EPIDEMIOLOGY OF *CLOSTRIDIOIDES DIFFICILE* INFECTIONS IN BELGIAN HOSPITALS

—

National report
Data up to and including 2022

MILENA CALLIES • LOUISE VAES • KARL MERTENS

WHO WE ARE

Sciensano can count on more than 950 staff members who are committed to health every day.
As our name suggests, science and health are central to our mission. Sciensano's strength and uniqueness lie within the holistic and multidisciplinary approach to health. More particularly we focus on the close and indissoluble interconnection between human and animal health and their environment (the "One health" concept). By combining different research perspectives within this framework, Sciensano contributes in a unique way to everybody's health.
For this, Sciensano builds on the more than 100 years of scientific expertise.

Sciensano

Epidemiology and public health **-** Healthcare-associated infections and antimicrobial resistance

February 2024 • Brussels • Belgium
Internal reference number: D/2024.14.440/8

M. Callies[1]
•
L. Vaes[1]
•
M. Mertens[1]

In collaboration with
A. Anantharajah[2], B. Kabamba Mukadi[2], M. Delmée[2], A. Buchelot[2], A-T. Pâques[2], S. Comblez[2], E. Ngyuvula Mantu[2], K. Soumillion[2]

1. Sciensano, Epidemiology and public health, Healthcare-associated infections and antimicrobial resistance, Brussels
2. National Reference Center *Clostridioides difficile,* Brussels

Contactperson: Milena Callies • T+32 4 73 13 31 58 • Milena.Callies@sciensano.be

With the financial support of

service public fédéral SANTE PUBLIQUE, SECURITE DE LA CHAINE ALIMENTAIRE ET ENVIRONNEMENT
federale overheidsdienst VOLKSGEZONDHEID, VEILIGHEID VAN DE VOEDSELKETEN EN LEEFMILIEU
BRUSSELS HOOFDSTEDELIJK GEWEST
Vlaanderen is zorg
Wallonie familles santé handicap
AVIQ

Please cite as: M. Callies, L. Vaes, K. Mertens. Epidemiology of *Clostridioides difficile* infections in Belgian hospitals: National report, data up to and including 2022 (Catry B., Ed). Brussels, Belgium : Sciensano ; 2024.
Depot Number: D/2024.14.440/8

Acknowledgments

The authors wish to thank all the participating hospitals for their continuous efforts to provide data, the members of the Working Group '*Clostridioides difficile* infections' for their help in improving the *Clostridioides difficile* infections surveillance, the Healthdata team for the maintenance of the data collection and reporting tool, Els Duysburgh and Laure Mortgat for the development of this report and the coordination of the surveillance in prior years, and Hilde Jansens and An Caluwaerts for their feedback.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

BR	Brazier (European ribotype classification)
CDI	*Clostridioides (Clostridium) difficile* infection
C. difficile	*Clostridioides (Clostridium) difficile*
CI	Confidence interval
COVID-19	Coronavirus Disease 2019
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
FPS	Federal Public Service (SPF/FOD)
GDH	Glutamate dehydrogenase
HA-CDI	Hospital associated *Clostridioides (Clostridium) difficile* infection
HAI	Healthcare-associated infections
HD	Healthdata
ICD-9 (10)-CM	International classification of diseases, 9th (10th) version, clinical modification
IPC	Infection prevention and control
INAMI/RIZIV	Institut national d'assurance maladie-invalidité/Rijksinstituut voor ziekte- en invaliditeitsverzekering
LTCF	Long term care facility
MIC	Minimal inhibitory concentration
N or n	Number
NAAT	Nucleic acid amplification test
NIHDI	National Institute for Health and Disability Insurance
NRC	National Reference Centre (Laboratory)
PCR	Polymerase chain reaction
RD	Royal Decree
RHM/MZG	Résumé hospitalier minimum/Minimale ziekenhuis gegevens (Minimum hospital data set)
SPMA	Standardised procedures for Mortality Analysis
UCL	Université catholique de Louvain (Belgian ribotype classification)
UCLouvain	Université catholique de Louvain

GLOSSARY

***Clostridioides difficile* infection (CDI)**
A patient who meets one or more of the following criteria:

1. Diarrhoea or toxic megacolon, and a positive laboratory test for *C. difficile* toxin A and/or B in the stools or a toxin-producing strain identified in the stools, by culture or another method;
2. Pseudomembranous colitis identified by endoscopy of the lower gastro-intestinal tract;
3. Histopathology characteristic of *C. difficile* in the colon (with or without diarrhoea) on a biopsy obtained during endoscopy, colectomy or autopsy.

Community associated *Clostridioides difficile* infection (CA-CDI)
Onset of symptoms less than two days after admission in the reporting hospital with no previous admission in any healthcare facility in the previous 12 weeks.

Hospital-associated *Clostridioides difficile* infection (HA-CDI)
Onset of symptoms 2 days or more after admission in the reporting hospital, or within four weeks of discharge from a healthcare facility. In this report, it is calculated as: date of onset - date of admission ≥ 2.

Recurrent CDI
CDI occurring after end of treatment, more than two weeks and less than eight weeks after the start of the previous episode.

Hospitalisation-days (or patient-days or hospital-days)
Number of invoiced days for every patient admitted in a hospital as defined by the Belgian minimal hospital data classification (*Résumé hospitalier minimal/minimale ziekenhuisgegevens*, RHM/MZG). Ambulatory patients, day hospitalisations, or emergency room stays without overnight stay are not included.

Number of hospitalisations
Number of standard hospitalisations with overnight stay, as defined by the Belgian minimal hospital data classification (*Résumé hospitalier minimal/minimale ziekenhuisgegevens,* RHM/MZG). Ambulatory patients, day hospitalisations, or emergency room stays without overnight stay are not included.

Mean cumulative incidence
Sum of cases reported by participating hospitals for a given period, divided by the sum of hospitalisations for that period and the concerned hospitals. Numerator is all episodes or episodes deduplicated by hospitalisations and patient (indicated by an asterisk).

Mean incidence density
Sum of cases reported by participating hospitals for a given period, divided by the sum of hospitalisation-days for that period and the concerned hospitals.

Primary hospitals
Primary hospitals are hospitals that are defined as hospitals without university characteristics by the Belgian Ministry of health in a list dated December 2022[1]. (In this report, the hospital type is provided at INAMI/RIZIV code level, and not at campus level).

Secondary hospitals
Secondary hospitals are hospitals that are defined as hospitals with university characteristics by the Belgian ministry of health in a list dated December 2022[1]. (In this report, the hospital type is provided at INAMI/RIZIV code level, and not at campus level).

Tertiary hospitals
Tertiary hospitals are hospitals that are defined as university hospitals by the Belgian ministry of health in a list dated December 2022[1]. (In this report, the hospital type is provided at INAMI/RIZIV code level, and not at campus level).

[1] List of hospitals provided by the Belgian Ministry of health (Dienst Datamanagement – Directoraat - Generaal Gezondheidszorg); List dated December 2022.

KEY FINDINGS

- The participation rate of the national *Clostridioides difficile* surveillance in Belgian hospitals decreased slightly between 2021 and 2022, from 83% (85) to 79% (81), considering all eligible hospitals providing cases for at least one semester. Compared to the previous year about 250 additional cases were reported.

- The characteristics of *Clostridioides difficile* infections (CDI) have remained relatively similar in 2022 compared to previous years; For example, 10% of episodes are recurrent and most episodes are still occurring in geriatric patients. A small increase was observed in the percentage of hospital-associated *Clostridioides difficile* infection (HA-CDI), episodes labelled as “complicated”, and patients affected by CDI that possibly or definitely died because of their infection.

- An increase of incidence was observed between 2021 and 2022. From 1.31 HA-CDI per 10,000 hospitalisation-days in 2021 to 1.62 in 2022. Change in incidence was statistically significant (p-value < 0.001).

- About 67% (54) of all participating hospitals send maximum five strains to the national reference centre (NRC) per semester. Ribotype BR014 remained the most prevalent and widespread strain in Belgian hospitals (13% of all strains in 2022, compared to 11% in 2021). Ribotype BR002 came second (10% of all strains in 2022, compared to 7% in 2021), followed by BR078 (8% of all strains in 2022, compared to 9% in 2021).

- Similarly as to what was reported in 2021, 93.9 % of the total isolates tested were resistant to clindamycin in 2022. All isolates were susceptible to other tested antibiotics currently used for CDI treatment.

- The gap in incidence difference between the surveillance data and the hospital stay data remains big, with the surveillance data reporting 1.50 total CDI per 1,000 hospitalisations and the hospital stay data 2.04 in 2021 (most recent data available).

- There has been a substantial increase in total number of diagnostic tests for *Clostridioides difficile* billed in 2022. Contrarily to previous year, the number of tests billed in hospitalised patients increased. Similarly to 2021, the tests billed in ambulatory patients continued to increase.

- The mortality rate continues to decrease according the death registry. In 2020 (most recent data available), 57 deaths were reported specifically due to a CDI.

BELANGRIJKSTE RESULTATEN

- De deelname aan de nationale surveillance van *Clostridioides difficile* in Belgische ziekenhuizen daalde licht tussen 2021 en 2022, van 83% (85) naar 79% (81), rekening houdend met alle in aanmerking komende ziekenhuizen die gedurende ten minste één semester episodes rapporteerden. In vergelijking met het voorgaande jaar werden ongeveer 250 extra gevallen gerapporteerd.

- De kenmerken van *Clostridioides difficile* infecties (CDI) zijn in 2022 relatief gelijk gebleven ten opzichte van voorgaande jaren; zo is 10% van de episodes recurrent en komen de meeste episodes nog steeds voor bij geriatrische patiënten. Er is een kleine toename waargenomen in het percentage ziekenhuisgeassocieerde *Clostridioides difficile* infecties (HA-CDI), episodes die als "gecompliceerd" worden gecategoriseerd en patiënten die door CDI zijn getroffen en mogelijk of zeker zijn overleden als gevolg van hun infectie.

- Er was een toename van de incidentie tussen 2021 en 2022. Van 1,31 HA-CDI per 10.000 hospitalisatie-dagen in 2021 naar 1,62 in 2022. en 1,31 HA-CDI. Deze verandering in incidentie was statistisch significant (p-waarde < 0,001).

- Ongeveer 67% (54) van alle deelnemende ziekenhuizen stuurt maximaal vijf stammen per semester naar het nationaal referentiecentrum (NRC). Ribotype BR014 bleef de meest voorkomende en wijdverspreide stam in Belgische ziekenhuizen (13% van alle stammen in 2022, tegenover 11% in 2021). Ribotype BR002 kwam op de tweede plaats (10% van alle stammen in 2022, vergeleken met 7% in 2021), gevolgd door BR078 (8% van alle stammen in 2022, vergeleken met 9% in 2021).

- Net als in 2021 was 93,9% van het totaal aantal geteste isolaten in 2022 resistent tegen clindamycine. Alle isolaten waren gevoelig voor andere geteste antibiotica die momenteel worden gebruikt voor de behandeling van CDI.

- Het verschil in incidentie tussen de surveillancegegevens en de gegevens over ziekenhuisopnames blijft groot, waarbij de surveillancegegevens 1.50 CDI per 1,000 ziekenhuisopnames rapporteren en de gegevens over ziekenhuisopnames 2.04 in 2021 (meest recente beschikbare gegevens).

