EPIDEMIOLOGY OF *CLOSTRIDIOIDES DIFFICILE* INFECTIONS IN BELGIAN HOSPITALS

—

National report
Data up to and including 2021

MILENA CALLIES • LAURE MORTGAT • ELS DUYSBURGH

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ABBREVIATIONS

BR	Brazier (European ribotype classification)
CDI	*Clostridioides difficile (Clostridium)* infection
C. difficile	*Clostridioides (Clostridium) difficile*
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
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
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

Acute care hospital
An acute care hospital is a hospital that is defined as such by the National Institute for Health and Disability Insurance (NIHDI) (INAMI-RIZIV list updated April 2017[1]).

Chronic/Long-term care hospital
A chronic or long-term care hospital is a hospital that is defined as such by the National Institute for Health and Disability Insurance (NIHDI) (INAMI-RIZIV list updated April 2017[1]).

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.

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.

Mean incidence
Sum of cases reported by participating hospitals for a given period, divided by the sum of denominators (admissions or hospitalisation days) for that period and the concerned hospitals.

Number of admissions (or discharges)
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.

Primary hospitals
Primary hospitals are hospitals that are defined as acute hospitals without university characteristics by the Belgian Ministry of health in a list dated April 2019[2]. (In this report, the hospital type is provided at INAMI/RIZIV code level, and not at campus level).

[1] NIHDI – list hospitals - April 2017: acute / chronic / psychiatric hospitals.
[2] List of hospitals provided by the Belgian Ministry of health (*Dienst Datamanagement - Directoraat- Generaal Gezondheidszorg*); List dated April 2019: *Adressenlijst ziekenhuizen 04/2019 - Liste d'adresses des hôpitaux 04/2019*.

Secondary hospitals
Secondary hospitals are hospitals that are defined as acute hospitals with university characteristics by the Belgian ministry of health in a list dated April 2019[2]. (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 April 2019[2]. (In this report, the hospital type is provided at INAMI/RIZIV code level, and not at campus level).

KEY FINDINGS

- Participation rate of Belgian hospitals in the national surveillance of *Clostridioides difficile* infection (CDI) in hospitals remained good and comparable to 2020. In 2021, 87 (81%) out of the 107 eligible hospitals reported CDI cases for at least one semester, and 70 hospitals reported CDI cases all year long.

- Only 50 hospitals (57% of the participating hospitals) sent their strains to the national reference centre (NRC) for further typing in 2021. Worth remembering: the NRC also accepts toxigenic *C. difficile* positive stool samples should bacterial culture no longer be available in the local hospital laboratory. Only the first five samples should be sent.

- At national level, hospital-associated *Clostridioides difficile* infection (HA-CDI) incidence per 10,000 hospitalisation-days was 1.3 in 2021 (slightly lower than the previous year). Differences between regions, provinces and hospitals remained substantial. As in previous years, incidence was higher in Wallonia than in Flanders and Brussels. However, incidence in Wallonia has not been this low since 2014.

- The proportion of HA-CDI diagnosed among all CDI in Belgian hospitals decreased in the ten last years to reach 55% in 2021.

- We observed a slight increase in CDI originating from the 'community' among hospitalised patients (from 25% in 2020 to 27% in 2021).

- In 2021, the number of tests billed among hospitalized patients (82,306) for *C. difficile* was the lowest since 2016 (81,583). However, the total number of tests billed (among hospitalized and ambulatory patients) increased compared to 2020.

- As for previous years, about 10% of CDI episodes were recurrent. Geriatric patients were, as observed previous years, the most affected.

- Hospital stay data recorded around 3,761 CDI cases in 2020 (most recent data), less than in 2019 (4,256). The incidence of total CDI per 10,000 hospitalisation-days was 3.3, while the national surveillance reported an incidence 24% lower for the same year. The gap between findings from these two sources increased, and the trends they displayed were opposite.

- Around 14% of patients affected by CDI died from various causes, while 2% died possibly or definitely because of their CDI infection.

- Ribotype BR014 remained the most prevalent and widespread strain in Belgian hospitals. Ribotype BR020 came second, followed by BR078. The hypervirulent ribotype BR027 was identified in only two hospitals in 2021.

- All isolates tested for antimicrobial susceptibility were susceptible to the three antibiotics commonly used for the treatment of CDI: vancomycin, metronidazole and fidaxomicin.

- 89% of the hospitals who gave us information on their testing algorithms, used multistep algorithms and 73% of them used ESCMID-recommended algorithms (European Society of Clinical Microbiology and Infectious Diseases).

- In 2019, the most recent year for which mortality data was validated, the age-standardised mortality rate was the lowest since 2002. Mortality in Brussels increased again and was the highest across the three regions.

- Opposite to other hospital associated infection we did not observe, based on surveillance or MZG data, a clear increase in HA-CDI incidence in Belgian hospitals. A more comprehensive reflection on the impact of COVID-19 on HA-CDI in Belgian hospitals will be included in our next report, including also 2022 data and expected to be published in summer 2023.

EXECUTIVE SUMMARY

Clostridioides difficile infection (CDI), is a major cause of infectious diarrhoea acquired in healthcare institutions. Symptoms range from mild diarrhea to a severe life-threatening infection, resulting in a high clinical, social and economic burden. This report aims to describe the epidemiology of CDI in Belgian hospitals, focusing on the year 2021. It summarises the data from four different sources, being: (1) the national surveillance of CDI in hospitals, including data from the national reference laboratory (NRC 2010 – 2021); (2) hospitals stays (RHM/MZG 2010 – 2020); (3) billing of diagnostic tests (INAMI/RIZIV 2010 – 2021), and (4) the death registry (2008 – 2019).

NATIONAL SURVEILLANCE OF CDI IN HOSPITALS

Participation in the national surveillance system slowly decreased since 2015. In 2021, 87 hospitals (81%) out of the 107 hospitals eligible for CDI surveillance registered 2,051 CDI cases. Among them, 82 hospitals (77%) provided both numerators (cases) and denominators (number of hospitalisation-days and number of admissions) for at least one semester, while 68 hospitals (64%) provided these data for the whole year.

The proportion of “hospital-associated” cases (HA-CDI, with date of onset ≥ 2days after admission) among all registered CDI cases was 55% in 2021, compared to 62% in 2010. The proportion of cases possibly originating from the “community” increased slightly to reach 27% compared to 25% in 2020. As observed in the previous years, around 10% of cases were recurrent and female were more affected (55%) than male, as were elderly people (median age of 76 years old). Geriatrics, gastroenterology and oncology departments remained the most affected wards. In 2021, 14% of CDI patients died for whatever reason, while 2% died because of their infection. The proportion of cases reported as “complicated” remained low (7%).

Out of all the hospitals who gave us information on their diagnosis algorithms for CDI, 89% used multistep algorithms in 2021, and 73% of them used ESCMID-recommended algorithms (European Society of Clinical Microbiology and Infectious Diseases). The mean rate of CDI testing, using surveillance data, was 78.68 stool tests per 10,000 patient-days in 2021, and positivity rate was about 3%.

Since 2010, at national level, based on surveillance data, the mean CDI incidence in acute care hospitals remains more or less stable, but shows a non-significant decreasing trend since 2018. In 2021, it reached 2.4/10,000 hospitalisation-days for total CDI and 1.3/10,000 hospitalisation-days for HA-CDI. Incidence was higher in Wallonia than in Flanders and Brussels, but the differences are small (see Figure 1). There was a variability in the reported incidence of CDI and HA-CDI between provinces and hospitals.

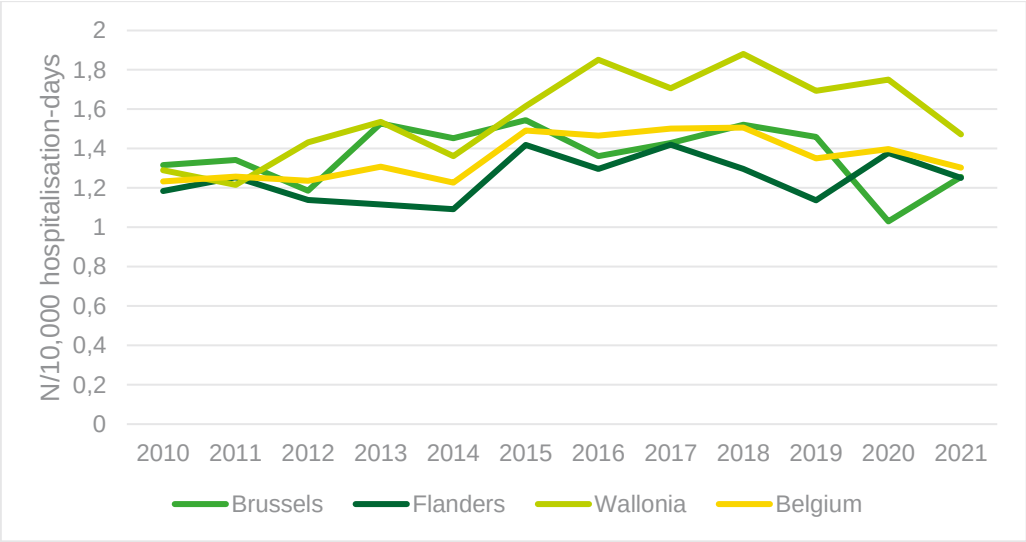


Figure 1: Mean incidence of HA-CDI/10,000 hospitalisation-days in acute care hospitals, per region, Belgium, 2010-2021 (HA-CDI: hospital-associated *Clostridioides difficile* infection; N: number)

Note: Hospital-associated-Clostridioides difficile infection (HA-CDI): onset of symptoms ≥ 2 days after admission. Incidence calculation: inclusion of all acute care hospitals that provided complete data (numerators and denominators) for at least one semester/year in the national surveillance.

In 2021, 50 Belgian hospitals sent 504 toxigenic strains to the NRC for typing for surveillance purposes. The number of strains sent have been constantly decreasing since 2014 and are lower than ever. Ribotype BR[3]014 remained the most prevalent and widespread strain type in Belgian hospitals, followed by ribotype BR020. The hypervirulent strain BR078 came third; while BR027 was found in only two hospital. All isolates tested for antimicrobial susceptibility were susceptible to vancomycin, metronidazole and fidaxomicin. These are three antibiotics commonly used for the treatment of CDI.

HOSPITAL STAYS

As shown in Figure 2 and based on most recent available hospital stay data from the federal public service (FOD/SPF), CDI incidence approached 3.2/10,000 hospitalisation-days in 2020, which is comparable to 2019. The CDI incidence according to the surveillance data was 2.5/10,000 hospitalisation-days. Since 2018, the gap between these two sources has been increasing. However, as hospital stay data are comprehensive, they are supposed to give a better estimate of CDI burden in Belgium. In 2020, 3,761 hospital stay records mentioned CDI as primary or secondary diagnosis, 11% less than in 2019.

[3] BR: European Brazier classification of ribotypes.

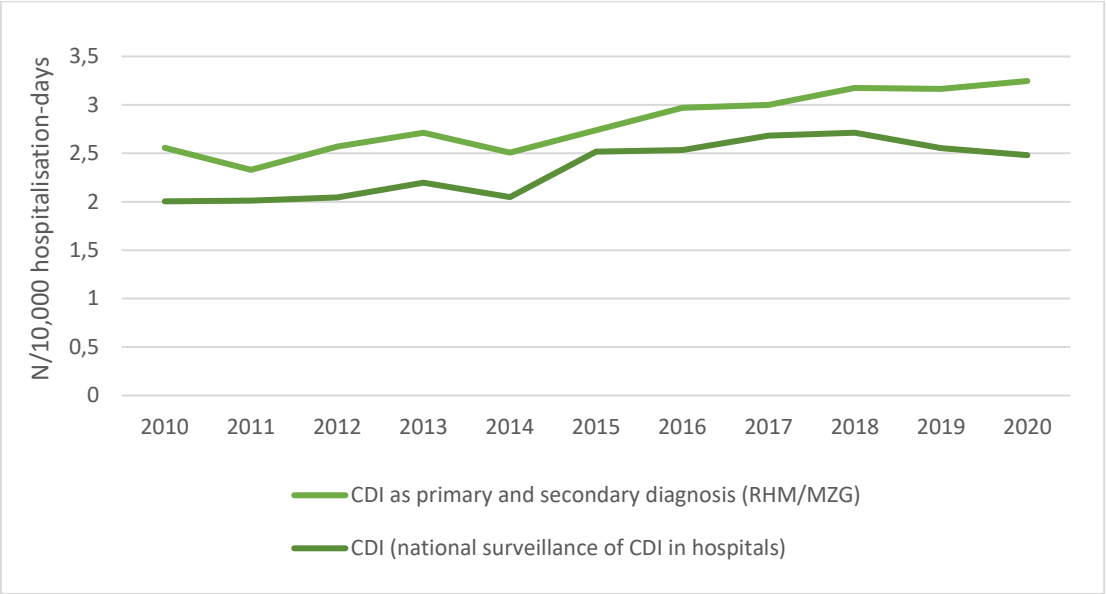


Figure 2: CDI incidence in Belgian hospitals, per 10,000 hospitalisation-days, 2010-2020 (CDI: *Clostridioides difficile* infections; N: Number)

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 year 2015. Surveillance data: incidence calculation by including CDI episodes reported by all acute care hospitals that provided complete data (numerators and denominators) for at least one semester/year.

