

TECHNICAL DOCUMENT



European Surveillance of *Clostridioides (Clostridium)* *difficile* infections

Surveillance protocol version 2.4

2019

ECDC TECHNICAL DOCUMENT

**European surveillance of *Clostridioides*
(*Clostridium*) *difficile* infections**

Surveillance protocol version 2.4



This technical document is an update of 'European Surveillance of *Clostridium difficile* infections. Surveillance protocol version 2.3'. Data collected according to protocol versions 2.2 and 2.3 are compatible with data collected according to this protocol version. A full list of changes is provided in the section 'Differences between protocol versions 2.3 and 2.4' on page 3.

Each version of the protocol (2.1 — 2.4) resulted from direct consultation at ECDC network meetings and webinars with epidemiologists and microbiologists designated by each EU/EEA Member State; expert consultations, e.g. with consortium members from the ECDC project 'ECDIS-Net' (2009—2013) and 'ECDIS-Net-2' (2013—2015); and presentation of the initial protocol to the ECDC Advisory Forum prior to publication. Annex 3 contains a list of relevant publication dates; ECDC meetings; and all consulted experts, to whom ECDC is extremely grateful. The current protocol (version 2.4) was prepared by Pete Kinross and Carl Suetens.

Addition of optional variables to record structure and process indicators of infection prevention and control. Data collection for these new indicators is recommended from 1 October 2020 onwards, although the ECDC TESSy database can receive, from National Coordinating Competent Bodies, data on these variables collected before that date.

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Contents

Abbreviations	iv
Background	1
Objectives	2
Objectives of CDI surveillance in the EU.....	2
Objectives of this protocol	2
Differences between protocol versions 2.1 and 2.2	2
Differences between protocol versions 2.2 and 2.3	3
Differences between protocol versions 2.3 and 2.4	4
Definitions and inclusion/exclusion criteria.....	5
Acute care hospitals	5
Long-term care facility	5
Healthcare facility	5
Community	5
Wards.....	5
Patient (denominator) data.....	6
Definition of <i>Clostridioides difficile</i> infection (CDI)	6
Case (numerator) data	6
New cases of CDI and recurrent cases of CDI.....	7
CDI case origin.....	8
Data collection: the three options.....	9
Who collects the data?	9
Form H: Hospital-based data.....	10
Definitions.....	10
Form C: Case-based data	15
Definitions.....	15
Form M: Isolate-level data	20
Definitions.....	20
References	23
Annex 1. Specialty code list.....	24
Annex 2. Other hospital variables that must be added at national level before submission to The European Surveillance System	25
Annex 3. Previous protocol versions — development and acknowledgements	26

Figures

Figure 1 Designation of new CDI episodes as a recurrent case and/or a new case, based the date of positive laboratory tests for CDI	7
Figure 2. Designation of CDI cases as healthcare-associated or community-associated based on location and time of onset of symptoms.....	8

Tables

Table 1. Information collected for different CDI surveillance options.....	9
Table 2. Definitions of hospital types	10
Table 3. McCabe score categories for classification of underlying medical conditions	16

Abbreviations

AHG	Administrative Hospital Group
ARHAI	Antimicrobial resistance and healthcare-associated infections
ATC	Anatomical Therapeutic Chemical classification system
CA CDI	Community-associated <i>Clostridioides difficile</i> infection
CDI	<i>Clostridioides difficile</i> infection, previously also referred to as <i>Clostridium difficile</i> infection and <i>C. difficile</i> associated diarrhoea (CDAD)
DDD	Defined daily dose
ECDIS-Net	European <i>Clostridium difficile</i> Infection Network project
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
ESGCD	ESCMID Study Group for <i>Clostridioides difficile</i>
EIA	Enzyme immunoassay
GDH	Glutamate dehydrogenase
HA CDI	Healthcare-associated <i>Clostridioides difficile</i> infection
HAI	Healthcare-associated infection
ICU	Intensive care unit
IPC	Infection prevention and control
LTCF	Long-term care facility
MIC	Minimum inhibitory concentration
NAAT	Nucleic acid amplification test
NFP	National Focal Point
NUTS	Nomenclature of Territorial Units for Statistics
PCR	Polymerase chain reaction
SPI	Structure and process indicator
TcdA	<i>Clostridium difficile</i> toxin A
TcdB	<i>Clostridium difficile</i> toxin B
Toxin A/B EIA	Enzyme immunoassay for both toxins A and B
UA CDI	Unknown association CDI
UNK	Unknown

Background

In response to the emerging problems with *Clostridioides (Clostridium) difficile* infections (CDIs), the European Centre for Disease Prevention and Control (ECDC) in collaboration with the US Centers for Disease Control and Prevention (CDC), published background information about the changing epidemiology of CDIs, agreed on CDI case-definitions and issued recommendations for the surveillance of CDIs [1]. An ECDC-funded survey performed in 2008 [2] revealed a mean incidence of 4.1 per 10 000 patient-days per hospital (range: 0.0–36.3), almost 70% higher than that reported in a previous European surveillance study [3] performed in 2005 (2.45 per 10 000 patient-days per hospital, range: 0.13–7.1), although each survey had a different design. Standardised periodic or continuous surveillance of the incidence of CDI is more likely to facilitate the identification of epidemiological changes and is an essential tool for CDI prevention and control [4,5]. Microbiological data supplements surveillance data, allowing further insights into epidemiological changes.

Facing the lack of standardised surveillance of CDI in EU/EEA countries, ECDC launched a call for tender to support capacity building for surveillance of CDIs at the European level in 2010. The contract was awarded to a consortium that carried out the European *Clostridium difficile* Surveillance Network (ECDIS-Net) project from 20 December 2010 to 30 November 2014¹. The ECDIS-Net project developed a protocol for the surveillance of CDI, which was pilot tested in 37 hospitals in 14 countries in 2013 [6]. This protocol (version 2.4) incorporates feedback from countries and hospitals that participated in the pilot survey, feedback from the final meeting of the ECDIS-Net project, as well as discussion with the ESCMID Study Group for *C. difficile* (ESCGD) to obtain information about its draft and final versions of the ESCMID guidelines 'Update of the diagnostic guidance document for *Clostridium difficile* infection' and 'Guidance document for prevention of *Clostridium difficile* infection in acute healthcare settings'.

On 1 January 2016, ECDC started the coordination of surveillance of CDI in acute care hospitals in EU/EEA countries, with data reported to ECDC annually. During a 'start-up wave', EU/EEA countries were encouraged to recruit at least one hospital to participate for at least one month between January and March 2016. At least 20 countries participated in this first phase, with the majority continuing data collection throughout 2016. The CDI surveillance data for 2016 are reported in the ECDC Annual Epidemiological Report [7], available on the ECDC website, including its webpage² dedicated to ECDC CDI activities.

ECDC will coordinate another wave of participation in October–December 2020. In this second phase, countries that do not participate in European CDI surveillance are encouraged to recruit at least one hospital for at least one month; and countries that do participate are encouraged to recruit additional hospitals for at least one month (recommended three months). ECDC is also working with countries with national CDI surveillance that are compatible with this protocol to convert their national dataset into a compatible format for joint analyses. Those seeking further information about options to participate should contact their National Focal Point for Healthcare-Associated Infections in their country³.

¹ Consortium composed of Leiden University Medical Center, the Netherlands (E.J. Kuijper, coordination), University of Leeds and the Health Protection Agency, England, United Kingdom (M. Wilcox), University Hospital of Wales, Cardiff, United Kingdom (V. Hall), Centre for Infectious Disease Control, RIVM, Bilthoven, the Netherlands (D. Notermans), Charité - Universitätsmedizin Berlin, Germany (P. Gastmeier, A. Kola).

² European Centre for Disease Prevention and Control. *Clostridium difficile* infections. URL: <https://ecdc.europa.eu/en/clostridium-difficile-infections>

³ European Centre for Disease Prevention and Control. Information on the Competent Bodies. URL: <https://www.ecdc.europa.eu/en/about-us/governance/competent-bodies>

Objectives

Objectives of CDI surveillance in the EU

The objectives for the surveillance of CDIs are:

- to estimate the incidence of CDIs in European acute care hospitals;
- to assess the burden of CDIs (including recurrent CDI cases) in European acute care hospitals;
- to provide participating hospitals with a standardised tool to measure and monitor their own incidence rates, and to compare incidence rates with those observed in other participating hospitals;
- to assess adverse outcomes of CDIs including death;
- to describe the epidemiology of *C. difficile* at the local, national and European level, in terms of factors such as antibiotic susceptibility, PCR ribotype, presence of *Clostridium difficile* toxin A (TcdA), *Clostridium difficile* toxin B (TcdB) and binary toxin genes, morbidity and mortality of infection, and the detection of new/emerging types;
- to promote use of CDI diagnostic practices that have a high diagnostic accuracy;
- to assess the implementation of structure and process indicators (SPIs) of infection prevention and control (IPC) in European acute care hospitals.

Objectives of this protocol

This protocol prescribes the methodology, and provides the data collection tools required to achieve the objectives of European surveillance of CDIs. This requires national or regional coordinators to choose one of three CDI surveillance options for data collection by data collectors at the hospital level. Each option corresponds to the collection of progressively more detailed information:

- the minimal CDI surveillance option corresponds to collection of only aggregated numerator and denominator data;
- the light surveillance option necessitates collection of case-based numerator data and aggregated denominator data;
- the enhanced surveillance option necessitates collection of microbiological data, i.e. molecular characterisation and antimicrobial susceptibility testing data, for the isolates corresponding to at least the first 5 consecutively detected CDI cases in each healthcare facility (see section 'Data collection').

Data collected using these forms should, in each Member State, be sent to the country institution designated by the country's Coordinating Competent Body¹. These institutions are then requested to upload the data to the European Surveillance System (TESSy) at ECDC, according to the same methodology used for other communicable diseases and related special health issues within Decision 1082/2013/EU², i.e. verifying that patient identifiers are not included and adding information for the variables listed in Annex 2.

