset (community onset, community acquired); or the onset of symptoms occurred within 48 hours after admission to a health care facility and the patient had no prior stay in a health care facility within the 12 weeks before symptom onset (health-care-facility onset, community acquired).1-3

Using these definitions, Kutty and colleagues found that 34% of 604 patients in North Carolina with community-onset C. difficile infection truly had community-acquired infection. Most of the cases acquired in health care facilities that had a community onset occurred within 4 weeks after discharge. Community-acquired C. difficile infection has also been reported in otherwise healthy children, pregnant women and adults without known risk factors. Klein and colleagues found an unexpectedly high rate of C. difficile infection of 6.7% among children with diarrhea who presented to a pediatric emergency department. Rouphael and coauthors described 10 previously healthy women who had severe C. difficile infection during pregnancy. Only 3 of the women had a history of hospital admission and had used antibiotics within the 3 months before symptom onset. The US Centers for Disease Control and Prevention reported an increase in severe community-acquired C. difficile infection in populations previously considered to be at low risk. Of 33 patients in whom C. difficile infection developed, 8 (24%) reported no direct exposure to antimicrobial agents within the 3 months before symptom onset, but 3 of them reported having had close con-
tact with an individual who had diarrhea. Finally, a surveillance study of community-acquired *C. difficile* infection in Connecticut revealed an incidence of 6.9 per 100 000 inhabitants.\(^1\) Of 241 patients, 36% had no history of antibiotic use within 3 months before symptom onset, and 25% had no underlying medical condition or recent hospital admission and, moreover, were younger than 45.

Community-acquired *C. difficile* infection is almost certainly underdiagnosed. However, there is an increasing interest worldwide in recognition of this new disease entity. In a well-designed prospective study in Germany, Weil and colleagues\(^9\) found that immunoassay results were positive for *C. difficile* toxins A and B in 66 (9.4%) of the stool samples submitted by general practitioners of 703 patients with diarrhea. Of these 66 patients, 35 (53%) truly had community-acquired infection. Recent use of antibiotics was reported by 52% of the 66 patients, most frequently cephalosporins (33%) and fluoroquinolones (33%). In a prospective surveillance study in the United Kingdom, Wilcox and colleagues\(^10\) found that 2.1% of 2000 randomly selected fecal samples were positive for *C. difficile* cytotoxin. Although exposure to antibiotics in the 4 weeks before symptom onset and hospital admission in the 6 months before onset were significantly associated with *C. difficile* infection, about one-third of cases had neither risk factor. In a third, recently completed study, in the Netherlands, Bauer and colleagues\(^11\) identified *C. difficile* infection in 37 (1.5%) of 2423 patients with diarrhea attending general practitioners. Of the patients with *C. difficile* infection, 65% had not been admitted to a health care institution in the year before symptom onset, 42% had not used antibiotics during the 6 months before symptom onset, and 23% had neither risk factor.

The results of these studies indicate that it is worthwhile to test for community-acquired *C. difficile* infection in patients with diarrhea who have no known risk factors. Practitioners cannot rely on classic risk factors such as recent antibiotic use, prior hospital stays, comorbidity and age of 65 years or more.\(^12\) There is an urgent need to identify and better characterize potential risk factors for community-acquired *C. difficile* infection to explain the large proportion of cases not linked to recent antibiotic therapy or hospital stays. Moreover, the role of animal reservoirs should be explored in this respect, since *C. difficile* strains from humans and animals often belong to similar polymerase chain reaction (PCR) ribotypes and have identical virulence factors.\(^13,14\)

This article has been peer reviewed.

**Competing interests:** The authors have received an unrestricted grant from Genzyme to study community-acquired *Clostridium difficile* infection.

**Contributors:** Both authors contributed to the content of this article and approved the version submitted for publication.

### REFERENCES

1. Kuijper EJ, Coignard B, Toll P. Emergence of *Clostridium difficile*-associated disease in North America and Europe. *Clin Microbiol Infect* 2006;12(Suppl 6):2-18.
2. Dial S, Kezouh A, Dascal A, et al. Patterns of antibiotic use and risk of hospital admission because of *Clostridium difficile* infection. *CMAJ* 2008;179:767-72.
3. McDonald LC, Coignard B, Dubberke E, et al. Recommendations for surveillance of *Clostridium difficile*-associated disease. *Infect Control Hosp Epidemiol* 2007;28:140-5.
4. Kutty PK, Benoit SR, Woods CW, et al. Assessment of *Clostridium difficile*-associated disease surveillance definitions. *Infect Control Hosp Epidemiol* 2008;29:197-202.
5. Klein EJ, Boster DR, Stapp JR, et al. Diarrhoea etiology in a children’s hospital emergency department: a prospective cohort study. *Clin Infect Dis* 2006;43:807-13.
6. Rouphael NG, O’Donnell JA, Bhatnagar J, et al. *Clostridium difficile*-associated diarrhoea: an emerging threat to pregnant women. *Am J Obstet Gynecol* 2008;198:e1-6.
7. Centers for Disease Control and Prevention. Severe *Clostridium difficile*-associated disease in populations previously at low risk — four states. *MMWR Morb Mortal Wkly Rep* 2005;54:1201-5.
8. US Centers for Disease Control and Prevention. Surveillance for community-associated *Clostridium difficile* — Connecticut, 2006. *MMWR Morb Mortal Wkly Rep* 2008;57:340-3.
9. Weil HP, Fischer-Briidge U, Harmanus C, et al. High incidence of *Clostridium difficile*-associated diarrhoea in a hyperendemic region in Germany [abstract O329]. In: 17th ECCMID/25th ICC abstracts — abstracts of the 17th European Congress of Clinical Microbiology and Infectious Diseases, and 25th International Congress of Chemotherapy. *Int J Antimicrob Agents* 2007;29(Suppl 2):S69.
10. Wilcox MH, Mooney L, Bendall R, et al. A case-control study of community-associated *Clostridium difficile* infection. *J Antimicrob Chemother* 2008;62:388-96.
11. Bauer MP, Veenendaal D, Verhoef L, et al. Community-onset *Clostridium difficile*-associated diarrhoea: Is it truly community-acquired? [abstract P1488]. 18th European Congress of Clinical Microbiology and Infectious Diseases; 2008 Apr 19-22; Barcelona, Spain.
12. Bauer MP, Goochhaus A, Koster T, et al. Community-onset *Clostridium difficile*-associated diarrhoea not associated with antibiotic usage—two case reports with review of the changing epidemiology of *Clostridium difficile*-associated diarrhoea. *Neth J Med* 2008;66:207-11.
13. Rugnik M. Is *Clostridium difficile*-associated infection a potentially zoonotic and foodborne disease? *Clin Microbiol Infect* 2007;13:457-9.
14. Goochhaus A, De bast SB, van Leengoed LA, et al. *Clostridium difficile* PCR ribotype 078: An emerging strain in humans and in pigs? *J Clin Microbiol* 2008;46:1157.

---

**Correspondence to:** Dr. Ed J. Kuijper, Department of Medical Microbiology, Rm. E4-64, Leiden University Medical Center, PO Box 9600, 2300 RC, Leiden, The Netherlands; fax 31 71 5248148; e.j.kuijper@lumc.nl