BILLING OF DIAGNOSTIC TESTS

Around 159,500 tests applied for faecal toxin-producing *C. difficile* detection were billed in 2021, resulting in 14 tests reimbursed per 1,000 insured inhabitants. Until 2019 the total number of billed tests was mostly driven by the number of billing tests in hospitalized patients. Starting from 2020, we can see that the trend in total billed tests is depending on the number of billing tests in ambulatory patients.

DEATH REGISTRY

In the death registry, 60 deaths due to *C. difficile* were recorded in 2019 (most recent available mortality data). The age-adjusted specific mortality rate was 0.50 deaths/100,000 inhabitants, which is a substantial decrease compared to the last 16 years. Mortality in Brussels was still the highest among the three regions. In 2019, 85% of deaths occurred in people aged 80 years or more.

In conclusion, the burden of CDI in Belgian hospitals did not change substantially during the last years. Participation in the epidemiological surveillance, especially the shipment of strains or stool samples to the NRC, should be further encouraged. Finally, given their association with CDI (1), antimicrobial stewardship programmes and infection prevention and control measures in hospitals and ambulatory practices should be continuously encouraged and evaluated

NEDERLANDSE SAMENVATTING

Clostridioides difficile infectie (CDI), voorheen bekend als "*Clostridium difficile*" infectie, is een belangrijke oorzaak van infectieuze diarree verworven tijdens acute of chronische zorg. De symptomen variëren van milde diarree tot een ernstige levensbedreigende infectie, met als gevolg een hoge medische, sociale en economische belasting. Dit rapport heeft als doel de epidemiologie van CDI in Belgische ziekenhuizen te beschrijven, met de focus op het jaar 2021. Het rapport vat de gegevens uit vier verschillende bronnen samen, namelijk: (1) de nationale surveillance van CDI in ziekenhuizen, inclusief gegevens van het nationale referentielaboratorium (NRC 2010 - 2021); (2) minimale ziekenhuisgegevens (MZG 2010 - 2020); (3) facturatie van diagnostische tests (RIZIV 2010 - 2021), en (4) het overlijdensregister (2008 - 2019).

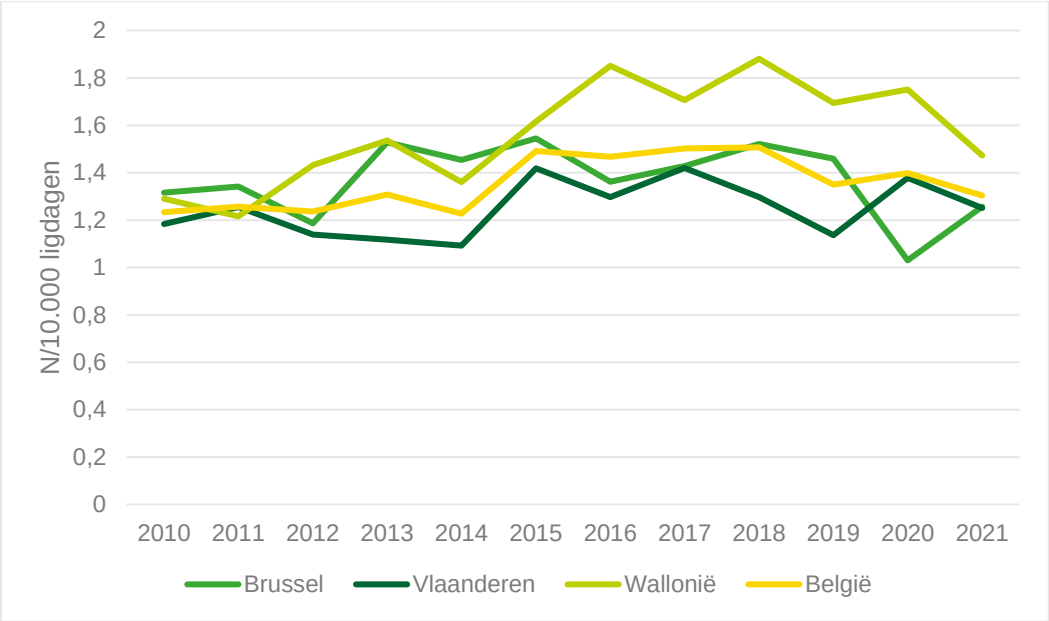
NATIONAAL SURVEILLANCE VAN CDI IN ZIEKENHUIZEN

Deelname aan de nationale surveillance nam sinds 2015 langzaam af. In 2021 hebben ongeveer 87 (81%) van de 107 ziekenhuizen die voor de CDI surveillance in aanmerking kwamen 2.051 CDI-gevallen gerapporteerd. Van hen leverden 82 ziekenhuizen (77%) zowel tellers (gevallen) als noemers (ligdagen en aantal opnames) voor ten minste één semester, terwijl 68 ziekenhuizen (64%) deze gegevens voor hele jaar rapporteerden.

De proportie "ziekenhuis-geassocieerde" gevallen (HA-CDI, met startdatum ≥ 2 dagen na opnamedatum) onder alle geregistreerde CDI, bedroeg 55% in 2021, in vergelijking met 62% in 2010. Het aandeel van de gevallen die vermoedelijk uit de "gemeenschap" kwamen, steeg licht naar 27% in vergelijking met 25% in 2020. Vergelijkbaar met vorige analyses ging het in ongeveer 10% om wederkerende gevallen, waren er iets meer vrouwelijke patiënten (55%), en waren patiënten voornamelijk ouderen (mediaanleeftijd van 76 jaar). Evenzo bleven geriatrie-, gastro-enterologie- en oncologie de meest getroffen afdelingen. In 2021, overleed 14% van de CDI-patiënten omwille van diverse redenen, terwijl 2% stierf als gevolg van hun infectie. De proportie van de als "gecompliceerd" gerapporteerde gevallen bleef laag (7%).

Van alle ziekenhuizen die hun CDI diagnose algoritmen rapporteerde, gebruikte 89% meerstapsalgoritmen in 2021, en 73% van hen gebruikte door ESCMID aanbevolen algoritmen (European Society of Clinical Microbiology and Infectious Diseases). Het gemiddelde percentage CDI-tests, berekend via surveillancegegevens, was 78.68 ontlastingstests per 10.000 ligdagen in 2021, en het aantal positieve testen bedroeg ongeveer 3%.

Sinds 2010, bleef de gemiddelde CDI-incidentie in acute ziekenhuizen, berekend op basis van de surveillancegegevens, min of meer stabiel op nationaal niveau, maar vertoonde een niet-significante dalende trend sinds 2018. In 2021, veroorzaakte dit 2,4/10.000 ligdagen voor het totaal aantal CDI gevallen en 1,3/10.000 ligdagen voor het aantal HA-CDI gevallen. De incidentie was hoger in Wallonië dan in Vlaanderen en Brussel (zie Figuur 1), maar de verschillen blijven klein. Er waren verschillen in de gerapporteerde incidentie van CDI en HA-CDI tussen provincies en ziekenhuizen.



Figuur 1: Gemiddelde incidentie van HA-CDI/10.000 ligdagen in acute ziekenhuizen, per regio, België, 2010-2021

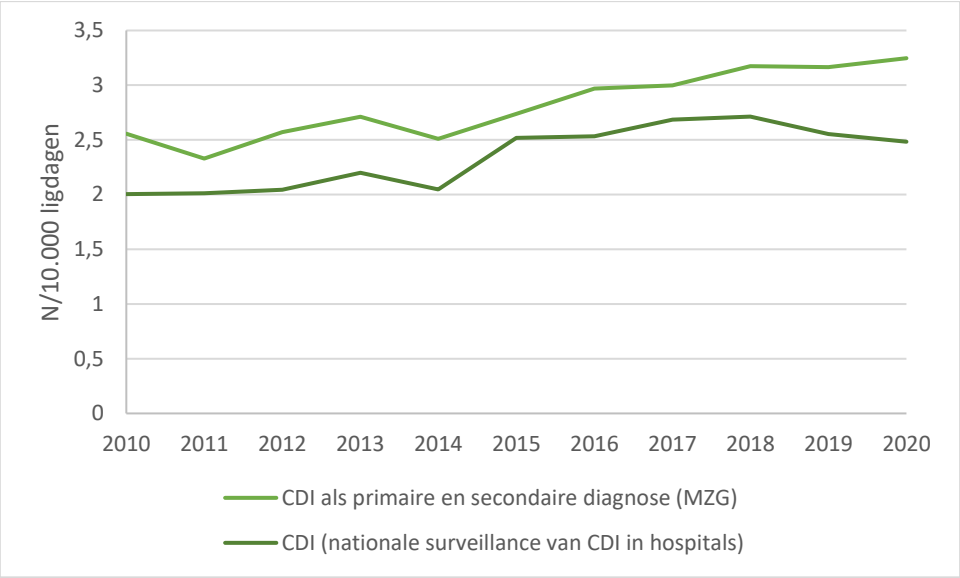
Opmerking: Ziekenhuis-geassocieerde Clostridioides difficile infectie (HA-CDI): begin van de symptomen ≥ 2 dagen na opname. Incidentieberekening: omvat alle acute ziekenhuizen die volledige gegevens (tellers en noemers) verstrekten voor ten minste één semester/jaar.

In het kader van de surveillance werden er in 2021, door 50 Belgische ziekenhuizen, 504 toxigene stammen naar het NRC gestuurd voor typering. Het aantal opgestuurde stammen is sinds 2014 voortdurend gedaald en zijn lager dan ooit. Ribotype BR[4]014 bleef het meest voorkomende en wijdverspreide stam-type in Belgische ziekenhuizen, gevolgd door ribotype BR020. De hypervirulente stam BR078 kwam op de derde plaats, terwijl BR027 in slechts twee ziekenhuizen werd aangetroffen. Alle isolaten die getest waren voor antimicrobiële gevoeligheid waren gevoelig voor vancomycine, metronidazol en fidaxomicine. Dit zijn drie antibiotica die meestal worden gebruikt voor de behandeling van CDI.

MINIMALE ZIEKENHUISGEGEVENS

Zoals blijkt uit Figuur 2 en op basis van de meest recente beschikbare minimale ziekenhuisgegevens van de federale overheidsdienst (FOD), was in 2020 de CDI-incidentie ongeveer 3,2/10.000 ligdagen, wat vergelijkbaar is met de gegevens van 2019. De CDI-incidentie bedraagt, volgens de surveillance gegevens, 2,5/10.000 ligdagen. Sinds 2018, stijgt de kloof tussen deze twee gegevensbronnen. Aangezien deze gegevens alle gevallen omvatten, worden ze echter verondersteld een betere schatting te geven van de CDI-belasting (burden) in België. In 2020 vermeldden 3.761 ziekenhuisverblijven CDI als primaire of secundaire diagnose, 11% minder dan in 2019.

