C. Difficile Surveillance in Public Hospitals

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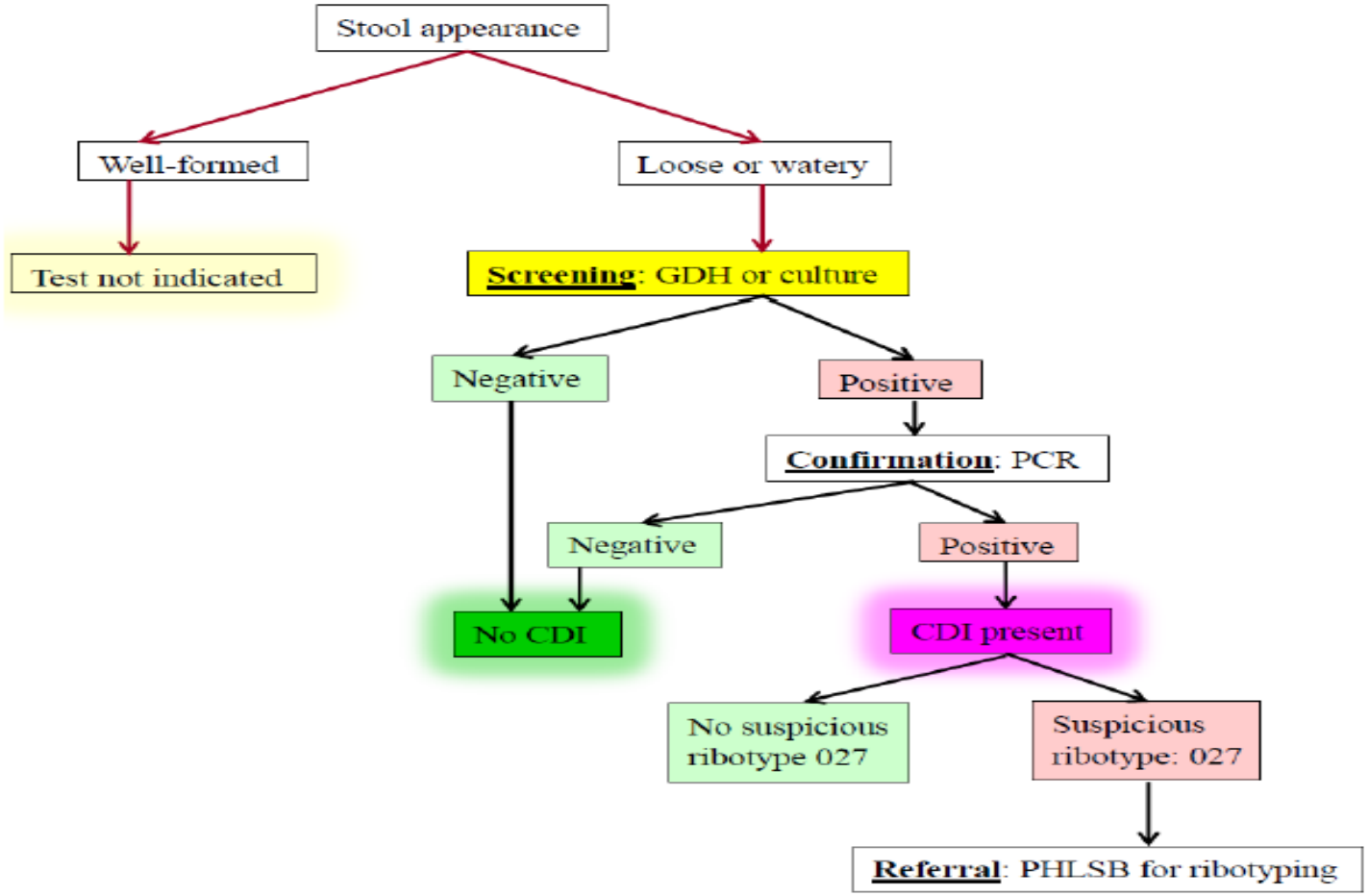
Background

- Objective: To standardize the surveillance definition and methodology among public hospitals on *Clostridioides difficile* Infection (CDI) with the following characteristics:
  - Features real-time information flow and data compilation
  - Captures territory-wide healthcare-associated CDI statistics that constitutes a basis for policy decision
  - Monitors infection rates to assess efficacy of infection control measures
  - Provides feedback to users on a need-to-know basis
  - Generates data for future research studies
- Collaboration between ICB/CHP and HA

Current Laboratory Algorithm



CD testing in HA clusters

- Screening
  - GDH
  - ChromID agar +/- MALDI-TOF MS
  - Direct stool cell culture cytotoxin neutralization assay
- Confirmation
  - PCR toxin gene detection
  - Direct stool cell culture cytotoxin neutralization assay
- Further testing:
  - If 18 base pair deletion of tcdC gene is detected by PCR or severe case suspected of ribotype O27, culture isolate will be sent to PHLSB for confirmation
  - ‘Second-look’ C diff cytotoxin assay for BMT patients

