Clinical Microbiology and Infection xxx (2018) 1–10

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative review

New insights into transmission of *Clostridium difficile* infection—narrative review

A. Durovic [1], A.F. Widmer [2], S. Tschudin-Sutter [2], *

[1] *Medical University Department, Division of Oncology and Hematology, Kantonsspital Aarau, Aarau, Switzerland*
[2] *Department of Infectious Diseases & Hospital Epidemiology, University Hospital Basel, University Basel, Basel, Switzerland*

ARTICLE INFO

Article history:
Received 1 October 2017
Received in revised form
22 January 2018
Accepted 27 January 2018
Available online xxx

Editor: L. Leibovici

Keywords:
Clostridium difficile
Transmission
Sources
Hospital-acquired
Community-acquired
Acquisition

ABSTRACT

Background: Traditionally, *Clostridium difficile* has been considered a typical healthcare-associated pathogen—that is, one transmitted within healthcare facilities and thus prevented by implementation of standard infection control measures. Recently this concept has been challenged by studies suggesting a relevant role for community acquisition of *C. difficile.*
Aims: To discusses the current literature, compiled during the last decade, reporting on sources of acquisition of *C. difficile* and subsequent transmission.
Sources: The databases PubMed, Medline, Embase and the Cochrane Database were searched for articles published from 1 January 2007 to 30 June 2017 reporting on possible transmission pathways of *C. difficile* and/or suggesting a source of acquisition of *C. difficile.* All study types reporting on adult populations were considered; case reports and series were excluded. The PRISMA guidelines for the reporting of systematic reviews were followed.
Content: Among 24 original articles included, 63% report on transmission of *C. difficile* in healthcare settings and 37% investigate sources and transmission of *C. difficile* in the community. Contact with symptomatic carriers (53.3%), the hospital environment (40.0%) and asymptomatic carriers (20%) were the most commonly reported transmission pathways within healthcare settings. The leading sources for acquisition of *C. difficile* in the community include direct contact with symptomatic and asymptomatic carriers in the community, including infants (30%) and residents of long-term non—acute care facilities (30%), followed by contact with contaminated environments in outpatient care settings (20%) and exposure to livestock or livestock farms (20%).
Implications: In healthcare settings, future control efforts may need to focus on extending cleaning and disinfection procedures beyond the immediate surroundings of symptomatic carriers. Potential targets to prevent acquisition of *C. difficile* in the community include household settings, long-term care facilities and outpatient settings, while the role of livestock in entertaining transmission requires further investigation. **A. Durovic, Clin Microbiol Infect 2018;■:1**

Introduction

Traditionally, *Clostridium difficile* has been considered a typical healthcare-associated pathogen—that is, transmitted within healthcare facilities and thus prevented by implementation of standard infection control measures.

This concept has recently been challenged. Screening at admission studies have revealed colonization with *C. difficile* at hospital admission is an important a risk factor for development of subsequent infection, suggesting that relevant acquisition of *C. difficile* may be occurring outside rather than inside healthcare settings [1,2]. This concept is further supported by studies associating whole genome sequencing (WGS) data with epidemiologic relationships, revealing a relevant proportion of genetically distinct cases reflecting diverse sporadic sources of *C. difficile* [3] rather than few sources located within single institutions. Along these lines, a growing body of evidence points to the efficacy of antibiotic

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* Corresponding author. S. Tschudin-Sutter, Division of Infectious Diseases & Hospital Epidemiology, University Hospital Basel, Petersgraben 4, CH-4031 Basel, Switzerland.
E-mail address: sarah.tschudin@usb.ch (S. Tschudin-Sutter).

https://doi.org/10.1016/j.cmi.2018.01.027

Please cite this article in press as: Durovic A, et al., New insights into transmission of *Clostridium difficile* infection—narrative review, Clinical Microbiology and Infection (2018), https://doi.org/10.1016/j.cmi.2018.01.027

stewardship interventions to prevent development of *C. difficile* infection (CDI) [4,5].

Here we discuss the current literature, compiled during the last decade, regarding sources of acquisition of *C. difficile* and subsequent transmission.

Methods

We searched the databases PubMed, Medline, Embase and the Cochrane Database for articles published from 1 January 2007 to 30 June 2017 using the following search terms: '*Clostridium difficile*' or '*C. difficile*' in combination with any of the following: 'transmission,' 'acquisition,' or 'source,' as well as the following MeSH terms: '*Clostridium difficile*' or '*Clostridium* infections' in combination with 'disease reservoirs' or 'disease transmission, infectious.' Reference lists of selected reports were searched to identify additional publications.