[4] BR: Europese Brazier classificatie voor ribotypes



Figuur 2: *Clostridioides difficile* infectie (CDI) incidentie in Belgische ziekenhuizen, 2009-2020

Bron: Federale Overheidsdienst Volksgezondheid (FOD). Aantal ICD-9-CM 008.45 (2000-2014) en ICD-10-CM A04.7 (2016-2018) codes (Enterocolitis als gevolg van Clostridioides difficile) opgenomen in de minimale ziekenhuisgegevens databank als primaire of secundaire diagnose. Extrapolatie gemaakt voor 2015[5] *.*

FACTURATIE VAN DIAGNOSTISCHE TESTS

In 2021 werden ongeveer 159.500 testen voor het opsporen van fecaal toxine-producerende *C. difficile* gefactureerd, en bijna 14 tests werden terugbetaald per 1.000 verzekerde inwoners. Tot 2019 was het totale aantal gefactureerde testen het meest bepaald door het aantal gefactureerde testen bij gehospitaliseerde patiënten. Sinds 2020 zien we dat dat de trend in de totale aantal gefactureerde testen afhankelijk is van het aantal gefactureerde testen in ambulante patiënten.

OVERLIJDENSREGISTER

In het overlijdensregister werden in 2019 (meest recente gegevens) 60 sterfgevallen als gevolg van *C. difficile* geregistreerd. Het "*age-adjusted specific mortality rate*" bedroeg 0,50 sterfgevallen/100.000 inwoners, wat een grote daling is ten opzichte van de laatste 16 jaar. De sterfte in Brussel was de hoogste van de drie gewesten. In 2019 deed 85% van de sterfgevallen zich voor bij mensen van 80 jaar of ouder.

Samengevat kan worden gesteld dat de CDI-belasting (burden) in Belgische ziekenhuizen de laatste jaren niet wezenlijk veranderde. Deelname aan de epidemiologische surveillance, met name het verzenden van stammen of ontlasting monsters naar de NRC, moet verder worden aangemoedigd. Ten slotte moeten antimicrobiële stewardship-programma's en infectiepreventie- en controlemaatregelen in ziekenhuizen en in de ambulante praktijk, gelet op het verband met CDI (1), continue worden aangemoedigd en geëvalueerd.

[5] Als gevolg van de overgang van ICD-9 naar ICD-10 waren gegevens voor 2015 niet beschikbaar en werden deze berekend als het gemiddelde tussen 2014 en 2016.

RÉSUMÉ EN FRANÇAIS

L'infection à *Clostridioides difficile* (ICD), anciennement connue sous le nom d'infection à «*Clostridium difficile*», est une cause majeure de diarrhée infectieuse acquise dans les établissements de soins de santé aigus et chroniques. Ses symptômes peuvent varier d'une diarrhée légère à une infection sévère voire mortelle, entraînant une charge clinique, sociale et économique élevée. Ce rapport vise à décrire l'épidémiologie des ICD dans les hôpitaux belges, en se concentrant sur l'année 2021. Il résume les données provenant de quatre sources différentes, à savoir: (1) la surveillance nationale des ICD dans les hôpitaux, y compris les données du laboratoire national de référence (CNR 2010–2021); (2) les séjours hospitaliers (RHM 2010 – 2020); (3) la facturation des tests diagnostiques (INAMI 2010 – 2021), et (4) le registre des décès (2008 – 2019).

SURVEILLANCE NATIONALE DES ICD DANS LES HÔPITAUX

La participation au système national de surveillance a légèrement diminué depuis 2015. En 2020, 87 (81%) des 107 hôpitaux éligibles à cette surveillance ont enregistré 2.051 cas d'ICD. Parmi eux, 82 hôpitaux (77%) ont fourni à la fois des numérateurs (cas) et des dénominateurs (nombre de journées d'hospitalisation et nombre d'admissions) pendant au moins un semestre, tandis que 68 hôpitaux (64%) ont fourni ces données tout au long de l'année.

La proportion de cas «associés à l'hôpital» (dont la date de début des symptômes est ≥ 2 jours après la date d'admission) parmi tous les cas ICD enregistrés était de 55% en 2021, par rapport à 62 % en 2010. La proportion de cas probablement provenant de la «communauté» a légèrement augmenté pour atteindre 27% comparativement à 25% en 2020. Comme d'habitude, environ 10% des cas étaient récurrents et les femmes étaient légèrement plus touchées (55%) que les hommes, tout comme les personnes âgées (âge médian de 76 ans). De même, les services de gériatrie, de gastroentérologie et d'oncologie sont restés les services les plus touchés. En 2021 14% des patients atteints d'ICD sont décédés pour une raison quelconque, tandis que 2% sont décédés à cause de leur infection. La proportion de cas déclarés comme «compliqués» (admission aux soins intensifs, infection nécessitant une chirurgie ou un traitement hospitalier, décès en lien avec l'ICD dans les 30 jours) restait faible (7%).

Sur l'ensemble des hôpitaux qui nous ont fourni des informations sur leurs algorithmes de diagnostic de l'ICD, 89% ont utilisé des algorithmes en plusieurs étapes en 2021, et 73% d'entre eux ont utilisé des algorithmes recommandés par l'ESCMID (European Society of Clinical Microbiology and Infectious Diseases). Le taux moyen de tests diagnostiques des ICD, calculé à l'aide des données de surveillance, était de 78,68 analyses de selles pour 10.000 journées d'hospitalisation en 2021, et le taux de positivité était d'environ 3%.

À l'échelle nationale, l'incidence moyenne des ICD dans les hôpitaux aigus calculée à partir des données de surveillance est demeurée plus ou moins stable depuis 2010, mais a affiché une tendance à la baisse non significative depuis 2018. En 2021, cette incidence approchait 2,4/10.000 journées d'hospitalisation pour les ICD totales et 1,3/10.000 journées d'hospitalisation pour les ICD associées à l'hôpital. L'incidence était plus élevée en Wallonie

qu'en Flandre et à Bruxelles (voir Figure 1), mais les différences restent minimes. Elle variait également d'une province à l'autre et d'un hôpital à l'autre.

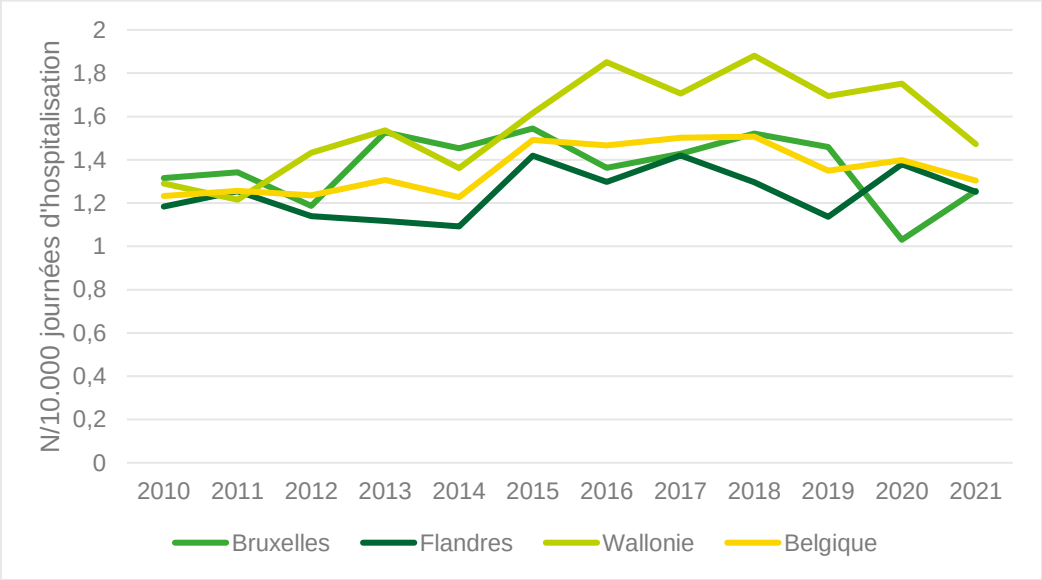


Figure 1: Incidence moyenne des ICD associées à l'hôpital, par 10.000 journées d'hospitalisation dans les hôpitaux aigus, par région, Belgique, 2010-2021

Remarque : ICD associées à l'hôpital : début des symptômes ≥ 2 jours après l'admission. Calcul de l'incidence : inclusion de tous les hôpitaux aigus ayant fourni des données complètes (numérateurs et dénominateurs) pendant au moins un semestre/année.

En 2021, 50 hôpitaux belges ont envoyé 504 souches toxinogènes au CNR pour un typage à des fins de surveillance. Le nombre de souches envoyées sont en constante diminution depuis 2014 et sont plus faibles que jamais. Le ribotype BR[6]014 est resté la souche la plus fréquente et la plus répandue dans les hôpitaux belges, suivi du ribotype BR020. La souche hypervirulente BR078 s'est retrouvée en troisième position; tandis que BR027 n'a été trouvé que dans un deux hôpitaux. Tous les isolats testés pour la sensibilité aux antimicrobiens étaient sensibles à la vancomycine, au métronidazole et à la fidaxomicine. Il s'agit de trois antibiotiques couramment utilisés pour le traitement de l'ICD.

SEJOURS HOSPITALIERS

Comme le montre la Figure 2 et sur la base des dernières données disponibles du service public fédéral (FOD/SPF) sur les séjours hospitaliers, l'incidence des ICD approchait 3,2/10.000 journées d'hospitalisation en 2020, ce qui est comparable à 2019. L'incidence des ICD selon les données de surveillance était de 2,5/10 000 journées d'hospitalisation. Depuis 2018, l'écart entre ces deux sources s'est creusé. Cependant, les données sur les séjours hospitaliers étant exhaustives, elles sont censées donner une meilleure estimation de la charge que représentent les ICD en Belgique. En 2020, 3.761 séjours hospitaliers ont mentionné l'ICD comme diagnostic primaire ou secondaire, soit 11% de moins qu'en 2019.

[6] Classification européenne des ribotypes (Brazier).

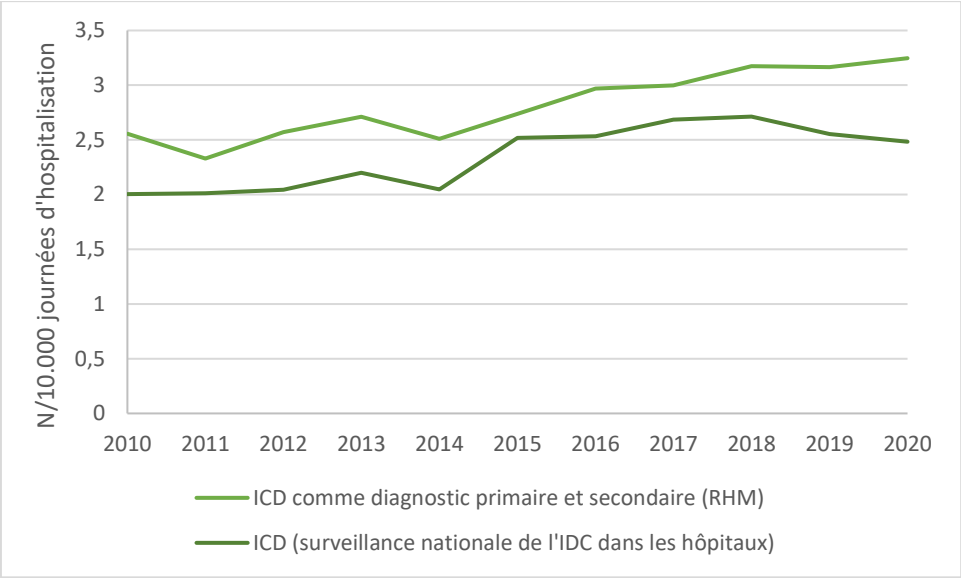


Figure 2: Incidence des infections à *Clostridioides difficile* dans les hôpitaux belges, 2009-2020

Source : Service public fédéral (SPF) santé publique. Nombre de codes ICD-9-CM 008.45 (2000- 2014) et ICD-10-CM A04.7 (2016-2018) (entérocolite à Clostridioides (Clostridium) difficile) repris dans la base de données des séjours hospitaliers comme diagnostic primaire ou secondaire. Extrapolation faite pour 2015[7].

FACTURATION DES TESTS DIAGNOSTIQUES

Environ 159.500 tests pour la «recherche de *C. difficile* toxinogène dans les selles» ont été facturés en 2021, et près de 14 tests ont été remboursés pour 1.000 habitants assurés. Jusqu'en 2019, le nombre total de tests facturés dépendait principalement du nombre de tests facturés aux patients hospitalisés. À partir de 2020, on constate que l'évolution du nombre total de tests facturés dépend du nombre de tests facturés chez les patients ambulatoires.