- Het totale aantal gefactureerde diagnostische testen voor *Clostridioides difficile* is in 2022 aanzienlijk gestegen. In tegenstelling tot vorig jaar was het aantal gefactureerde testen bij ziekenhuispatiënten gestegen. Zoals in 2021 blijft het aantal gefactureerde testen bij ambulante patiënten stijgen.

- Het sterftecijfer blijft dalen volgens het overlijdensregister. In 2020 (meest recente beschikbare gegevens) werden 57 sterfgevallen gemeld die specifiek te wijten waren aan een CDI.

PRINCIPAUX RÉSULTATS

- Le taux de participation à la surveillance de *Clostridioides difficile* dans les hôpitaux belges a légèrement diminué entre 2021 et 2022, passant de 83 % (85) à 79 % (81), si l'on considère que tous les hôpitaux éligibles ont fourni des cas pendant au moins un semestre. Par rapport à l'année précédente, environ 250 cas supplémentaires ont été déclarés.

- Les caractéristiques des infections à *Clostridioides difficile* (ICD) sont restées relativement similaires en 2022 par rapport aux années précédentes. Par exemple, 10 % des épisodes sont récurrents et la plupart des épisodes surviennent toujours chez des patients gériatriques. Une légère augmentation a été observée dans le pourcentage d'infections à *Clostridioides difficile* associées à l'hôpital (HA-ICD), les épisodes catégoriser comme "compliqués", et les patients atteints d'ICD qui sont probablement ou certainement décédés à cause de leur infection.

- Une augmentation de l'incidence a été observée entre 2021 et 2022. De 1,31 HA-ICD pour 10 000 journées d'hospitalisation dans 2021 jusqu'à 1,62 dans 2022. La différence de l'incidence était statistiquement significative (valeur $p < 0,001$).

- Environ 67% (54) de tous les hôpitaux participants ont envoyé au maximum cinq souches au centre national de référence (CNR) par semestre. Le ribotype BR014 est resté la souche la plus prévalente et la plus répandue dans les hôpitaux belges (13 % de toutes les souches en 2022, contre 11 % en 2021). Le ribotype BR002 est arrivé en deuxième position (10 % de toutes les souches en 2022, contre 7 % en 2021), suivi par le BR078 (8 % de toutes les souches en 2022, contre 9 % en 2021).

- Comme en 2021, 93,9 % des isolats testés étaient résistants à la clindamycine en 2022. Tous les isolats étaient sensibles aux autres antibiotiques testés qui sont actuellement utilisés pour le traitement de l'ICD.

- L'écart d'incidence entre les données de surveillance et les données sur les séjours hospitaliers reste grand, les données de surveillance faisant état de 1,50 IDC totales pour 1 000 hospitalisations et les données sur les séjours hospitaliers de 2,04 en 2021 (données disponibles les plus récentes).

- Le nombre total de tests diagnostiques de *Clostrioides difficile* facturés en 2022 a considérablement augmenté. Contrairement à l'année précédente, le nombre de tests facturés chez les patients hospitalisés a augmenté. Comme en 2021 le nombre de tests facturés chez les patients ambulatoires a augmenté.

- Le taux de mortalité continue de diminuer selon le registre des décès. En 2020 (données les plus récentes disponibles), 57 décès ont été signalés comme étant spécifiquement dus à une ICD.

INTRODUCTION

1. Background

*Clostridioides (*previously *Clostridium) difficile* is an anaerobic, Gram-positive, spore-forming bacterium often found in the intestinal tract of healthy individuals and different animals. It can become harmful once the normal balance of the gut microbiota (flora) is disturbed, a phenomenon known as “dysbiosis”. The intestinal microbiota can be impacted by various environmental or individual factors, such as genetics, immune defence system, diet, stress, and medication, in particular antibiotic agents (1). Pathogenic *C. difficile* strains produce toxins (toxin A and/or B, and/or binary toxin) responsible for symptoms ranging from mild diarrhoea to a severe life-threatening infection, depending on host susceptibility and the virulence of the infecting strain. Antibiotic exposure, being the main trigger for dysbiosis, is therefore the major risk factor for the development of *C. difficile* infection (CDI), together with advanced age, presence of co-morbidities and increased length of hospitalisation (2). *C. difficile* can survive for long periods in the environment and its potential for spreading and generating outbreaks in healthcare facilities is particularly high. Treatment usually involves a long course of antibiotics and can be challenging, due to for example the antimicrobial resistance of *C. difficile* (3). Furthermore it has been documented that the infection is recurrent in around 20% of the cases who initially respond to treatment, and this risk further increases with the number of previous recurrences (4). CDI is the most important cause of infectious diarrhoea acquired in healthcare institutions and is responsible for around 4.9% of healthcare-associated infections (HAI) in European hospitals (5). CDI therefore results in a high clinical, social and economic burden due to increased duration of hospitalisation, re-admission, and management of complications. Therapeutic success for recurrent cases can be obtained by faecal microbiota transplantation (6).

Surveillance of CDI in Belgian hospitals was implemented in 2007. The objectives of the surveillance are to:

- Monitor CDI incidence, burden and trends at hospital and national level;
- Identify and monitor the microbiological characteristics of strains isolated in Belgian hospitals through collaboration with the National Reference Laboratory (NRC).

Data used in this report comes from four sources, being: (1) the national surveillance of CDI in hospitals, including data from the NRC (2010 – 2022); (2) hospital stays (Résumé hospitalier minimum/Minimale ziekenhuis gegevens: RHM/MZG 2010 – 2021); (3) billing of diagnostic tests (Institut national d'assurance maladie-invalidité/Rijksinstituut voor ziekte- en invaliditeitsverzekering: INAMI/RIZIV (2010 – 2022) and (4) the death registry (2008 – 2020). Main results are presented in the body of the report while more detailed data can be consulted in the annex. As of this year the data processing is different compared to previous years. Hence, some small changes are made to the results, retrospectively.

The objective of this report is to describe the epidemiology of CDI in Belgium, with a focus on year 2022 of the national surveillance data in combination with the most recent related information from other sources. It aims to present an estimate of CDI incidence in Belgium hospitals and its trends during the last years, to assess the burden and adverse outcomes of CDI, to describe its microbiological characteristics, and to give recommendations if relevant.

METHODS

1. National surveillance of CDI in hospitals

HOSPITAL DATA

Participation in the CDI surveillance was mandatory until 2014 for all Belgian hospitals. Since 2015, these hospitals have to participate in at least one out of the four following surveillance program: CDI surveillance, surgical site infections, vancomycin-resistant enterococci, and ventilation-associated pneumonia and bloodstream infections in intensive care units. The hospital wide surveillances of bloodstream infections, methicillin-resistant *Staphylococcus aureus*, and multi-resistant Gram-negative bacteria remain by default mandatory for all hospitals[2]. Only data from these hospitals are included in this report.

Participation to the CDI surveillance involves the registration of all cases identified in hospitalised patients in the facility for a minimum of one semester per year (January to June, or July to December) as well as the shipment of five consecutive strains per surveillance period to the NRC for further typing. Hospital data and NRC data are related via an unique code that is generated automatically for each individual hospital record and sent to the NRC with the corresponding strain.

Denominators, being the monthly number of hospitalisations and number of hospitalisation-days must also be provided by each participating hospital. One-day hospitalisations are excluded. The methodology used for data collection is given in detail in the surveillance protocol, available at our website in Dutch (https://www.sciensano.be/nl/biblio/surveillance-van-clostridium-difficile-infecties-belgische-ziekenhuizen) and French (https://www.sciensano.be/fr/biblio/surveillance-des-infections-a-clostridium-difficile-dans-les-hopitaux-belges). This protocol is closely aligned with the European surveillance protocol of CDI (enhanced option) (7). The differences between the Belgian and European surveillance are described in the protocol of the CDI surveillance. Definitions used are described in the protocol, and summarised in the glossary of this report.

Since mid-2017, all data have been collected via Healthdata (HD) (https://healthdata.sciensano.be/en/home, https://www.healthdata.be/dcd/#/collection/NSIH-CDIF/version/12). This platform enables data collection, storage, and analysis, while reporting is done via their data visualisation platform "Healthstat" (https://www.healthstat.be/). In the HD application hospitals are identified by their hospital and campus number defined by the INAMI/RIZIV, allowing for a better standardisation.

This report includes surveillance data up to 2022 (database data labelled as 'Approved' in HD on 12 July 2023). Data that is entered later will be added retrospectively in the report of next year.

[2] General hospitals with the exception of Sp hospitals palliative care are legally required to participate according to the Royal Decree: Koninklijk besluit van 25 april 2002 betreffende de vaststelling en de vereffening van het budget van financiële middelen van de ziekenhuizen, Art 56, Par 2, wijziging van 10 september 2020/ Arrêté royal du 25 avril 2002 relatif à la fixation et à la liquidation du budget des moyens financiers des hôpitaux, Art 56, Par 2, modification du 10 septembre 2020.

NATIONAL REFERENCE LABORATORY DATA

Each participating hospital is required to send maximum five consecutively isolated strains per surveillance period to the NRC, managed by the “Institut de Recherche Expérimentale et Clinique” of the Université catholique de Louvain (UCLouvain). Each strain must be accompanied by a minimal set of case information, including the automatically generated code, that links hospital and NRC data. In addition, an hospital may send locally isolated strains to the NRC for typing in order to support the investigation of a local increase in the number of cases or a suspected outbreak. These strains are not considered in this report.

Each received sample is confirmed and typed. The currently applied method of ribotyping is capillary-based polymerase chain reaction (PCR). In Belgium, the NRC has developed an in-house ribotype classification (UCL), which was readapted in 2019. Over six hundred different profiles have already been identified. Ongoing work to harmonise the nomenclature is performed in collaboration with different European groups. To allow for an international comparison, this report will use the European Brazier classification (BR), whose correspondence with the new and previous UCL nomenclature – when available – can be found in the Sciensano website (https://www.sciensano.be/en/projects/national-surveillance-clostridioides-difficile-infections-belgian-hospitals).

NRC data were transmitted to Sciensano via HD (when operational) or via an Excel sheet manually uploaded in the HD environment.

Antibiotics susceptibility, including antibiotics known to be significantly risk-associated to CDI (erythromycin, clindamycin, rifampicin, chloramphenicol, ciprofloxacin and moxifloxacin) or used for CDI treatment (metronidazole, vancomycin and fidaxomicin) are evaluated against 100 clinical isolates sent to the NRC (sample representing the most common ribotypes circulating in Belgium).

DATA ANALYSIS

CDI episodes are deduplicated per hospitalisation except for those who are defined as being a recurrent CDI. CDI deaths, age group and gender were deduplicated on patient level.

For the calculation of CDI incidence per hospitalisations or per hospitalisation-days, all hospitals that provided numerators and denominators for at least one semester, were included. The way incidences are computed are described in the glossary.
For the description of the characteristics of CDI, all valid cases were considered, irrespective of whether the corresponding hospital provided denominators. Results are presented at the level of hospital group (RIZIV/INAMI number), and not at campus level.

Concerning the NRC microbiological data, analysis was performed using the first five consecutive strains sent by the participating hospitals and for which a corresponding CDI case was identified in the hospital CDI surveillance database.

Data analysis was performed using SAS Enterprise guide 7.13. Graphical representations were made with Excel (Windows) and statistical analysis with R 4.2.2.

