

Clostridium difficile infection in Europe

A CDI Europe report: Executive summary

1. INTRODUCTION: CDI — WHAT IS THE PROBLEM?

Clostridium difficile infection (CDI), an infection of the large intestine, is the leading cause of healthcare-associated diarrhoea in Europe. CDI is usually a consequence of antibiotic use and most cases occur in the elderly. In severe cases, CDI can cause serious bowel conditions that can be life-threatening.

Healthcare-associated infections (HAIs) are a major healthcare priority and a major focus of current European and national strategies to improve patient safety. In addition to its impact on individual patients, CDI accounts for a substantial drain on healthcare resources and costs. As a prominent HAI, CDI must be considered within efforts to prevent and control HAIs. However, in many countries, CDI remains under-recognised by health policymakers and managers, healthcare professionals and by the public.

This report presents an overview of the clinical and economic burden of CDI, highlights the current deficiencies in CDI management in Europe, and proposes strategies to address these within the framework of relevant on-going European Union health policy initiatives.

Introducing CDI EUROPE

CDI Europe is an expert-led initiative focused at the healthcare policy level with the aim to translate research on CDI into meaningful policy responses to help: raise awareness of CDI; improve and standardise disease surveillance and reporting; promote a better standard of care for CDI management across Europe; and ultimately to improve patient outcomes. CDI Europe is supported by Astellas Pharma Europe Ltd.

How common is CDI? CDI is thought to occur in approximately 1 in 436 hospital admissions across Europe, and is now more common than HAIs caused by methicillin-resistant *Staphylococcus aureus* (MRSA). The incidence has been reported to be rising in some countries and there have been outbreaks of particularly severe CDI due to specific strains of *C. difficile* (e.g. ribotype 027). An increasing fraction of CDI cases appear to be community-associated. CDI is also an important problem in nursing homes, although few data are available.

Who is at risk of CDI? Recent antibiotic use, advanced age, underlying illness and recent hospitalisation are key risk factors. However, many patients do not fall into conventional risk groups and the possibility of CDI should be considered in any patient with unexplained diarrhoea.

What are the clinical outcomes of CDI? One in ten cases of CDI cause, or contribute to, intensive care unit admission or death, or lead to surgery to remove part of the bowel. CDI typically extends hospitalisation by around 6–21 days. Up to 25% of treated patients have a recurrence within a month after successful therapy. CDI may increase the risk of in-hospital death by three-fold, and is thought to cause or contribute to 40% of deaths that occur within 3 months of diagnosis. Elderly patients are particularly vulnerable to poor outcomes.

What does CDI cost? On average, hospital-acquired CDI adds costs of approximately €2,500–€14,000 to the cost per hospitalisation case. The total cost of healthcare-associated CDI in Europe is estimated at around €3,000 million/year. This burden is anticipated to increase with the projected growth of the elderly population.

2. DIAGNOSIS

How is CDI diagnosed? CDI is diagnosed based on clinical symptoms (e.g. diarrhoea) together with laboratory evidence of toxin-producing *C. difficile* in the stool. A two-step testing protocol is recommended, but important deficiencies in diagnosis exist across Europe.

Clinical diagnosis – a lack of awareness: In many countries there is an inadequate level of awareness of CDI and its risk factors among doctors and other healthcare workers. The lack of clinical suspicion can result in under-diagnosis or mis-diagnosis of CDI, with important implications: 1) Treatment is delayed or omitted, risking severe disease and complications. 2) Infection control measures are delayed, risking outbreaks. 3) The incidence of the disease is underestimated. 4) Unnecessary and costly diagnostic tests may be used.

Laboratory diagnosis – poor standardisation: Variety exists across Europe, with only a third of countries having a nationally recommended diagnostic test algorithm for CDI. Services for *C. difficile* testing in nursing homes and the community are particularly limited. The costs of improving *C. difficile* testing are expected to be offset by the avoidance of complications, hospitalisation and outbreaks. Organisational and education barriers also hamper the improvement of CDI diagnosis.

CDI Europe Recommendations

Awareness and clinical suspicion

- *Managers of healthcare systems and institutions must be encouraged to assign a higher organisational priority to CDI in order to drive education programmes.*
- *Awareness of the signs and symptoms of CDI, and the patients at high risk, needs to be improved among healthcare staff so that rates of testing and diagnosis are increased.*
- *Education should encourage a low threshold of clinical suspicion for diagnostic testing. Many patients with CDI do not fall into conventional high-risk categories and a focus only on elderly patients receiving antibiotics will miss many cases, especially in the community.*

- Educational programmes should target nurses, nursing assistants/auxiliary healthcare staff, as well as doctors.
- There is a need for research to develop and validate a system for predicting the risk of severe outcomes in patients with CDI.