REGISTRE DES DÉCÈS

Dans le registre des décès, 60 décès dus à *C. difficile* ont été enregistrés en 2019 (données de mortalité disponibles les plus récentes). Le taux de mortalité spécifique standardisé pour l'âge était de 0,50 décès/100.000 habitants, ce qui représente une diminution substantielle par rapport aux 16 dernières années. La mortalité à Bruxelles reste la plus élevée des trois régions. En 2019, 85% des décès sont survenus chez des personnes âgées de 80 ans ou plus.

En conclusion, la charge des ICD dans les hôpitaux belges n'a pas changé de manière substantielle au cours des dernières années. La participation à la surveillance épidémiologique, en particulier l'envoi de souches ou d'échantillons de selles au CNR, devrait être davantage encouragée. Finalement, compte tenu de leur association avec l'ICD (1), les programmes de gestion des antimicrobiens et les mesures de prévention et de contrôle des infections dans les hôpitaux et dans la pratique ambulatoire doivent être encouragés et évalués en permanence.

[7] En raison du passage de l'ICD-9 à l'ICD-10, les données de 2015 n'étaient pas disponibles et ont été calculées comme étant la moyenne des données de 2014 et de 2016.

INTRODUCTION

1. Background

Clostridioides 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 (2). 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 *Clostridioides difficile* infection (CDI), together with advanced age, presence of co-morbidities and increased length of hospitalisation (3). *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. 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 therefore results in a high clinical, social and economic burden due to increased duration of hospitalisation, re-admission, and management of complications.

CDI is the most important cause of infectious diarrhoea acquired in healthcare institutions and is responsible for around 3.6% of healthcare-associated infections (HAI) in European hospitals (5). A few years ago, various countries around the world reported an increase in incidence of CDI, with, however, wide variations between countries (6–8). This increase was attributed to different factors such as changes in the prevailing ribotypes and emergence of hypervirulent strains like BR027[8]/NAP1[9], the ageing of the population, and an overall increase in antibiotic consumption. More recent evidence suggest that, following global and intense efforts to mitigate this infection, healthcare-associated CDI rates are decreasing, (1) although this doesn't seem to be the case for community-associated CDI (9).

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 – 2021); (2) hospital stays (Résumé hospitalier minimum/Minimale ziekenhuis gegevens: RHM/MZG 2010 – 2020); (3) billing of diagnostic tests (Institut national d'assurance maladie-invalidité/Rijksinstituut voor ziekte- en invaliditeitsverzekering: INAMI/RIZIV (2010 – 2021) and (4) the death registry (2008 – 2019).

[8] European Brazier classification of *C.difficile* ribotypes based on polymerase chain reaction.
[9] North American classification of *C.difficile* strains based on pulsed-field gel electrophoresis.

Main results are presented in the body of the report while more detailed data can be consulted in the annex.

2. Objectives

The objective of this report is to describe the epidemiology of CDI in Belgium, with a focus on year 2021 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 acute care 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 acute care hospitals. Since 2015, these hospitals have to participate in at least one out of the four following surveillance program: CDI, 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 acute care hospitals (RD 22/06/2017).

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 a 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 admission and number of hospitalisation-days must also be provided by each participating hospital. One-day admissions 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)(10), and is regularly updated. The differences between the Belgian and European surveillance are described in our protocol.

Since mid-2017, all data have been collected via Healthdata (https://healthdata.sciensano.be/en/home, https://www.healthdata.be/dcd/#/collection/NSIH-CDIF/version/6). This platform enables data collection, storage, and analysis, while reporting is done via their data visualisation platform "Healthstat" (https://www.healthstat.be/). In the Healthdata application hospitals are identified by their hospital and campus number defined by the INAMI/RIZIV, allowing for a better standardisation.

To be considered for registration, a CDI case must fulfil at least one 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.

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 Annex 3 (Table 8).

Data are currently transmitted to Sciensano via an Excel sheet but Healthdata onboarding is planned to become operational in the near future.

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

DATA ANALYSIS

Data validation was performed using SAS Entreprise guide 7.1, and consolidated manually. Only validated records were included in the analysis. Merging of hospital and NRC data and the analysis presented in this report were done using STATA 16.1. For the calculation of CDI incidence per admission or per hospitalisation-days, all acute care hospitals that provided complete data, including numerators and denominators for at least one semester, were included. For the description of the characteristics of CDI, all valid CDI 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.

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 hospital stays with code A04.7 from 2010 to 2020 (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 admissions 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, and crossed checked with Statbel data, the Belgian statistical office.

The RHM/MGZ data are exhaustive as they include all hospital stays in Belgium. They should therefore provide an accurate view on the total number of CDI in Belgian hospitals as well as CDI trends over the years. They can be applied for validation of surveillance data.

Analysis was done in Excel, and data for year 2015 was 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[10]. 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 2021 (most recent available year) was analysed using Excel. INAMI/RIZIV also provided denominators, being: the yearly number of patient admissions[11](available until year 2020) 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.

[10] Every inhabitant of Belgium is enrolled in the healthcare insurance system.
[11] 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 – 2019 (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 region of death, and not to 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 and validated by comparing with Statbel data.

RESULTS

1. National surveillance of CDI in hospitals

HOSPITAL DATA

Participation

Participation of Belgian hospitals in the national CDI surveillance decreased slowly since 2015, the year in which the surveillance became no longer mandatory. The migration, in July 2017, to Healthdata probably also contributed in this decrease. In 2021, out of 107 hospitals eligible for participation (101 acute and 6 long-term care, based on the last version of the list provided by the INAMI/RIZIV in April 2017), 70 (65%) hospitals (68 acute and 2 long-term care hospitals) registered their cases during the whole year. Among these hospitals, 68 also provided denominator data. At semester level, 82 hospitals provided both numerator and denominator data for at least one semester, which represents around 77% of the eligible hospitals.

In 2021, 87 hospitals registered 2,051 CDI cases (after data cleaning and validation), belonging to 1,882 patients. The maximum number of registered cases per hospital per semester was 65 with a median of 10. About 9% of participating hospitals-semesters reported zero cases. These data are detailed in Annex 1 (Table 3).

Characteristics of CDI cases

For 55% of the CDI episodes, symptoms occurred 2 days or more after admission in the reporting hospital; they were therefore considered “hospital-associated” (HA-CDI). This proportion was more or less stable during the five last years, but slowly decreased over the past 10 years (in 2010, 62% of all CDI cases). This is consistent with the fact that the proportion of CDI with a presumed origin defined as “acute hospital” decreased from 69% in 2010 to 56% in 2021. The proportion of cases arising from the “community” was 27% (compared to 25% last year). The number of cases with a reported origin being a “long-term care facility” (LTCF) did not change substantially across the years, and accounted for about 5% of the cases in 2021.

In 2021, as in previous years, the majority of cases were females (55%). Half of the patients were older than 75 years of age. Patients with HA-CDI had a median age of 76, four years more than the median age of patients with an infection not considered as “hospital-associated” (median age of 72).

Similar to previous years, 10% of the reported CDI were labelled as “recurrent”. The most affected wards were geriatrics (29%) and gastroenterology (9%), followed by oncology (6%), pneumology (4%) and hematology (4%). In 2021, we recorded the same amount of episodes labelled as “complicated”, than 2020 (7% of CDI).

In 2021, 14% (286) of patients with a CDI died. Thirteen % (36) of these deaths were reported to be related to CDI, meaning that 2% of patients affected by CDI died possibly or definitely because of their infection.

Testing practices

Out of the 87 hospitals that participated at least one semester in 2021, 45 (52%) provided information on the algorithm they used for CDI diagnosis in >80% of the cases. Forty of these hospitals used multistep algorithms: 29 used ESCMID-recommended algorithms (11) while screening with glutamate dehydrogenase (GDH) and confirmation with nucleic acid amplification test (NAAT) was used by the majority 9 of the 11 remaining hospitals.

A subgroup of 35 hospitals documented their billing: for this subgroup 28,673 stool tests for *C.difficil*e detection were reported, of which 3.2% were positive. The mean rate of CDI testing was 78.68 stool tests per 10,000 patient-days and 46.64 per 1,000 admissions.

CDI trends and incidences

Between 2010 and 2021, at national level, no trend in CDI and HA-CDI incidence is observed. The mean CDI incidence per 1,000 admissions or 10,000 hospitalisation increased in 2015, but decreased again since 2018. In 2021, CDI incidence was 1.47 CDI cases per 1,000 admissions (Figure 1) and 2.40 CDI cases per 10,000 hospitalisation-days. For HA-CDI, these numbers were respectively 0.80 and 1.30 (Figure 1 and 2).

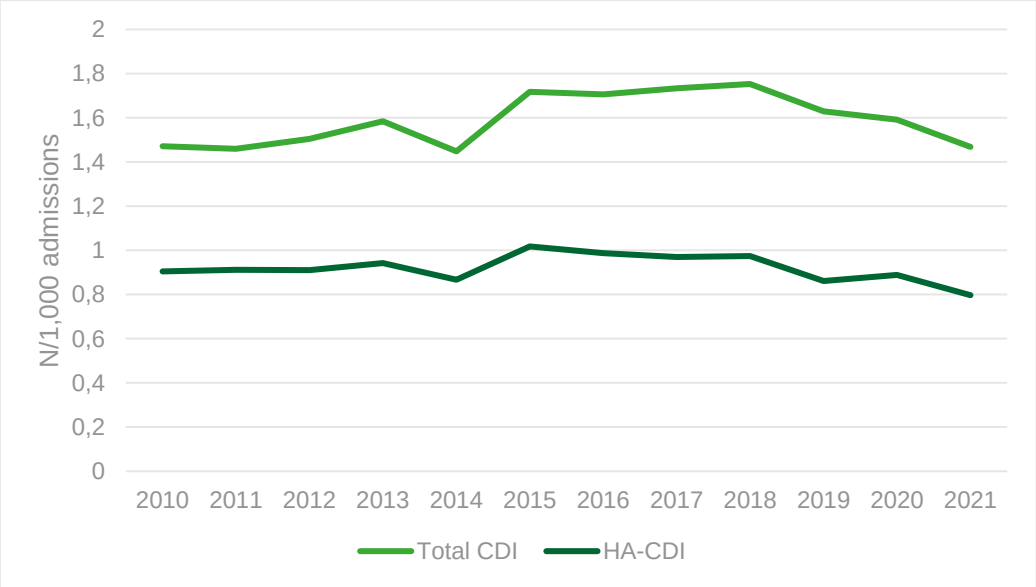


Figure 1: Mean incidence of CDI in acute care hospitals per 1,000 admissions, Belgium 2010-2021 (CDI: *Clostridioides difficile* infection; HA-CDI: hospital-associated-CDI; N: number)

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

In 2021, the incidence of CDI per 10,000 hospitalisation-days remained highest in Wallonia. Compared to 2020, the incidence in Flanders decreased while in Brussels it increased (Figure 2). However, the differences between the regions currently are small.