Differences between protocol versions 2.1 and 2.2

- Form E has been removed. It was used in the enhanced surveillance option to collect additional case-based data. Its variables have been incorporated into Form C (i.e. for the light surveillance option) and labelled as 'optional' with the exception of 'Ward speciality'.
- On Form C, 'Ward speciality' has been simplified to 12 categories, to match the other ECDC surveillance modules, including the ECDC point prevalence survey of healthcare-associated infections (HAIs) and antimicrobial use in European acute care hospitals (see Annex 1).
- On Form C, 'Consultant/Patient speciality' has been added; the variable contains a larger number of categories than 'Ward speciality' (see Annex 1).
- On Form H, the options for 'Algorithms used for CDI diagnosis' have been updated incorporating the November 2015 update of the ESCMID diagnostic guidance document for CDI [8].
 - In the previous protocol (version 2.1), algorithms were categorised in three categories with decreasing order of expected diagnostic accuracy. The current protocol (version 2.2) only has two groups: 'ESCMID-recommended' and 'Other'.
 - Eight of the original 12 listed diagnostic algorithms are unchanged, including the category 'Other, please specify...'

¹ European Centre for Disease Prevention and Control. Information on the Competent Bodies. <https://www.ecdc.europa.eu/en/about-us/governance/competent-bodies>

² Decision No 1082/2013/EU of the European Parliament and of the Council of 22 October 2013 on serious cross-border threats to health and repealing Decision No 2119/98/EC

- One algorithm has been deleted, i.e. 'Multiple methods for the same stool specimen', as these can be reported within 'Other, please specify...'
- Two algorithms have been amalgamated, resulting in the second algorithm within the category 'ESCMID-recommended', i.e. 'Screening with both GDH and toxin A/B EIA, optional confirmation with NAAT or toxigenic culture'.
- One algorithm is new, listed within the category 'ESCMID-recommended', i.e. 'Screening with GDH EIA, confirmation with toxin A/B EIA, optionally second confirmation with NAAT or toxigenic culture'.
- Other minor language and format edits.

Differences between protocol versions 2.2 and 2.3

- In the section 'Definitions and inclusion/exclusion criteria':
 - Addition of definitions for healthcare facility (particularly the requirement for an overnight stay), community and 'new episode of CDI'.
 - Clarifications to current definitions, including CDI case origin and recurrent cases. In particular, the definition of healthcare-associated CDI now includes explicit text advising inclusion of cases who were discharged from a healthcare facility within the past four weeks and had onset of symptoms on the day of admission or on the following day.
- On Form H:
 - Addition of variables for whether the participating hospital is part of an administrative hospital group (also referred to as 'trusts', 'mergers', 'fusions', 'boards', 'chains', etc.). These match variables used in other ECDC HAI-Net surveillance systems, e.g. the ECDC point prevalence survey (PPS) of HAIs and antimicrobial use in European acute care hospitals.
 - Clarification of definitions of variables, particularly CDI case origin (see changes to 'Definitions and inclusion/exclusion criteria').
 - Addition of the text 'do include cases that have an unknown recurrence status' to the definitions of 'number of healthcare-associated CDI (HA CDI) cases' and 'number of Community-associated CDI (CA CDI) cases and CDI cases of unknown origin'.
 - Clarification of the categories of algorithms for CDI diagnosis that are suitable to align with current ESGCD guidance [8].
- On Form C:
 - Addition of the variable 'Reason for typing'.
 - Addition of a subcategory to 'previous healthcare admission (optional)' to indicate previous admission to both hospitals and long-term care facilities (LTCFs).
 - Removal of the subcategory 'Other healthcare facility with overnight stay' as the 'CDI case origin' for HA CDI because the subcategory is redundant.
 - Clarification of definitions of variables, particularly CDI case origin (see changes to 'Definitions and inclusion/exclusion criteria'). Other clarifications to definitions include 'Ward/unit ID', 'complicated course of CDI' and 'date of discharge/in-hospital death'.
 - The definition of HA CDI now contains a prioritisation algorithm to help data collectors assign the 'origin of the infection' for cases with multiple recent healthcare contacts.
 - Simplification of the variable 'Ward/unit speciality' through provision of a shorter list of specialties (see Annex 1).
- On Form M:
 - The title has been changed from 'isolate shipment data sheet' to 'isolate data sheet'.
 - Minimum participation in the enhanced surveillance option has been reduced to: isolates from 5 consecutive patients per surveillance period per hospital. There is no maximum defined in this protocol. Hospitals that participate in the enhanced surveillance option and have fewer than 5 cases per surveillance period should collect data on all these cases. Protocol version 2.2 requested collection of 10 sequential isolates.
 - Other format edits (e.g. Annex 1) and minor language edits. Addition of references 4–8.
- Other minor language and format edits.

Differences between protocol versions 2.3 and 2.4

- Data collected with protocol versions 2.2 and 2.3 are compatible with data collected with protocol version 2.4.
- Form H and Form C contain five new optional variables, selected with designated representatives of EU/EEA countries at the 'ECDC CDI Network Meeting 2019', Stockholm, Sweden on 22–23 May 2019, from the recommendations of document 'Guidance document for prevention of *Clostridium difficile* infection in acute healthcare settings', from the ESCMID Study Group for *Clostridioides Difficile* (ESGCD) [9].
- In the section 'Definitions and inclusion/exclusion criteria':
 - Clarification of the definitions for cases and recurrent cases.
 - Adaption of definitions such as CDI case origin, to support countries that convert existing national CDI surveillance datasets that predominantly derived from laboratory data.
 - Explicit clarification that the minimum surveillance period is one month, with the recommended minimum remaining at three months.
- On Form H:
 - Addition of a mandatory variable 'Total CDI cases', principally to provide an internal consistency check of the data provided on Form H and Form C.
 - Addition of five (maximum 14) optional variables to record SPIs of IPC, IPC training and antimicrobial consumption, i.e.:
 - The number of single patient rooms (see definition) in the participating hospital, in order to estimate the hospital capacity to isolate patients.
 - The hours of IPC training of hospital staff during the previous calendar year; and the proportion of this IPC training that was specific for CDI.
 - There is strong evidence for the effectiveness of antimicrobial stewardship and reductions in antimicrobial consumption in controlling CDI [9-11]. Therefore, protocol v2.4 includes collection of the number of defined daily doses (DDDs) per 100 patient-days during the previous calendar year, most preferably for fluoroquinolones (Anatomical Therapeutic Chemical Classification System (ATC) J01MA), and also, if possible, for the total 'antibacterials for systemic use' (J01), cephalosporins (J01D), amoxicillin-clavulanic acid (J01CR02, 'co-amoxiclav') and clindamycin (J01FF01). The wording of the definitions in this protocol are purposefully aligned with that in the ECDC ESAC-Net reporting protocol¹ and with that of the WHO Collaborating Centre for Drug Statistics Methodology².
- On Form C:
 - Addition of two new optional variables to record SPIs of IPC for descriptive analyses: use of contact precautions and the start date for treatment.
 - In protocol v2.3, date of onset of CDI symptoms was mandatory for cases with symptom onset during hospitalisation, and not collected for cases with CDI signs/symptoms present on admission. In protocol v2.4, this variable remains mandatory for cases with onset during hospitalisation, but it can now also be collected for cases with signs/symptoms on admission.
- On Form M:
 - Addition of optional variables to record the location of the positive sample, which can be either the location the sample was acquired or analysed. The maximum resolution of analysis by ECDC will be a geographical area corresponding to 800 000 — three million population (i.e. NUTS 1) if this is provided by countries. Otherwise, the resolution of analysis will be 3–7 million population (i.e. NUTS 2). Previously, ECDC provided geographical analysis at national-level resolution, i.e. 460 000 (Malta) — 67 million (France) population.
 - Addition of the variable 'Toxin detection method'.
- Other minor language and format edits.

¹ URL: <https://ecdc.europa.eu/en/antimicrobial-consumption/surveillance-and-disease-data/database>

² URL: https://www.whooc.no/ddd/definition_and_general_considera/

Definitions and inclusion/exclusion criteria

This section provides definitions and inclusion/exclusion criteria for reference. It is recommended that they are read before surveillance activities. The definition of each variable collected using a surveillance form is provided within the section of this protocol dedicated to that particular form.

Acute care hospitals

An objective of this CDI surveillance protocol is to estimate the incidence of CDIs in European acute care hospitals.

An acute care hospital is defined according to national definitions. **All acute care hospitals are eligible for inclusion.** There is no minimum size of hospitals.

Countries can include an acute care hospital in a surveillance period of ECDC CDI surveillance (i.e. at least one month) if denominator data can be provided for that hospital for that same surveillance period.

It is preferable for hospitals with more than one geographical site to report each site that has a separate infection control team/unit separately, if this is feasible. Otherwise, it is sufficient to report for the entire hospital group.

The participation of hospitals in the national surveillance of CDI may be voluntary or mandatory, depending on the country. ECDC acknowledges that acquisition of data from a nationally representative sample of hospitals may currently not be practicable in most EU/EEA countries.

Long-term care facility

A long-term care facility (LTCF) is defined as a facility in which residents need constant supervision (24 hours); need 'high-skilled nursing care' (i.e. more than 'basic' nursing care and assistance for daily living); are medically stable and do not need constant 'specialised medical care' (i.e. administered by specialised physicians); and do not need invasive medical procedures (e.g. ventilation). Examples include, but are not limited to, nursing homes, residential homes and mixed long-term care facilities.

Healthcare facility

For the purposes of establishing 'CDI case origin' and facilitating data collection regarding a 'previous healthcare admission', a healthcare facility is defined as a facility that provides services for patients (or residents) that require an overnight stay, i.e. 'acute and chronic care hospitals and long-term care facilities'.

