



EUROPEAN SURVEILLANCE OF CLOSTRIDIUM DIFFICILE
INFECTIONS (ECDIS-Net)

Pilot Surveillance Protocol
Version 1.2

May 2013

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Background

In response to the emerging problems with *Clostridium difficile* infections (CDI), a working group of 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 CDI, agreed on CDI case-definitions and issued recommendations for the surveillance of CDI [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) though the surveys 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 in epidemiological changes. However, strain typing and susceptibility testing 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 in 2010 a call for tender to support capacity building for surveillance of *Clostridium difficile* infections at the European level (OJ/2010/07/09-PROC/2010/035). The contract was awarded to the European *Clostridium difficile* Surveillance Network (ECDIS-Net) project [4]¹. As part of the project, ECDIS-Net developed a protocol for the surveillance of CDI, composed of two modules: 1) a “light” protocol, which collects aggregated denominator data and case-based data on CDI cases in hospitals, and 2) an “enhanced” protocol, which collects additional risk factors and detailed microbiological data (typing and susceptibility testing). The current protocol (v1.2) is the pilot version of the CDI surveillance protocol and will be tested for a period of 3 months. In this pilot study, we combine the light version with the enhanced version restricted to a maximum of 10 patients.

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Objectives

The objectives of the surveillance of *C.difficile* infections are:

- to estimate the incidence of *Clostridium difficile* infections in European acute care hospitals
- to assess the total burden of CDI (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 CDI such as complications and death
- to describe the epidemiology of *C. difficile* concerning antibiotic susceptibility, PCR ribotype, presence of TcdA, TcdB and binary toxin and detect new emerging types, at the local, national and European level.

The objectives of the current pilot protocol are:

- to assess the feasibility and workload of the light protocol, both with case-based and aggregated numerator data
- to assess the added value of case-based numerator data (“light” protocol) over aggregated numerator data (“minimal data collection”)
- to assess the feasibility and workload of the enhanced protocol, in particular for the additional epidemiological and microbiological data
- to assess the feasibility and workload of the linkage of microbiological data collected using the enhanced protocol with the epidemiological data collected in the light protocol
- to assess the appropriateness of the different protocol modules to achieve the objectives of the CDI surveillance

Future objectives are to estimate the costs of the study and to harmonize the diagnostics of CDI.

Inclusion / exclusion criteria

Hospitals

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

Wards

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

Patients

All hospitalized patients should be included in the denominator. A patient is considered as hospitalized 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.

- Exclude day cases, e.g.:
 - one day surgery;
 - patients seen at outpatient department;
 - patients in the emergency room;
 - dialysis patients (outpatients).

Sample design

Sampling of patients within the hospital

All eligible patients are included in the surveillance denominator. This will enhance the local usefulness of the results because of the larger sample size (see objectives).

Sampling of hospitals (for coordinating centres only)

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. As for other surveillance modules of healthcare-associated infections (HAI), surveillance of CDI is a tool for prevention and the goal should be to include as many hospitals as possible. In the pilot study, 2 to 3 hospitals for each participating country will be included.

Data Collection

The data collection includes variables at the hospital and the patient level.

In the **light CDI surveillance protocol**, hospital-based aggregated denominator data are collected for each hospital (number of hospital admissions and number of patient-days per hospital). Numerator data are collected for each patient with an active CDI. To test a minimal data collection scenario, numerator data are also aggregated per surveillance period at the hospital level.

In the **enhanced CDI surveillance protocol**, more clinical and epidemiological data will be collected for CDI cases and *C. difficile* isolates will be subjected to molecular characterization and susceptibility testing.

The **enhanced CDI surveillance will** always be performed in addition to the **light CDI surveillance protocol**.

Surveillance periods

In the **light CDI surveillance protocol**, data are collected prospectively and continuously, with a minimum time period of 3 uninterrupted months for each calendar year. In an average European hospital of 300 beds, 7 CDI cases are expected to occur in a period of 3 months (or 26 CDI cases per year) for an incidence of 3 CDI cases per 10 000 patient days. The resulting 95% confidence interval in such a case would be 3 (1.2-6.2) CDI cases per 10 000 patient days. To improve the precision around the incidence estimate at the hospital level and to allow timely detection of outbreaks, continuous surveillance is recommended.