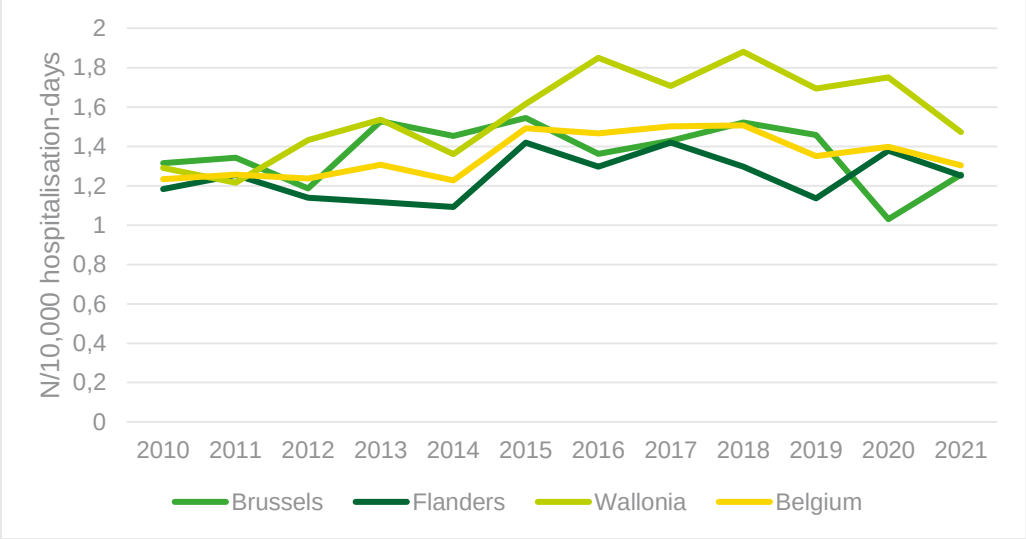


Figure 2: Mean incidence of HA-CDI/10,000 hospitalisation-days in acute care hospitals, per region, Belgium, 2010-2021 (HA-CDI: hospital-associated *Clostridioides difficile* infection; N: number)

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

CDI distribution

Figure 3 shows, as usual, a variability in the reported incidence of HA-CDI between provinces. Incidence was highest in the provinces of Hainaut, Eastern Flanders and Limburg (descending order) and lowest in the provinces of Walloon Brabant, Flemish Brabant, and Luxembourg (ascending order). There were no HA-CDI reported in Brabant Walloon (but only two hospital-semester participated). Categories are based on the distribution of data in Belgium (quartiles) to allow for benchmarking between provinces. Details on incidences are presented in Annex 2 (tables 5, 6 and 7).

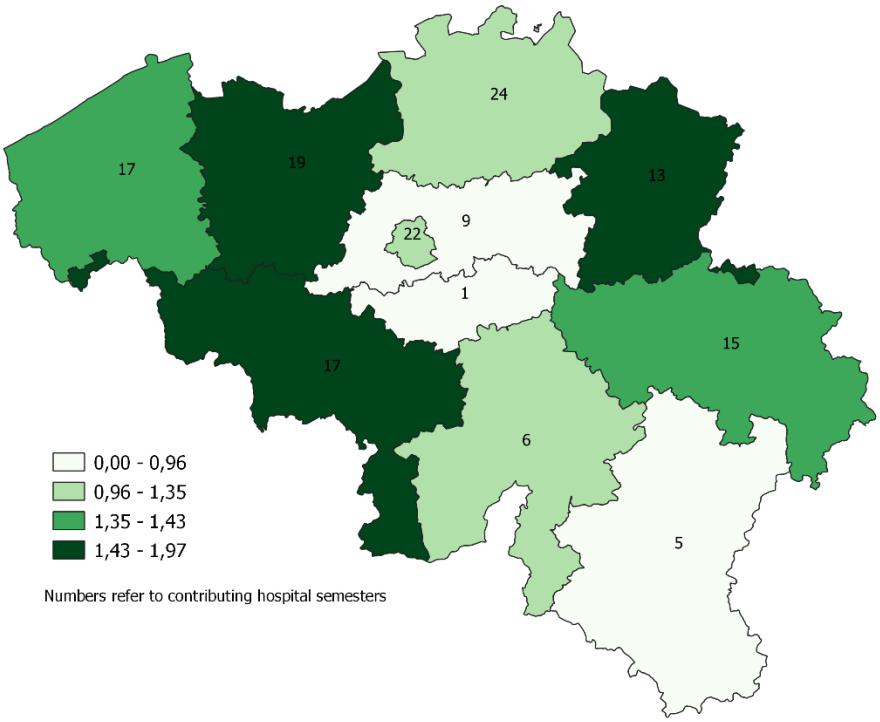


Figure 3: Mean incidence of HA-CDI/10,000 hospitalisation-days in acute care hospitals, per province, Belgium, 2021 (HA-CDI, hospital-associated *Clostridioides difficile* infection)

Note: Mean incidence of episodes reported by all acute care hospitals that provided complete data (numerators and denominators) for at least one semester. The number given in each province indicates the number of contributing hospital-semesters. Categories are based on distribution quartiles.

Similarly, we observed a large variability in HA-CDI incidence across the different Belgian hospitals, represented in the funnel plot[12] and box plot on Figure 4 and 5, respectively. In 2021, the mean of the HA-CDI incidences in primary hospitals was lower than in secondary and tertiary hospitals (Figure 5). However, these differences were not significant.

[12] Funnel plots are a graphical aid for hospital comparisons. An estimate of the parameter (here HA-CDI incidence/10,000 hospitalisation-days) is plotted against a measure of its precision (here number of hospitalisation-days). It is a useful display method when denominator sizes vary, indeed, in small hospitals, chances of variation are bigger. Funnel plots also give a visual identification of statistically significant outliers (those falling above or below the 95% and 99.8% confidence intervals), enabling further investigation and data validation.

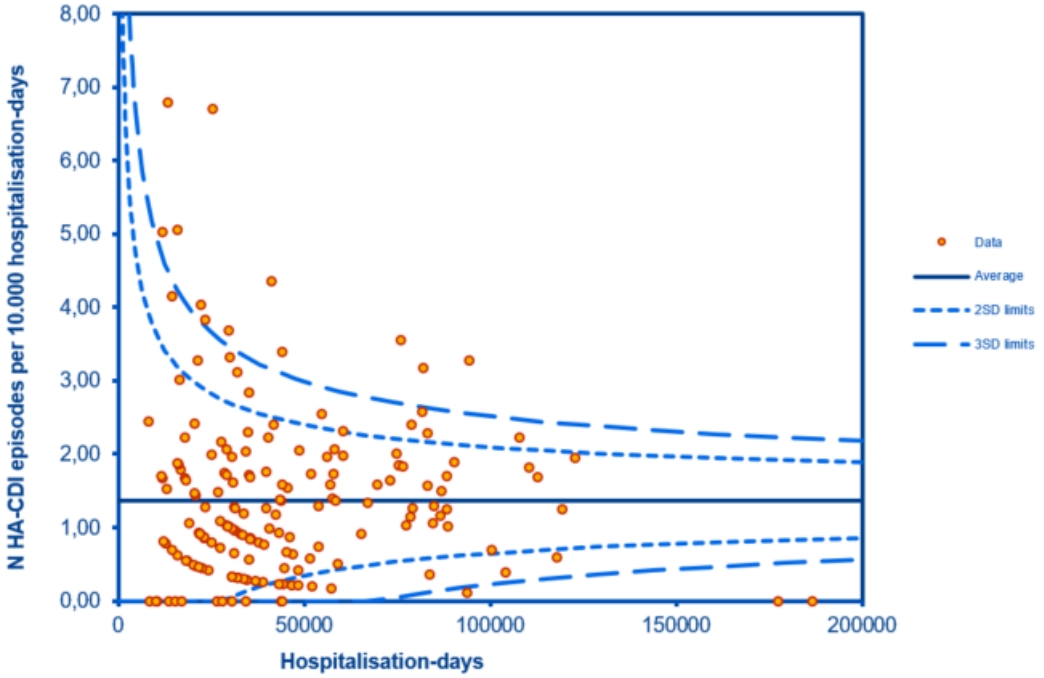


Figure 4: Incidence of HA-CDI per 10,000 hospitalisation-days per hospital-semester, Belgium, 2021 (HA-CDI: hospital-associated *Clostridioides difficile* infection; N: number)

Note: Each dot is the incidence for one hospital/semester plotted against the number of hospitalisation-days in that hospital during the semester. « Average » = mean of all incidences. Dots outside confidence intervals (95% and 99.8%, Poisson distribution) are statistical outliers. SD: standard deviation.

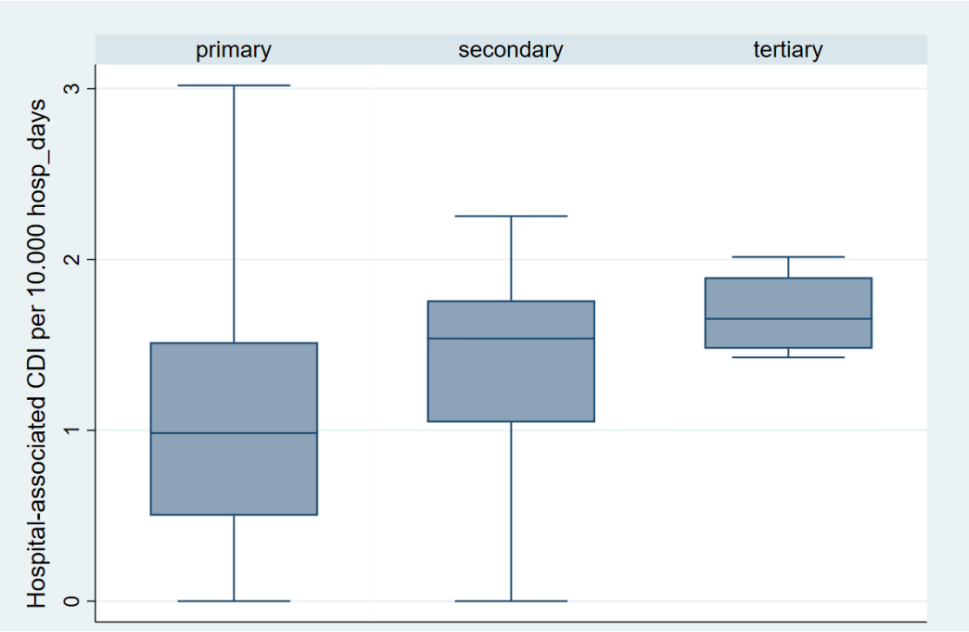


Figure 5: Distribution of HA-CDI per 10,000 hospitalisation-days, Belgium 2021 (CDI: *Clostridioides difficile* infection)

Note: Are included in the analysis 64 primary hospitals, 12 secondary hospitals and 4 tertiary hospitals, according to the classification provided by the Belgian ministry of health (list dated April 2019). Long-term care hospitals and specialised hospitals were excluded. The boxplots display the median (central line) and the 25th and 75th percentiles. The lower and upper whiskers run up to the minimum and maximum values. Outliers are excluded.

NATIONAL REFERENCE LABORATORY DATA

Participation

In 2021, a total of 504 strains were sampled and sent to the NRC in the context of surveillance, belonging to 50 (acute) hospitals (median: 5 strains/hospital/year). A cytopathogenic effect was detected in 456 (95%) of the confirmed strains (belonging to 49 hospitals). Both the number of strains sent and the number of participating hospitals have been constantly decreasing since 2015 (when 81 hospitals sent 1559 strains). To note, some strains sampled in a specific year were only received and typed the following year, so the number of strains sent in the year of the analysis is always slightly underestimated. Around 30 hospitals that participated in the surveillance and entered cases in Healthdata for 2021 did not send any strains to the NRC.

Ribotype distribution

When considering only the first five strains per hospital per semester, the most frequently isolated and widespread strain in 2021 remained, as in previous years, BR014, toxin A-positive and toxin B-positive. It represented 12.2% of the total samples and was found in 46.9% of the hospitals that sent samples to the NRC. Ribotype BR020 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 8.9% of the samples and found in 34.7% of the hospitals (Table 1 and 2). The most BR014 strains where found in Brussels, accounting for more than 5% of all the samples.

Table 1: Distribution of the five most frequently isolated ribotypes (number and %) among total samples of *Clostridioides difficile* typed in 2021 as part of the national surveillance, Belgium 2014-2021 (Brazier classification).

Year	2014		2015		2016		2017		2018		2019		2020		2021	
Total samples	496	*100%*	546	*100%*	470	*100%*	426	*100%*	423	*100%*	395	*100%*	308	*100%*	*246*	*100%*
BR014	74	*14.9%*	66	*12.0%*	63	*13.4%*	62	*14.6%*	54	*12.8%*	56	*14.2%*	49	*15.9%*	30	*12.2%*
BR020	56	*11.3%*	46	*8.4%*	26	*5.5%*	39	*9.2%*	38	*9.0%*	25	*6.3%*	21	*6.8%*	23	*9.3%*
BR078	36	*7.3%*	50	*9.2%*	27	*5.7%*	33	*7.7%*	38	*9.0%*	34	*8.6%*	25	*8.1%*	22	*8.9%*
BR106	15	*3.0%*	20	*3.7%*	20	*4.3%*	21	*4.9%*	20	*4.7%*	23	*5.8%*	20	*6.5%*	21	*8.5%*
BR002	33	*6.7%*	45	*8.2%*	40	*8.5%*	29	*6.8%*	31	*7.3%*	24	*6.0%*	18	*5.8%*	18	*7.3%*

Source: National reference center (NRC). BR: Brazier classification
Note: Are only considered the first five consecutive samples sent by hospital, by semester.