International surveillance platforms

	HA GL	ECDC (1)	US CDC (2)	US NHSN (3)
CDI case definition	A CDI case is defined as a case of clinically significant diarrhea or toxic megacolon without other known etiology that meets one or more of the following criteria: (i) either the stool sample yields a positive result for a laboratory assay for C. difficile toxin A and/or B or a toxin-producing C. difficile organism is detected in the stool sample by culture or other means, (ii) pseudomembranous colitis is seen on endoscopic examination or surgery, and (iii) pseudomembranous colitis is seen on histopathological examination.	A case of Clostridioides difficile infection (CDI) 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.	A case of CDI is defined as a positive C. difficile toxin assay or a positive C. difficile molecular assay (e.g. PCR) of a stool specimen from a resident of the surveillance catchment area who is at least 1 year old.	A positive laboratory test result for C. difficile toxin A and/or B, (includes molecular assays [PCR] and/or toxin assays) tested on an unformed stool specimen (must conform to the container). OR A toxin-producing C. difficile organism detected by culture or other laboratory means performed on an unformed stool sample (must conform to the container).

(1) ECDC. Surveillance and disease data for Clostridium difficile infections https://www.ecdc.europa.eu/en/clostridium-difficile-infections/surveillance-and-disease-data

(2) US CDC. Clostridioides difficile Infection (CDI) Tracking. https://www.cdc.gov/hai/eip/cdiff-tracking.html#:~:text=The%20CDI%20surveillance%20program%20also,monitoring%20effectiveness%20of%20prevention%20strategies

(3) US NHSN. Multidrug-Resistant Organism & Clostridioides difficile Infection (MDRO/CDI) Module https://www.cdc.gov/nhsn/PDFs/pscManual/12pscMDRO_CDADcurrent.pdf

International surveillance platforms (cont'd)

	HA GL	ECDC (1)	US CDC (2)	US NHSN (3)
Start date	CDI symptom onset date	CDI symptom end date / Date of positive lab test for CDI	Positive stool specimen was collected	Date of specimen collection
Location	Healthcare facility	Hospitalised patients	Hospital admission / long-term care facility / outpatient setting	Inpatient / Outpatient
Target population	5.3. Generally it is not advisable to test children under the age of 1 years in whom toxigenic strains of C. difficile may be present in the absence of symptoms	at least 2 year old	at least 1 year old	--
Healthcare Facility-Onset CDI	>72 hours after admission	>48 hours after admission / On day 3 or later, following admission to a healthcare facility on day one	>3 calendar days after hospital admission	On or after HD 4 where HD 1 is day of admission
Outcome measure	Cases per 1,000 patient-days	Cases per 10,000 patient-days	Cases per 100,000 persons (population based)	Denominator Data: Patient days and admissions (for inpatient locations), and encounters (for outpatient locations.

ECDC Protocol

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	• **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 5 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. 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.			

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.

European surveillance of Clostridioides (Clostridium) difficile infections Surveillance protocol version 2.4

HA guideline

(i) either the stool sample yields a positive result for a laboratory assay for *C. difficile* toxin A and/or B or a toxin-producing *C. difficile* organism is detected in the stool sample by culture or other means,
(ii) pseudomembranous colitis is seen on endoscopic examination or surgery, and
(iii) pseudomembranous colitis is seen on histopathological examination.

3.2. Surveillance Definitions: [26]

3.2.1. Healthcare facility–onset, healthcare facility–associated CDI:
CDI symptom onset more than 72 hours after admission to a healthcare facility

3.2.2. Community-onset, healthcare facility–associated CDI:
CDI symptom onset in the community or less than or equal to 72 hours from admission, provided symptom onset was less than 4 weeks after the last discharge from a healthcare facility.

3.2.3. Community-associated CDI:
CDI symptom onset in the community or less than or equal to 72 hours after admission to a healthcare facility, provided that symptom onset was more than 12 weeks after the last discharge from a healthcare facility.

3.2.4. Indeterminate onset CDI:
CDI case patient who does not fit any of the above criteria for an exposure setting (eg, onset in the community greater than 4 weeks but less than 12 weeks after the last discharge from a healthcare facility)

3.2.5. Unknown: Exposure setting cannot be determined because of lack of available data.

3.2.6. Recurrent CDI:
An episode of CDI that occurs less than or equal to 8 weeks after the onset of a previous episode, provided that CDI symptoms from the earlier episode resolved.

HA Infection Control Guideline on Clostridium difficile infection

Surveillance Definitions

Definition of a CDI episode:

- A stool or rectal swab sample yielding a positive result for a laboratory assay for C. difficile toxin A and/or B or a toxin-producing C. difficile organism is detected in the sample by culture or other means e.g. PCR toxin gene detection.

Based on HA Infection Control Guideline on Clostridium difficile Infection CCIDER-CDI-001(V3)

C. diff classification

HO-HCFA (Healthcare facility-onset, healthcare facility-associated) CDI:

- The first positive diagnostic sample taken more than 72 hours after admission to a healthcare facility.

CO-HCFA (Community-onset, healthcare facility-associated) CDI:

- The first positive diagnostic sample taken less than or equal to 72 hours after admission, provided that symptom onset was less than 4 weeks after the last discharge from a healthcare facility.

CA (Community-associated) CDI:

- The first positive diagnostic sample taken less than or equal to 72 hours after admission to a healthcare facility, provided that symptom onset was more than 12 weeks after the last discharge from a healthcare facility.