In the **enhanced CDI surveillance protocol**, strains and additional case-based data are collected in March-June and October-December with a maximum of 10 consecutively collected patients with CDI per participating healthcare facility and per 3-months period (or maximum 20 cases per surveillance year). In the duration of the pilot study (3 months, mid-May - mid-August 2013), a maximum of 10 patients per hospital is allowed.

Who will collect 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 involved.

Data processing

The standard scenario will be that data are collected on forms (such as the examples provided in this protocol) and subsequently entered in a computer system after data verification.

For the pilot study, ECDIS-Net will provide a web-based data entry system (webCDI) to the national coordinators (NCs). WebCDI is in English only. The NCs have to register themselves in webCDI. Afterwards they can choose between two data entry modes: light and enhanced surveillance protocol. WebCDI offers the appropriate data entry forms for hospital data and CDI data.

Hospitals should send their completed paper-based surveillance forms to the NCs. The NCs will enter the hospital surveillance data into webCDI. In the pilot study, NCs can delegate the authority to use WebCDI to the local hospital coordinators (HCs). In this case, HCs have to register – please inform ecdis@charite.de how you want to proceed.

If EU-wide surveillance is approved by Member States after the pilot study, data from different hospitals will be appended by the national coordination centres. National centres will then submit the national database to ECDC, using ECDC's TESSy system, after which ECDC reports will be available. In case of EU-wide CDI surveillance after the pilot, ECDC will also provide software support for participating hospitals, probably through a CDI surveillance module in the HelicsWin.Net software developed for the ECDC Point Prevalence Survey of HAI and antimicrobial use.

Overview of collected data

Data collected at the hospital level conform to the following two types of protocol:

Light CDI surveillance protocol:

- Case data (Form C): one form per CDI case (see case definition below).
- Hospital data (Form H): one form per hospital.

Enhanced CDI surveillance protocol

In addition to Form C and H:

- Additional case data (Form E): one form per CDI case and *C. difficile* strain.
- Microbiological data (Form M): strain typing, characterization and susceptibility testing of the isolated *C. difficile* strains.

Pilot study:

In addition to Form C, H, E and M:

- Feasibility of the surveillance protocol (Form F), collected at hospital level.

Case (numerator) data

Numerator data are collected for all eligible hospitalised patients suffering from CDI (both those who already showed symptoms of CDI at admission and those who developed symptoms after admission) according to the following definition:

Definition of *Clostridium difficile* infection (CDI)

A *Clostridium difficile* infection (previously also referred to as *Clostridium difficile* associated diarrhoea, or CDAD) must meet at least one of the following criteria:

- 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;*
- pseudomembranous colitis revealed by lower gastro-intestinal endoscopy;
- colonic histopathology characteristic of *C. difficile* infection (with or without diarrhoea) on a specimen obtained during endoscopy, colectomy or autopsy.

* e.g. by positive PCR result

Note: In general, the detection of *C. difficile* in faces of children under the age of two with diarrhea should not be considered as CDI because many children are asymptotically colonized with *C. difficile*. Such findings in children <2 years old should only lead to the inclusion of these patients as CDI cases in the numerator if there is compelling clinical evidence for CDI.

Include a case of CDI if:

- the date of onset of CDI falls within the surveillance period, even if the patient was already admitted before the start of the surveillance period
- the patient is admitted to the hospital during the surveillance period with signs and symptoms of CDI present at admission
- recurrent cases of CDI should be included if the date of onset of the recurrent episode falls within a period > 2 weeks and ≤ 8 weeks following the onset of a previous episode
- CDI cases with onset later than 8 weeks after the onset of a previous episode are included as new CDI cases

Form C: Case-based data (light protocol)

Form C: Case-based data (light protocol)

Hospital code:

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

Patient counter: _____

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

Sex: M F

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

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

Yes No Unknown

Symptoms of CDI present at admission: Yes No Unknown

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

- CDI origin:
- Healthcare-associated (a case of CDI with onset of symptoms at least 48 h (>48 h) following admission to a healthcare facility or with onset of symptoms in the community within 4 weeks following discharge from a healthcare facility).
 - current hospital
 - other hospital
 - long term care facility
 - other
 - Community-associated (a case of CDI with onset of symptoms while outside a healthcare facility, and without discharge from a healthcare facility within the previous 12 weeks or with onset of symptoms within 48 h following admission to a healthcare facility without residence in a healthcare facility within the previous 12 weeks.
 - Unknown