Table 2: Distribution of the five most frequently isolated *Clostridioides difficile* ribotypes (number and %) among hospitals that sent samples to NRC in 2021 as part of the national surveillance, Belgium 2014-2021 (Brazier classification)

Year	2014		2015		2016		2017		2018		2019		2020		2021	
Total Hospitals	87	*100%*	81	*100%*	70	*100%*	72	*100%*	65	*100%*	61	*100%*	48	*100%*	*49*	*100%*
BR014	44	*50.6%*	43	*53.3%*	39	*55.7%*	36	*51.4%*	35	*53.8%*	33	*54.1%*	33	*68.8%*	*23*	*46.9%*
BR078	23	*26.4%*	36	*44.4%*	21	*30.0%*	26	*36.1%*	31	*47.7%*	25	*41.0%*	18	*37.5%*	*18*	*36.7%*
BR106	13	*14.9%*	16	*19.8%*	14	*20.0%*	15	*20.8%*	17	*26.2%*	19	*31.1%*	15	*31.3%*	*17*	*34.7%*
BR020	39	*44.8%*	34	*42.0%*	21	*30.0%*	26	*36.1%*	27	*41.5%*	19	*31.1%*	15	*31.3%*	*17*	*34.7%*
BR002	23	*26.4%*	31	38.3%	27	*38.6%*	25	*34.7%*	24	*36.9%*	18	*29.5%*	14	*23.0%*	*16*	*32.7%*

Source: National reference center (NRC). BR: Brazier classification.
Note: Are only considered the first five consecutive samples sent by hospital, by semester

Out of the 36 CDI episodes that resulted in death, seven strains were sent to the NRC and ribotyped, and for all of them well-known ribotype were identified: BR003 (found twice), BR014, BR015, BR017, BR056 and BR078. From the 147 complicated episodes 19 strains were ribotyped. Four of these strains corresponded to BR078, two corresponded to BR002. Three corresponded to a 'rare' UCL type (ribotyping profile was not recognized by the European Brazier and/or Belgium database). Regarding the 207 recurrent episodes, 28 were typed, 5 belonged to BR078, 3 to BR020, 2 to BR002, 2 to BR005, 2 to BR014, 2 to BR056, 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 2021 can be found in Annex 3 (Table 8).

Antimicrobial susceptibility

To monitor antimicrobial susceptibility, 70 isolates (a representative sample of strains sent in 2021 to the NRC in the context of surveillance), were tested by disk diffusion for moxifloxacin, tetracycline, erythromycin, clindamycin, chloramphenicol and rifampicin suseptibility (CA-SFM 2021 guidelines) and by E-test for metronidazole and vancomycin suseptability (EUCAST V11 guidelines). For the first year, we also evaluated by agar dilution method the sensitivity to fidaxomicin since it has been recently recommended as first-line CDI treatment by the European Society of Clinical Microbiology and Infectious Diseases (12).
All isolates were susceptible to the three antibiotics commonly used for the treatment of CDI : vancomycin (Minimal inhibitory concentration (MIC) ≤2 mg/L), metronidazole (MIC ≤2 mg/L) and fidaxomicin (MIC ≤0.125 mg/L). Compared to 2020 the resistance rates to all antibiotics remained stable. BR078 (8.9% of all *C. difficile* isolates received in 2021), BR012 (2.4%), BR017 (1.5%), BR027 (1.2%) were associated with multiple antimicrobial resistance.

Percentage resistance of *Clostridioides difficile* isolates (n=70, 2021)

Antibiotics	%R
Chloramphenicol	4.29
Clindamycin	94.29
Erythromycin	21.43
Moxifloxacin	11.43
Rifampicin	1.43
Tetracycline	4.29
Fidaxomicin	0.00
Vancomycin	0.00
Metronidazole	0.00

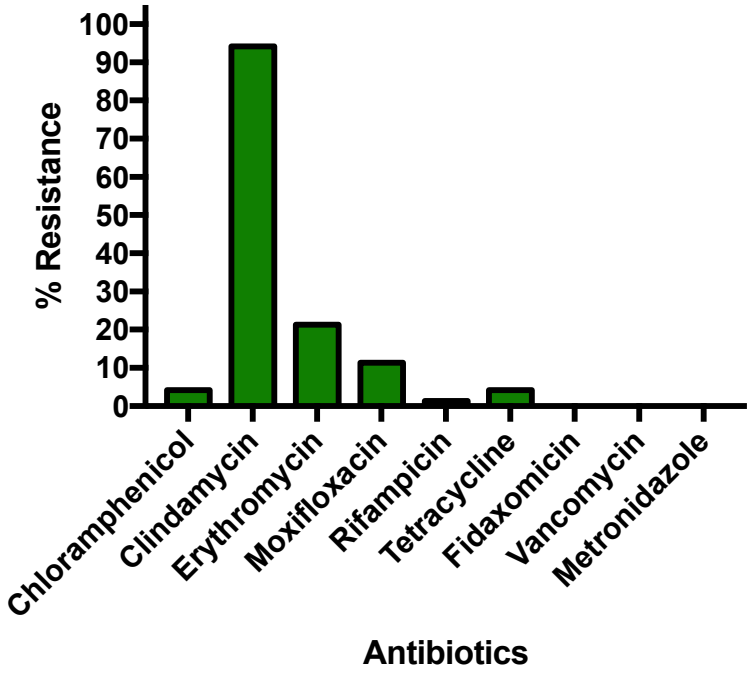


Figure 6: Rates (%) of *Clostridioides difficile* isolates resistant to antibiotics, Belgium 2021.

Source: National reference center (NRC), R: resistance

2. Hospital stays

In 2020 (most recent available data), 3,761 hospital stay records mentioned CDI as primary or secondary diagnostic code. The incidence of total CDI in the hospital was 2.2 per 1,000 admissions and 3.3 per 10,000 hospitalization-days. These numbers are comparable to the previous years. Observed changes since year 2010 are displayed in Figures 7 and 8.

Comparing with data obtained from the national surveillance of CDI in hospitals, 56% of CDI cases identified via hospital stay records in 2020 were reported in the surveillance. For the same year, the incidence of CDI per 10,000 hospitalization-days found in the national surveillance was 24% lower than the incidence found using the hospital stay data, and this difference reached 30% when using admissions as denominator. The gap in reported incidence between these two sources increased compared to the previous years. Since 2019, CDI trends seemed slightly different throughout both sources, as shown in Figure 8. Further details are given in Annex 4, Table 9.

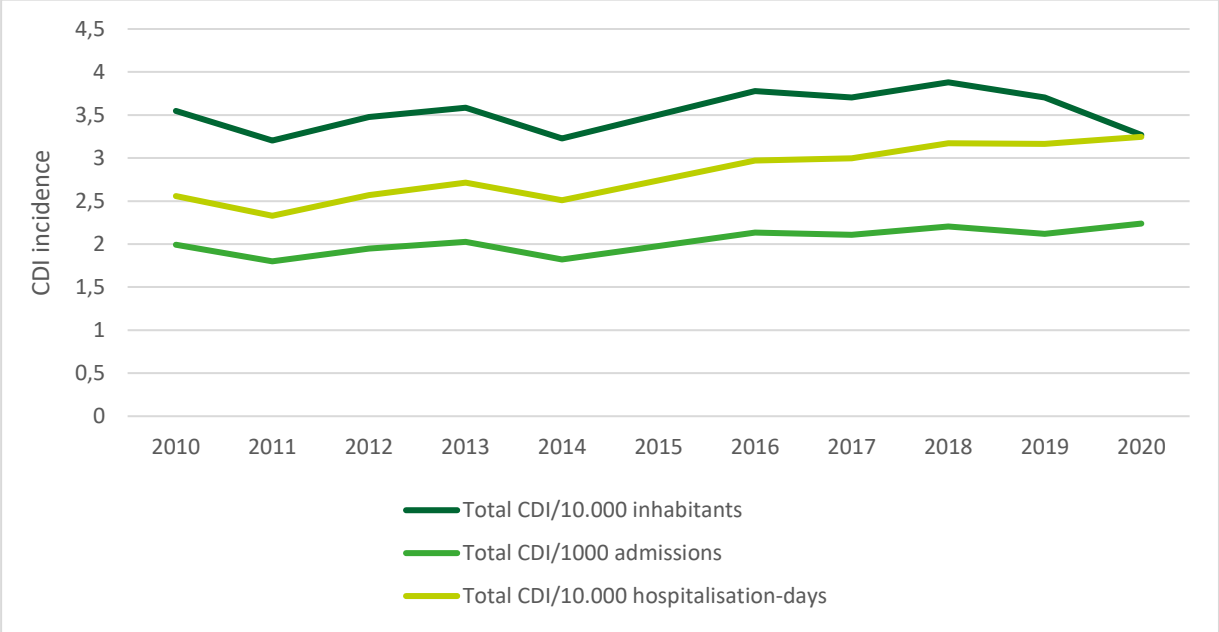


Figure 7: CDI incidence in Belgian hospitals, 2010-2020 (CDI: *Clostridioides difficile* infections; N: Number)

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.*

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 2020, it represented 23.1% of the total stays with a diagnostic code of CDI (Figure 8). Among the total number of CDI cases, the percentage of cases “not present at admission” approached 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.

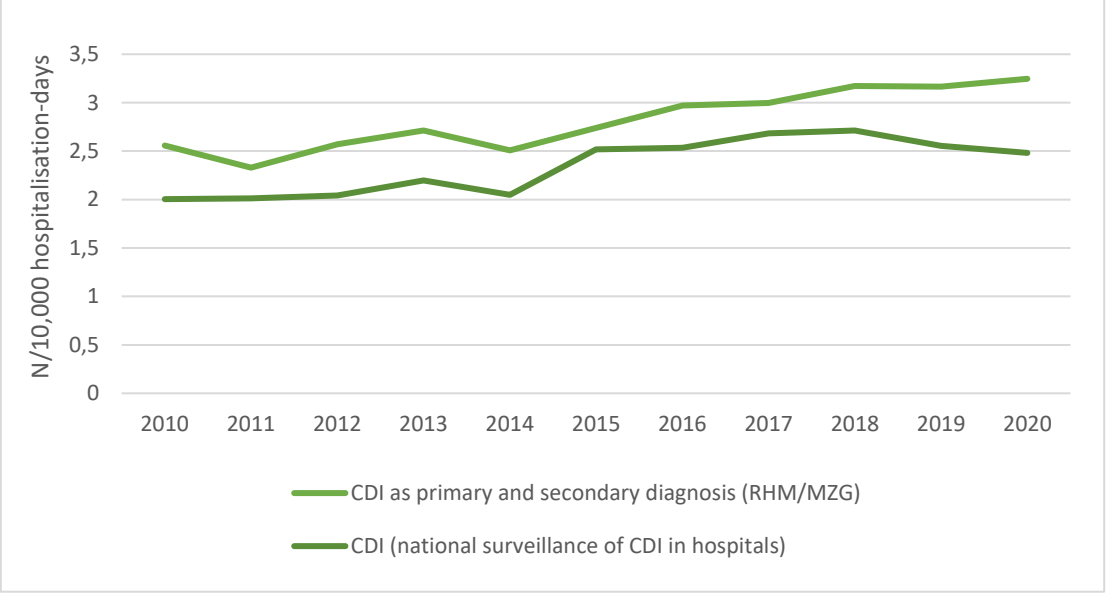


Figure 8: CDI incidence in Belgian hospitals, per 10,000 hospitalization-days, 2010-2020 (CDI: *Clostridioides difficile* infections; N: Number)

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 year 2015. Surveillance data: incidence calculation by including CDI episodes reported by all acute care hospitals that provided complete data (numerators and denominators) for at least one semester/year.*

3. Billing of diagnostic tests

In 2021, there were around 82,306 tests billed for hospitalised patients and around 77,247 tests billed for ambulatory patients in Belgium. Compared with 2020, the total number of tests searching for faecal toxin-producing *C. difficile* billed in Belgium increased (Figure 9). In 2021, we observed a similar increase up to 14.0 tests reimbursed per 1,000 insured Belgian inhabitants. This increase is fully explained by the increase in test among ambulant patients.

