



Guidelines

Guidance document for prevention of *Clostridium difficile* infection in acute healthcare settings

S. Tschudin-Sutter^{1,*}, E.J. Kuijper², A. Durovic¹, M.J.G.T. Vehreschild³, F. Barbut⁴, C. Eckert⁴, F. Fitzpatrick⁵, M. Hell⁶, T. Norèn⁷, J. O'Driscoll⁸, J. Coia⁹, P. Gastmeier¹⁰, L. von Müller¹¹, M.H. Wilcox¹², A.F. Widmer¹ on behalf of the Committee†

¹ Division of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, University Basel, Basel, Switzerland

² Department of Medical Microbiology, Centre for Infectious Diseases, Leiden University Medical Center, Leiden, The Netherlands

³ Department I of Internal Medicine, University Hospital of Cologne, Cologne, Germany and German Centre for Infection Research (DZIF), Partner Site Bonn-Cologne, Germany

⁴ National Reference Laboratory for *Clostridium difficile*, Paris, France

⁵ Departments of Clinical Microbiology, Royal College of Surgeons in Ireland and Beaumont Hospital, Ireland

⁶ Department of Medical Microbiology and Infection Control, Academic Teaching Laboratories-Medilab OG, Paracelsus Medizinische Privatuniversität (PMU), Salzburg, Austria

⁷ Department of Laboratory Medicine, Clinical Microbiology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

⁸ Department of Medical Microbiology, Stoke Mandeville Hospital, Aylesbury, UK

⁹ Scottish Microbiology Reference Laboratories, Glasgow, UK

¹⁰ Institute of Hygiene and Environmental Medicine, Charité, Universitätsmedizin Berlin, Berlin, Germany

¹¹ Institute for Medical Microbiology and Hygiene, University of Saarland Medical Center, State Laboratory of Saarland, Consiliary Laboratory for *Clostridium difficile*, Homburg/Saar, Germany

¹² Department of Microbiology, Leeds Teaching Hospitals & University of Leeds, Leeds, UK

ARTICLE INFO

Article history:

Received 29 June 2017

Received in revised form

23 January 2018

Accepted 3 February 2018

Available online 2 March 2018

Editor: L. Leibovici

ABSTRACT

Scope: *Clostridium difficile* infection (CDI) is the most important infective cause of healthcare-associated diarrhoea in high income countries and one of the most important healthcare-associated pathogens in both Europe and the United States. It is associated with high morbidity and mortality resulting in both societal and financial burden. A significant proportion of this burden is potentially preventable by a combination of targeted infection prevention and control measures and antimicrobial stewardship. The aim of this guidance document is to provide an update on recommendations for prevention of CDI in acute care settings to provide guidance to those responsible for institutional infection prevention and control programmes.

Methods: An expert group was set up by the European society of clinical microbiology and infectious diseases (ESCMID) Study Group for *C. difficile* (ESGCD), which performed a systematic review of the literature on prevention of CDI in adults hospitalized in acute care settings and derived respective recommendations according to the GRADE approach. Recommendations are stratified for both outbreak and endemic settings.

Questions addressed by the guideline and recommendations: This guidance document provides thirty-six statements on strategies to prevent CDI in acute care settings, including 18 strong recommendations. No recommendation was provided for three questions. **S. Tschudin-Sutter, Clin Microbiol Infect 2018;24:1051**

© 2018 European Society of Clinical Microbiology and Infectious Diseases. Published by Elsevier Ltd. All rights reserved.

* Corresponding author. S. Tschudin-Sutter

E-mail address: Sarah.Tschudin@usb.ch (S. Tschudin-Sutter).

† On behalf of the Committee: F. Allerberger, Austrian Agency for Health and Food Safety (AGES), Vienna, Austria; O.A. Cornely, Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), University of Cologne, Cologne, Germany; Department I of Internal Medicine, University Hospital of Cologne, Cologne, Germany; German Centre for Infection Research (DZIF), partner site Bonn-Cologne, Germany; M. Delmée, Université Catholique de Louvain, Microbiology Unit, Brussels, Belgium; B. Olesen, Department of Clinical Microbiology, Herlev Hospital, Herlev, Denmark; Johan van Broeck, Université Catholique de Louvain, Microbiology Unit, Brussels, Belgium.