2. Hospital stays

In Belgium, each hospital stay has to be registered in a “minimum hospital data set” (RHM/MZG). Since 2016, diagnoses are registered using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM). The transition from ICD-9-CM to ICD-10-CM was done in 2015 for which no data is available. The code used to identify a “Enterocolitis due to *Clostridium difficile*” is the code A04.7, regrouping “recurrent” (A04.71) and “not specified recurrent” (A04.72) cases

We analysed the national hospital stays with code A04.7 from 2010 to 2021 (most recent available year) included in the RHM/MZG dataset. This data was provided to us by the Belgian Federal Public Service (FPS) of Public Health. For each hospital stay, the RHM/MZG dataset reports both a “primary diagnosis”, that is the condition considered to be the primary reason for the patient’s admission, and “secondary diagnosis”, that are the conditions present at admission or that developed thereafter and influenced patient care during the current hospitalisation. Information on whether these diagnosis (either primary, either secondary) were made at hospital admission or during hospitalisation was also provided when available.

Additionally, RHM/MZG provided denominators, being the total yearly number of hospitalisations and of hospitalisation-days, excluding day-care and ambulatory care provided in the emergency room. To calculate incidence per 10,000 inhabitants, we used the mid-year Belgian population, obtained on SPMA (Standardized Procedures for Mortality Analysis), a software application developed by Sciensano to facilitate the analysis of vital statistics for Belgium by year.

The RHM/MZG data are used to compare with our national surveillance data. It is important to keep in mind that there are some differences between both sources. For example, the use of other definitions for a CDI.

Analysis is done in Excel, and data for year 2015 (administrative transitional year) were extrapolated by calculating the average between results for year 2014 and 2016.

3. Billing of diagnostic tests

The INAMI/RIZIV is the Belgian public social security institution that manages and supervises the Belgian health care insurance system[3]. Reimbursement of healthcare services is obtained via nomenclature codes for each service provided.

We analysed the billing codes for "faecal toxin-producing *C. difficile* testing" for ambulatory and hospitalised patients, that are codes "549850" and 549861" respectively. Data from year 2010 to 2022 (most recent available year) was analysed using Excel. INAMI/RIZIV also provided denominators, being: the yearly number of patient admissions[4](available until year 2021) and the yearly number of persons insured in Belgium. We used these data, along with the mid-year Belgian population obtained on SPMA to compute specific incidences.

[3] Every inhabitant of Belgium is enrolled in the healthcare insurance system.
[4] Admissions relate to “classical hospitalisations”, excluding day-care, emergency room, long stay and rehabilitation.

It should be noted that billing data are only provided for health services covered by the Belgian healthcare insurance system (e.g. costs of health services linked to a work-related accident are covered by another insurance system).

4. Death registry

Mortality data was obtained via SPMA, that receives their data from the FPS Economy. FPS Economy centralises mortality information from the Belgian communities. The mortality cause is coded according to the ICD-10 classification.

We analysed deaths with code A04.7 as underlying cause of death, representing “deaths due to a *Clostridium difficile* related enterocolitis” for the years 2008 – 2020 (latest available data) using Excel. The underlying cause of death is considered to be the original disease causing the chain of events immediately leading to death.

Deaths were analysed according to the region of death, and not to the region of residence of the deceased. The age standardised mortality rate was based on direct standardisation using the Belgian mid-year 2015 population as reference population and three age groups (0-64, 65-79, > 80).

The population data for each region and for the whole country was obtained on SPMA (cfr. supra).

RESULTS

1. National surveillance of CDI in hospitals

HOSPITAL DATA

Participation

In 2022, out of the 102 hospitals eligible for participation (hospitals funded for RD on surveillance of nosocomial infections), 81 (79%) hospitals registered their cases for at least one semester. Among these hospitals, 79 also provided denominator data. In total, 62 (78%) are primary hospitals, 13 (16%) are secondary hospitals and 4 (5%) are tertiary hospitals (Annex 3, Table 8)[5]. Of all hospitals providing both numerator and denominator there were 14% in Brussels, 53% in Flanders and 33% in Wallonia (Annex 3, Table 7). This corresponds to the overall regional distribution of hospitals, which is 14%, 50% and 36% for Brussels, Flanders and Wallonia, respectively.
Participation in 2022 did slightly decrease (four less hospitals participating) compared to 2021. However since 2018 the participation rate has remained relatively stable (between 79 - 83%).

In 2022, hospitals registered 2,294 CDI cases (after data cleaning and validation), belonging to 2,094 patients. The maximum number of registered cases per hospital per semester was 62 with a median of 13.

Overall participation is detailed in Annex 1 (Table 4).

Characteristics of CDI

CDI characteristics are summarised in Annex 2 (Table 5) for the period of 2019 until 2022.

In 2022, as in previous years, the majority of the patients were females (55%). About three fourths of the patients were more than 64 years of age. In 2022, 16% of patients with a CDI died. Of these 340 deaths, 51 (15%) were reported to be related to CDI, meaning that 2% of patients affected by CDI possibly or definitely died because of their infection.

Similar to previous years, 10% of the reported CDI were labelled as “recurrent”. In 2022, we recorded slightly more episodes labelled as “complicated”, than in 2021 (from 7% to 9% of CDI). CDI affected mostly the following wards: geriatrics (27%), gastroenterology (11%) and oncology (8%). Additionally, the category ‘Other medical department’ contained 13% of the CDI.

For 58% (1340) of all the CDI episodes, symptoms occurred 2 days or more after admission in the reporting hospital; they were therefore considered “hospital-associated” (HA-CDI). This is consistent with the fact that the proportion of CDI with a presumed origin defined as “acute care facility” was 56% in 2022. Between this reported presumed origin and our calculated HA-CDI there is an overlap of 1125 episodes (Table 1).
The proportion of cases that are presumed to arise from the ‘community’ was 29% (compared to 27% last year). The number of cases with a reported (presumed) origin being a ‘long-term

[5] Out of the 102 eligible hospitals 78 (76%) are primary, 17 (17%) are secondary and 7 (7%) are tertiary hospitals.

care facility' (LTCF) did not change substantially across the years, and accounted for about 5% of the cases in 2022.

Table 1 • Absolute number episodes that are categorised as HA-CDI (calculated from surveillance data) and presumed origin being 'acute care facility' (reported in surveillance data) and the row percentages. Belgium, 2022.

		Calculated		
		N HA-CDI	N Other CDI	N Total CDI
Reported	N Presumed origin 'acute care facility' (%)	1,125 (87.9)	155 (12.1)	1,280 (100)
	N All other presumed origin (%)	215 (21.2)	799 (78.8)	1,014 (100)
	N Total presumed origin	1,340	954	2,294

Note: hospital-associated Clostridioides difficile infection (HA-CDI): onset of symptoms ≥ 2 days after admission. Incidence calculation: inclusion of episodes reported by all hospitals that provided complete data (numerators and denominators) for at least one semester/year.
N: number.

Testing practices

Out of the hospitals that participated at least one semester in 2022, only 36 provided information on the algorithm they used for CDI diagnosis in >80% of the cases. A multistep algorithm was used by 31 hospitals: 22 used ESCMID-recommended algorithms (8) while screening with glutamate dehydrogenase (GDH) and confirmation with nucleic acid amplification test (NAAT) was used by the nine remaining hospitals.

CDI incidences and trends

In 2022, CDI incidence was 1.60[6] CDI cases per 1,000 hospitalisations (Figure 1) and 2.78 CDI cases per 10,000 hospitalisation-days. For HA-CDI, these numbers were respectively 1.01[6] and 1.62 (Figure 1 and Figure 2).

Compared to 2021, the incidence increased in all regions except for Brussels in 2022 (Figure 2). The difference in incidence of CDI per 10,000 hospitalisation-days remains small between Wallonia and Flanders.

In 2022, the mean of the HA-CDI incidences per 10,000 hospitalisation-days in primary hospitals was lower than in secondary and tertiary hospitals (Figure 3). However, these differences were not statistically significant.

The increase of the CDI incidence density between 2021 and 2022 of 2.41 (95CI 2.31 – 2.52) to 2.78 (95CI 2.66 – 2.89) per 10,000 hospitalisation-days was statistically significant using a Poisson regression model. For the HA-CDI incidence increase of 1.31 (95CI 1.24 – 1.39) to 1.62 (95CI 1.53 – 1.71) per 10,000 hospitalisation-days the same could be observed. This upward shift completely corrects the decreasing trend observed over multiple years (2018 – 2021).

[6] Episodes deduplicated by hospitalisation and patient

The incidence density of HA-CDI compared to the incidences generated using episodes with a presumed origin being ‘acute care facility’ overlaps nicely, following closely the same trend (Figure 4).

Figure 1 • Mean incidence of CDI in hospitals per 1,000 hospitalisations. Belgium, 2010-2022.

Note: hospital-associated Clostridioides difficile infection (HA-CDI): onset of symptoms ≥ 2 days after admission. Incidence calculation: inclusion of episodes reported by all hospitals that provided complete data (numerators and denominators) for at least one semester/year. Including only hospitals funded for Royal Decree on surveillance of nosocomial infections

*CDI: Clostridioides difficile infection; N: number; * : deduplicated by hospitalisation and patient*

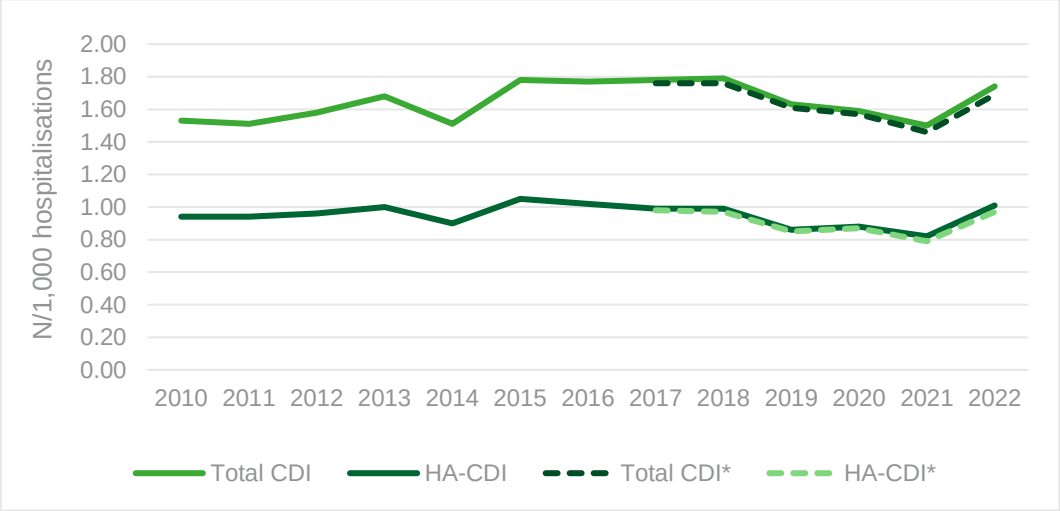


Figure 2 • Mean incidence of HA-CDI/10,000 hospitalisation-days in hospitals, per region. Belgium, 2010-2022.