The following locations should be excluded: outpatient and other ambulatory care centres, hostel care (hotel without any kind of nursing care), sheltered care houses, day centres, home-based centres, protected living or any other healthcare facility where patients (or residents) **do not** stay overnight.

Community

The community is considered to be all locations that are not healthcare facilities as defined above.

Wards

Include all wards in acute care hospitals, including, for example, chronic care and long-term care wards, acute psychiatric wards and neonatal intensive care units (ICUs).

Wards can be excluded if they are for patients who do not have an overnight stay, e.g. day surgery and haemodialysis wards. Accident and emergency departments can be excluded, except for wards attached to accident and emergency departments where patients are monitored for more than 24 hours.

Patient (denominator) data

All hospitalised patients should be included in the denominator, including children age 2 years or less. A patient is considered as hospitalised when they are registered as such in the local hospital administration system and will therefore contribute to the denominator data (number of admissions or discharges, number of patient-days). Usually, this involves at least one overnight stay in the hospital.

A bed-day is a day during which a person is confined to a bed and in which the patient stays overnight in a healthcare facility. Day cases (patients admitted for a medical procedure or surgery in the morning and released before the evening) should be excluded. (Source: <http://stats.oecd.org/glossary/detail.asp?ID=194>)

Definition of *Clostridioides difficile* infection (CDI)

A case of *Clostridioides difficile* infection (CDI) (previously also referred to as *C. difficile* infection or *C. difficile*-associated diarrhoea or CDAD) must meet at least one of the following criteria [1,12]:

- diarrhoeal stools or toxic megacolon AND a positive laboratory assay for *C. difficile* toxin A and/or B in stools or a toxin-producing *C. difficile* organism detected in stool via culture or other means e.g. a positive PCR result;
- OR
- pseudomembranous colitis revealed by lower gastro-intestinal endoscopy¹;
- OR
- colonic histopathology characteristic of *C. difficile* infection (with or without diarrhoea) on a specimen obtained during endoscopy, colectomy or autopsy.

Case (numerator) data

Numerator data are collected for all hospitalised patients that meet the definition of CDI, and meet at least one of the following inclusion criteria.

Inclusion criteria:

- the date of CDI symptom onset was within the surveillance period (even if the patient was admitted before the start of the surveillance period)
- OR
- the patient was admitted to the hospital during the surveillance period with signs and symptoms of CDI present at admission, even if this episode of CDI was already diagnosed prior to admission (e.g. at the outpatient department)
- OR
- recurrent cases of CDI (see definition below).

Exclusion criteria:

- day cases, e.g. one day surgery; patients in the emergency room; dialysis patients (outpatients).

It is recognised that many children are asymptotically colonised with *C. difficile*. Detection of *C. difficile* in children of less than 2 years of age should only lead to the inclusion of these patients as CDI cases in the numerator if there is compelling clinical evidence for CDI.

¹ Microbiological or histopathological confirmation of CDI should be considered in patients with pseudomembranous colitis, as this pathology has other causes (Tang DM. Cleveland Clinic J. Med. 2016; 83:5:361-366).

New cases of CDI and recurrent cases of CDI

ECDC records cases, including recurrent cases; but not repeat positives.

Case of CDI

All cases should meet the case definition for CDI (see page 5). Cases with a positive laboratory test for CDI more than 14 days (two weeks) after the last positive specimen are considered a new case. Therefore, for surveillance purposes, an individual may be classified and captured as a new case if 14 days (two weeks) weeks have elapsed since their last *C. difficile*-positive test (Figure 1). If a case has had a previous episode of CDI and there are data on symptoms available, there should be evidence of clear improvement of symptoms, either after completion of initial treatment, or within a week of CDI symptom onset if no treatment for CDI was given.

Recurrent cases

CDI cases with a positive *C. difficile* stool specimen between two to eight weeks of the last positive specimen are considered recurrent cases (Figure 1). In clinical practice, it is not possible to differentiate between a relapse involving the same strain and re-infection with a different strain. The term 'recurrence' is used as a designation for both.

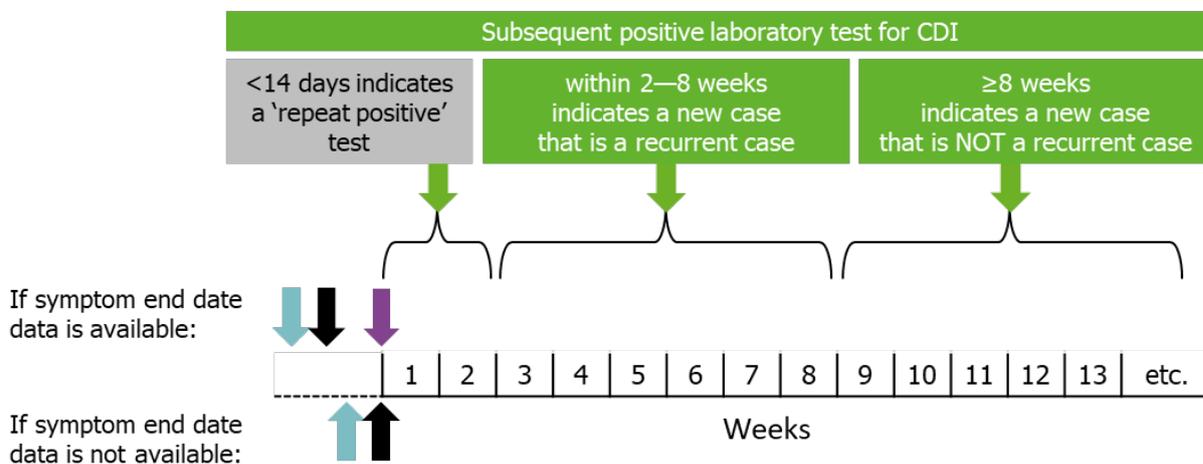
Repeat positives

CDI cases with a positive *C. difficile* stool specimen less than 14 days since the last positive specimen are considered duplicate episodes, and are not reported as separate cases (Figure 1).

Figure 1. Designation of new CDI episodes as a recurrent case and/or a new case, based the date of positive laboratory tests for CDI

Key:

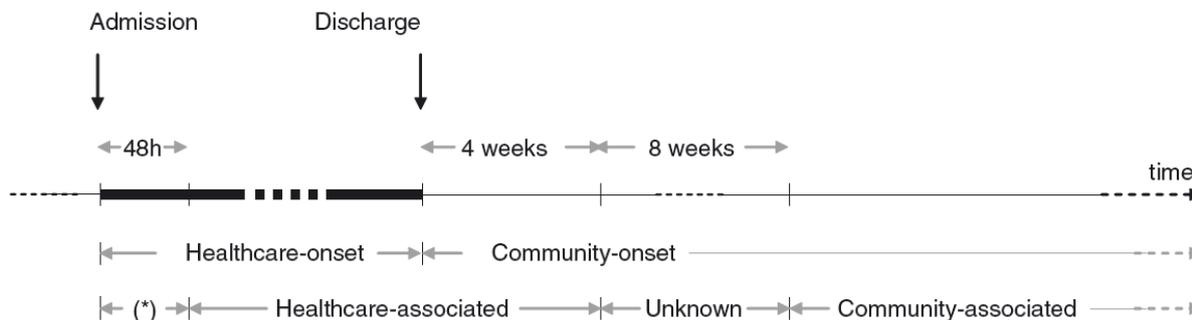
-  CDI symptom onset date
-  First positive laboratory test for CDI
-  Symptom end date
-  Subsequent positive laboratory test for CDI



CDI case origin

The origin of a CDI case can be healthcare-associated, community-associated or unknown, based on the date and location of the onset of CDI symptoms (Figure 2). If information on the date of onset is unavailable, then the date of the first positive sample can be used as a proxy.

Figure 2. Designation of CDI cases as healthcare-associated or community-associated based on location and time of onset of symptoms



48h — In practice, for this protocol, '48h' is interpreted as on the day of admission or on the following day; * — may be community-associated, healthcare-associated or have an unknown association, depending on the case's history.

Source: Figure from Kuijper EJ, Coignard B, Tull P, ESCMID Study Group for *Clostridium difficile*, EU Member States, European Centre for Disease Prevention and Control (ECDC). Emergence of *Clostridium difficile*-associated disease in North America and Europe. *Clin Microbiol Infect.* 2006 Oct;12 Suppl 6:2-18. [1].

Healthcare-associated CDI (HA CDI) is defined as a case of CDI with onset of symptoms:

- on day three or later, following admission to a healthcare facility on day one,
OR
- within four weeks of discharge from a healthcare facility (including the current hospital or a previous stay in any other healthcare facility) EITHER in the community OR on the day of admission to a healthcare facility (day 1) or on the following day (day 2).

Community-associated CDI (CA CDI) is defined as a case of CDI with onset of symptoms:

- outside of healthcare facilities
AND without discharge from a healthcare facility within the previous 12 weeks,
OR
- on the day of admission to a healthcare facility or on the following day
AND not resident in a healthcare facility within the previous 12 weeks.

Unknown association CDI (UA CDI) is defined as a case of CDI with onset of symptoms:

- outside of healthcare facilities
AND discharged from a healthcare facility within the previous 4–12 weeks,
OR
- on the day of admission to a healthcare facility (day 1) or on the following day (day 2)
AND resident in a healthcare facility within the previous 4–12 weeks.

Data collection: the three options

Data are collected following either the 'minimal', the 'light' or the 'enhanced' CDI surveillance option. As shown in Table 1, the 'minimal' surveillance option requires collecting information with only Form H, for longer than one month (preferably 3 consecutive months). The 'light' surveillance option requires collecting information with Form H and Form C, and the 'enhanced' surveillance option requires collecting information with Forms H and C as well as Form M.