Indeterminate CDI:

- CDI case patient who does not fit any of the above criteria for an exposure setting (e.g., onset in the community greater than 4 weeks but less than 12 weeks after the last discharge from a healthcare facility).

Recurrent CDI:

- An episode of CDI that occurs within 2 and 8 weeks of a previous episode.

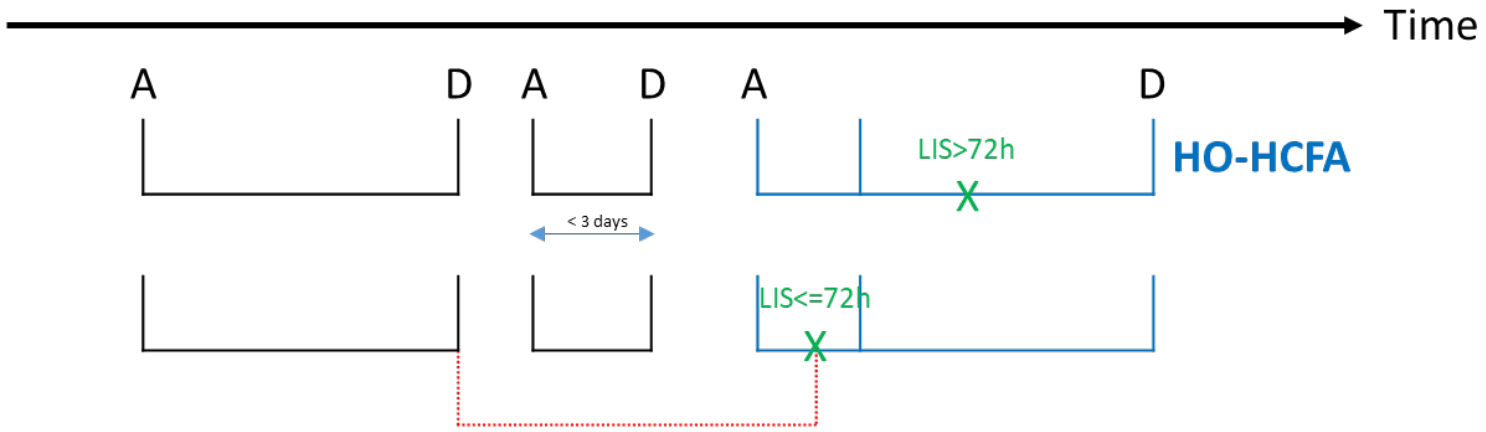
Total CDI

- The sum of all five categories of CDIs mentioned above

No. of Patient Days:

- Number of hospital patient days in the current surveillance period.

Counting rule



CO-HCFA 0-28 days (0-4 weeks)

Indeterminate 29-84 days (>4-12 weeks)

CA >84 days (>12 weeks)

Recurrent 14-56 days (2-8 weeks)

- **Focus on HO-HCFA**
- LIS = specimen collection date-time
- Episode of hospital stay is counted only if LOS>=3 days
- Positive test within 14 days of last positive is not counted

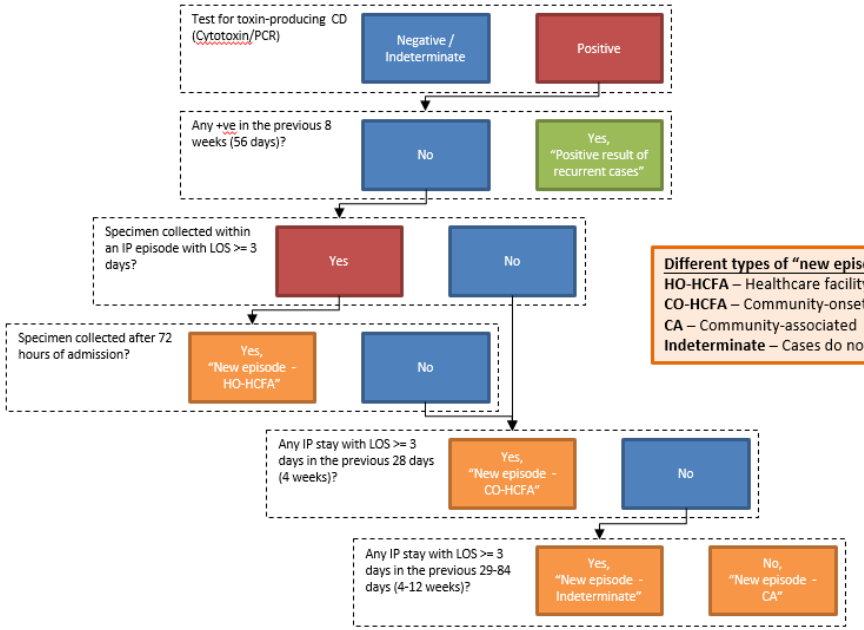
HO-HCFA: healthcare-onset, healthcare facility-associated
CO-HCFA: community-onset, healthcare facility-associated
CA: community-associated

Automatic CDARS standard report generation

IT system

- Step 1: Extract positive test result & linked episode & previous episode
- Step 2: Download & classify
- Step 3: Retrieve any episode in the past 84 days to further classify (for previous episode LOS<3days & test collected <=72hr)
- Step 4: Extract monthly patient-days to calculate the rate