Note: hospital-associated Clostridioides difficile infection (HA-CDI): onset of symptoms ≥ 2 days after admission. Incidence calculation: inclusion of episodes reported by all hospitals that provided complete data (numerators and denominators) for at least one semester/year. Including only hospitals funded for Royal Decree on surveillance of nosocomial infections

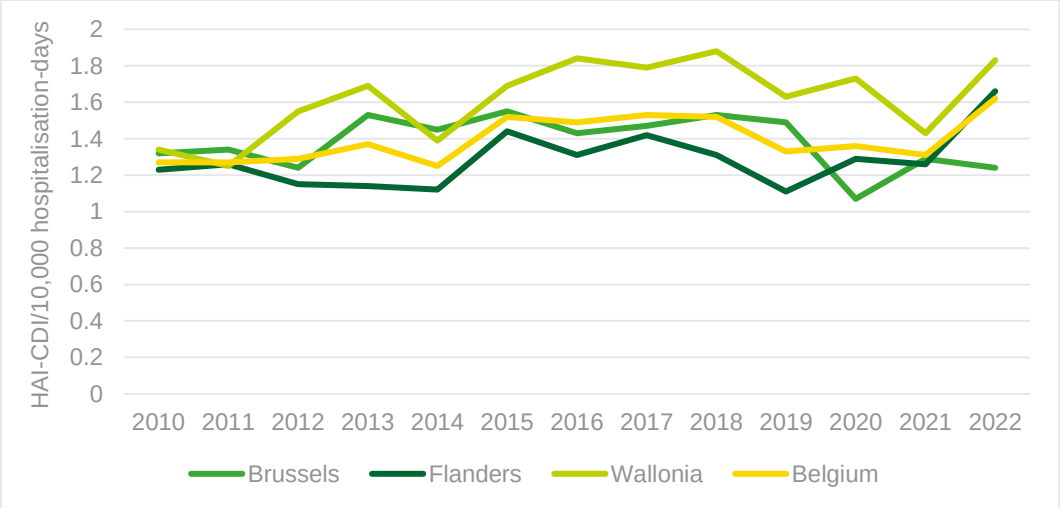


Figure 3 • Mean incidence of HA-CDI/10,000 hospitalisation-days in hospitals, per type hospital. Belgium, 2010-2022.

Note: hospital-associated Clostridioides difficile infection (HA-CDI): onset of symptoms ≥ 2 days after admission. Incidence calculation: inclusion of episodes reported by all hospitals that provided complete data (numerators and denominators) for at least one semester/year. Including only hospitals funded for Royal Decree on surveillance of nosocomial infections

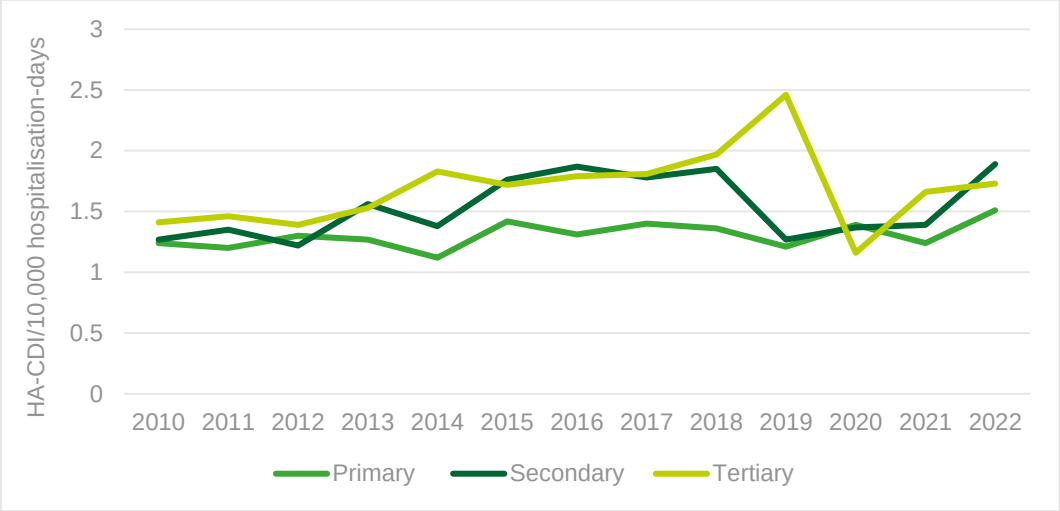
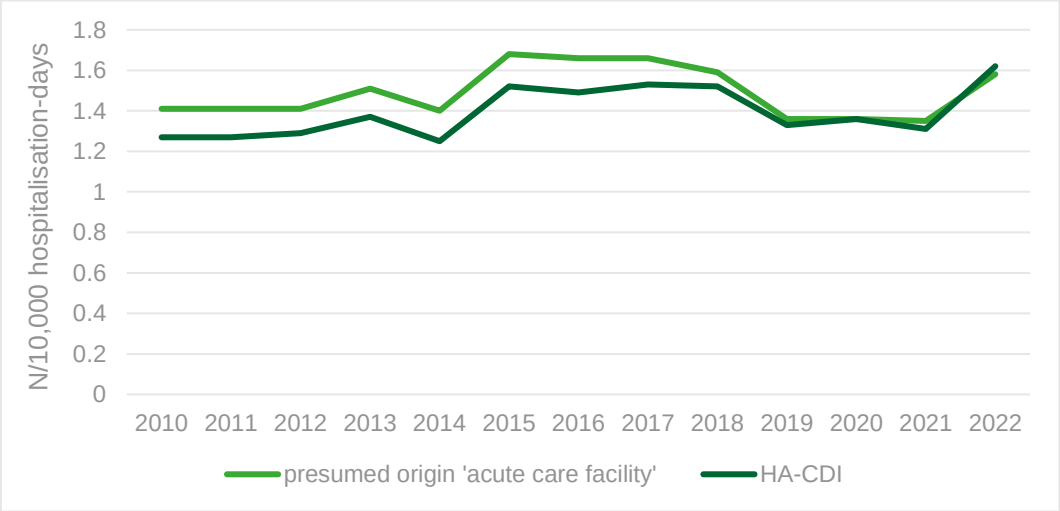


Figure 4 • Mean incidence of HA-CDI and episodes with presumed origin 'acute care facility' per 10,000 hospitalisation-days in hospitals. Belgium, 2010-2022.

Note: hospital-associated Clostridioides difficile infection (HA-CDI): onset of symptoms ≥ 2 days after admission. Incidence calculation: inclusion of episodes reported by all hospitals that provided complete data (numerators and denominators) for at least one semester/year. Including only hospitals funded for Royal Decree on surveillance of nosocomial infections.



Incidence data are detailed in Annex 3 (Table 6, Table 7 and Table 8).

NATIONAL REFERENCE LABORATORY DATA

Participation

In 2022, a total of 335 strains were sampled by the NRC in the context of surveillance, belonging to 54 (acute) hospitals (median: 4 strains/hospital/semester). A cytopathogenic effect was detected in 323 (96%) of the confirmed strains (belonging to 54 hospitals). Of all the

acute hospitals reporting cases at least for one semester, 67% also send strains to the NRC. Some strains sampled in a specific year are only received and typed the following year, hence the number of strains sent in the year of the analysis is always slightly underestimated. The number of hospitals sending CDI strains throughout the years are detailed in Annex 1 (Table 4).

Ribotype distribution

When considering only the first five strains per hospital per semester, the most frequently isolated and widespread strain in 2022 remained, as in previous years, BR014, toxin A-positive and toxin B-positive. It represented 13% of the total samples and was found in 52% of the hospitals that sent samples to the NRC. Ribotype BR002 was the second most frequently encountered ribotype, while the hypervirulent strain BR078, toxin A-positive, toxin B-positive and binary toxin-positive, came third, accounting for 8.2% of the samples and found in 31% of the hospitals (Table 2 and Table 3). The most BR014 strains where found in Brussels, accounting for more than 5% of all the samples.

Table 2 • Distribution of the five most frequently isolated ribotypes (number and %) among total samples of *Clostridioides difficile* from 2022 as part of the national surveillance. Belgium, 2015-2021.

Year	2015		2016		2017		2018		2019		2020		2021		2022	
Total Samples	539	*100%*	470	*100%*	406	*100%*	388	*100%*	353	*100%*	311	*100%*	335	*100%*	323	*100%*
BR014	75	*13%*	67	*14%*	73	*17%*	41	*11%*	39	*11%*	41	*13%*	40	*11.0%*	42	*13.0%*
BR002	41	*7.3%*	41	*8.5%*	27	*6.4%*	32	*8.3%*	25	*6.9%*	19	*5.9%*	23	*6.6%*	34	*10.0%*
BR078	46	*8.2%*	33	*6.8%*	28	*6.6%*	34	*8.8%*	35	*9.7%*	27	*8.4%*	30	*8.6%*	27	*8.2%*
BR106	19	*3.4%*	18	*3.7%*	19	*4.5%*	20	*5.2%*	19	*5.3%*	18	*5.6%*	28	*8.0%*	27	*8.2%*
BR020	46	8.2%	25	*5.2%*	30	*7.1%*	34	*8.8%*	22	*6.1%*	22	*6.9%*	26	*7.4%*	21	*6.4%*

Source: National reference center (NRC).
Note: Only the first five consecutive samples (with cytopathogenic effect) sent by hospital, by semester, are considered.
BR: Brazier classification

Table 3 • Distribution of the five most frequently isolated *Clostridioides difficile* ribotypes (number and %) among hospitals that sent samples to NRC in 2022 as part of the national surveillance. Belgium, 2015-2022.

Year	2015		2016		2017		2018		2019		2020		2021		2022	
Total Hospitals	78	*100%*	68	*100%*	71	*100%*	59	*100%*	55	*100%*	49	*100%*	55	*100%*	54	*100%*
BR014	43	*53%*	39	*57%*	41	*58%*	28	*47%*	26	*47%*	30	*60%*	28	*51%*	28	*52%*
BR002	31	*38%*	28	*41%*	22	*31%*	26	*44%*	20	*36%*	16	*32%*	18	*33%*	26	*48%*
BR106	16	*20%*	14	*21%*	14	*20%*	17	*29%*	17	*31%*	14	*28%*	23	*42%*	18	*33%*
BR020	34	*42%*	20	*29%*	23	*32%*	21	*36%*	18	*33%*	15	*30%*	20	*36%*	17	*31%*
BR078	36	44%	23	*34%*	23	*32%*	28	*47%*	23	*42%*	17	*34%*	22	*40%*	17	*31%*

Source: National reference center (NRC).
Note: Only the first five consecutive samples (with cytopathogenic effect) sent by hospital, by semester, are considered.
BR: Brazier classification

Out of the 51 CDI episodes that resulted in death, eight strains were sent to the NRC and ribotyped. Following seven well-known ribotypes were identified: BR002 (found twice), BR106 (found twice), BR014, BR015 and BR017. From the 202 complicated episodes 31 strains were ribotyped. Seven of these strains corresponded to BR002, and five to BR078. Four corresponded to a 'rare' UCL type (ribotyping profile was not recognized by the European Brazier and/or Belgium database). Regarding the 239 recurrent episodes, 29 were typed: 5 were classified as a 'rare' UCL type, 4 belonged to BR078, 4 to BR002, 4 to BR014, 2 to BR020, 2 to BR106, and each of the remaining strains corresponded to another ribotype.