In 2020 (most recent data), there were around 25 tests billed for hospitalised patients per CDI diagnosed in hospitals, which has increased compared to the previous years (positivity rate of about 4%). So has the number of tests per 1,000 admissions, approaching 54.8. Detailed data are presented in Annex 5, Table 10.

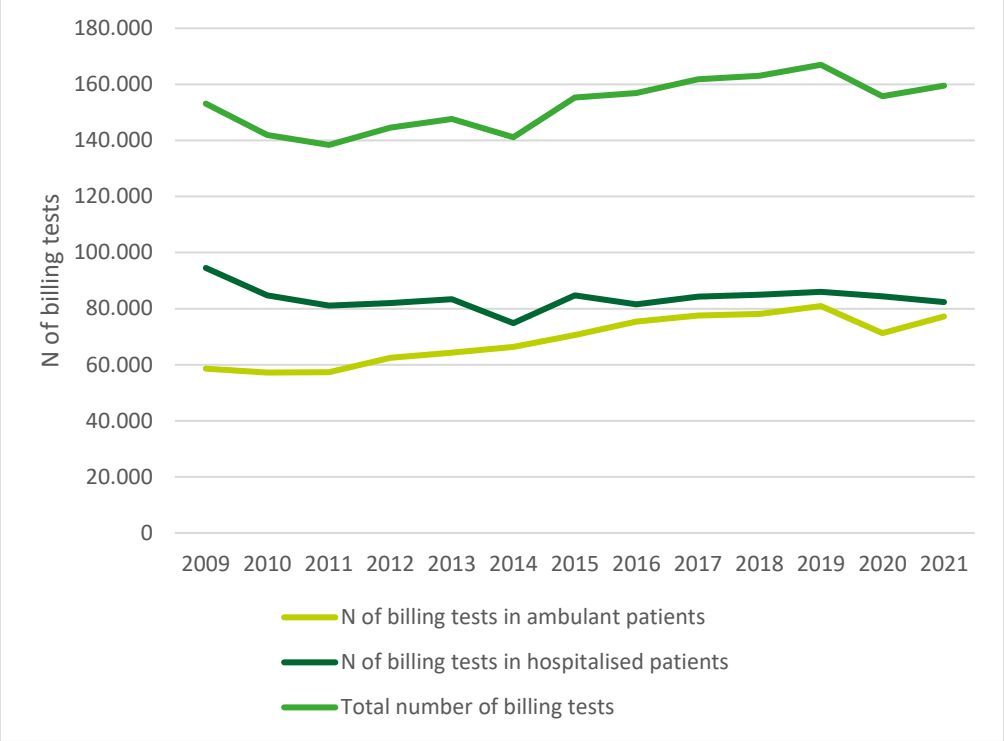


Figure 9: Number of tests billed for *C. difficile* testing in ambulatory and hospitalised patients. Belgium, 2010-2021 (N: Number)

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

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 2019 (most recent available data), 60 recorded deaths. In 2019, the majority of deaths (85%) occurred in people aged 80 years or more, and this proportion seems to be increasing. Crude and adjusted mortality rates were respectively 0.52 and 0.50 deaths/100,000 inhabitants in 2019 (Figure 11). In Brussels, the mortality rate is the highest compared to the other regions (Annex 6, Table 11).

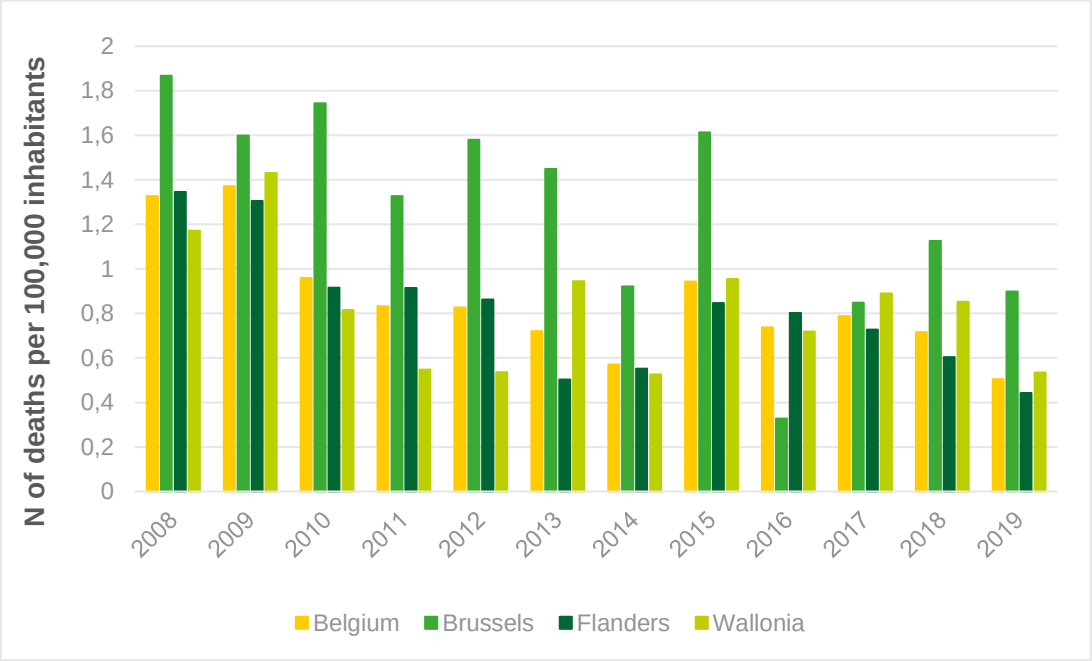


Figure 10: Age-standardised mortality rates, enterocolitis due to *Clostridioides difficile*, by region, Belgium, 2008-2019 (N: Number)

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.

DISCUSSION

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 (81%) and is comparable to 2020 findings. However, this number slightly decreases each year. The number of strains send to the NRC keeps decreasing as well, although, in 2021 five additional hospitals send strains compared to 2020. Still, 32 participating hospitals did not send (maximum) five samples, which is required according to the protocol.

Out of the 45 hospitals that provided information on the algorithm they used for CDI diagnosis, 40 (89%) used multistep algorithms. In total, 29 of these hospitals used ESCMID-recommended algorithms (11).

The main characteristics of CDI cases did not change much in 2021. Between 2010 and 2021, we did not observe a trend in CDI and HA-CDI incidence. Compared to 2019, in 2021, we observed a decrease in the HA-CDI incidence from 1.35 HA-CDI per 10,000 hospitalisation days in 2019 to 1.30 HA-CDI per 10,000 hospitalisation days in 2021. This decrease could be explained by mitigation measures or other aspects present during the SARS-CoV-2 pandemic and should certainly be looked at more closely in report on 2022 data.

CDI incidence, using the hospital stay data, does not substantially change since 2016. These data are comprehensive and therefore allow for a better estimation of the real burden of CDI in Belgium. Hospital stay data could be used to validate data collected through the national surveillance of CDI in hospitals. However, since 2018, differences in CDI incidence using these two sources increased. This discrepancy should be explored further in the future.

In 2019, compared to previous years, the death registry data reported a decline in mortality. It has not been this low in 17 years. New treatments or improved case detection could be involved here. It will be interesting to see the effect on COVID-19 when the mortality data of 2020 is available.

In 2021, compared to 2020, the total number of tests billed increased, however, the number of tests billed in hospitalised patients decreased (lowest since 2014) but the number of tests billed in ambulant patients increase with about 6,000 billed tests. The trend of increase in billed tests in ambulant patients and decrease in billed tests in hospitalised patients started in 2020. This might be caused by a lack of availability of care and by a fear of seeking care related to the COVID-19 pandemic, as well as the increased ease of testing among ambulant patients. It will be interesting to know if we still observe this trend in 2022.

All these findings indicate that the CDI burden in Belgium can and should be still reduced. Certainly when considering that the 70 tested isolates were susceptible to the three most used antibiotics (Figure 6). Hence, stewardship programs, participation in local and national CDI surveillance systems and IPC measures in and outside hospitals should be strengthened.

RECOMMENDATIONS

To policy makers, we recommend the following:

- Continue support the national surveillance of CDI in Belgian hospitals, as a key element in CDI prevention and control. This is also crucial to assess the impact of COVID-19 on HAI, including CDI, and to draw appropriate mitigation measures.
- Continue support researchers in their surveillance tasks.
- Ensure adequate support (structural, educational and financial) to IPC teams and related ICT infrastructure in Belgian hospitals, even more so in the light of the current pandemic.
- Consider extending the CDI surveillance to related mitigation measures like faecal microbial transplantation.
- Continue promoting good quality of care practices in Belgian hospitals, especially focused on IPC and antimicrobial stewardship.
- Mandatory forwarding of those strains isolated from deaths to the reference laboratory for detailed subtyping should be discussed within the working group.

To hospitals, we recommend the following:

- Assess if it still is possible to decrease CDI incidence in their hospital, and if so, implement or improve implementation of appropriate IPC measures.
- Continue or resume registering CDI in the national surveillance program in order to monitor CDI incidence at hospital level as well as contribute to national and international CDI epidemiological surveillance.
- Continue collaboration with the NRC, by ensuring the shipment of five CDI strains / stool samples per semester for confirmation and typing.
- Hospitals should be encouraged to share the individual healthstat feedbacks on their dedicated website,

To researchers of Sciensano involved in the CDI national surveillance program, we recommend the following:

- Validate surveillance data, starting with an in-depth comparison with hospital stay data (RHM/MZG).
- Continue promoting participation in the surveillance, both in terms of hospital recruitment and in terms of data completeness.
- Continue encouraging hospitals to send their strains or stool samples to the NRC.
- Continue improving accessibility and usability of both the data collection and reporting tools, in collaboration with Healthdata.
- Update the current protocol, and try to align it with the ECDC protocol version 2.4.
- Update the CDI working group and organize a meeting in 2023 to discuss previous points.
- Ensure the timely publication of the following report.
- Investigating further the impact of COVID-19 on CDI incidence.
- Investigate further CDI in the community, as well as the role of the environment and food producing animals in the disease (one-health approach).
- Continue trying to extend the surveillance to related mitigation measures like faecal microbial transplantation.

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ANNEXES

1. Hospital contributing data to the national surveillance of CDI

Table 3: Participation of Belgian hospitals in the national surveillance of CDI in hospitals. Belgium, 2010-2021

2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
N hospitals providing cases for at least one semester											
103	103	104	105	104	104	100	99	91	89	89	87
N hospitals providing numerators and denominators for at least one semester											
101	101	102	103	103	101	98	91	89	85	86	82
N hospitals providing cases for the whole year											
81	80	82	84	82	88	83	75	75	71	72	70
N hospitals providing numerators and denominators for the whole year											
78	78	78	81	81	84	82	56	74	66	69	68
Total hospital-semesters providing numerators and denominators											
179	179	180	184	184	185	180	147	163	151	155	150
N hospitals sending CDI strains to the NRC											
NA	43	78	84	88	81	70	72	65	60	45	50
% hospital-semesters with zero case											
4	4	4	5	5	3	5	5	1	3	3	9
N cases per hospital per semester: median											
9	10	11	11	9.5	12	11	11	13.5	12.5	10	10
N cases per hospital per semester: maximum											
67	94	96	83	114	77	79	73	74	84	58	65
Total number of registered cases											
2,451	2,496	2,505	2,664	2,414	2,977	2,804	2,691	2,690	2,515	2,119	2,051

Source: surveillance data.

Note: Including long-term care hospitals.