First or only test used for diagnosis of CD (screening test or single test):

- Toxin EIA
- Toxin PCR
- Toxinogenic culture
- CDI diagnosed by means other than microbiology
- Unknown
- GDH EIA
- GDH PCR
- Cell cytotoxicity test

Confirmation test for diagnosis of CDI (if any):

- Toxin EIA
- Toxinogenic culture
- Unknown
- Toxin PCR
- Cell cytotoxicity test

Enhanced data (Form E) collected for this patient: Yes No Unknown

Enhanced microbiological data (Form M) collected for this patient: Yes No Unknown

Definitions of case-based data

Hospital code. Hospital identifier/code assigned by national/regional ECDIS coordinating centre; unique code per surveillance/ECDIS network. Required.

Surveillance period. Start and end date for the ECDIS in the entire hospital. Required, needed for the link with the denominator data. Include the case if the Date of onset of CDI falls within the surveillance period.

Patient counter. Number: anonymised patient number that allows establishing the link between patient data and microbiological typing/susceptibility data, and between patient data from the light and the enhanced protocol. Not the actual patient identifier. Unique within each hospital. Required.

Age in years. Patient age in years; number; if missing=UNK.

Age in months. Patients age in months if the patient is less than two years old.

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

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

Recurrent CDI. A recurrence can correspond to a relapse involving the same strain or to a reinfection with a different strain. In clinical practice, it is not possible to differentiate between relapse and re-infection. The term recurrence is used as a designation for both. An episode of CDI (return of diarrhoeal stools with a positive laboratory tests after the end of treatment) which falls within a period > 2 weeks and ≤ 8 weeks following the onset of a previous episode should be included as recurrent CDI. CDI cases with onset later than 8 weeks after the onset of a previous episode are included as new CDI cases.

Symptoms of CDI present at admission. Patient already showed symptoms of CDI (see above, definition of CDI) at admission, Yes/No/Unknown. Required.

Date of onset. Date of onset of the infection (dd/mm/yyyy). Not to be recorded if signs/symptoms are present at admission, but mandatory if onset during current hospitalisation. Record the date of first signs or symptoms of the infection; 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.

Note: If clinical signs of *Clostridium difficile* infection appear in 28 days after hospital discharge, CDI must be defined as healthcare-associated infection. Required if onset during current admission.

Origin:

- **Healthcare-associated CDI:** A case of CDI with onset of symptoms at least 48 h (>48 h) following admission to a healthcare facility or with onset of symptoms in the community within 4 weeks following discharge from a healthcare facility. This may apply to the current hospital or a previous stay in a healthcare facility (other hospital, long term care or other healthcare facilities like outpatient departments etc.).
- **Community-associated CDI:** A case of CDI with onset of symptoms while outside a healthcare facility, and without discharge from a healthcare facility within the previous 12 weeks or with onset of symptoms within 48 h following admission to a healthcare facility without residence in a healthcare facility within the previous 12 weeks.
- **Unknown case:** This is a CDI patient who was discharged from a healthcare facility 4–12 weeks before the onset of symptoms.

First or only test used for the diagnosis of CDI (screening or solitary test). First or only test applied on feces samples to diagnose CDI.

- **Toxin EIA:** Enzyme immuno assay for the detection of *C. difficile* TcdA and/or TcdB;
- **GDH EIA:** Enzyme immuno assay for the detection of glutamate dehydrogenase of *C. difficile*;
- **Toxin PCR:** Polymerase chain reaction for the detection of TcdA and/or TcdB genes;
- **GDH-PCR:** Polymerase chain reaction for the detection of glutamate dehydrogenase of *C. difficile*;
- **Toxicogenic culture:** Culture method for the detection of toxin-producing *C. difficile*;
- **Cell cytotoxicity test:** Cell culture cytotoxicity assay for the detection of toxin-producing *C. difficile*;
- **CDI diagnosed by means other than microbiology:** CDI diagnosed by colonoscopy or colonic histopathology;
- **Unknown**

Confirmation test for diagnosis of CDI (if any): Laboratory test applied on feces samples to recognize the presence of toxin producing *C. difficile* as confirmation of the positive screening test.