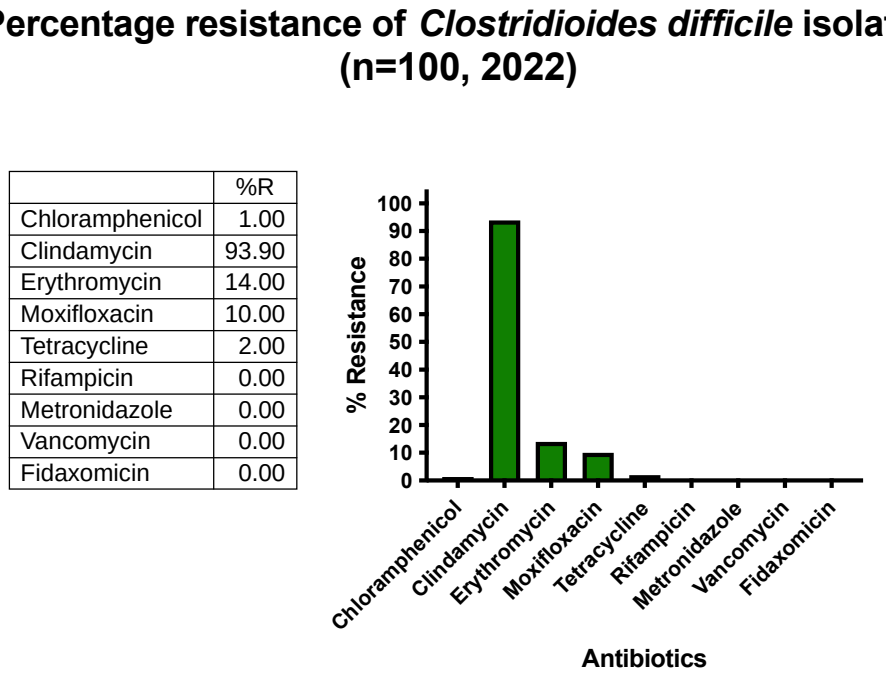
A comprehensive list with the number of strains per ribotype (UCL classification), and the number of hospitals in which each ribotype was isolated in 2022 can be found in Annex 4 (Table 9).

Antimicrobial susceptibility

Since 2019, data has been collected on antimicrobial susceptibility including antibiotics known to be significantly risk-associated with CDI or used in CDI treatment, through testing a representative sample of strains sent to the NRC. All isolates were susceptible to antibiotics currently used in CDI treatment such as vancomycin (MIC ≤2 mg/L), metronidazole (MIC ≤2 mg/L) and fidaxomicin (MIC ≤0.125 mg/L) (Figure 5). BR012, BR027, BR126 and BR078, one of the most common ribotypes in Belgium, were associated with resistance to multiple antimicrobials. Compared to 2019, the resistance to erythromycin (20.5% in 2019 vs 14.0% of isolates in 2022), moxifloxacin (26.0 vs 10.0%), tetracycline (6.8 vs 2.0%) and rifampicin (4.11 vs 0.0%) decreased (Annex 4, Table 10). Antibiotic resistance rates are lower in Belgium when compared to EU levels, except for clindamycin, for which the reported resistance rate has doubled since 2015 (93.9 % of the total isolates tested were resistant to clindamycin in 2022 vs 56% in 2015) (9).

Figure 5 • Rates (%) of *Clostridioides difficile* isolates resistant to antibiotics. Belgium, 2022.

Source: National reference center (NRC)
R: resistance



	%R
Chloramphenicol	1.00
Clindamycin	93.90
Erythromycin	14.00
Moxifloxacin	10.00
Tetracycline	2.00
Rifampicin	0.00
Metronidazole	0.00
Vancomycin	0.00
Fidaxomicin	0.00

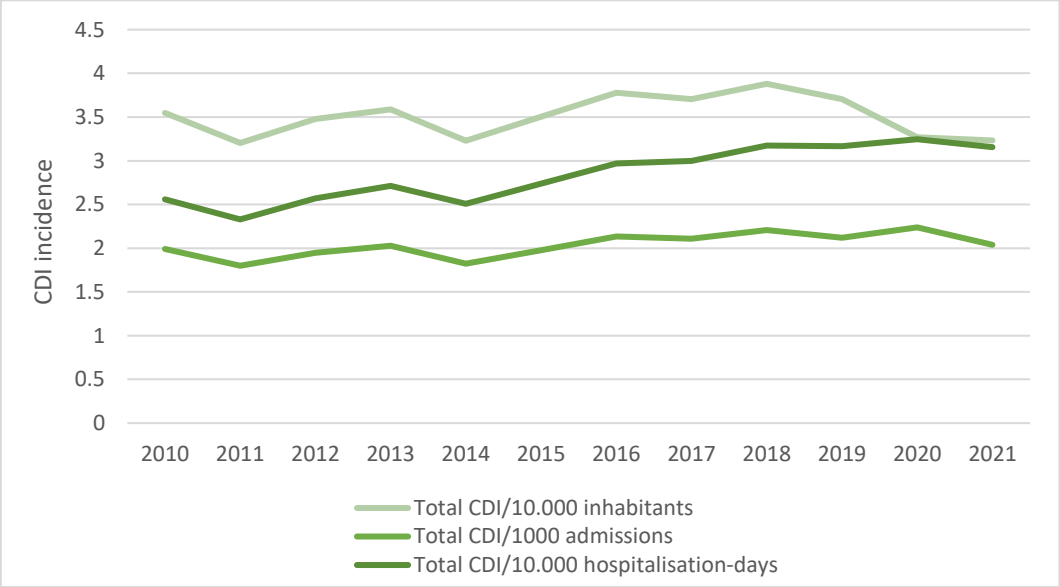
2. Hospital stays

In 2021 (most recent available data), 3,733 hospital stay records mentioned CDI as primary or secondary diagnostic code. The incidence of total CDI in the hospital was 2.0 per 1,000 admissions and 3.2 per 10,000 hospitalisation-days. These numbers are comparable to the previous years. Observed changes since year 2010 are displayed in Figure 6 and Figure 7.

The percentage of stays with a primary diagnostic code of CDI – presumed in this case to be the reason for admission – remained stable across the years. In 2021, it represented 23.5% of the total stays with a diagnostic code of CDI. Among the total number of CDI cases, the percentage of cases "not present at admission" is still 33%. It should be noted here that this number, which we would tend to associate with hospital-associated cases, should be interpreted with caution, partly because there might have been cases for which the presence or absence of the CDI diagnosis at admission was difficult to establish or uncertain.

Figure 6 • *Clostridioides difficile* infection (CDI) incidence in hospitals according to three denominators (inhabitants, admission, hospital-days). Belgium, 2010-2021.

Source: Federal Public Service of public health (SPF/FOD). Number of ICD-9-CM 008.45 (2009-2014) and ICD-10-CM A04.7 (2016-2020) codes (Enterocolitis due to Clostridium difficile) included in the hospital stay database as primary or secondary diagnosis. Extrapolation made for 2015.



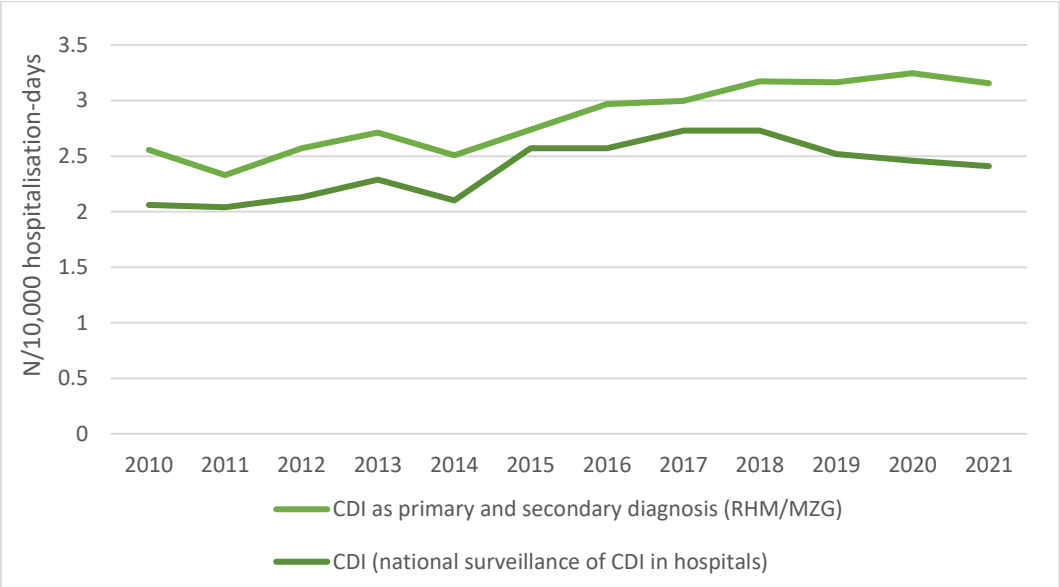
Comparing with data obtained from the national surveillance of CDI in hospitals, we can observe a difference in incidence. Since 2017, the gap in reported incidence between these two sources has increased (Figure 7), with seemingly different trends.

Further details are given in Annex 5 (Table 11).

Figure 7 • *Clostridioides difficile* infection incidence in hospitals as collected in two monitoring systems, both expressed per 10,000 hospitalization-days. Belgium, 2010-2021.

Source: Federal Public Service of public health (SPF/FOD): Number of ICD-9-CM 008.45 (2009-2014) and ICD-10-CM A04.7 (2016-2021) codes (Enterocolitis due to Clostridium difficile) included in the hospital stay database as primary or secondary diagnosis. Extrapolation made for year 2015. Surveillance data: incidence calculation by including CDI episodes reported by all hospitals that provided complete data (numerators and denominators) for at least one semester/year.

N: Number; CDI: Clostridioides difficile infection;



3. Billing of diagnostic tests

In 2022, there were 87,037 tests billed for hospitalised patients and 87,689 tests billed for ambulatory patients in Belgium. Compared with 2021, the total number of tests searching for faecal toxin-producing *C. difficile* billed in Belgium increased (Figure 8). In 2022, 15 tests were reimbursed per 1,000 insured Belgian inhabitants, which is an increase compared to the previous year. Over the last 12 years, the number of tests for hospitalised patients has remained stable (about 8 per 1,000 insured inhabitants). For the ambulatory patients there has been an increase from 5 tests per 1,000 insured inhabitants in 2010 to 8 per 1,000 in 2022.

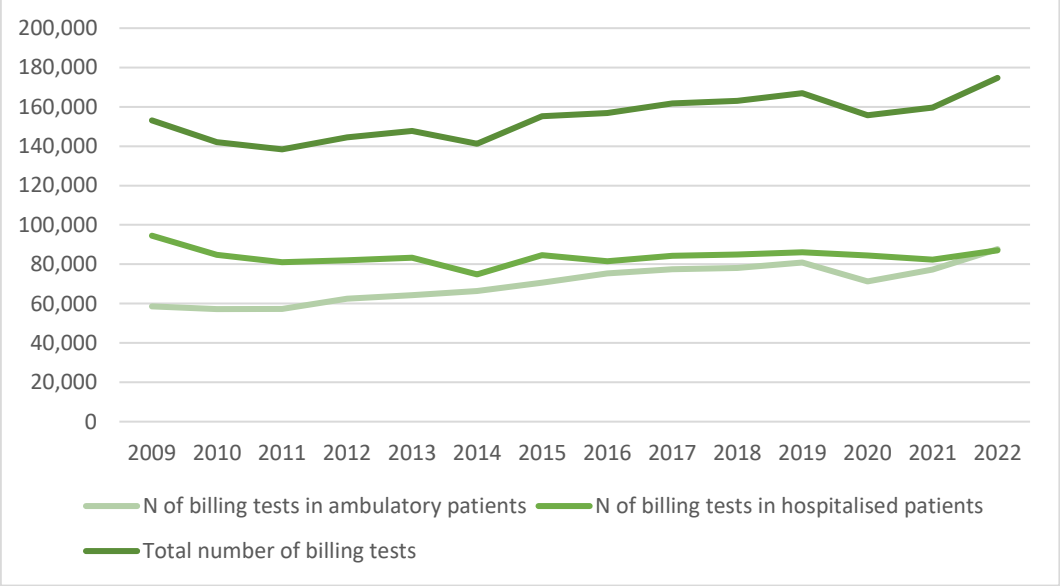
In 2021 (most recent data), there were 22 tests billed for hospitalised patients per CDI diagnosed in hospitals, which is comparable to previous years (positivity rate of about 5%). The number of tests billed for hospitalised patients per 1,000 admissions is 49.