Method - Episode counting and classification



Different types of "new episodes"
HO-HCFA – Healthcare facility-onset, healthcare facility-associated
CO-HCFA – Community-onset, healthcare facility-associated
CA – Community-associated
Indeterminate – Cases do not fit any of the above classifications

Remark: Based on the concept of "HO-HCFA" episode (CD +ve specimen collected after 72 hours of admission), the episode should be attributed to the HCF only when the exposure in the HCF is > 72 hours. **In our calculation, definition of "CO-HCFA" episode requires IP stay in the previous 28 days (4 weeks) with LOS >= 3 days (72 hours).**

Case Exclusion

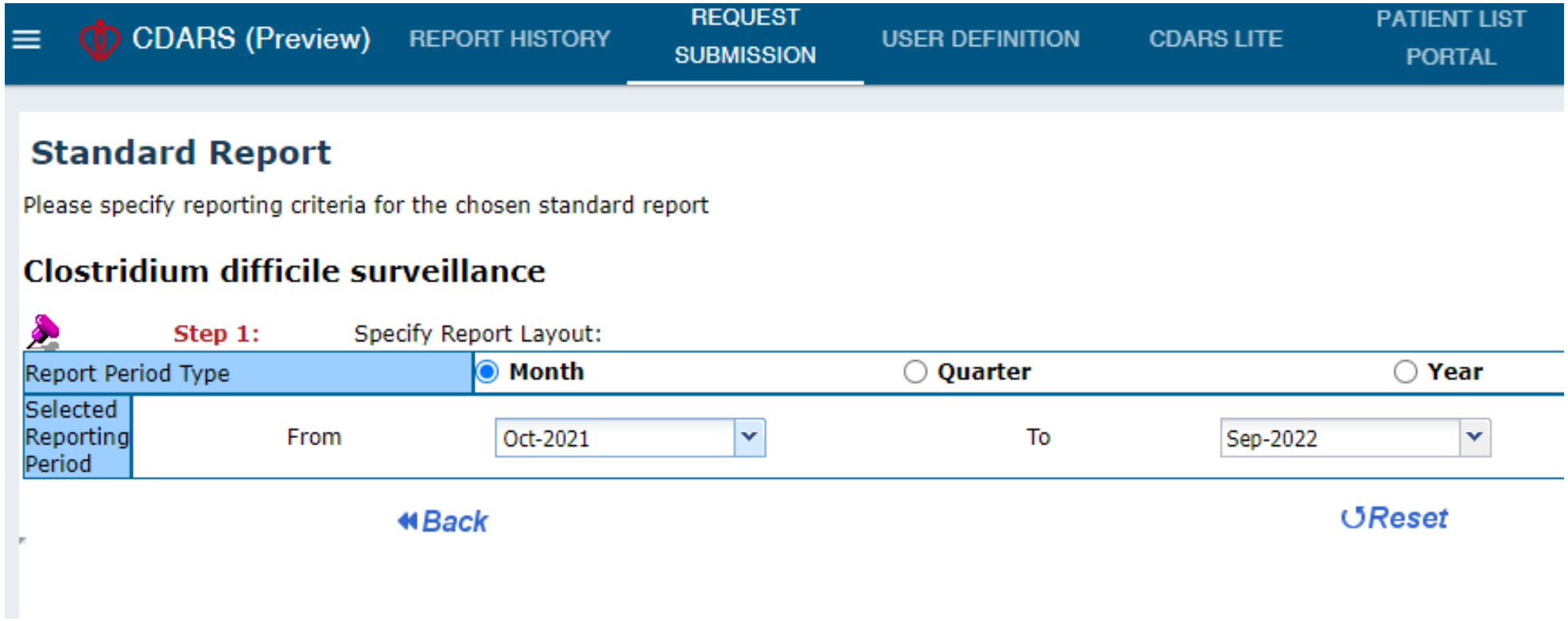
In line with ECDC surveillance protocol, the followings are excluded:

- An episode of CDI that occurs less than 2 weeks of a previous episode (Re-positive CDI)
- Age < 2 years old

Development Timeline of the *Clostridioides difficile* Infection (CDI) Surveillance

COVID-19 pandemic

Screen caps of CDARS user interface



Screen caps of CDARS user interface

This is the CDARS Production-**Preview** Environment, the data is only for data verification purpose. For production data, please retrieve from CDARS.home