The search was restricted to full-length articles published in English. Original research studies reporting on possible transmission pathways of *C. difficile* and/or suggesting a source of acquisition of *C. difficile* were included. Studies merely reporting on a decline of *C. difficile* transmission, acquisition or rates after the introduction of specific interventions were excluded, although such an intervention may point to a possible source or transmission pathway. All study types were considered; case reports and case series were excluded. We only included articles reporting on adult populations.

All identified studies were screened for eligibility by two independent reviewers. Using standardized data collection forms, we extracted key data on study design, population investigated, reported transmission pathways and sources, and typing methodology used to confirm transmission.

The PRISMA guidelines for the reporting of systematic reviews were followed [6]; however, the concept of using the proposed PICO format (participants, interventions, comparisons, outcomes, and study design) to state the specific research questions to be addressed could not be applied, as the aim of this review was to identify specific sources and transmission chains of *C. difficile*, which is not related to interventional studies.

Results

Included studies

Over the last decade, 24 studies specifically reporting on sources of CDI and specific transmission pathways within and beyond healthcare facilities (Fig. 1) were published and are included in this review. Sources and transmission pathways occurring within healthcare institutions, community settings or both are described in 13, eight, and two studies, respectively (Tables 1 and 2).

Transmission

Successful transmission of *C. difficile* is considered to be the result of the interplay between host susceptibility, strain transmissibility and exposure to the pathogen, mainly *C. difficile* spores.

Host factors

Well-established risk factors increasing host susceptibility include the prior use of antimicrobials and proton pump inhibitors as well as age. Exposure to antimicrobials, most importantly fluoroquinolones, clindamycin and broad-spectrum penicillins and cephalosporins, disrupts the composition of the normal gut flora,

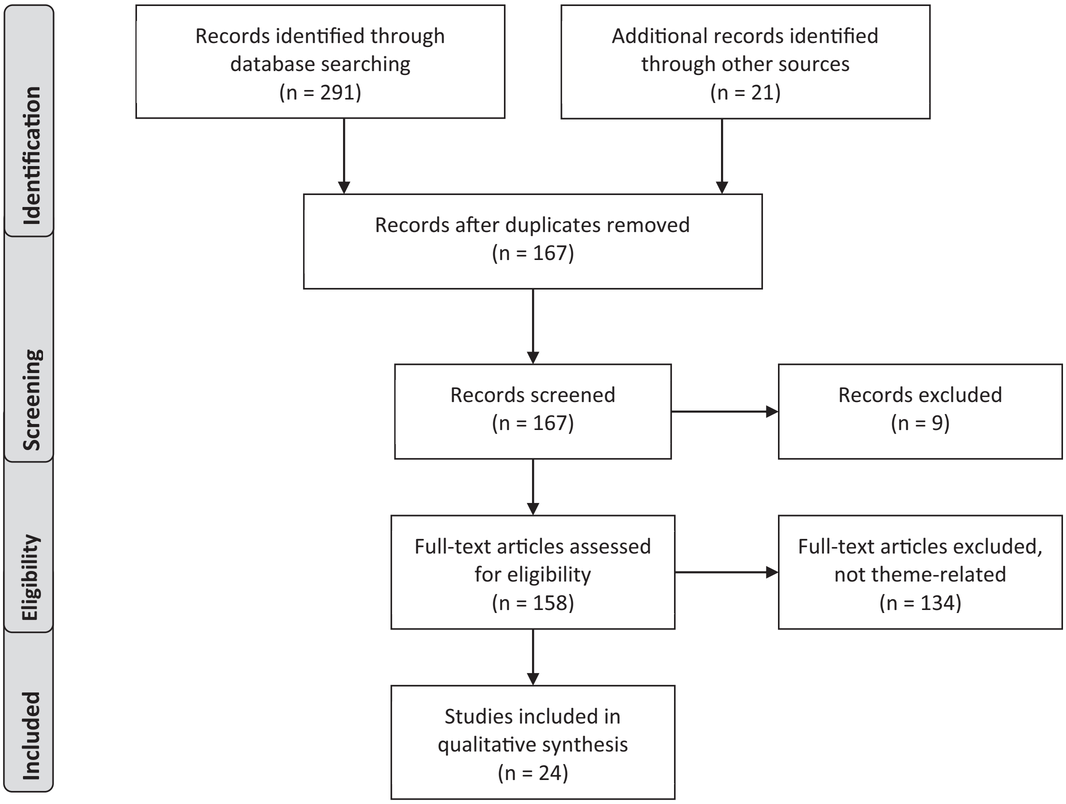

Fig. 1. Flowchart of included studies according to PRISMA recommendations [7].

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