EPIDEMIOLOGY AND SURVEILLANCE OF C. DIFFICILE

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Royal College of Surgeons in Ireland
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DISCLOSURES

- **Tillotts Pharma: consultancy, research**

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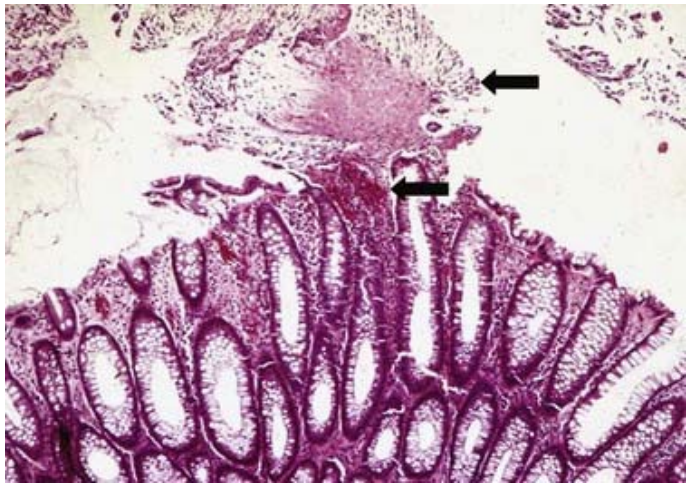
CLOSTRIDIOIDES DIFFICILE



(Hematoxylin and eosin stain ×105.5) (From Feldman M, Friedman LS, Brandt LJ [eds]: Sleisenger and Fordtran's Gastrointestinal and Liver Diseases, 8th ed. Philadelphia, WB Saunders, 2006.)

- **Spore-forming, toxin-producing anaerobic bacterium**
  - **Survive in environment**
  - **Need to wash hands**
- **Carried asymptomatically**

- ***C. difficile* infection (CDI): Toxin-mediated disease**
  - **Major virulence factor in *C. difficile* = toxins A/B**
- **In Europe: Common HAI: one in twenty HAI (48% of gastrointestinal HAI)**
- **Antibiotics = main risk factor for infection**
- **2-step testing recommended**

Source: ECDC Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2011-2012
European Society of Clinical Microbiology and Infectious Diseases: update of the diagnostic guidance document for *Clostridium difficile* infection. Clin Microbiol Infect. 2016;22 Suppl 4:S63-81.

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SYMPTOMS

- Variable (depends on the patient/resident)
- Asymptomatic to potentially fatal
  - Diarrhoea
  - Stomach cramps
  - Fever
  - Nausea
  - Loss of appetite
  - Acute abdomen /Pseudomembraneous colitis