Clostridium difficile surveillance

Period From: 01-Oct-2021
Period To: 30-Sep-2022
As of Day: 12-Oct-2022

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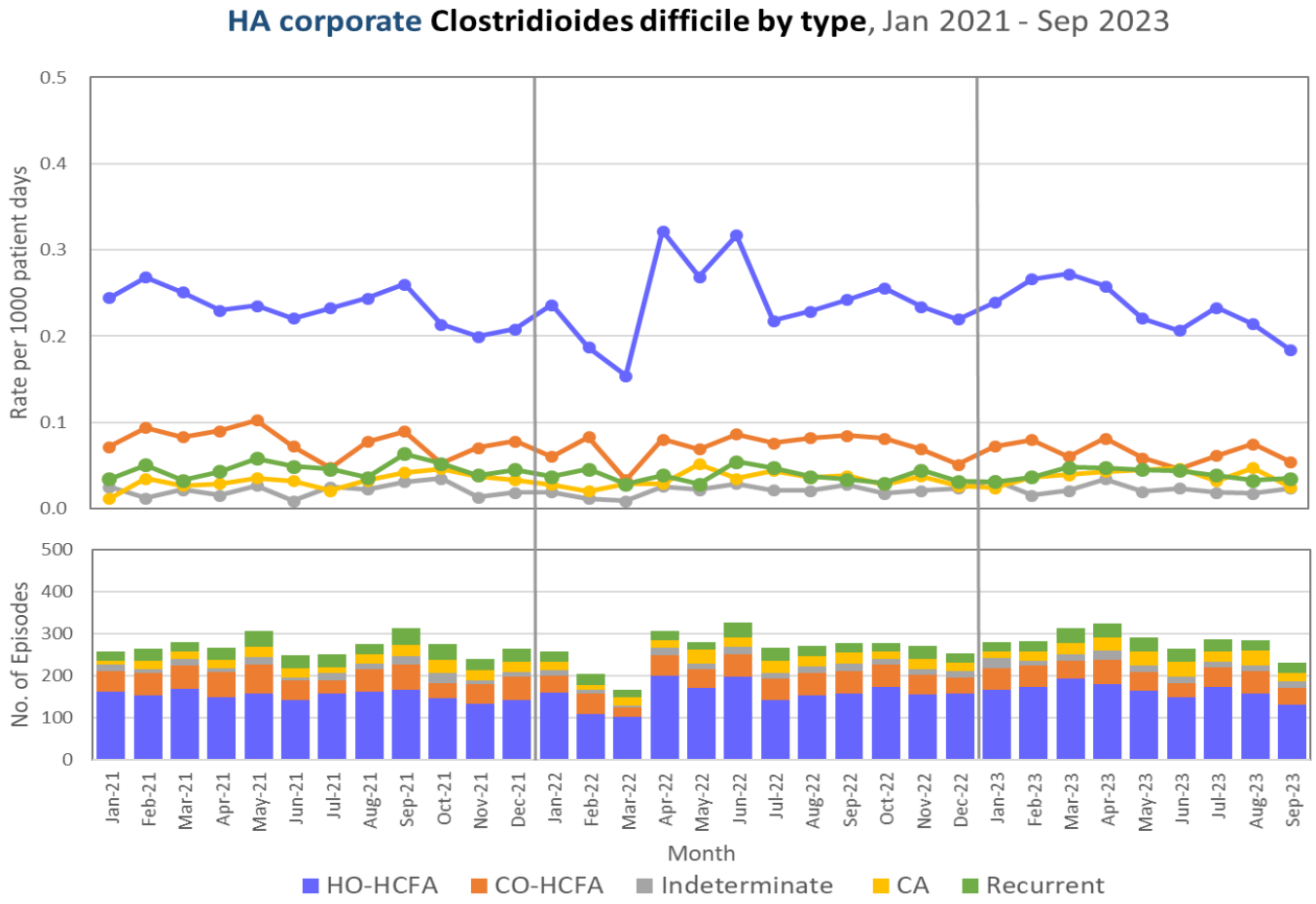
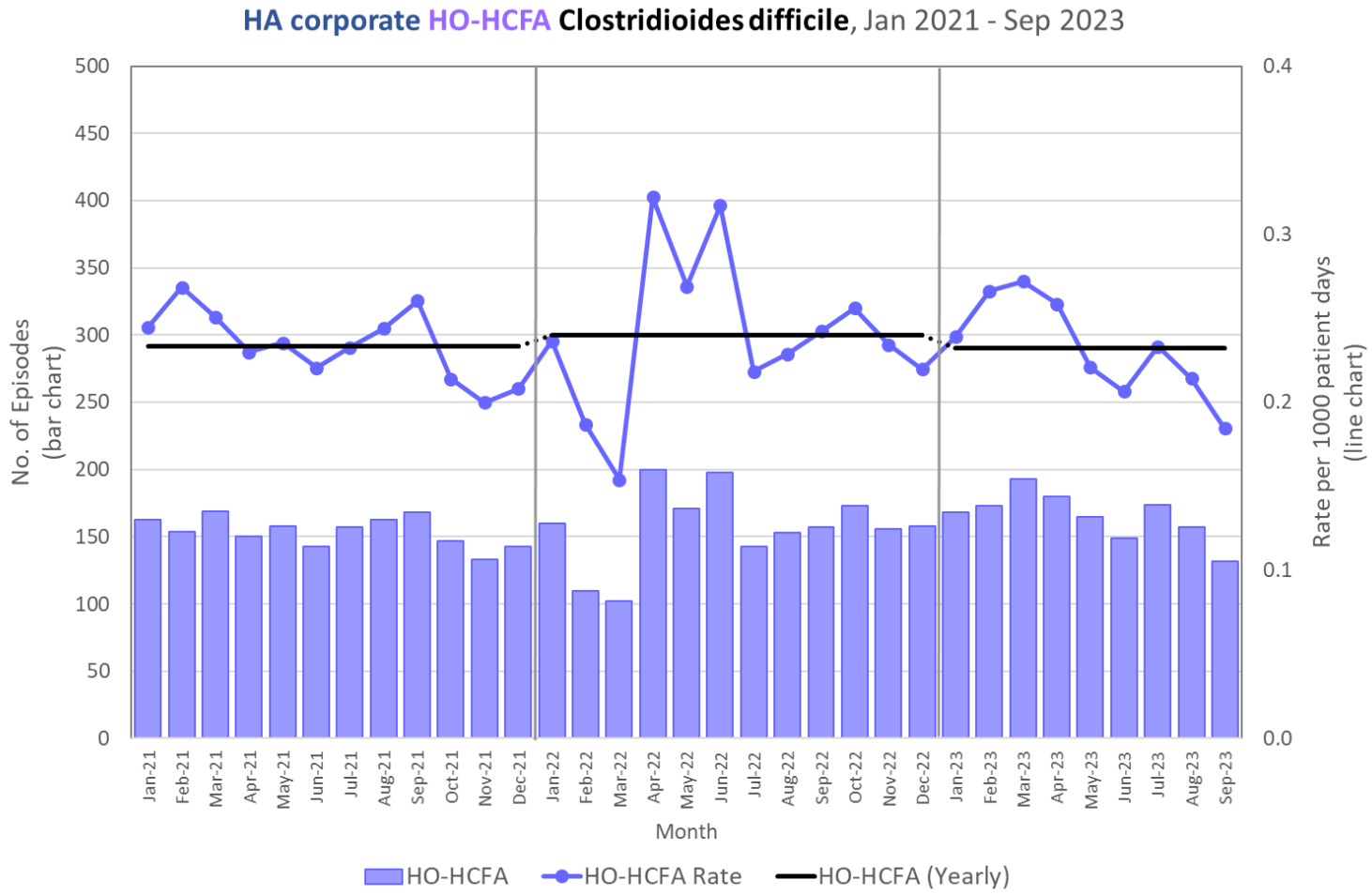
Period	Cluster	Hospital	HO-HCFA Cases	CO-HCFA Cases	Indeterminate Cases	CA Cases	Recurrent Cases	No. of Patient Days	HO-HCFA Cases / 1000 No. of Patient Days	CO-HCFA Cases / 1000 No. of Patient Days	Indeterminate Cases / 1000 No. of Patient Days	CA Cases / 1000 No. of Patient Days	Recurrent Cases / 1000 No. of Patient Days
2021-10			1	0	0	0	0	5502	0.1818	0.0000	0.0000	0.0000	0.0000
2021-10			8	3	2	4	1	40983	0.1952	0.0732	0.0488	0.0976	0.0244
2021-10			2	0	1	1	0	13694	0.1460	0.0000	0.0730	0.0730	0.0000
2021-10			0	0	0	0	0	222	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			1	0	0	0	0	6293	0.1589	0.0000	0.0000	0.0000	0.0000
2021-10			0	0	0	0	0	4571	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			0	0	0	0	0	1203	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			0	0	0	0	0	5056	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			0	0	0	0	0	8853	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			0	0	0	0	0	1555	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			1	0	2	0	0	32019	0.0312	0.0000	0.0625	0.0000	0.0000