If a hospital has zero cases within a surveillance period, it should still complete Form H as this form is used to collect valuable denominator data.

Table 1. Information collected for different CDI surveillance options

	Minimal surveillance	Light surveillance	Enhanced surveillance	Form
Collected information	<ul style="list-style-type: none"> • Minimum CDI surveillance for each hospital (aggregated numerator data) • Hospital data for each hospital (aggregated denominator data) 	<ul style="list-style-type: none"> • Minimum CDI surveillance for each hospital (aggregated numerator data) • Hospital data for each hospital (aggregated denominator data) 	<ul style="list-style-type: none"> • Minimum CDI surveillance for each hospital (aggregated numerator data) • Hospital data for each hospital (aggregated denominator data) 	<ul style="list-style-type: none"> • Form H (aggregated numerator and denominator data)
		<ul style="list-style-type: none"> • Information on each CDI case (case-based numerator data) 	<ul style="list-style-type: none"> • Information on each CDI case (case-based numerator data) 	<ul style="list-style-type: none"> • Form C (case-based numerator data)
			<ul style="list-style-type: none"> • Microbiological data (for the first 5 consecutively detected cases in each participating healthcare facility: characterisation, susceptibility testing and typing of each <i>C. difficile</i> isolate) 	<ul style="list-style-type: none"> • Form M (one form for each <i>C. difficile</i> isolate)
Surveillance period	<p>Recommended: continuous surveillance for 12 months, starting on the first* day of the month. The recommended minimum surveillance period is three consecutive months, preferably from 1 October to 31 December, or from 1 January to 31 March. The absolute minimum surveillance period is one month, starting on the first day of the month. *The pilot study demonstrated that completion of Form H is made much easier by starting surveillance on the first day of a month.</p>			

Who collects the data?

The composition of the team responsible for data collection may vary from one hospital to another. It is recommended that hospital infection control personnel as well as the team in charge of the patients are both involved. It is likely that most hospitals using the enhanced surveillance module will acquire microbiological data (Form M) from clinical microbiology laboratory personnel.

Form H: Hospital-based data

This form is used to collect denominator data in the minimal, light and enhanced surveillance options. The minimum requirement for CDI surveillance is completion of Form H alone.

Hospital-based aggregated denominator data are collected for all eligible patients within a participating hospital. Participating hospitals with no case during a surveillance period should still complete Form H as it is used to collect valuable denominator data. One Form H should be filled out for each surveillance period. The recommended minimum surveillance period is three consecutive months, from 1 October to 31 December, or from 1 January to 31 March, with an absolute minimum of one month.

In addition to the denominator data, the following aggregated data are collected for each surveillance period at the hospital level:

- Basic hospital characteristics: hospital type and size, necessary for stratification of incidence rates;
- Aggregated numerator data: together with the denominator data, these data allow the calculation of the incidence of healthcare-associated (and total) CDI in participating hospitals, and therefore correspond to the minimal data set for CDI surveillance. The number of cases reported on this form should correspond to the number of completed case files in the light surveillance option;
- Frequency of testing for CDI and diagnostic tests in use: process indicator of surveillance sensitivity.

If a hospital has several facilities located on different sites, data should be only merged for those sites which are related in terms of infection control.

Definitions

Hospital code (required): hospital identifier/code is assigned by the national/regional CDI surveillance coordinator. Hospital codes should be unique within each surveillance network, and kept constant between the ECDC Antimicrobial Resistance and Healthcare-Associated Infection (ARHAI) surveillance protocols and from one year to the next.

Hospital type (required): designate the hospital as being Primary, Secondary, Tertiary or Specialised, using Table 2 as a guide. If the hospital is 'Specialised', please specify the specialisation (e.g. paediatric hospital, infectious diseases hospital), after having consulted the categories of speciality listed in the Annex 1.

Table 2. Definitions of hospital types

Primary	Few specialities (mainly internal medicine, obstetrics-gynaecology, paediatrics, general surgery or only general practice). Limited laboratory services are available for general, but not for specialised pathological analysis. Often corresponds to a general hospital without teaching function.
Secondary	Often referred to as a 'provincial hospital'. Hospital is highly differentiated by function with five to ten clinical specialities, such as haematology, oncology, nephrology, ICU. Takes some referrals from other (primary) hospitals. Often corresponds to a general hospital with teaching function.
Tertiary	Often referred to as a 'central', 'regional' or 'tertiary-level' hospital. Highly specialised staff and technical equipment (ICU, haematology, transplantation, cardio-thoracic surgery, neurosurgery); specialised imaging units. Clinical services are highly differentiated by function. Provides regional services and regularly takes referrals from other (primary and secondary) hospitals. Often a university hospital or associated with a university.
Specialised	Single clinical specialty, possibly with sub-specialties. Highly specialised staff and technical equipment.

Hospital type. Free text. Include hospital specialty if specialised hospital (e.g. paediatric, infectious diseases, etc.). If possible, please use the specialty codes listed in Annex 1, e.g. PED=Paediatrics.

Hospital is part of administrative hospital group (AHG): Yes/No. The hospital is part of an administrative group of hospitals (AHG, including entities referred to as 'trusts', 'mergers', 'fusions', 'boards', 'chains', etc.).

Data apply to single hospital site or to AHG/trust. If the hospital is part of an AHG, specify if the data in Form H apply to a single hospital (i.e. a hospital with a single address, or a hospital site within an AHG) (S); or to the entire AHG (T).

AHG code. Free text, selected and generated by countries. Unique code/identifier for the AHG. Please ensure that the AHG code/identifier is identical for all hospital sites belonging to that AHG, if applicable. The code should remain identical in different surveillance periods and years. It can be identical to the hospital code if the data apply to the AHG.

AHG type. Primary/Secondary/Tertiary/Specialised (see definition of 'Hospital type' above). If the hospital is part of an AHG, specify the 'hospital type' of the entire AHG. Report the highest level of specialisation for the AHG, e.g. 'TERT' if a group with four sites contains one specialised, one primary, one secondary and one tertiary hospital. Note that the combined services of an AHG may increase the overall level of specialisation, above any one hospital within the AHG, i.e. the combination of clinical specialties provided by primary and/or specialised hospitals may result in the AHG matching the definition of a secondary hospital).

Surveillance period (required for each surveillance period): start and end date for the CDI surveillance period.

Exclusion of Wards/Units (required): All wards/units should be included for the surveillance of CDI. If, despite this recommendation certain wards/units were excluded, it is crucial that the aggregated denominator data are provided for the included wards/units only.

Number of beds (required): number of hospital beds for the current surveillance period. All wards should be included for the surveillance of CDI, exclusion of wards is not allowed.

Number of discharges or admissions (required): number of hospital discharges in the current surveillance period. Use number of admissions if discharges are not available. Do include children age 2 years or less.

Number of patient-days (required): number of hospital patient-days in the current surveillance period. Do include children age 2 years or less.

Number of HA CDI cases (required): number of healthcare-associated CDI cases within the surveillance period (i.e. with onset on day three or later, following admission to a healthcare facility on day one, OR in the community within four weeks of discharge from any healthcare facility). Exclude recurrent cases. Do include cases that have an unknown recurrence status.

Number of CA CDI cases and CDI cases of unknown origin (required): number of community-associated CDI cases and cases of unknown origin within the surveillance period i.e. include cases with onset outside of healthcare facilities, AND without discharge from a healthcare facility within the previous 12 weeks, OR onset on the day of admission to a healthcare facility or on the following day AND not resident in a healthcare facility within the previous 12 weeks, OR a CDI case discharged from a healthcare facility 4–12 weeks before the onset, OR cases for which the origin is unknown. Exclude recurrent cases. Do include cases that have an unknown recurrence status.

Number of recurrent CDI cases (required): number of CDI episodes with onset within two and eight weeks of a previous episode (including recurrent cases that are healthcare-associated, community-associated or have an unknown association).

Total CDI cases (required): this new variable is an internal consistency check. This should be equal to the [Number of HA CDI case] + [Number of CA CDI cases and CDI cases of unknown origin] + [Number of recurrent CDI cases]. The only scenario in which this calculation would not equal the total CDI cases will be for countries that transfer a pre-existing national CDI surveillance dataset that had systematically excluded a subset of CDI cases. In this rare scenario, national teams must communicate this national policy to ECDC.

Number of stool specimens tested for CDI: number of stool specimens tested for CDI within the surveillance period. Each specimen should only be counted once, even if more than one test was performed on that specimen.

Number of stool specimens that tested positive for CDI: number of stools tested for CDI with a positive test result within the surveillance period. Each specimen should only be counted once.

Algorithm used for CDI diagnosis: laboratory test(s) applied on faeces samples to recognise the presence of toxin-producing *C. difficile*, either as a solitary test or as a combination of screening and confirmatory tests. If no algorithms match your algorithm, indicate the algorithm which matches most closely. If multiple algorithms are applied (i.e. depending on work hours or patient categories), please indicate the most frequently applied algorithm(s), that is/are used for more than 80% of the samples tested for *C. difficile*.

Toxin A/B EIA	Enzyme immunoassays, including enzyme-linked immunosorbent assays (ELISA), that test for both toxins A and B in stool samples or cultures.
GDH EIA	Enzyme immunoassays, including enzyme-linked immunosorbent assays (ELISA), that test for both Glutamate dehydrogenase in stool samples or cultures.
NAAT	Nucleic acid amplification tests (e.g. polymerase chain reaction, PCR).
Cytotoxicity assay	Demonstration that stool sample supernatant kills a cell monolayer in the absence of a <i>C. difficile</i> toxin-neutralising antibody.
Toxigenic culture	Demonstration that a <i>C. difficile</i> culture is able to produce toxins in vitro, e.g. by cytotoxicity assays, Toxin A/B EIA or NAAT from colonies.
Toxin detection	Detection of toxins, in stool samples or cultures, e.g. by toxin A/B EIA or cell cytotoxicity assays.