- Risk of recurrence increases with each recurrence

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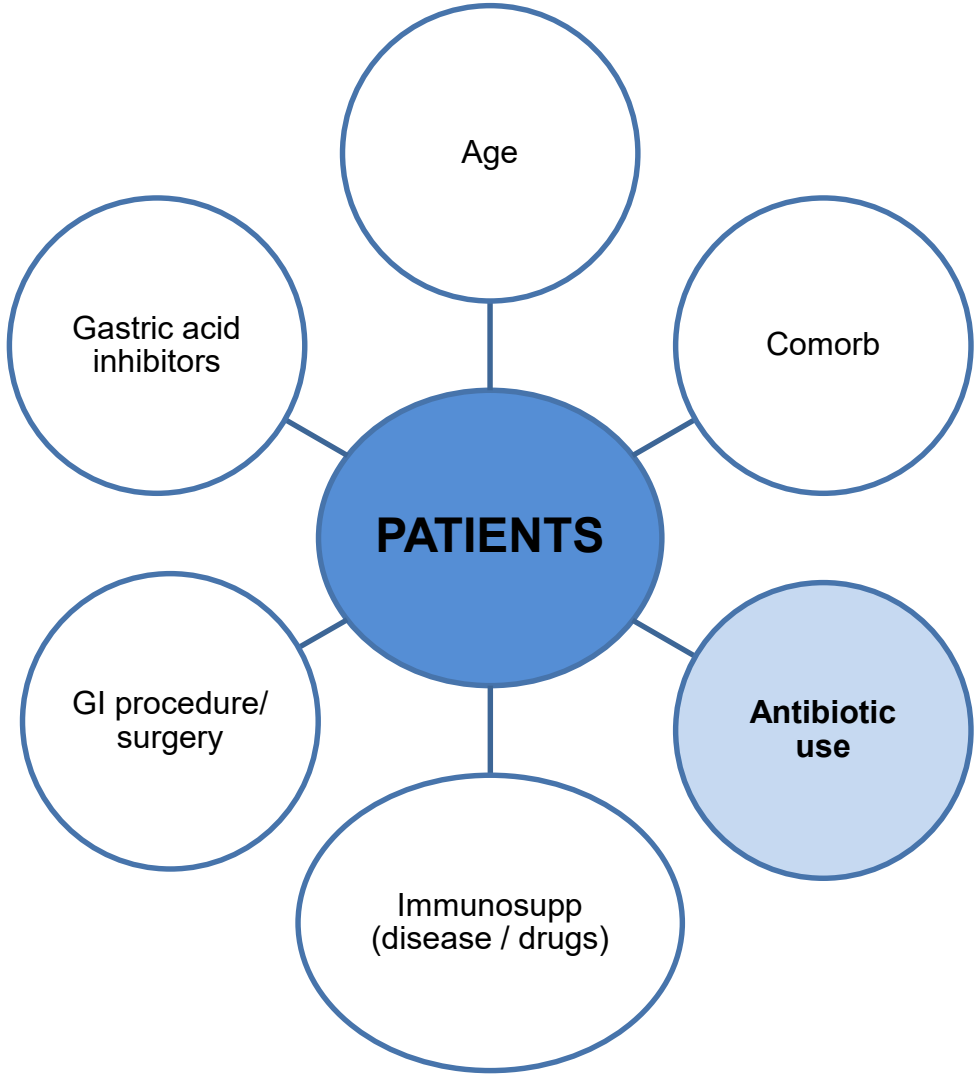
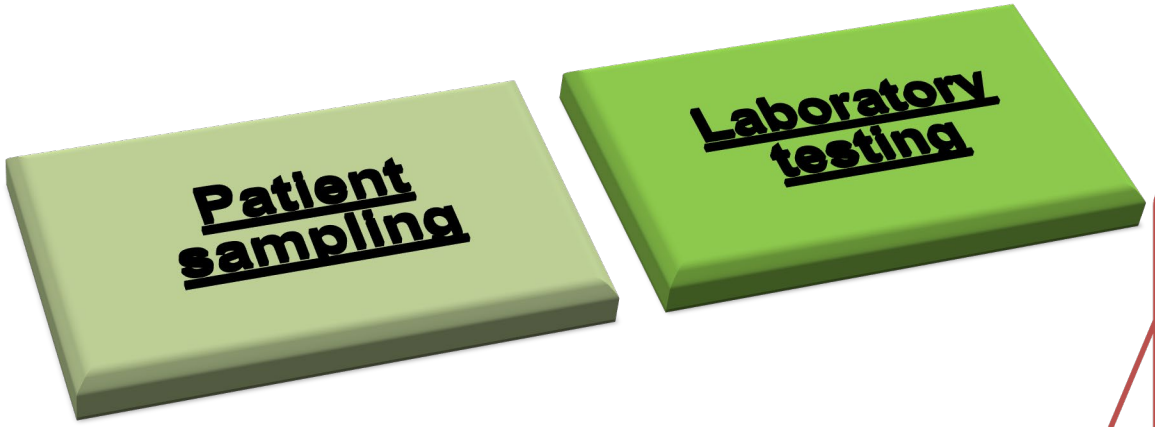
DRIVERS OF *C. DIFFICILE* EPIDEMIOLOGY





Slide adapted with permission: Dr. Jon Otter

WE CAN'T TALK ABOUT EPIDEMIOLOGY WITHOUT DISCUSSING TESTING

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WHO TO TEST?