2021-10			0	0	0	0	0	5978	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			0	0	0	0	0	0	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			1	0	0	0	1	11234	0.0890	0.0000	0.0000	0.0000	0.0890
2021-10			1	1	0	0	1	3731	0.2680	0.2680	0.0000	0.0000	0.2680
2021-10			0	0	0	0	0	154	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			3	0	0	1	4	35622	0.0842	0.0000	0.0000	0.0281	0.1123
2021-10			4	1	1	1	0	21127	0.1893	0.0473	0.0473	0.0473	0.0000
2021-10			3	0	0	0	0	5251	0.5713	0.0000	0.0000	0.0000	0.0000
2021-10			17	7	5	5	5	50857	0.3343	0.1376	0.0983	0.0983	0.0983
2021-10			3	1	0	0	0	11699	0.2564	0.0855	0.0000	0.0000	0.0000
2021-10			5	1	0	0	1	15032	0.3326	0.0665	0.0000	0.0000	0.0665
2021-10			12	2	0	1	2	19358	0.6199	0.1033	0.0000	0.0517	0.1033
2021-10			12	7	4	1	1	36841	0.3257	0.1900	0.1086	0.0271	0.0271
2021-10			8	0	0	1	1	29046	0.2754	0.0000	0.0000	0.0344	0.0344
2021-10			0	0	0	0	0	20799	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			0	0	0	0	0	4963	0.0000	0.0000	0.0000	0.0000	0.0000
2021-10			3	1	0	1	3	43614	0.0688	0.0229	0.0000	0.0229	0.0688