Enhanced data collected for this patient: Yes/No/UNK. If yes, please fill form E and collect microbiological data for this patient.

Hospital (denominator) data

Hospital-based aggregated denominator data are collected for all eligible patients within a participating hospital. A form (form H) should be filled for each surveillance period. The recommended minimum surveillance period is 3 months.

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, thus allowing minimally risk-adjusted inter-hospital comparison (using reference tables with percentile distributions of CDI incidence rates).
- **Aggregated numerator data:** together with the denominator data, these data allow to calculate 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 protocol.
- **Frequency of testing for CDI:** process indicator of surveillance sensitivity.

Form H: Hospital-based data by surveillance period

Form H: Hospital denominator data

Hospital code: _____

Hospital type: Primary Secondary Tertiary Specialised hospital; **please specify:** _____

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

Specify for surveillance period:

	Number
Number of beds	
Number of discharges/admissions	
Number of patient days	
Number of HA ^{1,3} CDI cases	
Number of CA ^{2,3} CDI cases or CDI cases of unknown origin	
Number of recurrent CDI cases	
Number of patients tested for CDI	
Number of positive tested patients	

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

Exclusion of wards: Yes No

If wards were excluded, which wards:

Important note: All wards should be included for the surveillance of CDI (also for the pilot study), 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!

Definition of aggregated data by hospital

Hospital code. Hospital identifier/code assigned by national/hospital ECDIS-Net coordinator; unique code per surveillance/ECDIS-Net network. Required.

Hospital type:

1 Primary

- Often referred to as 'district hospital' or 'first-level referral'.
- 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 general hospital without teaching function.

2 Secondary

- Often referred to as '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 general hospital with teaching function.

3 Tertiary

- Often referred to as 'central', 'regional' or 'tertiary-level' hospital.
- Highly specialised staff and technical equipment (ICU, haematology, transplantation, cardio-thoracic surgery, neurosurgery).
- Clinical services are highly differentiated by function.
- Specialised imaging units.
- Provides regional services and regularly takes referrals from other (primary and secondary) hospitals.
- Often a university hospital or associated to a university.

4 Specialised hospital

- Single clinical specialty, possibly with sub-specialties.
- Highly specialised staff and technical equipment.
- Specify (e.g. paediatric hospital, infectious diseases hospital), free text.

Required.

Surveillance period. Start and end date for the CDI surveillance period. Required for each surveillance period.

Number of beds. 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. If not available, provide number for entire hospital; specify 'included wards only OR total for hospital' in last column. Required.

Number of discharges/admissions. Number of hospital discharges in the current surveillance period, use number of admissions if discharges are not available; Required.

Number of patient days. Number of hospital patient days in the current surveillance period; Required.

Number of HA-CDI cases. Number of healthcare-associated CDI cases (both with onset during current hospital stay and with signs and symptoms present at admission but developed in association with another healthcare facility) for the surveillance period. Exclude recurrent cases. Required.

Number of CA-CDI cases and CDI cases of unknown origin. Number of community-associated CDI cases and cases of unknown origin (onset of symptoms between 4 and 12 weeks after a previous discharge from a healthcare institution) for the surveillance period. Exclude recurrent cases. Required.

Number of recurrent CDI cases: Number of CDI episodes which fall within a period > 2 weeks and ≤ 8 weeks following the onset of a previous episode (healthcare-associated and community-associated recurrent cases combined).

Number of patients tested. Number of patients tested for CDI in the surveillance period. Each patient should only be counted once.

Number of positive tested patients. Number of patients tested for CDI with a positive test result in the surveillance period. Each patient should only be counted once. Count patients with several negative results and one positive result as positive.