Total number of patient rooms (optional): Total number of rooms that are used for overnight stays for the entire hospital. If not all wards participated in this surveillance activity, only provide this number for the included wards.

Number of single patient rooms (optional): Total number of patient rooms with one single bed, for the entire hospital or the included wards. Please ensure that the number of single patient rooms was collected for the same year and wards (total for hospital OR included wards only) as the total number of patient rooms. Patient rooms with more than one bed that are designated for use as single occupancy as well as isolation rooms (e.g. for IPC purposes) must be included.

Total hours of training of hospital staff for infection prevention and control (IPC) (optional): the total number of hours of training related to IPC that were delivered for people working in this hospital during the previous calendar year, i.e. January to December.

Percentage of IPC training hours that was specific for CDI (optional): For example, if 15 minutes of a five-hour annual training course was dedicated to interventions to prevent and control CDI specifically, then 5% was specific to CDI.

Which of the following persons received education in prevention and control of CDI. Indicate the persons who received IPC training that was specific for CDI. The list is provided on page 2 of Form H.

Defined daily doses (DDDs) per 100 patient-days in the previous calendar year, for selected antimicrobial agents (optional): Provide the DDDs during the previous calendar year (i.e. January–December) for the entire hospital. If it is only possible to provide data for one antimicrobial group, provide this for fluoroquinolones (Anatomical Therapeutic Chemical Classification System (ATC) J01MA). Otherwise, also provide this data for the total ‘antibacterials for systemic use’ (J01), cephalosporins (J01D), amoxicillin-clavulanic acid (J01CR02, ‘co-amoxiclav’) and clindamycin (J01FF01).

A single DDD is defined by the World Health Organization (WHO) for each antimicrobial and route of administration. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. Only one DDD is assigned per ATC code and route of administration (e.g. oral formulation). It does not necessarily reflect the recommended or prescribed daily dose. Application of the ATC/DDD methodology makes it possible to aggregate consumption of different brands of medicines with different pack or content sizes and different strengths into units of measurement of active substances.

For more details on DDDs, see https://www.whocc.no/ddd/definition_and_general_considera/ and <https://ecdc.europa.eu/en/about-us/networks/disease-networks-and-laboratory-networks/esac-net-data>.

For more information about how to calculate the number of patient-days, see section ‘Patient (denominator) data’.



European surveillance of *Clostridioides difficile* infections Form H: Hospital-based data (all types of surveillance)

Hospital code: _____	Hospital type: <input type="checkbox"/> Primary <input type="checkbox"/> Secondary <input type="checkbox"/> Tertiary <input type="checkbox"/> Specialised (please specify: _____)
Hospital is part of administrative hospital group (AHG): <input type="checkbox"/> No <input type="checkbox"/> Yes	
<i>If yes: Data apply to:</i> <input type="checkbox"/> Hospital site only <input type="checkbox"/> All hospitals in AHG	
AHG type: <input type="checkbox"/> Primary <input type="checkbox"/> Secondary <input type="checkbox"/> Tertiary <input type="checkbox"/> Specialised	
Surveillance period: From ___ / ___ / 20___ (dd/mm/yyyy) to ___ / ___ / 20___ (dd/mm/yyyy)	

For the above surveillance period, for this hospital, please specify:

Attribute	Number
No. of beds	
No. of discharges (or admissions)	
No. of patient-days	
No. of HA ^{1,3} CDI cases	
No. of CA ^{2,3} CDI cases or CDI cases of unknown origin	
No. of recurrent CDI cases	
Total No of CDI cases	
No. of stool specimens tested for CDI	
No. of stool specimens that tested positive for CDI	

¹HA: healthcare-associated; ²CA: community-associated; ³recurrent cases excluded

Exclusion of wards/units: No (recommended) Yes (not recommended)

If some wards/units were excluded, specify which wards/units were excluded:

Important: All wards/units should be included. If, despite this recommendation, certain wards/units were excluded, it is crucial that aggregated denominator data are only provided for the included wards/units.

Algorithm used for CDI diagnosis: The diagnostic algorithms below are categorised in decreasing order of expected diagnostic accuracy (maximised sensitivity and specificity). If no algorithm is adequate, indicate the test algorithm which is the closest to the one that you apply. If you apply multiple algorithms, please indicate the most frequently applied algorithm(s), that is/are used for >80% of the samples tested for *C. difficile*.

ESCMID-recommended [8]*:

- Screening with NAAT, confirmation with toxin A/B EIA
- Screening with both GDH and toxin A/B EIA, optional confirmation with NAAT or toxigenic culture
- Screening with GDH EIA, confirmation with toxin A/B EIA, optionally second confirmation with NAAT or toxigenic culture
- Screening with GDH and screening or confirmation with toxin A/B EIA, but no laboratory capacity to confirm with NAAT or toxigenic culture.

Other:

- Screening with GDH, confirmation with NAAT
- Screening with GDH, confirmation with toxigenic culture
- NAAT alone
- Screening with toxin detection, confirmation with NAAT or toxigenic culture
- Toxigenic culture alone
- EIA for toxins alone
- Stool cytotoxicity assay alone
- Confirmation by NAAT of GDH positive, toxin A/B EIA negative isolates
- Other, please specify: _____



European surveillance of *Clostridioides difficile* infections
Form H: Hospital-based data (all types of surveillance)
Page 2 of 2

**Variables on this page are optional
and will be collected from 1 October 2020 onwards**

Hospital capacity to isolate infectious patients

Total number of patient rooms (optional): _____ rooms

Number of single patient rooms (see definition) (optional): _____ rooms

Infection prevention and control (IPC) training in the previous calendar year

Total hours of IPC training for hospital staff (optional): _____ hours

Percentage of IPC training hours that were specific for CDI (optional): _____ %

Which of the following persons received education in reduction of CDI (optional; tick all that apply):

- clinicians,
- nursing staff,
- environmental cleaning staff,
- other support staff,
- patients,
- visitors,
- other (please specify _____)

Antimicrobial consumption during this previous calendar year

Antimicrobial class (ATC code)	N of defined daily doses (DDDs)/100 patient-days
Fluoroquinolones (J01MA; optional, recommended)	
All antibacterials for systemic use (J01; optional)	
Cephalosporins (J01D; optional)	
Amoxicillin-clavulanic acid ('co-amoxiclav', J01CR02; optional)	
Clindamycin (J01FF01; optional)	

*Crobach MJ, Planche T, Eckert C, Barbut F, Terveer EM, Dekkers OM, et al. European Society of Clinical Microbiology and Infectious Diseases: update of the diagnostic guidance document for *Clostridium difficile* infection. Clin Microbiol Infect. 2016 Aug;22 Suppl 4:S63-81 [https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(16\)30025-8/fulltext](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(16)30025-8/fulltext)

Form C: Case-based data

This form is used to collect case-based numerator data in the light and enhanced surveillance options. Numerator data are collected for all hospitalised patients that meet the CDI case definition and inclusion criteria (see above), including both those with symptoms at admission and those who developed symptoms after admission.

Definitions

Hospital code (required): hospital identifier/code is assigned by the national/regional CDI surveillance coordinator. Hospital codes should be unique within each surveillance network and kept constant between ECDC ARHAI surveillance protocols and from one year to the next.

Surveillance period (required): start and end date for the surveillance in the entire hospital. This will be linked with the denominator data.

Patient counter (required): provide an anonymised patient number. In enhanced surveillance, this number should permit linkage of patient data with microbiological typing/susceptibility data and patient data from enhanced surveillance. Patient identifiers must not be used.

Sex: gender of the patient: M (male), F (female).

Age in years: patient age in years; if missing=unknown (UNK). Provide the patient's age in months if the patient is less than 2 years old.

Previous healthcare admission (optional): previous admission to a healthcare facility in the last three months relative to the onset of CDI: Yes/No/Unknown. If yes, was the case admitted (a) to a hospital or another healthcare facility e.g. LTCF, or (b) to both LTCF and hospital, or (c) to other/unspecified type(s) of healthcare facility. Collect these data from electronic records and/or patient notes, and/or by asking the patient.

Date of hospital admission (required): date patient was admitted to the hospital for the current hospitalisation (dd/mm/yyyy).

Ward/unit ID: abbreviated name of hospital ward where the case is located currently; the abbreviated name should be used consistently and should remain the same throughout different surveillance periods/years.

Ward/unit specialty (see code list): Main ward specialty ($\geq 80\%$ of patients requiring this specialty). PED=Paediatrics, NEO=Neonatal, ICU=Intensive care, MED=Medicine, SUR=Surgery, GO=Gynaecology/Obstetrics, GER=Geriatrics, PSY=Psychiatry, RHB=Rehabilitation, LTC=Long-term care, OTH=Other, MIX=Mixed. If fewer than 80%, report 'mixed ward' (MIX). See Annex 1.

Ward/unit name (optional): unique identifier for each ward/unit (abbreviated ward/unit name) within a hospital; should remain unchanged throughout different surveillance periods/years.

Consultant/patient specialty (optional – see code list): please enter the code for the specialty of the physician in charge of the patient; this may differ from the ward/unit specialty. See Annex 1 for the consultant/patient specialty code list.

McCabe score (optional): Classification of the severity of underlying medical conditions. Disregard the influence of an active CDI, i.e. estimate the score the patient had before the infection. Some examples of diseases and their different McCabe score categories are given in Table 3. These examples, in particular those of the second (ultimately fatal) category, are not meant to be exhaustive but rather serve as a guidance tool for the current protocol.