Introduction and rationale

Given the ongoing significance of *Clostridium difficile* infection (CDI) in Europe [1], the European society of clinical microbiology and infectious diseases (ESCMID) study group for *C. difficile* (ESGCD) initiated this guideline project with the purpose of updating the previous guideline, which covers the literature published up to December 2006 [2].

This updated guideline provides a current review of the literature on interventions to control CDI in adult populations in acute healthcare settings and derives specific infection control recommendations. It aims to provide guidance to those responsible for institutional infection control programmes, serving as a reference for best medical practice.

Methods

Summarized below are the key recommendations for prevention of CDI in adult populations in acute healthcare settings stratified for both the outbreak and endemic setting. The expert panel followed a process including performance of a systematic literature review and grading and classifying the quality of evidence using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach. A detailed description of the methods, background, and evidence summaries that support each of the recommendations can be found online in the full text of the guideline.

Results

I. Diagnostic approach for prevention of transmission

ESCMID has issued a recent guideline for the diagnosis of CDI [3]. Two-stage algorithms, based on the use of a first (screening) test that has high sensitivity for *C. difficile* (i.e. a nucleic acid amplification test (NAAT) for detection of toxin gene or an enzyme immunoassay (EIA) for detection of glutamate dehydrogenase (GDH)) followed by a highly specific test that detects free faecal *C. difficile* toxin(s), have been recommended for the laboratory diagnosis of CDI [3].

Recommendation for outbreak and endemic settings

1. A two-stage test (GDH or NAAT for toxin genes followed by a highly sensitive toxin test or GDH in combination with a toxin test) is recommended to diagnose CDI. In the case of a negative result of the toxin test, NAAT (if not already part of the first diagnostic step) or toxigenic culture can be performed based on clinical evaluation or local infection prevention requirements. (Strong recommendation, moderate-quality evidence as defined by the European Society of Clinical Microbiology and Infectious Diseases: update of the diagnostic guidance document for *Clostridium difficile* infection [3]).

II. Surveillance

Does surveillance of CDI in combination with appropriate feedback of infection rates lead to reduced CDI rates?

Recommendation for the outbreak setting

2. Perform surveillance of CDI in combination with timely feedback of infection rates on both the hospital and ward level (strong recommendation, very low quality of evidence).

Recommendation for the endemic setting

3. Perform surveillance of CDI in combination with timely feedback of infection rates (strong recommendation, very low quality of evidence).

III. Screening of asymptomatic patients and healthcare workers for *C. difficile* carriage

*Does screening for *C. difficile* identify colonized/carrier patients at increased or decreased risk of developing *C. difficile* infection?*

Recommendation for outbreak and endemic settings

4. We do not recommend screening for *C. difficile* to identify colonized/carrier patients as a way of altering the risk of developing CDI in either colonized subjects or other patients and thus reducing CDI rates (conditional recommendation, low level of evidence in the endemic setting).

*Are healthcare workers with contact to *C. difficile*-positive patients at risk for asymptomatic colonization or infection with *C. difficile* and should screening of healthcare workers for carriage of *C. difficile* to reduce CDI rates be recommended?*

Recommendation for outbreak and endemic settings

5. We do not recommend HCW screening for *C. difficile* gut colonization as a routine control measure for CDI (strong recommendation, very low level of evidence in the endemic setting).

IV. Hand hygiene

*Which are the most effective techniques/products for removal of *C. difficile* or its spores from hands?*

Recommendation

6. No specific recommendations regarding the most effective technique/product for removal of *C. difficile* spores can be made.

Is ethanol-based hand rub associated with increased CDI rates compared with hand washing?

Recommendation for the outbreak setting

7. Switch from alcohol-based hand rub (AHR) to hand washing because of the lack of *in vitro* activity of AHR against spores (conditional recommendation, very low quality of evidence).

Recommendation for the endemic setting

8. Do not switch from AHR to hand washing with soap and water to reduce the incidence of CDI (conditional recommendation, very low quality of evidence).

Is hand hygiene compliance associated with CDI transmission?

Recommendation for outbreak and endemic settings

9. Initiate interventions to increase hand hygiene compliance (conditional recommendation, very low quality of evidence).

V. Personal protective equipment (PPE)

How effective is the additional use of personal protective equipment (PPE) in reducing C. difficile infection/transmission, compared with standard precautions only?

Recommendation for the outbreak setting

10. Use PPE (gloves and gowns/disposable aprons) to decrease transmission of *C. difficile* or incidence of CDI (strong recommendation, very low quality of evidence).