23% = UNDER DIAGNOSIS OF CASES

Underdiagnosis of *Clostridium difficile* across Europe: the European, multicentre, prospective, biannual, point-prevalence study of *Clostridium difficile* infection in hospitalised patients with diarrhoea (EUCLID)

Kerrie A Davies, Christopher M Longshaw, Georgina L Davis, Emilio Bouza, Frédéric Barbut, Zsuzsanna Barna, Michel Delmée, Fidelma Fitzpatrick, Kate Ivanova, Ed Kuijper, Ioana S Macovei, Silja Mentula, Paola Mastrantonio, Lutz von Müller, Mónica Oleastro, Efthymia Petinaki, Hanna Pituch, Torbjörn Norén, Elena Nováková, Otakar Nyč, Maja Rupnik, Daniela Schmid, Mark H Wilcox

Lancet Infect Dis 2014; 14: 1208–19

Published Online November 5, 2014

Summary

Background Variations in testing for *Clostridium difficile* infection can hinder patients' care, increase the risk of transmission, and skew epidemiological data. We aimed to measure the underdiagnosis of *C difficile* infection across Europe.

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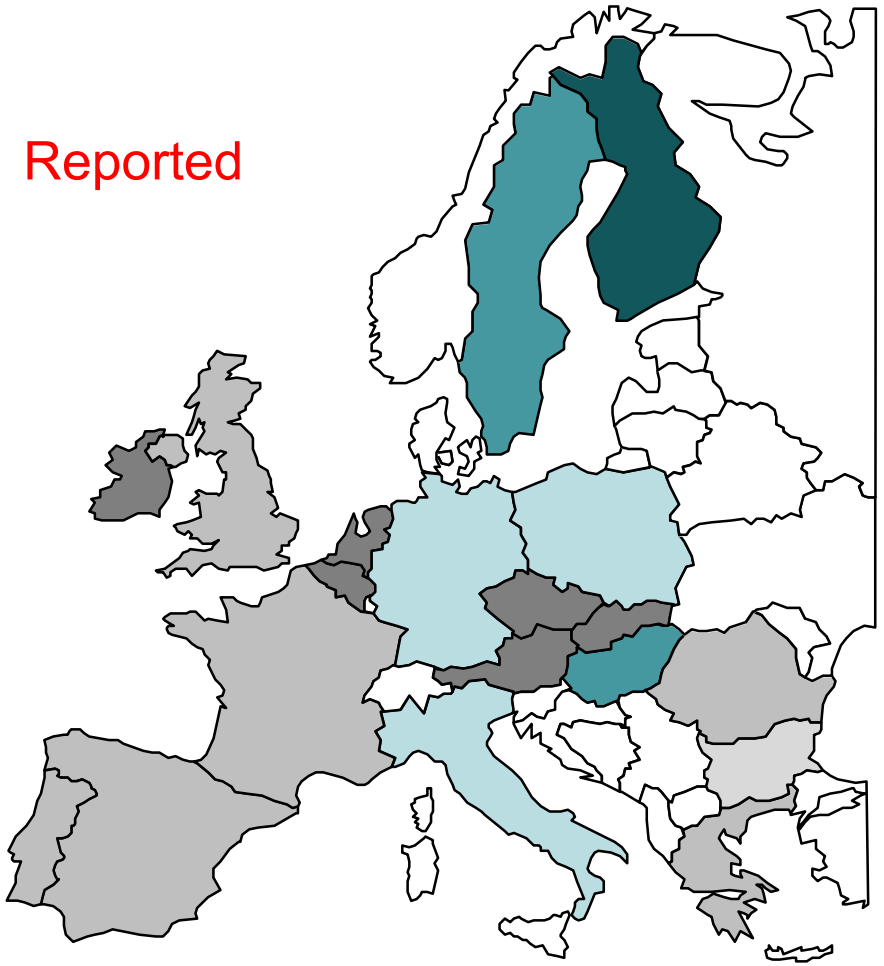
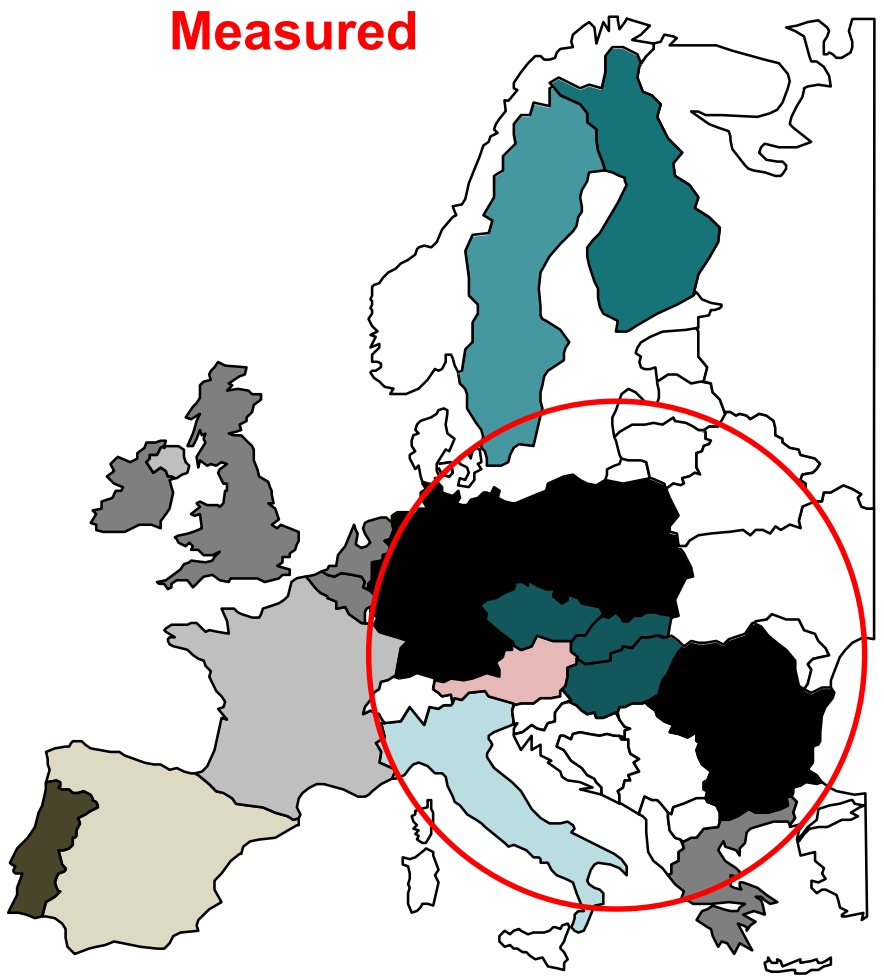
C. DIFFICILE INFECTION (CDI) IS UNDER REPORTED
I.E, CDI > REPORTED CDI