Table 3. McCabe score categories for classification of underlying medical conditions

McCabe score categories	Examples
Rapidly fatal (< one year)	<ul style="list-style-type: none"> End-stage haematological malignancies (unsuitable for transplant, or relapsed), heart failure (EF < 25%) and end-stage liver disease (unsuitable for transplant with recalcitrant ascites, encephalopathy or varices) Multiple organ failure on intensive care unit – APACHE II score > 30, SAPS II score >70 Pulmonary disease with cor pulmonale
Ultimately fatal: (one year to four years)	<ul style="list-style-type: none"> Chronic leukaemia's, myelomas, lymphomas, metastatic carcinoma, end-stage kidney disease (without transplant) Motor neuron disease, multiple sclerosis non-responsive to treatment Alzheimer's/dementia Diabetes requiring amputation or post amputation
Non-fatal (> five years)	<ul style="list-style-type: none"> Diabetes Carcinoma/haematological malignancy with > 80% five-year survival Inflammatory disorders Chronic GI, GU conditions Obstetrics Infections (including HIV, HCV, HBV – unless in above categories) All other diseases

EF: Ejection fraction, GI: Gastrointestinal, GU: Genitourinary, HCV: Hepatitis C virus, HBV: Hepatitis B virus

Symptoms of CDI present at admission (required): Yes/No/Unknown. Patient had CDI symptoms when admitted for this episode.

Date of onset of CDI symptoms: this is mandatory if symptom onset was during current hospitalisation, but not mandatory if signs/symptoms were present on admission. Record the date of the first signs or symptoms of the infection (dd/mm/yyyy). If unknown, record the date treatment was started for this infection or the date the first diagnostic sample was taken, whichever is first. If no treatment or sample, please estimate.

Date of first positive sample (optional): the date on which the first positive diagnostic stool sample was taken for this episode from the patient referred to on this form.

Reason for typing (optional): as the enhanced surveillance option collects data from the first 5 samples during a surveillance period, identify the rationale to type each sample, e.g. for routine surveillance activities; to investigate an outbreak/potential cluster; because it was a severe case; etc.

Recurrent CDI (required): Yes/No/Unknown. Choose yes if the patient had an episode of CDI (return of diarrhoeal stools with a positive laboratory test after the end of treatment) more than two weeks and less than eight weeks following the onset of a previous episode. When reporting recurrent cases, 'symptoms of CDI present at admission' and the 'date of onset of CDI symptoms' should be for this recurrent episode rather than for a previous episode.

CDI case origin (required): Choose one (for detailed definitions, see Definitions section):

- **Healthcare-associated CDI:** a case with onset of symptoms on day three or later, following admission to a healthcare facility on day one, OR within four weeks of discharge from any healthcare facility. The origin of the infection may have been the current hospital or another healthcare facility with overnight stay, e.g. another hospital or a LTCF.
- If the case had CDI on admission (or onset on the day of admission or the day following admission) and exposure to multiple healthcare facilities during the last 4 weeks, if possible use this prioritisation algorithm to associate the CDI to the healthcare facility with the highest risk of transmission/acquisition of *C. difficile*:
 1. Facility where the patient had a possible epidemiological link to another CDI case, e.g. shared a room with CDI patient or hospitalised on a ward with a CDI outbreak (if multiple facilities, select the most recent facility).
 2. If no known possible epidemiological link to another CDI case:
 - i. Facility where the patient received treatment with high-risk antibiotics, e.g. clindamycin, cephalosporins or fluoroquinolones (if multiple facilities, select the most recent one).
 - ii. Facility where the patient received treatment with lower-risk antibiotics, e.g. macrolides, sulphonamides (if multiple facilities, select the most recent one).
 3. If no known antimicrobial treatment: facility where the patient stayed the longest (if multiple facilities with same length of stay in previous month or if length of stay is unknown, select the most recent one).
- **Community-associated CDI:** a case with [onset outside of healthcare facilities, AND without discharge from a healthcare facility within the previous 12 weeks*] OR [onset on the day of admission to a healthcare facility or on the following day AND not resident in a healthcare facility within the previous 12 weeks].*

- **Unknown association:** a case who was discharged from a healthcare facility* 4–12 weeks before symptom onset.

*note: only consider healthcare facility contacts with overnight stay

Complicated course of CDI (optional): Yes/No/Unknown. CDI leading to any of the following:

- admission to a healthcare facility for treatment of community-onset CDI;
- admission to an intensive care unit for treatment of CDI or its complications (e.g. for shock requiring vasopressor therapy);
- surgery (colectomy) for toxic megacolon, perforation or refractory colitis;
- death within 30 days after onset if CDI is either a primary or contributing cause.

Personal protective equipment (PPE) used for this case (optional): indicate whether gloves, gowns and/or disposable aprons were used for this patient. If this information is unknown for this particular patient, indicate the hospital policy practiced during that surveillance period.

Received treatment for CDI (optional): indicate whether this CDI case received treatment for CDI (e.g. empiric or confirmed treatment with antimicrobial agent(s); faecal microbiota transfer; etc.) during this CDI episode, before admission to the current hospital, or during the current hospitalisation.

Start date of (confirmed/empiric) treatment of CDI (optional): start date of specific or empiric treatment for CDI for this CDI episode (dd/mm/yyyy). If antimicrobial treatment started prior to admission (e.g. cases transferred from another healthcare facility), report that treatment start date. If this date is unknown, leave this field blank.

Patient outcome (recommended): status of the patient at hospital discharge or at end of follow-up in the hospital. Two variables record the relationship between death and CDI, as assessed by a physician.

ECDC 3CAT is currently included in all ECDC HAI-Net protocols for healthcare-associated infection incidence surveillance. ECDC WHOCAT was developed in 2017 and compared to other methodologies to assess attributable mortality in an ECDC study in 11 countries (1). WHOCAT is an operationalisation of the World Health Organization categorisation for medical certification of cause of death (2). ECDC recommends collection of WHOCAT, but 3CAT can still be collected.

Patient outcome (ECDC WHOCAT; recommended)

- **Discharged alive:** patient was discharged alive; OR patient was still in the hospital and alive at end of follow-up during this hospital stay.
- **Sole cause:** CDI was the sole cause of death – no other disease or condition causing the death was present (sufficient condition).
- **Part of the causal sequence:** CDI was part of the causal sequence of events that led to death but not sufficient on its own.
- **Contributory cause:** CDI was a contributory cause but not related to the disease or condition causing the death.
- **No contribution:** CDI did not contribute to the death or the contribution was redundant, i.e. the patient would have died anyway.
- **Unknown or not verified:** Contribution of CDI to death of the patient unknown or not verified.

Patient outcome (ECDC 3CAT; optional):

- **Discharged alive:** patient was discharged alive; OR patient was still in the hospital and alive at end of follow-up during this hospital stay.
- **Death, CDI definitely contributed to death:** use this category if a causal link between CDI and death can be demonstrated.
- **Death, CDI possibly contributed to death:** use this category if no causal link between CDI and this case's death can be demonstrated, but it is still plausible that CDI was at least a contributory factor.
- **Death, unrelated to CDI:** use this category if the cause of death can be demonstrated not to be related to CDI.
- **Death, relationship to CDI unknown:** use this category if no evidence of contributory factors to the cause of death is available.
- **Unknown:** unknown patient outcome.

Date of discharge/in-hospital death: date the patient was discharged from the hospital; OR date of end of follow-up if the patient was still hospitalised and alive; OR date of death if patient died during the current hospitalisation. There is no requirement to 'follow up' patients beyond the end of the surveillance period. The 'patient outcome' of these patients meets the definition of 'discharged alive' (see above).

Microbiological data collected for this patient: Yes/No/Unknown. Indicate whether Form M has been completed.



European surveillance of *Clostridioides difficile* infections. Form C: Case-based data (light and enhanced surveillance)

Hospital code: _____

Surveillance period: From ___ / ___ / 20___ (dd/mm/yyyy) **to** ___ / ___ / 20___ (dd/mm/yyyy)

Patient counter: _____

Internal patient code (optional): _____

Sex:

- Male Female

Age in years: ____; age if < 2 years old: ____ months.

Previous healthcare admission in the last 3 months (optional): (tick one)

- Yes No Unknown

If yes, please specify: (tick one)

- Hospital
 Long-term care facility (LTCF)
 LTCF(s) and hospital(s)
 Other/not specified

Date of hospital admission: ___ / ___ / 20___ (dd/mm/yyyy)

Ward/unit ID (optional): _____

Ward/unit speciality (optional; see code list): _____

Ward/unit name (optional): _____

Patient/Consultant speciality (see code list): _____

McCabe score (optional):

- Non-fatal underlying disease (survival at least 5 years)
 Ultimately fatal underlying disease (survival 1–4 years)
 Rapidly fatal underlying disease (survival <1 year)
 Unknown

Symptoms of CDI present at admission:

- Yes No Unknown

Date of onset of CDI symptoms: ___ / ___ / 20___ (dd/mm/yyyy)

Date of first positive sample (optional): ___ / ___ / 20___ (dd/mm/yyyy)

Reason typing requested (optional): (tick one)

- Typing not requested
 Surveillance
 Investigation of outbreak/cluster
 Severe case
 Unknown



European surveillance of *Clostridioides difficile* infections. Form C: Case-based data (light and enhanced surveillance) - continued

Recurrent CDI (positive laboratory tests for CDI in diarrhoeal stools after the end of treatment for CDI occurring > 2 weeks and < 8 weeks following the onset of a previous episode):

- Yes No Unknown

CDI case origin: (tick one)

- Healthcare-associated** (symptom onset on day three or later following admission to a healthcare facility on day one, OR in the community within 4 weeks following discharge from any healthcare facility)

If yes, please specify the origin of the infection: (tick one)

- Current hospital
 Other hospital
 Long-term care facility
 Healthcare-associated, origin of the infection not specified

- Community-associated** (symptom onset [outside of healthcare facilities, AND without discharge from a healthcare facility within the previous 12 weeks], OR [on the day of admission to a healthcare facility or on the following day AND no residence in a healthcare facility within the previous 12 weeks])

- Unknown association** (including cases discharged from a healthcare facility 4–12 weeks before symptom onset)

Complicated course of CDI (optional):

e.g. admission to a healthcare facility for treatment of a community-onset CDI; CDI resulted in e.g. ICU admission, toxic megacolon, surgery or death

- Yes No Unknown

Personal protective equipment (PPE) used for this case (optional; tick all that apply):

- gloves gowns disposable aprons other unknown

Received treatment for CDI (optional; tick one):

- treatment started before current hospitalisation
 treatment started during current hospitalisation
 No treatment
 Unknown

Start date of (confirmed/empiric) treatment of CDI (optional): ___ / ___ / _____(dd/mm/yyyy)

Patient outcome:

ECDC WHOCAT (recommended, tick one):

- Discharged alive
 Sole cause
 Part of the causal sequence
 Contributory cause
 No contribution
 Death, relationship to CDI unknown
 Unknown

ECDC 3CAT (optional, tick one):

- Discharged alive
 Death, CDI definitely contributed to death
 Death, CDI possibly contributed to death
 Death, no relation to CDI
 Death, relationship to CDI unknown
 Unknown

Date of hospital discharge/in-hospital death: ___ / ___ / _____(dd/mm/yyyy)

Microbiological data (Form M) collected for this patient:

- Yes No Unknown

Form M: Isolate-level data

This form is only used in the enhanced surveillance option.