Enhanced protocol

The additional **enhanced protocol** should be implemented for two periods per year (starting in March and October), up to a maximum of 10 consecutive patients with CDI per participating centre. For the current pilot study, data should be collected from mid-May to Mid-August (3 months) with a maximum of 10 patients. Data to be collected in addition to the light protocol are:

- case-based patient data: additional data on risk factors.
- microbiological data from first episodes and recurrent episodes: strain typing and susceptibility testing of the isolated *C. difficile* strains. Therefore, for the pilot study, centers with microbiological facilities experienced with anaerobic culture of *C. difficile* are privileged for participation in the enhanced module. Alternatively, for a limited number of centers, *C. difficile* positive stool samples can be stored (4°C) and subsequently provided to the national reference centre for culturing and typing. Every strain identified, characterized and ribotyped by the national coordinator/reference lab should be sent to the Leiden University Medical Center (UMC) for repeated ribotyping (quality control).

Form E: Case-based data enhanced protocol

(to be combined with Form C of the light protocol)

Form E: Additional case-based data enhanced protocol (to be combined with form C)

Hospital code: _____ Patient counter: _____

Ward (Unit) ID: _____ Ward specialty (see code list): _____

Previous healthcare admission in the last 3 months: Yes No Unknown
If yes: Hospital other

Antibiotic treatment in the last 3 months: Yes No Unknown
If yes: One course Multiple courses

Physical status (McCabe Score): Non-fatal underlying disease (survival at least 5 years)
 Ultimately fatal underlying disease (1-4 years)
 Rapidly fatal underlying disease (less than 1 year)
 Unknown

Comorbidity:

- 1) Did the patient have liver cirrhosis? Yes No Unknown
- 2) Did the patient have NYHA class IV heart failure or angina when the stool sample was collected?
 Yes No Unknown
- 3) Did the patient have pulmonary disease as defined in the chronic health points score of APACHE II?
 Yes No Unknown
- 4) Did the patient receive chronic dialysis? Yes No Unknown

Immunocompromised status:

Was the patient immunocompromised as defined in the chronic health points score of APACHE II?
 Yes No Unknown

Complicated course of CDI: Yes No Unknown

Mortality: Did the patient die during the current admission?
 Yes, death related to CDI
 Yes, death unrelated to CDI
 Yes, relationship to CDI unknown
 No death

Date of hospital discharge/death (dd/mm/yyyy): ____ / ____ / _____

Definitions of enhanced case data

Hospital code. Hospital identifier/code assigned by national/regional ECDIS coordinating centre; unique code per surveillance/ECDIS network. Required.

Patient counter. Number: anonymised patient number that allows establishing the link between patient data and microbiological typing/susceptibility data, and between patient data from the light and the enhanced protocol. Not the actual patient identifier. Unique within each hospital. Required.

Ward (Unit) ID: Abbreviated name of hospital ward; should be used consistently and should remain the same in different surveillance periods/years.

Ward specialty (see code list): Main ward specialty; see specialty code list.

Previous healthcare admission. Previous admission in a healthcare facility in the last 3 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.)

Antibiotic treatment. History of antibiotic treatment in the last 3 month relative to the onset of CDI: Yes/No/Unknown. If it is possible: One course or multiple courses. Also include antimicrobial use reported by the patient but not documented in the patient charts.

Physical status. Classification of the severity of underlying medical conditions using the McCabe Score [5]. Answer categories: Non-fatal disease (expected survival at least five years); ultimately fatal disease (expected survival between one and five years); rapidly fatal disease (expected death within one year); unknown.

Although the prognosis of diseases varies in time and between hospitals due to changes in treatment options and their availability, using McCabe scores can still be helpful. 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.

Examples of diseases for different McCabe score categories:

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

Comorbidity.

1) Did the patient have **liver cirrhosis** as defined in the chronic health points score of APACHE II (biopsy- proven cirrhosis and documented portal hypertension; or episodes of upper gastrointestinal bleeding attributed to portal hypertension; or prior episodes of hepatic failure/encephalopathy/coma) Yes /No / Unknown.

2) Did the patient have NYHA class IV **heart failure or angina** when the stool sample was collected? Yes / No / Unknown.

3) Did the patient have **pulmonary disease** as defined in the chronic health points score of APACHE II (chronic restrictive, obstructive or vascular disease resulting in severe exercise restriction; i.e., unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythaemia, severe pulmonary hypertension (>40 mmHg) or respirator dependency) yes / no / Unknown.