Detailed data are presented in Annex 6 (Table 12).

Figure 8 • Number of tests billed for *Clostridioides difficile* testing in ambulatory and hospitalised patients. Belgium, 2010-2022.

Source: NIHDI (INAMI/RIZIV) for the number of billing tests for CDI.

N: number; CDI: Clostridioides difficile infection;



4. Death registry

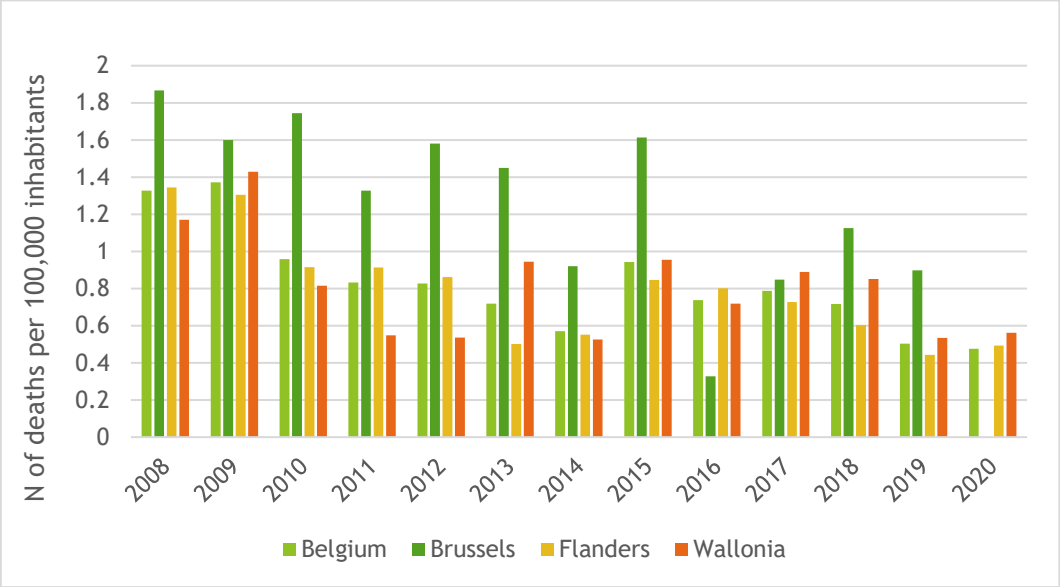
Mortality in Belgium with « enterocolitis due to *C. difficile* » as underlying cause, decreased steadily between 2009 and 2014, but increased in 2015, reaching 106 documented deaths. This was the highest number of deaths observed since 2009. Since 2015, a decreasing trend in mortality is observed, reaching in 2020 (most recent available data), 57 recorded deaths. For the same year, 46 deaths related to CDI were reported in the hospitals in the national surveillance (Annex 2, Table 5).

In 2020, the majority of deaths (80%) occurred in people aged 80 years or more according to the death registry data. Crude and adjusted mortality rates were respectively 0.50 and 0.48 deaths per 100,000 inhabitants in 2020 (Figure 9). In Brussels, for the first year since reporting, no death was documented with « enterocolitis due to *C. difficile* » as underlying cause.

Further details can be found in Annex 7 (Table 13).

Figure 9 • Age-standardised mortality rates, enterocolitis due to Clostridioides difficile, by region. Belgium, 2008-2020.

Source: Death registry, code ICD10 A047 as underlying cause of death. Direct standardisation using the Belgian mid-year 2015 population as reference population, according to 3 age groups (0-64, 65-79, 80+). Deaths are registered according to place of death and not place of residence.
N: number



MAIN FINDINGS AND RECOMMENDATIONS

See the section on Key findings for a summary of main results.

This report draws its strength from the use of four different data sources, providing a solid and broad overview of the epidemiology of CDI in Belgium.

The number of hospitals participating in the national CDI surveillance for at least one semester remains high (79%), considering it is not (completely) mandatory to participate. Although the number of participating hospitals has decreased with six hospitals compared to 2021, the number of hospitals sending strains remained similar (54). Still, 27 participating hospitals did not send (maximum) five samples, which is required according to the protocol. The regional and type hospital representativeness of the 79 hospitals providing numerator and denominator more or less corresponds to the regional and type hospital distribution of the 102 hospitals eligible for participation[7]. As for the use of Healthdata and Healthstat platforms for the registration and validation of surveillance data and analysis and reporting of results, we recommend to make these platforms more efficient and to address the technical problems that caused delays of results' reporting during the past year.

Comparing HA-CDI and episodes with presumed origin 'acute care hospital' shows that this self-reported variable seems accurate. Additionally, the number of 'unknown' and 'undetermined' presumed origin are relatively low. We could consider that the 29% of episodes with presumed origin 'community' gives us a correct indication on the number of CDI entering the hospital that occur outside of the healthcare setting. In the future, investigating CDI acquired in the community will be important, as has already been suggested in the literature (10).

In 2022 the CDI and HA-CDI incidence increased from 2.41 CDI per 10,000 hospitalisation-days to 2.78 CDI per 10,000 hospitalisation-days and from 1.31 HA-CDI per 10,000 hospitalisation-days to 1.62 HA-CDI per 10,000 hospitalisation-days. These are among the highest incidences of the last 10 years. Further investigation and analysis should clarify whether this increase is due to changes in hospital participation, patient population, antimicrobial use, and/or infection prevention and control practices.

The gap in results between national hospital stay and surveillance data remains big. Although similar trends seem to be observed in both data sources. It remains to be seen if the hospital stay data set will show the same increase we report in 2022. Furthermore, we recommend to evaluate further the use of hospital stays' data as a source for monitoring national and/or hospital CDI incidence.

In 2022, compared to previous years, the total number of billed tests increased, as well as the number of tests in hospitalised and ambulatory patients separately. In 2020 and 2021 only the number of tests in ambulatory patient increased, possibly due to a lack of availability of care and due to a fear of seeking care related to the COVID-19 pandemic, as well as the increased ease of testing among ambulant patients. In 2022, the number of tests billed in ambulatory and

[7] Region (79 hospitals - 102 hospitals): Brussels 14% - 14%, Flanders 53% - 50%, Wallonia 33% - 36%.
Type (79 hospitals - 102 hospitals): primary 78% - 76%, secondary 16% - 17%, tertiary 5% - 7%.

hospitalised patients was similar (about 87,000 tests). The number of tests in hospitalised patients has reached a similar number as in 2019. This might indicate that after 2021 more patients decided to sought out care in the hospital again.

In 2020, compared to previous years, the death registry data is still reporting a decline in mortality. In 2017 there were 91 deaths with CDI as underlying cause, while in 2020 (most recent available data) 57 deaths were registered. New treatments (6) or improved case detection could be the reason for this decline. To see the effect of the COVID-19 pandemic, data of 2021 will be needed.

REFERENCES

1. Messer Jeanette S. CEB. Microbial Physiology of the Digestive Tract and Its Role in Inflammatory Bowel Diseases. In: M. Said Hamid, editor. Physiology of the Gastrointestinal Tract, Sixth Edition. 2018. p. 795–810.

2. Freeman J, Bauer MP, Baines SD, Corver J, Fawley WN, Goorhuis B, et al. The changing epidemiology of Clostridium difficile infections. Clinical microbiology reviews. 2010 Jul;23(3):529–49.

3. Peng Z, Jin D, Kim HB, Stratton CW, Wu B, Tang YW, et al. Update on Antimicrobial Resistance in Clostridium difficile: Resistance Mechanisms and Antimicrobial Susceptibility Testing. J Clin Microbiol. 2017 Jul;55(7):1998–2008.

4. Song JH, Kim YS. Recurrent Clostridium difficile Infection: Risk Factors, Treatment, and Prevention. Gut and liver. 2019 Jan 15;13(1):16–24.

5. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals, 2016–2017. Stockholm: ECDC; 2023.

6. Baunwall SMD, Lee MM, Eriksen MK, Mullish BH, Marchesi JR, Dahlerup JF, et al. Faecal microbiota transplantation for recurrent Clostridioides difficile infection: An updated systematic review and meta-analysis. eClinicalMedicine [Internet]. 2020 Dec 1 [cited 2023 Nov 30];29. Available from: https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30386-2/fulltext

7. European Centre for Disease Prevention and Control. European Surveillance of clostridioides (Clostridium) difficile infections: surveillance protocol version 2.4. [Internet]. 2019 [cited 2021 Apr 5]. Available from: https://op.europa.eu/publication/manifestation_identifier/PUB_TQ0319947ENN

8. Crobach MJT, 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. Clinical Microbiology and Infection. 2016 Aug 1;22:S63–81.

9. Spigaglia P, Mastrantonio P, Barbanti F. Antibiotic Resistances of Clostridium difficile. In: Mastrantonio P, Rupnik M, editors. Updates on Clostridium difficile in Europe: Advances in Microbiology, Infectious Diseases and Public Health Volume 8 [Internet]. Cham: Springer International Publishing; 2018 [cited 2023 Nov 10]. p. 137–59. (Advances in Experimental Medicine and Biology). Available from: https://doi.org/10.1007/978-3-319-72799-8_9

10. Fu Y, Luo Y, Grinspan AM. Epidemiology of community-acquired and recurrent Clostridioides difficile infection. Therapeutic Advances in Gastroenterology [Internet]. 2021 [cited 2023 Dec 11];14. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8141977/

11. Vermeulen H, Hens N, Catteau L, Catry B, Coenen S. Impact of the COVID-19 pandemic on community antibiotic consumption in the EU/European Economic Area: a changepoint analysis. Journal of Antimicrobial Chemotherapy. 2023 Oct 1;78(10):2572–80.

ANNEXES

1. Hospitals contributing data to the national surveillance of CDI

Table 4 • Participation of Belgian hospitals in the national surveillance of CDI in hospitals. Belgium, 2010-2022.

2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
N hospitals providing cases for at least one semester												
99	99	100	100	100	100	95	95	88	87	87	85	81
N hospitals providing numerators and denominators for at least one semester												
97	97	98	98	99	98	93	86	86	84	86	83	79
N hospitals providing cases for the whole year												
74	74	75	76	74	84	78	69	73	69	63	70	67
N hospitals providing numerators and denominators for the whole year												
71	70	71	74	73	80	76	49	71	63	61	69	66
Total hospital-semesters providing numerators and denominators												
168	167	169	172	172	178	169	135	157	149	157	154	145
N hospitals sending CDI strains to the NRC												
NA	38	75	81	85	78	68	71	55	50	45	55	54
N cases per hospital per semester: median												
10	11	12	12	10	12	12	12	14	13	11	11	13
N cases per hospital per semester: maximum												
67	94	96	83	114	77	79	73	74	84	58	65	62
Total number of registered cases												
2,436	2,486	2,499	2,656	2,410	2,971	2,801	2,688	2,680	2,509	2,134	2,058	2,294
Total number of patients registered												
2,436	2,486	2,499	2,656	2,410	2,971	2,801	2,586	2,442	2,296	1,999	1,853	2,094
Total number of hospitals eligible for participation												
118	112	112	113	112	111	111	102	108	107	107	103	102

Source: surveillance data.