If possible, stool samples from a minimum of 5 consecutive patients per hospital with primary or recurrent CDI that tested positive for CDI should be stored at -20°C and cultured for the presence of toxin-producing *C. difficile* using the standard operating procedure for the culture and identification of *C. difficile* (available on request from ECDC), or national or local protocols. Consider storing samples for all CDI cases, in case further diagnostic or typing tests become available at a later date. Culture methods should be carried out under containment level 2 conditions using the principle of 'good laboratory practice', or containment level 3 if Hazard Group 3 organisms are suspected to be in the specimen.

C. difficile isolates should be sent for typing and characterisation to a laboratory designated at the national level by the national coordinator, accompanied by a partially filled Form M. If typing and characterisation is not available at the national level, support from a laboratory in another country should be sought. ECDC can be contacted for suggestions.

Definitions

Network-Id: Unique identifier for each surveillance network within a Member State, selected and generated by the Member State, e.g. for France, different regional networks; this field is combined with the hospital identifier to create a unique hospital code since different networks within one Member State may use the same hospital code. Can be omitted if the hospital identifiers are unique within the reporting Member State.

Hospital code (required): hospital identifier/code assigned by national/regional CDI surveillance coordinator. Hospital codes should be unique within each surveillance network and kept constant between ECDC ARHAI surveillance protocols and from one year to another.

Laboratory code (required): local laboratory identifier/code assigned by national/regional CDI surveillance coordinating centre. For the primary lab responsible for microbiological confirmation of CDI (not the code of the national/reference laboratory). It is recommended to use the same laboratory codes as in EARS-Net.

Patient counter (required): provide an anonymised patient number that will permit linkage of patient data and microbiological typing/susceptibility data, and between patient data from light and enhanced surveillance. Patient identifiers must not be used.

Hospital location (geo-tag) (optional): free text indicating the location where the sample was taken, or otherwise the location that the laboratory test was performed. The maximum geographical resolution in ECDC reports will be NUTS 2 level (corresponding to 800 000–3 million population), or otherwise NUTS 1 (3–7 million population), or otherwise national-level (See: <https://ec.europa.eu/eurostat/web/nuts/background>). Preferably provide a NUTS 2 code.

Type of geotag (optional): the type of Geo-tag data provided in the field 'Geo-tag', e.g. NUTS 2 code, NUTS 1 code, post code, address, latitude/longitude.

Start date of surveillance period (required): start date for the CDI surveillance period in the entire hospital, and should match the 'Surveillance period: From' on Form C.

Sample date (optional): the date on which the first positive diagnostic stool sample was taken from the patient referred to on this form if available. Otherwise, the date the stool sample was taken resulting in the results referred to on this form.

Age in years: patient age in years; if missing=UNK. Provide the patient's age in months if the patient is less than 2 years old.

Typing performed by a national/regional reference laboratory: typing of *C. difficile* isolates performed by a laboratory that provides diagnostic, analytical and advisory services to other laboratories, nationally or sub-nationally.

PCR ribotype of *C. difficile* isolate: *C. difficile* PCR ribotype as determined by conventional gel-electrophoresis or capillary-based PCR ribotyping.

Ribotyping method: Method used to acquire PCR ribotype information, e.g. capillary-based PCR ribotyping; conventional gel-electrophoresis; other, please specify, e.g. whole genome sequencing.

Production of toxins A and/or B: production of toxins A and/or B as determined by PCR of *tcdA* and *tcdB* or by EIA for TcdA and TcdB.

Toxin detection method (optional): laboratory method(s) used to detect toxins A and/or B:

Presence of binary toxin genes: detection of binary toxin (CDT) by NAAT of *cdtA* and *cdtB*

Antimicrobial susceptibility testing performed by the national/regional reference laboratory: Testing of *C. difficile* isolates for their susceptibility to antimicrobial agents performed by a laboratory that provides diagnostic, analytical and advisory services to other laboratories, nationally or sub-nationally.

Antimicrobial susceptibility testing: MIC (minimum inhibitory concentration), test used for the determination of the MIC and interpretation as S, I or R, i.e. susceptible, intermediate or resistant. Please report S, I or R using (in order of preference) EUCAST clinical breakpoints (http://www.eucast.org/clinical_breakpoints/), EUCAST ECOFFs, CLSI or national breakpoints.



European surveillance of *Clostridioides difficile* infections
Form M: Isolate-level data (enhanced surveillance)
(one form for each isolate)

Network-Id: _____ **Hospital code:** _____ **Laboratory code:** _____

Start date of surveillance period: From ___ / ___ / 20___ (dd/mm/yyyy)

Patient counter: _____

Internal patient code (optional): _____

Age in years: ___; age if <2 years old: ___ months

Sample date (optional): ___ / ___ / 20___ (dd/mm/yyyy)

Hospital location (geotag) (optional): _____

Type of geotag (optional): _____

Microbiological results:

Typing performed by the national/regional reference laboratory:

Yes No

PCR ribotype of *C. difficile* isolate: _____

Method used to acquire ribotype:

Capillary-based PCR (i.e. CE PCR)

Gel-based PCR

Other, please specify: _____

Production of toxins A and/or B:

Positive Negative Tests not performed

Toxin A/B detection method (optional):

PCR-based detection of *tcdA* and/or *tcdB*

EIA for TcdA and/or TcdB

Both PCR and EIA

Other

Unknown

Presence of binary toxin genes

Positive Negative Tests not performed

Antimicrobial susceptibility testing performed by the national/regional reference laboratory:

Yes No Tests not performed

Metronidazole MIC: _____ mg/l by (method): _____ SIR: _____

Vancomycin MIC: _____ mg/l by (method): _____ SIR: _____

Moxifloxacin MIC: _____ mg/l by (method): _____ SIR: _____

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Annex 1. Specialty code list

Specialty codes used for hospital specialisation, ward/unit specialty and consultant/patient specialty on Form C.

Categories (ward specialty)	Patient/consultant specialty code	Patient/consultant specialty name
Surgical specialties (SUR)	SURGEN	General surgery
Surgical specialties (SUR)	SURDIG	Digestive tract surgery
Surgical specialties (SUR)	SURORTR	Orthopaedics and surgical traumatology
Surgical specialties (SUR)	SURORTO	Orthopaedics
Surgical specialties (SUR)	SURTR	Traumatology
Surgical specialties (SUR)	SURCV	Cardio surgery and vascular surgery
Surgical specialties (SUR)	SURCARD	Cardio surgery
Surgical specialties (SUR)	SURVASC	Vascular surgery
Surgical specialties (SUR)	SURTHO	Thoracic surgery
Surgical specialties (SUR)	SURNEU	Neurosurgery
Surgical specialties (SUR)	SURPED	Paediatric general surgery
Surgical specialties (SUR)	SURTRANS	Transplantation surgery
Surgical specialties (SUR)	SURONCO	Surgery for cancer
Surgical specialties (SUR)	SURENT	ENT
Surgical specialties (SUR)	SUROPH	Ophthalmology
Surgical specialties (SUR)	SURMAXFAC	Maxillo-facial surgery
Surgical specialties (SUR)	SURSTODEN	Stomatology/Dentistry
Surgical specialties (SUR)	SURBURN	Burns care
Surgical specialties (SUR)	SURURO	Urology
Surgical specialties (SUR)	SURPLAS	Plastic and reconstructive surgery
Surgical specialties (SUR)	SUROTH	Other surgery
Medical specialties (MED)	MEDGEN	General medicine
Medical specialties (MED)	MEDGAST	Gastro-enterology
Medical specialties (MED)	MEDHEP	Hepatology
Medical specialties (MED)	MEDENDO	Endocrinology
Medical specialties (MED)	MEDONCO	Oncology
Medical specialties (MED)	MEDHEMA	Haematology
Medical specialties (MED)	MEDBMT	Bone marrow transplantation (BMT)
Medical specialties (MED)	MEDHEMBMT	Haematology/BMT
Medical specialties (MED)	MEDCARD	Cardiology
Medical specialties (MED)	MEDDERM	Dermatology
Medical specialties (MED)	MEDNEPH	Nephrology
Medical specialties (MED)	MEDNEU	Neurology
Medical specialties (MED)	MEDPNEU	Pneumology
Medical specialties (MED)	MEDRHEU	Rheumatology
Medical specialties (MED)	MEDID	Infectious diseases
Medical specialties (MED)	MEDTR	Medical traumatology
Medical specialties (MED)	MEDOTH	Other medical
Paediatrics (PED)	PEDGEN	Paediatrics general, not specialised
Neonatology (NEO)	PEDNEO	Neonatology (excl. healthy neonates)
Neonatology (NEO)	PEDBAB	Healthy neonates (paediatrics)
Neonatology (NEO)	ICUNEO	Neonatal ICU
Paediatrics (PED)	ICUPED	Paediatric ICU
Intensive Care Medicine (ICU)	ICUMED	Medical ICU
Intensive Care Medicine (ICU)	ICUSUR	Surgical ICU
Intensive Care Medicine (ICU)	ICUMIX	Mixed (polyvalent) ICU, general intensive or critical care
Intensive Care Medicine (ICU)	ICUSPEC	Specialised ICU
Intensive Care Medicine (ICU)	ICUOTH	Other ICU
Gynaecology/Obstetrics (GO)	GOOBS	Obstetrics /maternity
Gynaecology/Obstetrics (GO)	GOGYN	Gynaecology
Gynaecology/Obstetrics (GO)	GOBAB	Healthy neonates (maternity)
Geriatrics (GER)	GER	Geriatrics, care for the elderly
Psychiatrics (PSY)	PSY	Psychiatrics
Rehabilitation (RHB)	RHB	Rehabilitation
Long-term care (LTC)	LTC	Long-term care
OTHER (OTH)	OTH	Others not listed
Mixed (MIX)	MIX	Combination of specialties