4) Did the patient receive **chronic dialysis**? Yes / no / unknown

Immunocompromised status. Was the patient immunocompromised as defined in the chronic health points score of APACHE II (the subject has received therapy that suppresses resistance to infection, e.g., immunosuppression, chemotherapy, radiation, long term (during 30 days prior to hospitalization) or recent high dose steroids (> 15 mg/kg for ≥ 5 days); or has a disease that is sufficiently advanced to suppress resistance to infection, e.g., leukaemia, lymphoma, AIDS). Yes / No / Unknown.

Complicated course of CDI. CDI leading to any of the following:

-
- 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

Yes / No / Unknown.

Mortality. Did the patient die (due to whatever cause) during the current hospitalisation? Yes, death related to CDI/ Yes, death unrelated to CDI/ Yes, relationship death to CDI unknown / No death / Unknown.

Date of discharge/death. Date the patient was discharged from the hospital or date of end of follow-up for the current surveillance period if the patient was still hospitalised and alive at the time of end of data collection; date of death if patient died during current hospitalisation.

Microbiological and strain shipment data (enhanced protocol)

Stool samples from maximum 10 consecutive patients with primary or recurrent CDI that tested positive for CDI will be stored at -20° C and cultured for the presence of toxin-producing *C. difficile* using local or national protocols. A protocol is available at the ECDIS-website (<http://www.ecdisnet.eu/>, in “protocols and documents”). 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 also suspected in the specimen.

Isolated *C. difficile* strains will be sent as agreed with the national coordinator* for typing and characterisation and to Leiden University Medical Centre if typing capacity is not available at the national centre. If culture methods are not available locally, faces samples will be sent to the national coordinator or Leiden.

*if the national CDI surveillance coordinator (ECDIS-Net national representative) is not the national CDI reference laboratory, the procedure for shipment of samples should be clarified at the national level.

Form M: Strain shipment data sheet (enhanced protocol)

Form M: Strain shipment data sheet (one form for each strain)

Network-Id:

Hospital code:

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

Patient counter: _____

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

Laboratory code:

Microbiological results:

Performed by the national reference laboratory:	<input type="radio"/> yes	<input type="radio"/> no
PCR ribotype of <i>C. difficile</i> isolate:		
Production of toxins A and/or B	<input type="radio"/> positive	<input type="radio"/> negative
Presence of binary toxin genes	<input type="radio"/> positive	<input type="radio"/> negative
Performed by the national reference laboratory:	<input type="radio"/> yes	<input type="radio"/> no
MIC determination to metronidazole :.....mg/l by.....		
MIC determination to vancomycin :.....mg/l by.....		
MIC determination to moxifloxacin ;mg/l by.....		

Definitions of microbiological and strain shipment data (enhanced protocol)

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

Hospital code. Hospital identifier/code assigned by national/regional ECDIS coordinating centre; unique code per surveillance/ECDIS network. Required.

Surveillance period. Start and end date for the ECDIS in the entire hospital. Required.

Patient counter. Number: anonymised patient number allows establishing the link between patient data and CDI and typing/susceptibility data. Not the actual patient identifier. Unique for each hospital. Required.

Age in years. Patient age in years; number; if missing=UNK.

Age in months. Patients age in months if the patient is less than two years old.

Laboratory code: Local laboratory identifier/code assigned by national/regional ECDIS coordinating centre; unique code per surveillance/ECDIS network. Primary lab responsible for microbiological confirmation of CDI (not the code of the national/ref laboratory). Required.

Microbiological results: *C. difficile* PCR ribotype as determined by conventional gel-electrophoresis or capillary-PCR ribotyping and WebRibo database; production of toxins as determined by PCR of TcdA and TcdB or by EIA; MIC (minimal inhibitory concentration) and test used the determination of MIC

Feasibility questionnaire (pilot study only).

Form F: Feasibility variables.

