TECHNICAL DOCUMENT

European surveillance of *Clostridium difficile* infections

Surveillance protocol version 2.2

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This technical document is an update of 'European Surveillance of *Clostridium difficile* infections. Surveillance protocol version 2.1', for which a draft was sent for consultation to the ECDC National Focal Points for Healthcare-Associated Infections and to the ECDC Advisory Forum, and was published by ECDC on 5 May 2015. This updated version was prepared by Pete Kinross and Carl Suetens.

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Abbreviations

APACHE	Acute Physiology and Chronic Health Evaluation
ARHAI	Antimicrobial resistance and healthcare-associated infections
CA CDI	Community-associated *Clostridium difficile* infection
CDI	*Clostridium difficile* infection (previously also referred to as *C. difficile* associated diarrhoea (CDAD)
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
ECDIS-Net	European *Clostridium difficile* Infection Network project
ESGCD	ESCMID Study Group for *Clostridium difficile*
EIA	Enzyme immunoassay
GDH	Glutamate dehydrogenase
HA CDI	Hospital-associated *Clostridium difficile* infection
ICU	Intensive care unit
MIC	Minimum inhibitory concentration
NAAT	Nucleic acid amplification test
PCR	Polymerase chain reaction
TcdA	*Clostridium difficile* toxin A
TcdB	*Clostridium difficile* toxin B
Toxin A/B EIA	Enzyme immunoassay for both toxins A and B
UNK	Unknown

Background

In response to the emerging problems with *Clostridium difficile* infections (CDIs), the European Centre for Disease Prevention and Control (ECDC) in collaboration with the US Centres 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. Microbiological data may be an important supplement to surveillance data and allow further insights into epidemiological changes. However, molecular typing and antimicrobial susceptibility testing of isolates are mainly restricted to outbreaks of *C. difficile* or severe cases of CDI.

Facing the lack of standardised surveillance of CDI in EU Member States, ECDC launched a call for tender to support capacity building for surveillance of *Clostridium difficile* infections 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 2014 [4][i]. The ECDIS-Net project developed a protocol for the surveillance of CDI, which was piloted in 37 hospitals in 14 countries in 2013. The current protocol 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 guideline: update of the diagnostic guidance document for *Clostridium difficile* infection' [5].

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 compare their own 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, morbidity and mortality of infection, and the detection of new/emerging types.

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 surveyors 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
- the enhanced surveillance option necessitates collection of microbiological data, i.e. molecular characterisation and antimicrobial susceptibility testing data, for the isolates corresponding to the first 10 consecutively detected CDI cases in each healthcare facility (see section 'Data collection').

[i] 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), in collaboration with ECDC (C. Suetens, K. Weist, P. Kinross).

Data collected using these forms should, in each Member State, be sent to the country institution designated by the country's Coordinating Competent Body[i]. 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/EU[ii], 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 [5].
  - 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…'
  - 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.

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.

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.

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 practicable. Otherwise, it is sufficient to report for the entire hospital group.

The participation of hospitals to the national surveillance of CDI may be voluntary or mandatory, depending on the country. Representative sampling of hospitals is not required but is recommended.

Wards

Include all wards in acute care facilities, including long-term care wards. Exclusion of wards is not allowed.

[i] European Centre for Disease Prevention and Control. Information on the Competent Bodies. http://ecdc.europa.eu/en/aboutus/Competent%20bodies/Pages/Competent_bodies.aspx

[ii] 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

Long-term care facility

A long-term care facility 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).

Patient (denominator) data

All hospitalised patients should be included in the denominator, including children age two years or less. A patient is considered as hospitalised when he or she is 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.

Definition of *Clostridium difficile* infection (CDI)

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

- 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 endoscopy;

  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 asymptomatically colonised with *C. difficile*. Detection of *C. difficile* in children of less than two 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.

Recurrent CDI cases

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.