Annex 2. Other hospital variables that must be added at national level before submission to The European Surveillance System

RecordId. Unique identifier for each hospital within each network (combination of [NetworkId]+[HospitalId]+[DateStartSurvey]).

RecordType. The record type tells TESSy which protocol and level the data relate to. For CDI surveillance, the record type at hospital level (first level) is 'HAICDI' and 'HAICDI\$INF' for case-level, infection and microbiological information.

RecordTypeVersion. There may be more than one version of a record type.

Subject. Disease to report. For CDI, the subject is 'HAICDI'.

DataSource. One country can have several data sources. This should correspond to the name of the data source as defined in TESSy (e.g. CC-HAI, where 'CC' is a country code). One data source can be used to upload different HAI data (e.g. SSI, ICU and PPS) if the coordinating centre is the same for different surveillance protocols.

ReportingCountry. Country reporting the record. The codes are provided in the TESSy metadata 'coded values'.

DateUsedForStatistics. Start date of the survey in the hospital; this date allows to distinguish repeated surveys for the same institution. Hospitals can upload more than one surveillance period in a single year.

Status. Status of reporting can be NEW/UPDATE or DELETE (deactivate). If set to NEW/UPDATE or left empty, a new record is entered into the database. If set to DELETE, the record with the given RecordId will be deleted from the TESSy database (or, rather, invalidated).

NetworkId. Unique identifier for each surveillance network within a Member State, selected and generated by the Member State, e.g. for UK, EN, NI, SC or WA; for France, different Cclin networks; this field is combined with the hospital identifier to create a unique hospital code since different networks within one Member State may use the same hospital code. Can be omitted if the hospital identifiers are unique within the reporting Member State.

Hospital location (geotag). Region (NUTS 1 code) where the hospital is located; NUTS 1 codes are provided in the TESSy metadata 'coded values'. This variable is optional.

Hospital is part of national representative sample. 'Yes' if the hospital is part of a nationally representative sample. Must be filled in (or at least checked) by the national/regional coordinator.

Annex 3. Previous protocol versions — development and acknowledgements

Draft protocol version 2.1 was sent for consultation to the ECDC National Focal Points (NFPs) for Healthcare-Associated Infections (HAIs) and to the ECDC Advisory Forum, and was published by ECDC on 5 May 2015. ECDC would like to thank the contributing authors: Axel Kola, Michael Behnke, Petra Gastmeier (Charité - Universitätsmedizin Berlin, Germany); Sofie M van Dorp, Ed J Kuijper (Leiden University Medical Center, The Netherlands); and other members of the ECDIS-Net project surveillance working group for contributing to the CDI protocol meetings (Berlin, 27 Feb 2012; Berlin (ECCMID), 27 Apr 2013; Leiden, 22 Jan 2014), organising the pilot surveillance study in 2013 and/or commenting on protocol version 2.1: D Schmid, E Simons, F Allerberger (Austria); J van Broeck, M Delmée (Belgium); V Jindrák (Czech Republic); K EP Olsen (Denmark), A Pavelkovich, M Altmets (Estonia), O Lyytikäinen, S Mentula (Finland), F Barbut, A Collignon, B Coignard, S Vaux, K Chami (France), D Weitzel-Kage (Germany), A Hajdu, A Kurcz, K Borocz, K Antmann, Zs Barna (Hungary), A Ingebretsen, E Lingaas (Norway), D Notermans, S C de Greef, B van Benthem (the Netherlands), H Pituch, P Karpinski (Poland), I S Macovei (Romania), M Drakulovic, M Jovanovic (Serbia), T Åkerlund, J Struwe (Sweden), C Wiuff, J Coia, T Morris, M Wilcox (United Kingdom), Hospital Contact Points of the pilot CDI surveillance study. Declarations of interest were received from the contractors of the ECDIS-Net project, in accordance with ECDC's Independence Policy, and no conflict was identified.

Draft protocol version 2.2 was sent to NFPs for HAIs for comments in October 2015 and published on 17 November 2015. Draft version 2.3 was sent to NFPs for HAIs for comments on 13 October 2016 and published on 21 April 2017. ECDC would like to thank the nationally-designated attendees of the meeting 'Workshop and meeting on epidemiological surveillance of *Clostridium difficile* infections (HAI-Net CDI)' at ECDC on 14 September 2016, for their comments on potential updates to version 2.2 of this protocol: D Schmid (Austria); P Verroens (Belgium); E Dobрева (Bulgaria); A Budimir (Croatia); V Jindrák (Czech Republic); B Kristensen (Denmark); P Märtin (Estonia); O Lyytikäinen (Finland); F L'Héritau (France); F Barbut (France); B Weiss (Germany); F Maechler (Germany); A Hajdu (Hungary); A Elfarsdottir (Iceland); S Hennessy (Ireland); F Fitzpatrick (Ireland); E Ricchizzi (Italy); G Vizujė (Lithuania); M Debacker (Luxembourg); E Scicluna (Malta); E Astrup (Norway); O Kacelnik (Norway); H Pituch (Poland); PA Raposo Assunção Fernandes (Portugal); A Niculcea (Romania); S Litvová (Slovakia); J Kolman (Slovenia); A Asensio (Spain); P Gallego Berciano (Spain); EM Terveer (the Netherlands); EJ Kuijper (the Netherlands); R Hope (United Kingdom); C Wiuff (United Kingdom); M Morgan (United Kingdom).

Draft protocol version 2.4 was sent to NFPs for comments on 5 July and 10 October before publication on the ECDC website. ECDC would like to thank the nationally-designated attendees of the meeting 'ECDC *Clostridium difficile* infections Network Meeting 2019', Stockholm, 22–23 May 2019; and attendees of the 4th and the 20th September 2019 webinars for their comments on potential updates to version 2.3 of this protocol: Aleksander Indra, Samantha Rada, Reinhild Strauss (Austria); Laure Mortgat, Johan Van Broeck (Belgium); Elina Dobрева, Nadezhda Vladimirova (Bulgaria); Joseph Papaparaskevas, Kyriaki Tryfinopoulou (Greece); Nataša Boban, Zrinka Bošnjak (Croatia); Costas Constantinou, Christos Karagiannis (Cyprus); Lucie Bareková, Marcela Krůtová (Czech Republic); Manon Chaine, Sophie Gubbels, Søren Persson (Denmark); Liidia Dotšenko, Piret Mitt (Estonia); Luis Alcalá, Pilar Gallego, Mercedes Marín (Spain); Outi Lyytikäinen, Silja Mentula, Saija Toura (Finland); Frédéric Barbut, Mélanie Colomb-Cotinac (France); Mardjan Arvand, Mardjan Arvand, Friederike Maechler, Alexander Mellmann, Nicole Schmidt (Germany); Gabriella Hajbel-Vékony, Ágnes Hajdu (Hungary); Karen Burns, Tara Mitchell (Ireland); Stefania Iannazzo, Patrizia Spigaglia (Italy); Aistė Mierauskaitė, Matas Rutkauskas (Lithuania); Kate Vulāne, Reinis Zeltmans (Latvia); Karl Galea, Elizabeth Scicluna (Malta); Amoe Baktash, Jeroen Corver, Ed Kuijper, Daan Notermans, Karuna Vendrik (the Netherlands); Kirsten Gravninge, Øyunn Holen, André Ingebretsen (Norway); Jacek Czepiel, Michał Piotrowski (Poland); Filomena Martins, Andrea Santos (Portugal); Roxana Serban, Daniela Tălăpan (Romania); Barbro Mäkitalo, Kristina Rizzardi (Sweden); Uroš Glavan, Sandra Janežič (Slovenia); Martina Jamrichová (Slovakia); David Eyre, Russel Hope, Mark Wilcox (UK-England); Rachel Spiers (UK-Northern Ireland); A-Lan Banks (UK-Scotland); Mari Morgan, Trefot Morris (UK-Wales); Andi Koraqi (Abania); Nijaz Tihic (Bosnia and Herzegovina); Elena Trajkovska Dokic (North Macedonia); Predrag Stojanović (Serbia); Can Hüseyin Hekimoğlu, Belkis Levent (Turkey); Arsim Kurti (Kosovo¹); Sarah Tschudin Sutter (Switzerland); Saara Kotila, Tommi Kärki, Diamantis Plachouras, Carl Suetens, Pete Kinross (ECDC).

¹ This designation is without prejudice to positions on status, and is in line with UNSCR 1244/1999 and the ICJ Opinion on the Kosovo declaration of independence.

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