Recommendation for the endemic setting

11. Use PPE (gloves and gowns/disposable aprons) to decrease transmission of *C. difficile* or incidence of CDI (conditional recommendation, very low quality of evidence).

VI. Contact precautions

Are contact precautions for CDI patients effective in reducing the CDI rate/transmission of C. difficile in hospital settings?

Recommendation for the outbreak setting

12. Use contact precautions to decrease the transmission of *C. difficile* and reduce the incidence of CDI (strong recommendation, very low quality of evidence).

Recommendation for the endemic setting

13. Use contact precautions to decrease the transmission of *C. difficile* and reduce the incidence of CDI (strong recommendation*, very low quality of evidence).

*The authors acknowledge that institutions may choose to forgo contact precaution measures, providing strict surveillance of CDI rates and implementation of other prevention strategies for CDI (see respective details outlined in the full text of the guideline).

VII. Environmental cleaning and disinfection

Does environmental disinfection of rooms of patients with CDI decrease the transmission of C. difficile compared with routine cleaning?

Recommendation for the outbreak setting

14. Introduce daily environmental sporicidal disinfection and terminal disinfection of rooms of patients with CDI to decrease the transmission of CDI (strong recommendation, very low quality of evidence).

Recommendation for the endemic setting

15. Introduce daily and terminal environmental sporicidal disinfection of rooms of patients with CDI to decrease the transmission of CDI (conditional recommendation, very low quality of evidence).

Are no-touch disinfection systems as effective as hypochlorite to reduce the environmental contamination in rooms of patients with CDI?

Recommendation

16. The panel concludes that no-touch disinfection systems are as effective as hypochlorite in reducing environmental contamination with *C. difficile* (very low quality of evidence).

Are no-touch disinfection systems effective in reducing transmission/incidence of C. difficile?

Recommendation for outbreak and endemic settings

17. The panel concludes that both in the outbreak and the endemic setting, no-touch disinfection systems may be effective in reducing transmission/incidence of CDI (very low quality of evidence).

VIII. Infrastructure

Are infrastructural changes effective in reducing transmission of C. difficile in hospitals?

Recommendation for outbreak and endemic settings

18. The panel agreed that no specific strength of recommendation can be assigned as the term 'infrastructure' includes too many different interventions.

IX. Antibiotic stewardship

Is restriction of antibiotic agents/classes effective in reducing CDI rate in hospitals?

Recommendation for the outbreak setting

19. Restriction of antibiotic agents/classes is effective in reducing CDI rates (strong recommendation, low quality of evidence).

Recommendation for the endemic setting

20. Restriction of antibiotic agents/classes is effective in reducing CDI rates (strong recommendation, moderate quality of evidence).

Is reducing length of antibiotic therapy effective in reducing CDI rates in hospitals?

Recommendation for outbreak and endemic settings

21. Reducing the duration of antibiotic therapy is effective in reducing CDI rates (strong recommendation, very low quality of evidence).

X. Early treatment (focus on prevention of transmission)

Can early treatment of suspected/diagnosed patients with CDI reduce the transmission of C. difficile?

Recommendation for outbreak and endemic settings

22. Initiate early treatment in patients diagnosed with CDI (conditional recommendation, very low quality of evidence).

XI. Education

Is specific education required to enhance knowledge regarding prevention of CDI?

Recommendation for the outbreak setting

23. Educate healthcare workers on prevention of CDI to enhance their knowledge and skills on prevention strategies (strong recommendation, because of the lack of studies elucidating the impact of education of healthcare workers in outbreak settings formal grading of the evidence was not performed).

Recommendation for the endemic setting

24. Educate healthcare workers on prevention of CDI to enhance their knowledge and skills on prevention strategies (strong recommendation, very low quality of evidence).

How does implementation of intensified teaching, e-learning, direct observation, testing influence C. difficile transmission/prevalence in hospitals?

Recommendation for outbreak and endemic settings

25. Implement intensified teaching in conjunction with other intervention measures to reduce CDI rates (conditional recommendation, very low quality of evidence).

Does specific education enhance thoroughness of cleaning in the context of CDI prevention?

Education of environmental service personnel proved to be of particular importance for prevention of CDI as reducing environmental *C. difficile* contamination was associated with lower *C. difficile* prevalence in hospitals. Environmental service personnel require repeated training and regular quality control measurements (e.g. by labelling of surface areas before cleaning with a fluorescence marker) to ensure sustained high-quality cleaning.