Laboratory diagnosis

- Healthcare systems must offer appropriate *C. difficile* testing services.
- *C. difficile* testing should be performed on stools from all patients presenting with healthcare-associated diarrhoea.
- In the community, *C. difficile* tests should be considered in all patients who present to their general practitioner with diarrhoea and who have had recent antibiotic exposure, or are aged over 65 years, or have negative tests for other types of bowel infection. Further efforts are required to educate laboratories and to promote standardised testing according to guidelines.
- Tests of antibiotic resistance in *C. difficile* are not necessary for clinical purposes, but may be performed as part of disease surveillance programmes.
- Improved co-operation between hospitals, nursing homes and community healthcare providers is necessary in laboratory testing and in the interpretation and use of the results.
- The impact of improved *C. difficile* testing on overall healthcare costs needs to be assessed. Managers should take into account the potential savings, as well as benefits for patients, resulting from improved CDI management and the avoidance of costly outbreaks.
- The approval of new laboratory tests for *C. difficile* should be supported by robust evidence of their accuracy, clinical validity and cost-effectiveness compared with existing tests.

3. TREATMENT

How is CDI treated? Moderate or severe CDI is treated using antibiotics active against *C. difficile* in the intestines.

Current situation. Europe-wide treatment guidelines are widely accepted but the extent of compliance is unclear. Recurrence is the principal challenge of therapy.

CDI Europe recommendations

- Awareness of, and compliance with, CDI treatment guidelines needs to be improved among healthcare professionals, in conjunction with education on diagnosis.
- Further research is required to answer outstanding questions about optimal CDI treatment, in particular to establish the relative benefit of treatment options on mortality in CDI patients and to support improved guidance in special clinical cases where data are presently limited.
- Existing guidelines should be updated when necessary in order to take account of new published data. Future guidelines should better define 'severe' CDI in order to guide therapy.
- As new treatment options become available there is an increasing need for ways of identifying in clinical practice which patients will benefit from the available therapies.

4. INFECTION CONTROL AND PREVENTION

What is infection control? Infection control and prevention in CDI involves antibiotic stewardship, prompt and reliable diagnosis, isolation or cohort nursing, hand hygiene, disinfection of the healthcare environment, and additional measures during outbreaks.

Current situation. Compliance with these measures in hospitals and nursing homes is limited and variable both within and between countries owing to insufficient governmental and organisational prioritisation, a lack of education and awareness among healthcare staff, difficulty and inconvenience of disinfection regimens, and resource and cost limitations.

CDI Europe recommendations

- Improvements in CDI diagnosis and treatment are vital to infection control and prevention, as well as to optimise the standard of care for individual patients.
- Policymakers need to support and communicate the need for CDI-specific interventions and guidance to be integrated within policies and initiatives on patient safety and HAI prevention and control.
- Infection control should be a priority in all relevant aspects of healthcare management, including facility design and planning.

- *Improving compliance with infection control measures for all HAIs, among all healthcare staff, is crucial. Routine infection control should be encouraged through high-profile education and communications directed to all staff throughout institutions. Compliance should be audited regularly.*
- *CDI-specific performance indicators should be assessed and used to help drive up patient safety and quality of care. Infection control data should ideally be publicly available. Sharing best practice internationally may help improve standards.*
- *Specific protocols for cleaning and disinfection against *C. difficile* should be developed and implemented.*
- *Infection control procedures in nursing homes need to be assessed and improved where necessary.*
- *New, user-friendly disinfectants active against *C. difficile* are required. To help the development and evaluation of new agents, policymakers at European and national levels should support the introduction of standardised tests and laboratory services.*
- *Further research is required to address outstanding questions regarding the sources of *C. difficile* contamination, modes of transmission, and the optimal, cost-effective means of infection prevention and control.*

5. SURVEILLANCE

What is disease surveillance? Disease surveillance is used to monitor the epidemiology of HAIs and to evaluate and guide policies on their prevention and control.

Current situation. The European Council recommended in 2009 that Member States should establish or strengthen HAI surveillance systems at national, regional and institutional levels. There are marked variations between countries in national-level CDI surveillance. Some countries have established national surveillance systems with standardised methods and mandatory reporting of data. These features exist in varying degrees in other countries. CDI surveillance data are particularly lacking in nursing homes and the community.

CDI Europe recommendations

- *CDI must be considered a ‘targeted infection type’ for which healthcare institution surveillance should be supported at the European and national levels.*
- *All Member States should institute national-level surveillance systems for hospital-acquired CDI. These should utilise standardised case definitions and laboratory tests according to current recommendations. Ribotyping services should be available, as strain typing is important for outbreak investigations. However, surveillance should not focus on certain so-called ‘hypervirulent’ types. Data reporting should ideally be mandatory and public. Countries setting up such systems may benefit from the experience of others that have successfully implemented and evaluated such systems.*
- *Surveillance systems should be developed for community and nursing home CDI. The application of clear, standardised definitions of CDI in each setting will be important in order to provide comparable data across studies.*
- *The European Commission should provide on-going support for the European CDI Surveillance Network project (ECDIS-Net), in order to facilitate European-level surveillance and national and international capacity building and education for CDI testing services.*

6. PATIENT EMPOWERMENT

What does patient empowerment mean in CDI? Patients and the public have important roles to play in reducing the incidence and impact of CDI.