Source: Prof Kerrie Davies

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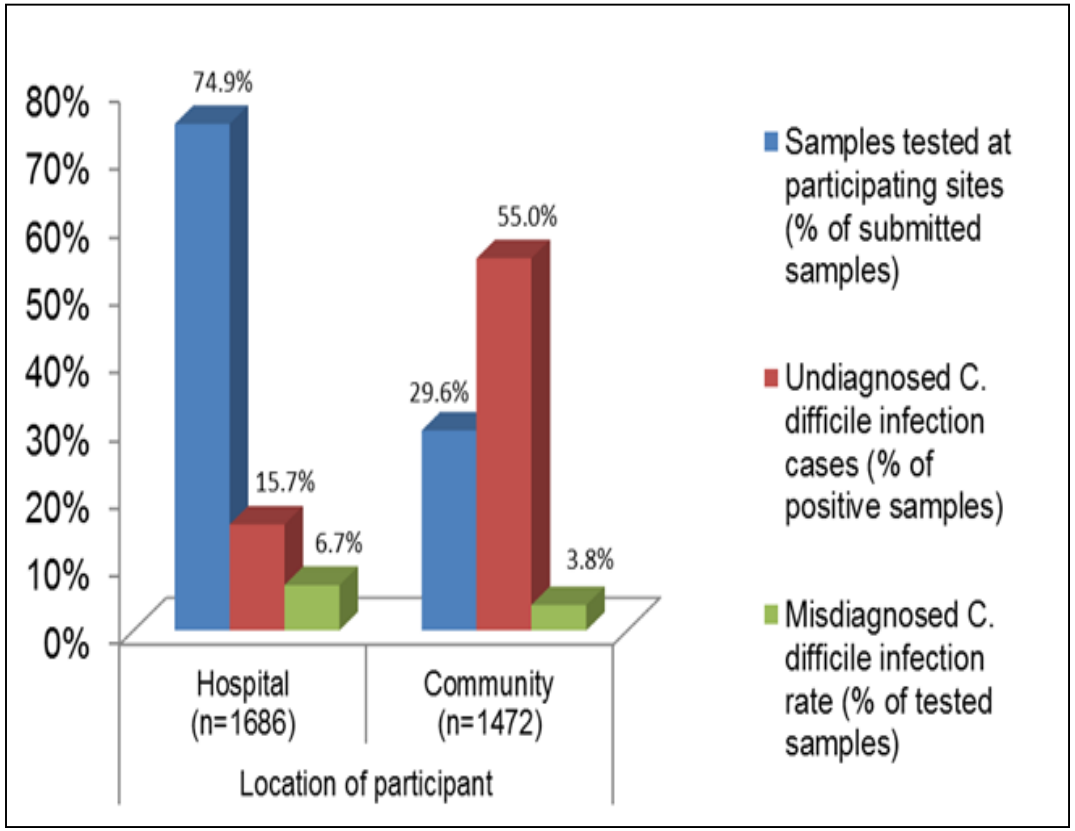
THIS IS A PARTICULAR PROBLEM IN THE COMMUNITY