Should CDI patients and visitors be educated on prevention measures for CDI?

Recommendation for outbreak and endemic settings

26. Educate CDI patients and visitors on prevention measures for CDI (strong recommendation, because of the paucity of studies elucidating the impact of education of patients and/or visitors formal grading of the evidence was not performed).

Transparency declaration

STS is a member of the AstellasFidaxomicin Advisory Board and a member of the MSD *C. difficile* Advisory Board. She has received unrestricted research grants from Astellas and has a grant from the Swiss National Science Foundation NRP72 (407240_167060). EK reports consulting fees from Astellas, Merck, and Sanofi-Pasteur, as well as grants from Valneva, Vedanta, and Quiagen. AD has nothing to disclose. MJGTV reports grants from Seres Therapeutics, grants

and personal fees from Organobalance, grants and personal fees from MSD/Merck, grants and personal fees from Astellas Pharma, grants from Da Volterra, outside the submitted work. FB reports grants, personal fees, and non-financial support from Astellas, personal fees from Pfizer, grants and personal fees from Sanofi Pasteur, grants and non-financial support from Anios, grants, personal fees and non-financial support from MSD, grants from Biomérieux, grants from QuidelBuhlman, grants from Diasorin, grants from Cubist, grants from Biosynex, grants from GenePoc, outside the submitted work. FP has nothing to disclose. CE reports personal fees and non-financial support from Astellas, non-financial support from bioMérieux, non-financial support from QuidelBuhlmann, non-financial support from Diasorin, non-financial support from Biosynex, non-financial support from Hain, grants from Theradiag, outside the submitted work; non-financial support from Alere, grants and non-financial support from Astellas, grants from BioMérieux, grants and non-financial support from Mobidiag, grants and non-financial support from Anios, grants from GenePoc, outside the submitted work. MH has nothing to disclose. TN has nothing to disclose. JOD has nothing to disclose. JC reports personal fees from MSD, outside the submitted work. PG has nothing to disclose. LVM has nothing to disclose. MHW has received consulting fees from Abbott Laboratories, Actelion, Antabio, Astellas, AstraZeneca, Bayer, Biomérieux, Cerexa, Cubist, Durata, The European Tissue Symposium, The Medicines Company, MedImmune, Merck, Motif Biosciences, Nabriva, Optimer, Paratek, Pfizer, Qiagen, Roche, Sanofi-Pasteur, Seres, Summit, and Synthetic Biologics; lecture fees from Abbott, Alere, Astellas, Astra-Zeneca, Merck, Pfizer & Roche; and grant support from Abbott, Actelion, Astellas, Biomérieux, Cubist, Da Volterra, MicroPharm, Morphochem AG, Sanofi-Pasteur, Seres, Summit and The European Tissue Symposium, Merck. AFW reports grants from National Science Foundation during the conduct of the study; he is a member of the AstellasFidaxomicin Advisory Board, and the MSD *C. difficile* Advisory Board. We thank Dr Thomas V. Riley, Dr Erik R. Dubberke, and Dr Anna-PelagiaMagiorakos (European Centre for Disease Prevention and Control) for critically revising the manuscript. We thank all members of the European Study group for *C. difficile* (ESGCD) for their professional support.

Acknowledgements

This work was funded in part by the ESCMID study group for *C. difficile* (ESGCD).

Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.cmi.2018.02.020>.

References

- [1] Davies KA, Longshaw CM, Davis GL, Bouza E, Barbut F, Barna Z, et al. Under-diagnosis of *Clostridium difficile* across Europe: the European, multicentre, prospective, biannual, point-prevalence study of *Clostridium difficile* infection in hospitalised patients with diarrhoea (EUCLID). *Lancet Infect Dis* 2014;14:1208–19.
- [2] Vonberg RP, Kuijper EJ, Wilcox MH, Barbut F, Tull P, Gastmeier P, et al. Infection control measures to limit the spread of *Clostridium difficile*. *Clin Microbiol Infect* 2008;14:2–20.
- [3] Crobach MJ, Planche T, Eckert C, Barbut F, Terveer EM, Dekkers OM, et al. European society of clinical Microbiology and infectious Diseases: update of the diagnostic guidance document for *Clostridium difficile* infection. *Clin Microbiol Infect* 2016;22:S63–81.