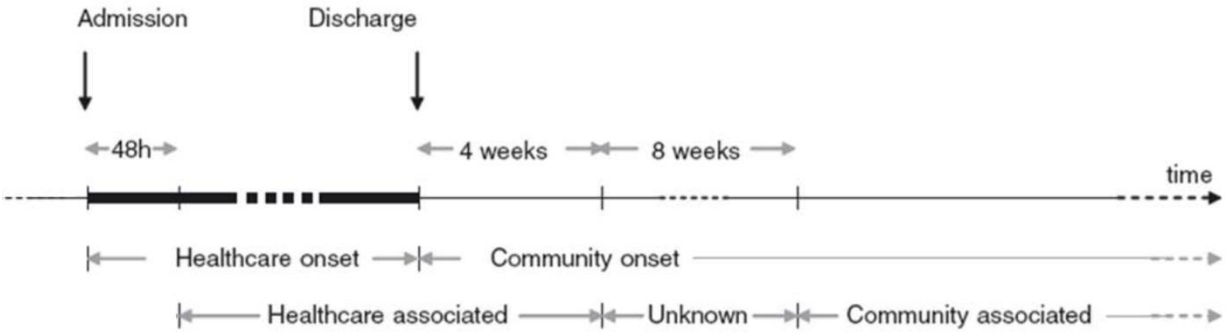
Recurrent CDI cases are patients meeting the CDI case definition with an episode of CDI (return of diarrhoeal stools with a positive laboratory test after the end of treatment) more than two weeks and less than eight weeks following the onset of a previous episode (no matter where that previous episode occurred).

CDI cases with symptom onset more than eight weeks after the onset of a previous episode are included as new CDI cases.

CDI case origin

The origin of a CDI case can be healthcare-associated, community-associated or unknown.

Figure 1. Designation of CDI cases as healthcare-associated or community-associated based on location and time of onset of symptoms.



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
- in the community within four weeks of discharge from a healthcare facility (including the current hospital or a previous stay in any other healthcare facility).

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: the CDI case was discharged from a healthcare facility 4–12 weeks before the onset of symptoms.

Data collection: the three options

Data are collected following either the 'minimal', the 'light' or the 'enhanced' CDI surveillance option. As shown in the table below, the 'minimal' surveillance option requires collecting information with only Form H, 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.

	Minimal surveillance	Light surveillance	Enhanced surveillance	Form
Collected information	• **Minimum CDI surveillance for each hospital** (aggregated numerator data) • **Hospital data for each hospital** (aggregated denominator data)	• **Minimum CDI surveillance for each hospital** (aggregated numerator data) • **Hospital data for each hospital** (aggregated denominator data)	• **Minimum CDI surveillance for each hospital** (aggregated numerator data) • **Hospital data for each hospital** (aggregated denominator data)	• **Form H** (aggregated numerator and denominator data)
		• **Information on each CDI case** (case-based numerator data)	• **Information on each CDI case** (case-based numerator data)	• **Form C** (case-based numerator data)
			• **Microbiological data** (for the first 10 consecutively detected cases in each participating healthcare facility: characterisation, susceptibility testing and typing of each *C. difficile* isolate)	• **Form M** (one form for each *C. difficile* isolate)
Surveillance period	**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. Note that on average, a 300-bed European hospital (with 100% bed occupancy) can expect seven CDI cases every three months, or 28 cases per year, for an incidence of three CDI cases per 10 000 patient-days. **The pilot study demonstrated that completion of Form H is made much easier by starting surveillance on the first day of a month.*			

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. 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.

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 the table below as a guide. If the hospital is 'Specialised', please specify the specialisation (e.g. paediatric hospital, infectious diseases hospital), after having consulted the categories listed in the annex.

Primary	Often referred to as a 'district hospital' or 'first-level referral' hospital.
	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.

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

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. If despite this recommendation certain wards were excluded, it is crucial that the aggregated denominator data are provided for the included wards only.

Number of discharges (or admissions) (required): number of hospital discharges in the current surveillance period, use number of admissions if discharges are not available.

Number of patient-days (required): number of hospital patient-days in the current surveillance period.

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.

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. 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. Exclude recurrent cases.

Number of recurrent CDI cases: number of CDI episodes with onset within two and eight weeks of a previous episode (including both healthcare-associated and community-associated recurrent cases).

Number of stool specimens tested: number of stool specimens tested for CDI in 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 in 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 none of the 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.
- Cytotoxicity assay — Demonstration that stool sample supernatant kills a cell monolayer in the absence of a *C. difficile* toxin-neutralising antibody.
- Toxigenic culture — Demonstration that a *C. difficile* 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.