Form F: Feasibility variables (for pilot study only):

Estimated person-days spent to collect hospital-based data (form H, this form): ____ days

Estimated person-days spent to collect CDI case-based surveillance data (form C): ____ days

Estimated additional person-days spent to collect epidemiological data for the enhanced protocol (form E): ____ days

Estimated additional person-days spent to collect microbiological data for the enhanced protocol, including lab analyses in your hospital and shipping of samples: ____ days

How would you assess the level of difficulty encountered during the completion of:

	Easy	Quite easy	Neutral	Quite difficult	Very difficult	Not applicable
1. Hospital-based data (form H)	<input type="radio"/>					
2. Case-based data (form C):	<input type="radio"/>					
3. Enhanced epi data (form E):	<input type="radio"/>					
4. Enhanced microbiological data:	<input type="radio"/>					

Comments on feasibility of data collection: _____

Definitions of feasibility variables (for pilot study only):

Estimated number of person-days spent for data collection of: (1 person-day = 7.5 person-hours)

- 1) hospital-based data (form H),
- 2) CDI case-based surveillance data (form C),
- 3) additional days spent to collect epidemiological data for the enhanced protocol (form E) and
- 4) collection of microbiological data for the enhanced protocol, including lab analyses in your hospital and shipping of samples.

Level of difficulty (scale from easy to very difficult) **encountered during data collection of:** 1) hospital-based data (form H), 2) CDI case-based surveillance data (form C), 3) epidemiological data for the enhanced protocol (form E; not applicable if the hospital did not participate in the enhanced module) and 4) collection of microbiological data for the enhanced protocol, including lab analyses in your hospital and shipping of samples (not applicable if the hospital did not participate in the enhanced module).

Annexes

Abbreviations

APACHE: Acute Physiology And Chronic Health Evaluation
ECDC: European Centre for Disease Prevention and Control
ECDIS: European *Clostridium difficile* Infection Surveillance
ECDIS-NET: European *Clostridium difficile* Infection Network
EEA: European Economic Area
EIA: Enzyme immuno assay
EU: European Union
CDAD: *Clostridium difficile* associated diarrhoea
CDC: Centres for Disease Control and Prevention, Atlanta
CDI: *Clostridium difficile* infections
GDH EIA: Glutamate dehydrogenase enzyme immuno assay
ICU: Intensive Care Units
NYHA: New York Heart Association
PCR: Polymerase Chain Reaction
TcdA: *Clostridium difficile* Toxin A
TcdB; *Clostridium difficile* Toxin B
TESSy: The European Surveillance System (ECDC's web-based data reporting system for the surveillance of communicable diseases)
UNK: unknown

Literature:

1. Kuijper EJ, Coignard B, Tull P. Emergence of *Clostridium difficile*-associated disease in North America and Europe. *Clin Microbiol Infect* 2006;12 Suppl 6:2-18
2. Bauer MP, Notermans DW, van Benthem BH, et al. *Clostridium difficile* infection in Europe: a hospital-based survey. *Lancet* 2011;377:63-73
3. Barbut F, Mastrantonio P, Delmee M, et al. Prospective study of *Clostridium difficile* infections in Europe with phenotypic and genotypic characterisation of the isolates. *Clin Microbiol Infect* 2007;13:1048-1057
4. <http://www.ecdisnet.eu/>
5. McCabe WR, Jackson GG. Gram-negative bacteremia: I. Etiology and ecology. *Arch Intern Med.* 1962;110:847-53.

Specialty code list

Specialty codes are used for ward specialty (Form E) and coding of the hospital specialisation (Form H).

Categories	Code	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	Ear, nose, throat or otorhinolaryngology
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

Categories	Code	Name
Paediatrics (PED)	PEDNEO	Neonatology
Paediatrics (PED)	PEDGEN	Paediatrics general, not specialised
Intensive Care Medicine (ICU)	ICUMED	Medical ICU
Intensive Care Medicine (ICU)	ICUSUR	Surgical ICU
Intensive Care Medicine (ICU)	ICUPED	Paediatric ICU
Intensive Care Medicine (ICU)	ICUNEO	Neonatal 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
Geriatrics (GER)	GER	Geriatrics, care for the elderly
Psychiatrics (PSY)	PSY	Psychiatrics
Rehabilitation (RHB)	RHB	Rehabilitation
OTHER (OTH)	OTH	Others not listed
Mixed (MIX)	MIX	Combination of specialties