Current situation. The public in Europe recognises that there are risks associated with healthcare, and HAIs are the most widely anticipated adverse events. HAIs are repeatedly the subject of media headlines and CDI is among the leading HAI in such coverage. The level of public knowledge about CDI is unclear and CDI patient advocacy is limited.

CDI Europe recommendations

- *Measures to help improve education and awareness of CDI among the general public need to be included within public health education programmes.*
- *Educational collaboration between CDI experts and patient organisations representing groups at risk of CDI should be supported at European and national levels to improve CDI awareness and encourage better communications with healthcare professionals.*
- *Patients and visitors should be encouraged to comply with infection prevention precautions within hospitals and nursing homes, especially concerning patient isolation and hand hygiene.*

7. CONCLUSIONS: IMPROVING PATIENT SAFETY AND CARE QUALITY

HAI and patient safety

Patient safety is a dominant healthcare concern internationally. The European Commission estimates that 8–12% of patients admitted to hospital suffer adverse effects while receiving healthcare. As HAIs are a leading form of healthcare-associated adverse events, their prevention and control is a principal aim of patient safety initiatives.

Many countries have implemented national strategies for HAI prevention and control, as recommended by the European Council. However, CDI is under-recognised within European policy on HAIs and at the national level in most Member States. The authors urge policymakers and other stakeholders to ensure that CDI-specific measures are included within the strategic patient safety and HAI intervention programmes at European, national and institutional levels.

Integrating CDI into HAI strategies

Organisational awareness and leadership: Sustained strategic prioritisation of HAI prevention and control, including CDI, is needed at EU, national and institutional board levels.

Implementation and audit of measures to improve CDI management and control: Evidence-based guidelines for the diagnosis, treatment and control of CDI should be implemented at the national and institutional level. CDI should be routinely considered a marker of care quality and hence one or more CDI measures should be included among performance indicators.

Education and training of healthcare staff and the public: Responsible authorities must ensure that healthcare staff in hospitals and nursing homes understand the risk factors and clinical signs and symptoms of CDI and the locally applied protocols for diagnostic testing, treatment, and infection prevention and control. Specific training of laboratory staff (and auditing) is necessary to implement the recommended diagnostic test protocol. Education of patients and the general public may also contribute to improving CDI management and control.

Disease surveillance: Disease surveillance is essential to improving CDI management and control across Europe. The activities of the ECDIS-Net to develop and co-ordinate laboratory capacity across the continent require sustained support from the European Commission. Nationally, CDI should be included as a target infection type when surveillance programmes are established or strengthened according to the European Council Recommendations.

Resourcing: The European Council recommends that Member States allocate the necessary resources for implementing the components of a national strategy on patient safety as part of the core funding for healthcare delivery. The European Commission has estimated that the implementation of national HAI prevention and control strategies should be highly cost effective owing to reductions in HAI incidence and associated costs. With regard to CDI, resourcing includes the costs of training healthcare professionals and the public, CDI laboratory testing according to current recommendations, infection control staff, facilities and measures.

Research: Further research is needed to address outstanding questions relating to: how CDI develops; epidemiology; mechanisms of *C. difficile* transmission; and the effectiveness and/or cost-effectiveness of diagnostic, therapeutic and infection control measures.

Conclusions

The European Commission is leading the development and implementation of European- and national-level strategic actions to improve patient safety through better HAI control and prevention. However, the importance of addressing CDI specifically is not recognised in these activities and this reflects a widespread under appreciation of the burden of CDI and the opportunities for addressing this.

CDI is a component of care quality and patient safety and the authors urge health policy makers and healthcare system managers to:

- Recognise the need to address the deficiencies that exist in many European countries with regard to CDI diagnosis, treatment, control and surveillance (see recommendations).
- Ensure that CDI is taken into account during the development and implementation of international and national programmes for improving HAI control and prevention, with inclusion of CDI-specific measures as necessary.
- Recognise that investing in better detection and management of CDI represents an investment in the quality of patient care, and that the costs are expected to be offset by savings in overall healthcare costs in addition to the reduced burden of illness among patients.

This report can be downloaded from www.epgonline.org/anti-infectives-knowledge-network/index.cfm and <http://www.dificlr.co.uk/section-choice>. Printed copies can be obtained from Astellas Pharma Ltd, 2000 Hillwood Drive, Chertsey, Surrey, KT16 0RS, United Kingdom.

Astellas Pharma Europe Ltd, in collaboration with the authors, provided financial and editorial support for the development of this report.