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

Hospital code: _____

Hospital type:

- ☐ Primary
- ☐ Secondary
- ☐ Tertiary
- ☐ Specialised hospital; (please specify:_____)

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

For the above surveillance period, 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	
No. of stool specimens tested for CDI	
No. of stool specimens that tested positive for CDI	

[1]HA: healthcare-associated; [2]CA: community-associated, [3]recurrent 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 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.

Algorithm used for CDI diagnosis: *The diagnostic algorithms below are categorised in decreasing order of expected diagnostic accuracy (maximised sensitivity and specificity). If none of the algorithms below 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 [5]*:

- ☐ 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

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
- ☐ Other, please specify: _____

* Crobach MJT, Planche T, Eckert C, et al., European Society of Clinical Microbiology and Infectious Diseases: update of the diagnostic guidance document for Clostridium difficile infection, Clin Microbiol Infect. 2015 (In press). Will be available here: https://www.escmid.org/research_projects/study_groups/clostridium_difficile/presentations_publications

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 two years old.

Previous healthcare admission (optional): previous admission in a healthcare facility in the last three months relative to the onset of CDI: Yes/No/Unknown, if yes: Admission in a hospital or another healthcare facility (long-term care, outpatient department, etc.). Collect 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; it should be used consistently and should remain the same in different surveillance periods/years.

Ward/unit specialty (see code list): please enter the code for the main ward specialty; see Annex 1 for the ward specialty code list.

Ward/unit name (optional): unique identifier for each ward/unit (abbreviated ward/unit name) within a hospital; should remain unchanged in 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 below. These examples, in particular those of the second (ultimately fatal) category, are not meant to be exhaustive but rather to serve as a guidance tool for the current protocol.

McCabe score categories	Examples
Rapidly fatal (< one year)	• 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)	• 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)	• 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): patient had CDI symptoms when admitted for this episode, Yes/No/Unknown.

Date of onset of CDI symptoms: this is mandatory if symptom onset was during current hospitalisation, but not recorded 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. 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 from the patient referred to on this form.

Recurrent CDI (required): 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.

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 in the community within four weeks of discharge from any healthcare facility. This may apply to the current hospital or a previous stay in another healthcare facility, e.g. in another hospital, a long-term care facility or other healthcare facilities (e.g. outpatient departments etc.)
- **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

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

- admission to a healthcare facility for treatment of community-associated 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 diagnosis if CDI is either a primary or contributing cause.

Patient outcome (required): status of the patient at hospital discharge or at end of follow-up in the hospital

- **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.

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

European surveillance of *Clostridium 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)**:**

- ☐ Yes
- ☐ No
- ☐ Unknown

If yes, please specify:

- ☐ Hospital
- ☐ Long-term care facility
- ☐ Other

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

Ward/unit ID (optional)**:** _____

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

Ward/unit name (optional)**:**_____

Patient/Consultant specialty (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)

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

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

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:
  - ☐ Current hospital
  - ☐ Other hospital
  - ☐ Long-term care facility
  - ☐ Other healthcare facility (e.g. outpatient)
- ☐ **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-associated CDI; CDI resulted in e.g. ICU admission, toxic megacolon, surgery or death)

- ☐ Yes
- ☐ No
- ☐ Unknown

Patient outcome *(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 shipment data sheet

This form is only used in the enhanced surveillance option.

Stool samples from a maximum of 10 consecutive patients 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. 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 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 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.

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 two 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.

Production of binary toxin genes: production of binary toxin (CDT) as determined by PCR 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 *Clostridium difficile* infections
Form M: Isolate shipment data sheet (enhanced surveillance)
(one form for each isolate)

Network-Id: _____

Hospital code: _____

Laboratory code: _____

Patient counter: _____

Internal patient code (optional)**:** _____

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

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

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

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
- ☐ Gel-based PCR
- ☐ Other, please specify: _____

Production of toxins A and/or B

- ☐ Positive
- ☐ Negative
- ☐ Tests not performed

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. Region (NUTS 1 code) where the hospital is located; NUTS 1 codes are provided in the TESSy metadata 'coded values'.

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.

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