Notes: Including only hospitals funded for Royal Decree on surveillance of nosocomial infections. Zero reporting is included since 2019.

2. CDI characteristics

Table 5 • CDI characteristics. Belgium, 2019-2022.

CDI characteristic (%)	2019	2020	2021	2022
Gender patients				
Male	1025 (44.6)	849 (42.5)	831 (44.9)	940 (44.9)
Female	1267 (55.2)	1149 (57.5)	1021 (55.1)	1149 (54.9)
Unknown	5 (0.2)	1 (0.1)	1 (0.1)	5 (0.2)
Age-groups patients				
0-64	661 (28.8)	527 (26.4)	564 (30.4)	540 (25.8)
65-79	715 (31.1)	628 (31.4)	604 (32.6)	732 (36.0)
80+	920 (40.1)	844 (42.2)	685 (37.0)	822 (38.2)
HA-CDI	1339 (53.4)	1200 (56.2)	1123 (54.6)	1340 (58.4)
Presumed origin CDI				
Community	696 (27.7)	544 (25.5)	549 (26.7)	654 (28.5)
Acute care facility	1371 (54.6)	1199 (56.2)	1153 (56.0)	1280 (55.8)
Long-term care facility	121 (4.8)	102 (4.8)	101 (4.9)	113 (4.9)
Other healthcare facility	31 (1.2)	25 (1.1)	30 (1.5)	34 (1.5)
Undetermined	77 (3.1)	63 (3.0)	73 (3.6)	68 (3.0)
Unknown	213 (8.5)	201 (9.4)	152 (7.4)	145 (6.3)
Recurrent CDI				
Yes	259 (10.3)	189 (8.9)	206 (10.0)	239 (10.4)
No	2003 (79.8)	1778 (83.3)	1642 (79.8)	1759 (76.7)
Unknown	247 (9.8)	167 (7.8)	210 (10.2)	296 (12.9)
Complicated CDI				
Yes	172 (6.9)	153 (7.2)	150 (7.3)	202 (8.8)
No	1913 (76.3)	1672 (78.4)	1683 (81.8)	1776 (77.4)
Unknown	424 (16.9)	309 (14.5)	225 (10.9)	316 (13.8)
Patient status after CDI				
Alive	1866 (81.3)	1646 (82.8)	1449 (80.9)	1656 (79.1)
Died, related to CDI	44 (1.9)	46 (2.3)	39 (2.1)	51 (2.4)
Died, not related to CDI	353 (15.4)	277 (13.9)	241 (13.0)	289 (13.8)
Unknown	33 (1.4)	30 (1.5)	74 (4.0)	98 (4.7)
Speciality ward				
Geriatrics	662 (26.4)	613 (28.7)	575 (27.9)	626 (27.3)
Other medical department	322 (12.8)	254 (11.9)	239 (11.6)	293 (12.8)
Gastro-enterology	259 (10.3)	213 (10.0)	174 (8.5)	252 (11.0)
Other	214 (8.5)	169 (7.9)	207 (10.1)	245 (10.7)
Hemato-oncology	237 (9.5)	190 (8.9)	196 (9.5)	189 (8.2)
Surgery	174 (6.9)	140 (6.6)	130 (6.3)	170 (7.4)
Intensive care unit	176 (7.0)	134 (6.3)	164 (8.0)	150 (6.5)
Pneumology	104 (4.2)	105 (4.9)	79 (3.8)	100 (4.3)
Cardiology	79 (3.2)	64 (3.0)	58 (2.8)	72 (3.1)
Paediatrics	75 (3.0)	29 (1.4)	77 (3.7)	61 (2.7)
Nephrology	66 (2.6)	62 (2.9)	61 (3.0)	60 (2.6)
Obstetrics/gynaecology	5 (0.2)	3 (0.1)	2 (0.1)	5 (0.2)
COVID-19 general department	NA	21 (1.0)	17 (0.8)	4 (0.2)
COVID-19 ICU	NA	1 (0.1)	8 (0.4)	0 (0)
Missing	136 (5.4)	136 (6.4)	71 (3.4)	67 (2.9)

Note: Including only hospitals funded for Royal Decree on surveillance of nosocomial infections. Speciality ward where CDI developed is not a mandatory field to register, hence missing data is possible.

CDI: Clostridioides difficile infection; HA-CDI: Healthcare-associated C. difficile infections; ICU: intensive care unit

3. CDI incidences in hospitals

Table 6 • Incidence of CDI in hospitals. Belgium, 2010-2022.

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Mean incidence, per 1,000 hospitalisations													
HA-CDI	0.94	0.94	0.96	1.00	0.90	1.05	1.02	0.99	0.99	0.86	0.88	0.82	1.01
Total CDI	1.53	1.51	1.58	1.68	1.51	1.78	1.77	1.78	1.79	1.63	1.59	1.50	1.74
Mean incidence* (deduplicated by hospitalisation and patient), per 1,000 hospitalisations													
HA-CDI	NA	NA	NA	NA	NA	NA	NA	0.98	0.97	0.85	0.87	0.79	0.97
Total CDI	NA	NA	NA	NA	NA	NA	NA	1.76	1.76	1.61	1.57	1.46	1.69
Mean incidence, per 10,000 hospitalisation-days													
HA-CDI	1.27	1.27	1.29	1.37	1.25	1.52	1.49	1.53	1.52	1.33	1.36	1.31	1.62
Total CDI	2.06	2.04	2.13	2.29	2.10	2.57	2.57	2.73	2.73	2.52	2.46	2.41	2.78
Numerators used													
HA-CDI	1,488	1,465	1,458	1,575	1,431	1,716	1,602	1,294	1,467	1,246	1,140	1,116	1,315
HA-CDI*	NA	NA	NA	NA	NA	NA	NA	1,274	1,432	1,228	1,120	1,075	1,263
Total CDI	2,409	2,357	2,407	2,639	2,403	2,897	2,764	2,320	2,637	2,364	2,054	2,050	2,254
Total CDI*	NA	NA	NA	NA	NA	NA	NA	2297	2,596	2,336	2,029	2,001	2,193
Denominators used													
N hosp	1,575,781	1,565,915	1,519,807	1,573,030	1,590,379	1,628,565	1,563,558	1,301,738	1,476,696	1,447,051	1,292,681	1,365,939	1,297,105
N hosp-days	11,706,116	11,541,993	11,311,307	11,514,364	11,418,213	11,252,546	10,752,007	8,484,312	9,665,404	9,370,163	8,356,025	8,496,459	8,117,178
N hospitals providing numerators and denominators for at least one semester													
	97	97	98	98	99	98	93	86	86	84	86	83	79

Note: Including only hospitals funded for Royal Decree on surveillance of nosocomial infections. Inclusion of episodes reported by all hospitals that provided complete data (numerators and denominators) for at least one semester/year). Mean incidence: total registered CDI or HA-CDI episodes for all hospitals and all semesters X 1,000 or 10,000/ total hospitalisations or hospitalisation-days for all corresponding semesters.

** : deduplicated by hospitalisation and patient; HA-CDI: Healthcare-associated C. difficile infections; hosp: hospitalisations*

Table 7 • Mean incidence of HA-CDI/10,000 hospitalisation-days in hospitals, per region. Belgium, 2010-2022.

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Mean incidence, HA-CDI per 10,000 hospitalisation-days													
Brussels	1.32	1.34	1.24	1.53	1.45	1.55	1.43	1.47	1.53	1.49	1.07	1.29	1.24
Flanders	1.23	1.26	1.15	1.14	1.12	1.44	1.31	1.42	1.31	1.12	1.29	1.27	1.66
Wallonia	1.34	1.25	1.55	1.69	1.39	1.69	1.84	1.79	1.88	1.63	1.73	1.43	1.83
Belgium	1.27	1.27	1.29	1.37	1.25	1.52	1.49	1.53	1.52	1.33	1.36	1.31	1.62
N HA-CDI													
Brussels	240	248	228	273	259	282	237	167	255	265	161	213	202
Flanders	818	781	693	709	692	897	760	721	669	559	610	606	722
Wallonia	430	436	537	593	480	537	605	406	543	422	369	297	391
Belgium	1,488	1,465	1,458	1,575	1,431	1,716	1,602	1,294	1,467	1,246	1,140	1,116	1,315
N hospitalisation-days													
Brussels	1,824,454	1,848,348	1,841,177	1,787,540	1,782,310	1,819,702	1,662,637	1,134,250	1,663,195	1,775,726	1,508,895	1,646,765	1,623,537
Flanders	6,677,041	6,192,506	6,005,391	6,207,993	6,180,636	6,247,387	5,804,100	5,076,247	5,112,927	5,000,724	4,715,998	4,779,657	4,354,733
Wallonia	3,204,621	3,501,139	3,464,739	3,518,831	3,455,267	3,185,457	3,285,270	2,273,815	2,889,282	2,593,713	2,131,132	2,070,037	2,138,908
Belgium	11,706,116	11,541,993	11,311,307	11,514,364	11,418,213	11,252,546	10,752,007	8,484,312	9,665,404	9,370,163	8,356,025	8,496,459	8,117,178
N hospitals contributing data (% hospitals/total hospitals)													
Brussels	11 (11.3)	11 (11.3)	11 (11.2)	11 (11.2)	11 (11.1)	13 (13.3)	12 (12.9)	10 (11.6)	12 (14.0)	12 (14.3)	12 (14.0)	12 (14.5)	11 (13.9)
Flanders	52 (53.6)	49 (50.5)	50 (51.0)	51 (52.0)	51 (51.5)	49 (50.0)	46 (49.5)	45 (52.3)	44 (51.2)	45 (53.6)	47 (54.7)	44 (53.0)	42 (53.2)
Wallonia	34 (35.1)	37 (38.1)	37 (37.8)	36 (36.7)	37 (37.4)	36 (36.7)	35 (37.6)	31 (36.0)	30 (34.9)	27 (32.1)	27 (31.5)	27 (32.5)	26 (32.9)
Belgium	97	97	98	98	99	98	93	86	86	84	86	83	79

Note: Including only hospitals funded for Royal Decree on surveillance of nosocomial infections. Inclusion of episodes reported by all hospitals that provided complete data (numerators and denominators) for at least one semester/year. Mean incidence: total registered HA-CDI episodes for all hospitals and all semesters X 10.000/ total hospitalisation-days for all corresponding semesters.

Table 8 • Mean incidence of HA-CDI/10,000 hospitalisation-days in hospitals, per type hospital. Belgium, 2010-2022.