2. CDI incidences in acute care hospitals, Belgium, 2010-2021

Table 4: Incidence of CDI in acute care hospitals, Belgium, 2010-2021

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Mean incidence, per 1,000 admissions												
Hospital-associated CDI	0.90	0.91	0.91	0.94	0.87	1.02	0.99	0.97	0.97	0.86	0.89	0.80
Total CDI	1.47	1.46	1.51	1.58	1.45	1.72	1.71	1.73	1.75	1.63	1.59	1.47
Mean incidence, per 10,000 hospitalisation-days												
Hospital-associated CDI	1.23	1.26	1.24	1.31	1.23	1.49	1.47	1.50	1.51	1.35	1.40	1.30
Total CDI	2.00	2.01	2.04	2.20	2.05	2.52	2.53	2.68	2.71	2.55	2.50	2.40
N acute care hospitals contributing data												
	95	96	97	98	98	95	92	88	86	83	85	81

Note: All acute care hospitals with complete numerator and denominator data for at least one semester are included in incidence computation. Mean incidence: total registered CDI or HA-CDI episodes for all hospitals and all semesters X 1,000 or 10,000/ total admissions or hospitalisation-days for all corresponding semesters.

Table 5: Mean incidence of HA-CDI/10,000 hospitalisation-days in acute hospitals, per region, Belgium, 2010-2021

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Mean incidence, HA-CDI per 10,000 hospitalisation-days												
Brussels	1.32	1.34	1.19	1.53	1.45	1.54	1.36	1.43	1.52	1.46	1.03	1.26
Flanders	1.18	1.25	1.14	1.12	1.09	1.42	1.30	1.42	1.30	1.14	1.38	1.25
Wallonia	1.29	1.22	1.43	1.54	1.36	1.62	1.85	1.71	1.88	1.69	1.75	1.47
Belgium	1.23	1.26	1.24	1.31	1.23	1.49	1.47	1.50	1.51	1.35	1.40	1.30
N acute care hospitals contributing data												
Brussels	11	11	11	11	11	12	11	10	12	12	12	11
Flanders	53	51	51	53	53	51	48	47	45	45	47	44
Wallonia	31	34	35	34	34	32	33	31	29	26	26	26
Belgium	95	96	97	98	98	95	92	88	86	83	85	82

Note: All acute care hospitals with complete numerator and denominator data for at least one semester are included in incidence computation. Mean incidence: total registered HA-CDI episodes for all hospitals and all semesters X 10.000/ total hospitalisation-days for all corresponding semesters.

Table 6: Incidence of HA-CDI in acute hospitals. per province. Belgium 2010-2021

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
	Mean incidence. HA-CDI per 10.000 hospitalisation-days											
Antwerp	0.85	1.21	0.88	1.03	0.93	1.50	1.41	1.27	1.01	0.80	0.97	1,02
Walloon Brabant	0.52	0.25	1.12	0.69	0.75	1.04	1.53	1.99	1.02	1.50	2.06	0
Brussels	1.32	1.34	1.19	1.53	1.45	1.54	1.36	1.43	1.52	1.46	1.05	1,26
Hainaut	1.18	1.26	1.49	1.76	1.61	1.67	1.91	1.86	2.18	2.19	1.89	1,97
Limburg	1.46	1.45	0.92	0.95	1.22	1.92	1.63	1.85	2.29	1.76	1.44	1,44
Liège	1.21	1.20	1.49	1.40	1.22	1.59	1.91	1.61	1.26	1.09	1.80	1,41
Luxembourg	1.32	1.29	1.10	1.74	0.72	0.89	1.30	1.76	0.93	0.55	0.74	0,91
Namur	2.02	1.43	1.27	1.28	1.29	1.93	1.73	0.88	2.91	2.44	1.50	1,35
Eastern Flanders	1.25	1.06	1.08	0.95	0.86	0.94	1.18	1.11	1.07	1.33	1.63	1,45
Flemish Brabant	1.09	1.39	1.37	1.13	1.64	0.52	0.75	1.13	0.77	0.80	1.42	0,65
Western Flanders	1.45	1.38	1.55	1.49	1.23	1.78	1.19	1.84	1.39	1.12	1.58	1,40

Note: All acute care hospitals with complete numerator and denominator data for at least one semester are included in incidence computation. Mean incidence: total registered HA-CDI episodes for all hospitals and all semesters X 10.000/ total hospitalisation-days for all corresponding semesters.

3. Ribotyping data

Table 7: Ribotypes isolated in Belgium in more than one hospital. 2021: number of isolates and number of hospitals (UCL new classification)

Ribotype (UCL-new)	Isolates N=246	Hospitals N=49
3	22	18
362	21	17
16	19	17
32	18	16
306	15	13
46	14	12
Rare	13	10
590	8	8
313	7	7
44	7	6
316	6	5
594	6	5
4	5	5
344	5	5
589	5	4
23	5	4
49	4	4
340	4	4
22	6	4
28	5	4
601	4	4
595	3	3
600	3	3
14	3	3
65	2	2
47	2	2
27	2	2
20	2	2
161	2	2
473	2	2
537	2	2

Note: Are only considered the first five consecutive strains per hospital per surveillance period.
Source: NRC. new UCL classification.

Table 8: Mapping between the current (new) Belgian UCL classification. the previous (old) and the European (Brazier) classification of *Clostridioides difficile* ribotypes

New UCL classification(valid from 2019 onwards)	Old UCL classification (valid until 2018 included)	Corresponding BRAZIER classification	New UCL classification (valid from 2019 onwards)	Old UCL classification (valid until 2018 included)	Corresponding BRAZIER classification
288	NA	001	344	23f	015
340	23b	001	469	NA	015
341	23c	001	576	NA	015
343	23e	001	578	NA	015
377	NA	001	617	23f*	015
541	NA	001	342	23d	015*
615	23b*	001	14	NA	017
635	NA	001	82	NA	019
32	NA	002	167	NA	019
283	NA	002	568	NA	019
598	32*	002	306	16a	020
49	NA	003	328	16z	020
521	NA	003	590	16a*	020
493	NA	004	633	NA	020
46	NA	005	4	NA	023
228	NA	005	337	22c	024
397	NA	005	48	NA	026
627	46'	005	208	NA	026
52	NA	006	505	NA	026
310	16e	007	027	NA	027
608	16e*	007	28	NA	029
122	NA	009	95	NA	031
513	NA	009	257	NA	032
36	NA	010	596	257*	032
266	NA	010	209	NA	033
22	NA	011	381	NA	033
413	NA	011	433	NA	034
44	NA	012	587	103*	035
490	NA	012	229	NA	036
531	NA	012	236	NA	036
118	NA	013	169	NA	038
16	NA	014	9	NA	039
316	16L	014	543	NA	039
326	16v	014	431	NA	042
474	NA	014	618	279*	042
589	16*	014	63	NA	043
604	16**	014	427	NA	043
605	16****	014	2	NA	045
609	16L*	014	487	NA	045
610	16L**	014	522	NA	045
262	NA	014*	612	2*	045
325	16u	014*	349	36a	046
23	NA	015	518	NA	046

New UCL classification(valid from 2019 onwards)	Old UCL classification (valid until 2018 included)	Corresponding BRAZIER classification	New UCL classification (valid from 2019 onwards)	Old UCL classification (valid until 2018 included)	Corresponding BRAZIER classification
637	NA	047	112	NA	100
403	NA	049	336	22b	101
35	NA	050	511	NA	101
165	NA	050	595	22a	103
246	NA	051	572	NA	104
26	NA	052	362	48d	106
565	NA	052	399	NA	106
395	NA	053	629	NA	106
437	NA	053	64	NA	107
15	NA	054	198	NA	110
55	NA	056	446	NA	118
600	55a	056	260	NA	119
86	NA	057	478	NA	123
56	NA	062	601	5a	126
379	NA	062	304	12a	127
613	20*	064	356	46d	128
232	NA	067	361	48c	131
47	NA	070	144	NA	137
31	NA	071	504	NA	137
67	NA	073	189	NA	139
141	NA	075	202	NA	139
307	16b	076	636	NA	139
592	16b*	076	245	NA	142
606	16b**	076	384	NA	147
21	NA	077	74	NA	150
195	NA	077	554	NA	150
442	NA	077	252	NA	151
3	NA	078	360	48b	151
300	3a	078	313	16i	154
619	3*	078	630	NA	154
620	3**	078	438	NA	155
33	NA	081	454	NA	155
178	NA	081	179	NA	157
621	33*	081	363	84a	159
548	NA	083	532	NA	159
597	265*	084	272	NA	161
110	NA	085	128	NA	163
369	110a	085	314	16j	169
24	NA	087	243	NA	173
269	NA	088	199	NA	174
290	NA	093	278	NA	174
334	21d	095	323	16s	175
514	NA	096	586	027*	176
57	NA	097	104	NA	181
282	NA	097	585	NA	181*

New UCL classification(valid from 2019 onwards)	Old UCL classification (valid until 2018 included)	Corresponding BRAZIER classification	New UCL classification (valid from 2019 onwards)	Old UCL classification (valid until 2018 included)	Corresponding BRAZIER classification
41	NA	183	302	9a	338
351	41a	186	43	NA	351
393	NA	190	162	NA	353
5	NA	193	392	NA	353
472	NA	203	256	NA	356
308	16c	207	372	NA	361
607	16c*	207	412	NA	361
408	NA	208	624	412*	361
20	NA	216	238	NA	375
319	16o	220	175	NA	411
491	NA	220	65	NA	414*
582	NA	220	382	NA	416
593	16o**	220	495	NA	423
322	16r	220*	161	NA	430
497	NA	234	292	NA	451
296	NA	243	556	NA	475
240	NA	247	287	NA	513
135	NA	248	275	NA	519
50	NA	251	558	NA	533
241	NA	251	545	NA	553
286	NA	251	457	NA	557
594	20a	258	461	NA	558
510	NA	261	383	NA	562
416	NA	262	355	46c	570
210	NA	263	420	NA	570
588	14a	265	536	NA	570
468	NA	273	599	46**	570
137	NA	276	417	NA	598
364	84b	278	473	NA	600
324	NA	282	448	NA	607
299	NA	284*	289	NA	608
507	NA	288	332	21b	629
303	11a	293	466	NA	629
114	NA	295	499	NA	641
489	NA	295	365	85a	668
333	21c	296	498	NA	668
435	NA	297	249	NA	695
626	435*	297	291	NA	695
244	NA	302	631	NA	709
297	NA	314	529	NA	770
51	NA	316	389	NA	808
259	NA	328	577	NA	808
367	100a	328	329	20b	864
368	100b*	328	200	NA	871
574	NA	328	546	NA	876
201	NA	338	374	NA	955

4. Hospital stays data

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Table 9: Number and incidence of enterocolitis due to *C. difficile* in hospital stay data. Comparison with incidence obtained via surveillance data. Belgium 2010-2020

2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
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
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
Incidence of total CDI per 1.000 admissions										
1.99	1.80	1.95	2.03	1.82	NA	2.13	2.11	2.21	2.12	2.24
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
Incidence of total CDI per 1.000 admissions from surveillance data (and % from incidence computed from hospital stay data)										
1.47 (74%)	1.46 (81%)	1.51 (77%)	1.58 (78%)	1.45 (79%)	1.72	1.71 (80%)	1.73 (82%)	1.75 (77%)	1.63 (77%)	1.58 (70%)
Incidence of total CDI per 10.000 hospitalisation-days from surveillance data (and % from incidence computed from hospital stay data)										
2.00 (78%)	2.01 (86%)	2.04 (79%)	2.20 (81%)	2.05 (82%)	2.52	2.53 (85%)	2.68 (90%)	2.71 (86%)	2.55 (80%)	2.48 (76%)
Total cases reported by surveillance (and % from cases reported in hospital stays data)										
2.451 (63%)	2.496 (71%)	2.505 (65%)	2.664 (67%)	2.414 (67%)	2.977	2.804 (66%)	2.691 (64%)	2.690 (61%)	2.515 (59%)	2119 (56%)

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

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5. Billing of diagnostic tests

Table 10: Number of diagnostic tests for *C. difficile* in stool samples billed to social insurance. Belgium 2010-2021

2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
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
N tests per 1.000 admissions											
48.16	45.61	45.65	46.37	41.37	46.47	44.38	45.82	46.02	46.62	54.80	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	NA
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
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

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.

6. Death registry data per region

Table 11: Specific mortality rates. enterocolitis due to *C. difficile*. per region. Belgium 2008-2019

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
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
Brussels	16	14	16	12	15	13	8	15	3	8	10	8
Flanders	75	76	55	56	55	33	37	58	56	52	44	33
Wallonia	36	45	26	18	18	32	18	33	25	31	30	19
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
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
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
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
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
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
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
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

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

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MORE INFORMATION

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