Prelim standard report results (trial)
Time period : 2021- 2023Q3

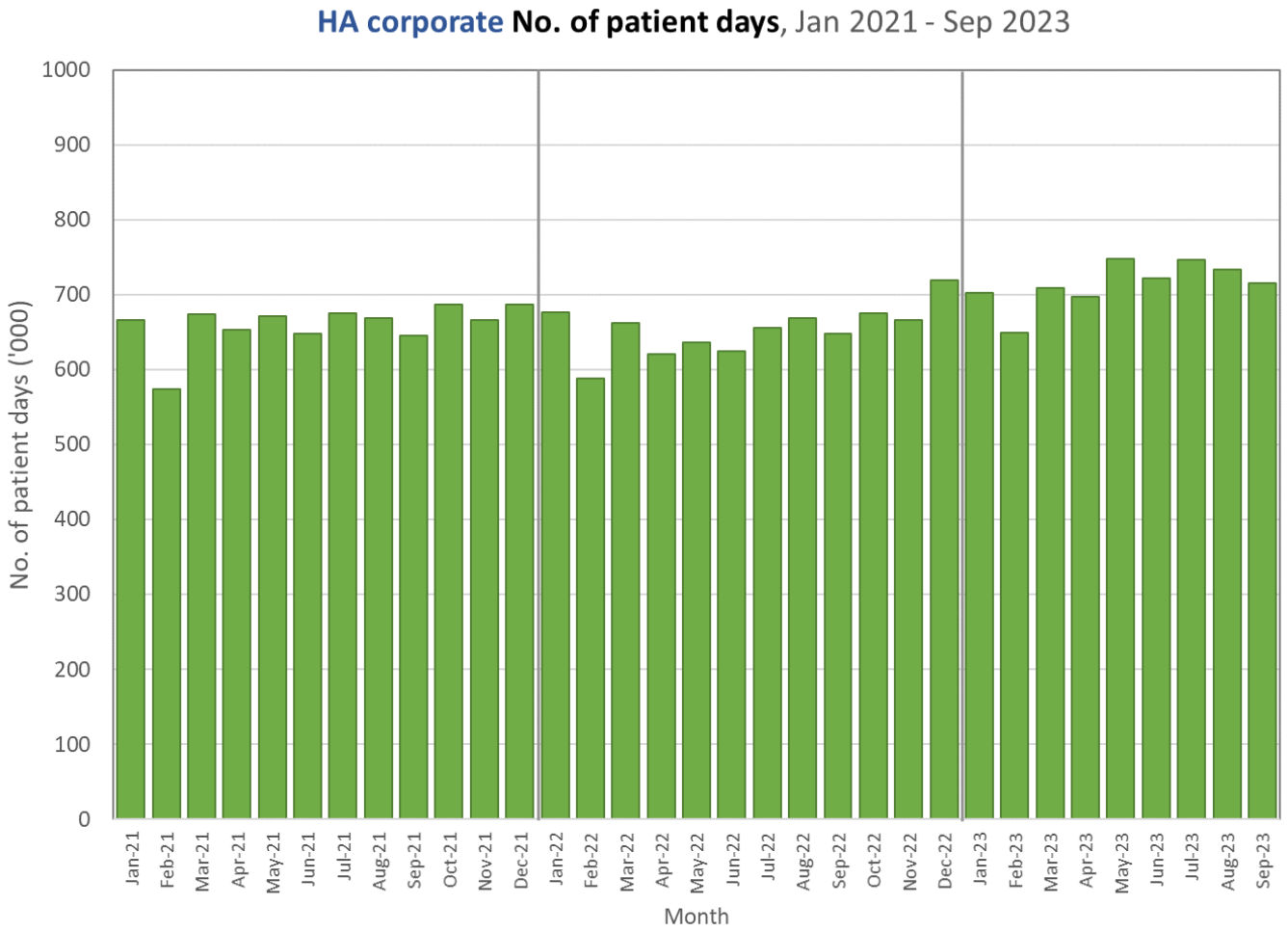
HA corporate *Clostridioides diffcile* by type Jan 2021 – Sep 2023



HA corporate HO-HCFA *Clostridioides difficile* Jan 2021 – Sept 2023



HA corporate No. of patient days Jan 2021 – Sep 2023



Incidence rate

- Incidence rate by this surveillance program in 2022Q4-2023Q3
- HO-HCFA = 0.2331 per 1,000 patient days

  = **2.331** per 10,000 patient days
- Total = 0.3965 per 1,000 patient days

  = **3.965** per 10,000 patient days

Overseas incidence rate

Source	Incidence rate	Numerator*
ECDC (1)	**Healthcare-associated CDI** in 2016–2017 • From 23 country / administration = 2.12 cases / 10 000 patient-days • UK-England = 1.93 cases / 10,000 patient-days • UK-Scotland = 1.43 cases / 10,000 patient-days • Netherlands = 1.40 cases / 10,000 patient-days	A+B
US CDC (2) - population- and laboratory-based surveillance system	**Healthcare-associated CDI** in 2019 • 57.9 cases per 100,000 persons	A+B+C
National Healthcare Safety Network (NHSN) , USA (3) - laboratory testing data	**Healthcare-facility–onset CDI** in 2011-2019 • The rates of HO-CDI were 7.58 and 6.94 per 10,000 patient days using the NHSN (>3 days) and the revised definitions (>72 hours), respectively.	A

- A: HO-HCFA; B: CO-HCFA; C: Indeterminate; D: CA; E: Recurrent

(1) ECDC. Clostridioides (Clostridium) difficile infections - Annual Epidemiological Report for 2016–2017 https://www.ecdc.europa.eu/en/publications-data/clostridiodes-difficile-infections-annual-epidemiological-report-2016-2017