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Mean incidence, HA-CDI per 10,000 hospitalisation-days													
Primary hospitals	1.24	1.2	1.3	1.27	1.12	1.42	1.31	1.4	1.36	1.21	1.39	1.24	1.51
Secondary hospitals	1.27	1.35	1.22	1.56	1.38	1.76	1.87	1.78	1.85	1.27	1.37	1.39	1.89
Tertiary hospitals	1.41	1.46	1.39	1.53	1.83	1.72	1.79	1.81	1.97	2.46	1.16	1.66	1.73
All hospitals	1.27	1.27	1.29	1.37	1.25	1.52	1.49	1.53	1.52	1.33	1.36	1.31	1.62
N HA-CDI													
Primary hospitals	905	871	954	943	855	1,072	945	815	918	748	784	712	830
Secondary hospitals	373	376	316	427	360	468	514	351	393	304	269	282	352
Tertiary hospitals	210	218	188	205	216	176	143	128	156	194	87	122	133
All hospitals	1,488	1,465	1,458	1,575	1,431	1,716	1,602	1,294	1,467	1,246	1,140	1,116	1,315
N hospitalisation-days													
Primary hospitals	7,271,960	7,272,392	7,356,759	7,436,414	7,618,980	7,562,820	7,200,059	5,808,092	6,749,249	6,183,998	5,651,878	5,727,284	5,491,418
Secondary hospitals	2,940,825	2,775,369	2,598,552	2,734,101	2,616,586	2,664,247	2,754,167	1,967,827	2,124,598	2,397,700	1,956,641	2,034,567	1,857,656
Tertiary hospitals	1,493,331	1,494,232	1,355,996	1,343,849	1,182,647	1,025,479	797,781	708,393	791,557	788,465	747,506	734,608	768,104
All hospitals	11,706,116	11,541,993	11,311,307	11,514,364	11,418,213	11252546	10,752,007	8,484,312	9,665,404	9,370,163	8,356,025	8,496,459	8,117,178
N hospitals contributing data (% hospitals/total hospitals)													
Primary hospitals	74 (76.3)	73 (75.3)	75 (76.5)	75 (76.5)	77 (77.8)	77 (78.6)	73 (78.5)	69 (80.2)	68 (79.1)	66 (78.6)	68 (79.1)	66 (79.5)	62 (78.5)
Secondary hospitals	16 (16.5)	17 (17.5)	16 (16.3)	16 (16.3)	16 (16.2)	16 (16.3)	16 (17.2)	13 (15.1)	14 (16.3)	14 (16.7)	14 (16.3)	13 (15.7)	13 (16.5)
Tertiary hospitals	7 (7.2)	7 (7.2)	7 (7.1)	7 (7.1)	6 (6.1)	5 (5.1)	4 (4.3)	4 (4.7)	4 (4.7)	4 (4.8)	4 (4.7)	4 (4.8)	4 (5.1)
All hospitals	97	97	98	98	99	98	93	86	86	84	86	83	79

Note: Including only hospitals funded for Royal Decree on surveillance of nosocomial infections. Inclusion of episodes reported by all hospitals that provided complete data (numerators and denominators) for at least one semester/year. Mean incidence: total registered HA-CDI episodes for all hospitals and all semesters X 10.000/ total hospitalisation-days for all corresponding semesters.

4. National reference laboratory data

Table 9 • Ribotypes isolated in Belgium in more than one hospital in 2022: number of isolates and number of hospitals (UCL new classification).

Ribotype (UCL-new)	Hospitals N=54	Isolates N=223	Ribotype (UCL-new)	Hospitals N=54	Isolates N=323
32	26	34	307	3	3
Rare	20	28	36	3	3
16	18	27	44	3	3
362	18	25	49	3	4
306	17	20	589	3	3
3	16	26	600	3	3
46	9	12	605	3	3
316	8	9	63	3	3
313	7	7	631	3	3
601	7	7	65	3	3
340	6	6	9	3	3
14	5	5	118	2	2
161	5	6	122	2	3
4	5	5	184	2	2
47	5	7	22	2	2
15	4	5	308	2	2
23	4	3	341	2	2
28	4	5	343	2	2
33	4	4	585	2	2
344	4	4	629	2	2
594	4	4	86	2	2
26	3	6			

Note: Only the first five consecutive strains send per hospital per surveillance period are considered. Only strains where cytopathic effect is detected. Rare strains are strains that do not have an UCL classification yet.
Source: NRC. new UCL classification.

Table 10 • Rates (%) of *Clostridioides difficile* isolates resistant to antibiotics. Belgium, 2019-2022.

	2019 (n=73)	2020 (n=74)	2021 (n=70)	2022 (n=100)
% Resistance to antibiotics				
Chloramphenicol	4.1	0.0	4.3	1.0
Clindamycin	97.3	98.6	94.3	93.9
Erythromycin	20.5	21.6	21.4	14.0
Moxifloxacin	26.0	12.2	11.4	10.0
Tetracycline	6.8	9.5	4.3	2.0
Rifampicin	4.1	1.4	1.4	0.0
Metronidazole	0.0	0.0	0.0	0.0
Vancomycin	0.0	0.0	0.0	0.0
Fidaxomicin*	NA	NA	0.0	0.0

Source: National reference center (NRC).

** : The Fidaxomicin susceptibility has been evaluated from 2021 onwards; NA: Non applicable.*

5. Hospital stays data

Table 11 • Number and incidence of enterocolitis due to *Clostridioides difficile* in hospital stay data. Belgium, 2010-2021.

2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Number of hospital stays with code ICD-10-CM A04.7 (Enterocolitis due to* Clostridium difficile*) as primary or secondary diagnosis											
3,867	3,522	3,848	3,990	3,609	NA	4,267	4,205	4,425	4,246	3,761	3,733
Incidence of total CDI per 10,000 inhabitants											
3.55	3.20	3.48	3.59	3.23	NA	3.78	3.71	3.88	3.70	3.27	3.23
Incidence of total CDI per 1,000 hospitalisations											
1.99	1.80	1.95	2.03	1.82	NA	2.13	2.11	2.21	2.12	2.24	2.04
Incidence of total CDI per 10,000 hospitalisation-days											
2.56	2.33	2.57	2.71	2.51	NA	2.97	3.00	3.17	3.17	3.25	3.16
N inhabitants (mid-year Belgian population)											
10,895,586	10,993,607	11,067,751	11,125,035	11,179,780	11,238,477	11,294,999	11,349,078	11,403,737	11,462,024	11,506,940	11,552,628
N hospitalisations											
1,940,817	1,956,739	1,973,762	1,967,414	1,980,068	NA	1,999,724	1,994,964	2,005,574	2,003,765	1,680,000	1,830,316
N hospitalisation-days											
15,119,717	15,119,171	14,965,785	14,707,710	14,388,742	NA	14,368,448	14,022,377	13,943,350	13,412,852	11,584,561	11,831,110

Source: Hospital stay data (RHM/MZG). Federal Public Service of public health (SPF/FOD).
Source: SPMA for number of inhabitants.

.

6. Billing of diagnostic tests

Table 12 • Number of diagnostic tests for *Clostridioides difficile* in stool samples billed to social insurance. Belgium, 2010-2022.

2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
N tests in hospitalised patients												
84,779	81,045	82,054	83,370	74,841	84,691	81,583	84,267	84,982	86,055	84,433	82,306	87,037
N tests per 1.000 hospitalisations												
48.16	45.61	45.65	46.37	41.37	46.47	44.38	45.82	46.02	46.62	54.80	48.93	NA
N tests billed per CDI diagnosed in the hospital												
21.92	23.01	21.32	20.89	20.74	NA	19.15	20.08	19.20	20.27	24.87	22.05	NA
N tests billed in hospitalised patients per 1,000 insured inhabitants												
7.91	7.50	7.53	7.61	6.80	7.66	7.34	7.54	7.57	7.63	7.45	7.24	7.60
N tests in ambulatory patients												
57,211	57,353	62,518	64,306	66,361	70,602	75,340	77,533	78,132	80,929	71,320	77,247	87,689
N tests billed in ambulatory patients per 1,000 insured inhabitants												
5.34	5.30	5.74	5.87	6.03	6.39	6.78	6.94	6.96	7.18	6.29	6.79	7.66
Total tests billed (hospitalised and ambulatory patients)												
141,990	138,398	144,572	147,676	141,202	155,293	156,923	161,800	163,114	166,984	155,753	159,553	174,726
Total tests billed per 1,000 insured inhabitants												
13.24	12.80	13.27	13.48	12.82	14.04	14.12	14.49	14.54	14.81	13.74	14.03	15.26

Source: INAMI-RIZIV for number of tests, number of admissions and number of insured persons. Nomenclature codes 549861 and 549850 are for hospitalised and ambulatory patients respectively.

Source: Hospital stay data (RHM/MZG). Federal Public Service of public health (SPF/FOD) for number of CDI diagnoses.

7. Death registry data per region

Table 13 • Specific mortality rates. enterocolitis due to *Clostridioides difficile*, per region. Belgium, 2008-2020.

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
Number of death records with code ICD10 A047 « enterocolitis due to C. difficile » as underlying cause of death													
Belgium	127	135	97	86	88	78	63	106	84	91	84	60	57
Brussels	16	14	16	12	15	13	8	15	3	8	10	8	0
Flanders	75	76	55	56	55	33	37	58	56	52	44	33	37
Wallonia	36	45	26	18	18	32	18	33	25	31	30	19	20
Crude specific mortality rate. per 100,000 inhabitants													
Belgium	1.19	1.25	0.89	0.78	0.80	0.70	0.56	0.94	0.74	0.80	0.74	0.52	0.50
Brussels	1.51	1.30	1.45	1.06	1.31	1.12	0.68	1.27	0.25	0.67	0.83	0.66	0.00
Flanders	1.21	1.22	0.88	0.88	0.86	0.52	0.58	0.90	0.86	0.80	0.67	0.50	0.56
Wallonia	1.04	1.29	0.74	0.51	0.51	0.90	0.50	0.92	0.69	0.86	0.83	0.52	0.55
Age-standardised specific mortality rate*. per 100,000 inhabitants													
Belgium	1.33	1.37	0.96	0.83	0.83	0.72	0.57	0.94	0.74	0.79	0.72	0.50	0.48
Brussels	1.87	1.60	1.74	1.33	1.58	1.45	0.92	1.61	0.33	0.85	1.13	0.90	0.00
Flanders	1.35	1.30	0.92	0.91	0.86	0.50	0.55	0.85	0.80	0.73	0.60	0.44	0.49
Wallonia	1.17	1.43	0.81	0.55	0.54	0.94	0.53	0.95	0.72	0.89	0.85	0.53	0.56

Source : death registries.

** : Indirect standardisation. Three age categories (0-64, 65-79, 80+) using 2015 Belgian population age structure as a standard.*

8. Report approval of various entities

Table 14 • Dates that the different entities have been sent and approved* this report.

Entity	Received	Approved
Sciensano	NA	19/12/2023
NRC *C. difficile*	12/12/2023	19/12/2023
BAPCOC	21/12/2023	26/01/2024
BICS		
Regional authorities	08/02/2024	21/02/2024
Cabinet of the National Secretary		
Hospitals		

* : includes passive approval

CONTACT
Milena Callies • T+32 4 73 13 31 58 • Milena.Callies@sciensano.be

MORE INFORMATION

–

Visit our website >www.sciensano.be or contact us at >info@sciensano.be

Sciensano • Rue Juliette Wytsmanstraat 14 • Brussels • Belgium • T + 32 2 642 51 11 • T press + 32 2 642 54 20 • info@sciensano.be • www.sciensano.be

Responsible editor: Christian Léonard. Managing director • Rue Juliette Wytsmanstraat 14 • Brussels • Belgium