(2) US CDC. Clostridioides difficile Infection (CDI) Tracking. https://www.cdc.gov/hai/eip/cdiff-tracking.html#:~:text=The%20CDI%20surveillance%20program%20also,monitoring%20effectiveness%20of%20prevention%20strategies

(3) Puri S, at al. Potential for the current National Healthcare Safety Network (NHSN)> 3 days after admission definition of laboratory-identified, healthcare-facility–onset, Clostridioides difficile infection (HO-CDI) to overestimate rates. Infection Control & Hospital Epidemiology. 2020 Apr;41(4):467-8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8121008/

Overseas incidence rate (cont'd)

Source	Incidence rate	Numerator*
US 775 hospitals (4) - based on diagnosis code	**Hospital-onset CDI** in 2019 and 2020 • Rates of HO-CDI per 10,000 patient days were similar between years: 3.3 in 2019 compared with 3.2 in 2020 (P = .0163).	A
Australian Commission on Safety and Quality in Health Care (5) - based on diagnosis code	**Healthcare-associated hospital-onset CDI** in 2019 • The average rate of non-principal CDI diagnoses flagged with a COF1 was 0.73 diagnoses per 10,000 patient bed days.	A
South Australian Healthcare-Associated Infection Surveillance Program (6) - ~ ECDC	**Healthcare associated–healthcare facility onset CDI** in 2019 and 2020 • The incidence rate for HCA-HCF CDI recorded a reduction, from 1.5 per 10,000 bed-days in 2019 to 1.4 per 10,000 bed-days in 2020.	A

- A: HO-HCFA; B: CO-HCFA; C: Indeterminate; D: CA; E: Recurrent

(4) Rose AN, et al. Trends in facility-level rates of Clostridioides difficile infections in US hospitals, 2019–2020. Infection Control & Hospital Epidemiology. Cambridge University Press; 2023;44(2):238–45. https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/trends-in-facilitylevel-rates-of-clostridioides-difficile-infections-in-us-hospitals-20192020/D20D0DAF36B4984E424908F8BAF913D3

(5) Australian Commission on Safety and Quality in Health Care. Clostridioides difficile infection 2019 Data Snapshot Report. https://www.safetyandquality.gov.au/sites/default/files/2022-02/cdi_2019_data_snapshot_report_-_december_2021.pdf

(6) South Australian Healthcare-Associated Infection Surveillance Program. Clostridioides difficile Infection. 2020 Annual Report. https://www.sahealth.sa.gov.au/wps/wcm/connect/cd789a74-ed24-43f7-832d-966aee240578/SA-HAI-CDI-2020-annual-report.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-cd789a74-ed24-43f7-832d-966aee240578-o5wuRGx

Overseas incidence rate (cont'd)

Source	Incidence rate	Numerator*
Singapore, a 1000-bed tertiary care hospital (7) - laboratory-confirmed CDI cases, SHEA guidelines	The incidence of laboratory-confirmed CDI in this hospital was 10.7/10 000 patient-days or 6.38/1000 discharges. **Hospital onset CDI** in 2012 • 50.0% were healthcare-facility-associated hospital onset (HCFA-HO)	A+B+C+D+E A
Asia (8) - meta-analysis, 51 studies	This yielded a pooled incidence of CDI of 5.3 per 10,000 patient-days (95% CI 4.0–6.7).	A+B+C+D+E

- A: HO-HCFA; B: CO-HCFA; C: Indeterminate; D: CA; E: Recurrent

(7) Tan XQ, et al. The emergence of community-onset Clostridium difficile infection in a tertiary hospital in Singapore: a cause for concern. International journal of antimicrobial agents. 2014 Jan 1;43(1):47-51. https://www.sciencedirect.com/science/article/pii/S0924857913003439?via%3Dihub

(8) Borren NZ, et al. The emergence of Clostridium difficile infection in Asia: A systematic review and meta-analysis of incidence and impact. PloS one. 2017 May 2;12(5):e0176797. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0176797

Limitations (points to note for results interpretation)

- The definitions employed are for surveillance purpose only and not to be used as clinical diagnosis and management. Despite consistent, it will not include every case nor exclude every non-case
- The incidence rate is based on laboratory detection of toxigenic *C. difficile* without clinical information on symptomatology. Since the date of collection of the first positive diagnostic test is used as a proxy for the date of onset of CDI symptoms, there could be overestimation of HO-HCFA CDI incidence rate if symptom onset occurs within, but specimen collection occurs after the first 72 hours of admission
- Admissions outside public hospitals are not considered.
- Incidence rate across hospitals may also be affected by:
  - Different types of laboratory tests and diagnostic methods adopted *
  - Difference in case-mixes, testing policies and test ordering practices
- Because of the above limitations, the surveillance data may not be strictly compared across hospitals and clusters. They are best used for individual hospital's trend monitoring to reflect the changing epidemiology of CDI and as a feedback tool on effectiveness of infection control measures.

*For example, one cluster uses cell culture cytotoxin assay while other clusters mainly use PCR-based tests for confirmation. Cytotoxin assay is considered more specific but less sensitive for diagnosis of CD infection compared to PCR-based tests.

Thank you