Testing ALL samples enabled detection of missed cases

- Undiagnosed CDI
  - **55% community cases missed**
  - **16% hospital cases missed**

Lack of clinical suspicion = lack of testing



Viprey et al Eurosurveillance 2022 Jun;27(26):2100704.

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WHO SHOULD WE TEST?

- **Symptomatic**
  - **Diarrhoea**
  - **Faecal sample takes the shape of the container**
- **Not on laxatives**

Avoid using

- *Age*
  - *Missed patients in EUCLID study = significantly younger than those diagnosed*
- *Hospital contact*
  - *Some community cases do not have healthcare contact*

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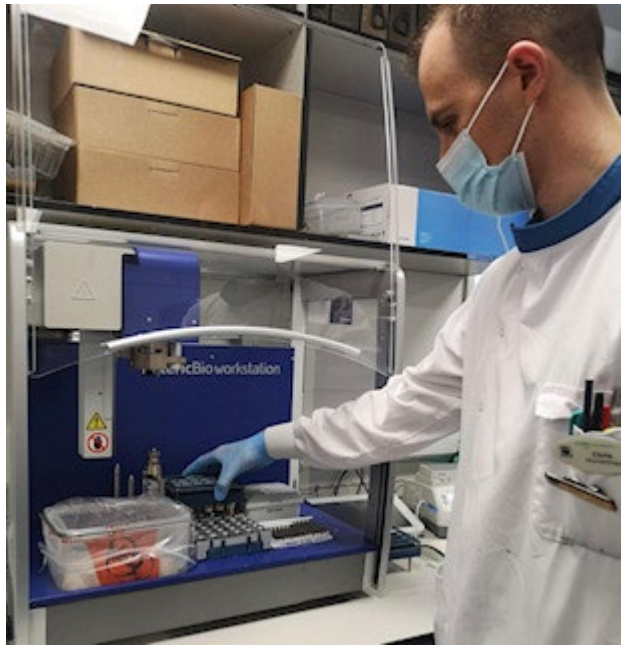
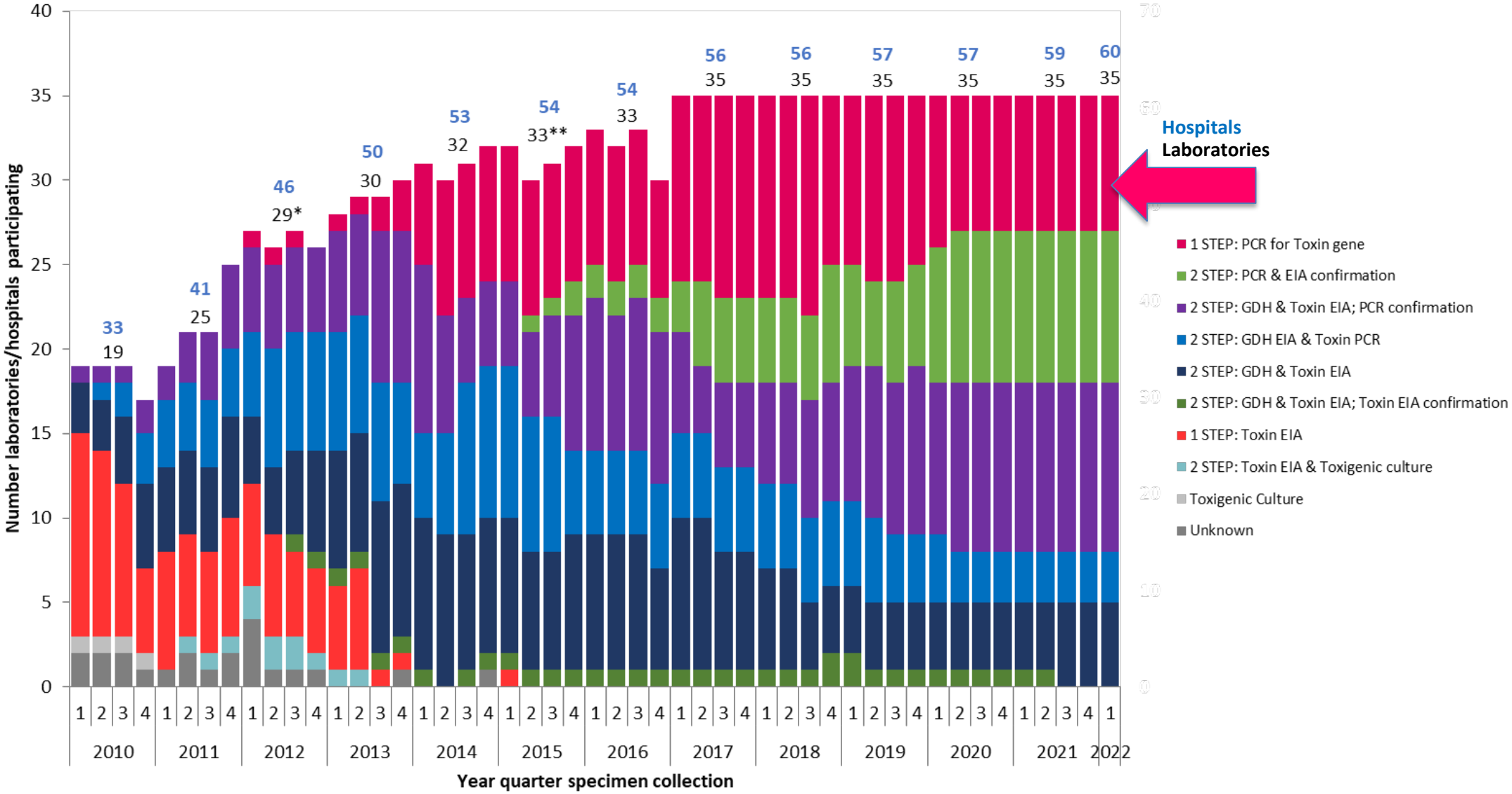


HOW TO TEST?

Test for?	How?	
The organism	1. Grow the organism (culture) 2. Cell surface protein (GDH)	More sensitive *C. difficile* carriage
The toxins	1. Toxin activity 2. Toxin protein	More specific Lack of sensitivity NB: not all EIA the same (69-93%)
DNA	Toxin genes (NAAT)	More sensitive *C. difficile* carriage

Eastwood et al J Clin Microbiol. 2009 Oct;47(10):3211-7

IRELAND: *C. DIFFICILE* LABORATORY TESTING



Unpublished data

Source: Tara Mitchell, HPSC

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HOW DO WE COUNT CASES?
CASE DEFINITIONS

CASE TYPE: NEW OR RECURRENT?

- **Diarrhoea* or toxic megagolon with either**
  - **Lab positive for *tcdA / tcdB***
  - **Toxin-producing *C. difficile* by culture**
- **PMC (colonoscopy)**
- **Histopathology indicating CDI**

CASE TYPE: NEW OR RECURRENT?

Previous CDI?

NO

NEW CDI CASE

YES

Was the positive test in the last 8 weeks?

NO

CASE TYPE: NEW OR RECURRENT?

Previous CDI?

YES

Positive test in the last 8 weeks?

YES

2-8 weeks since current treatment

SYMPTOMS RESOLVED BUT RETURNED = RECURRENT CDI CASE

CASE TYPE: NEW OR RECURRENT?

Previous CDI?

NO

NEW CDI CASE

YES

Positive test in the last 8 weeks?

NO

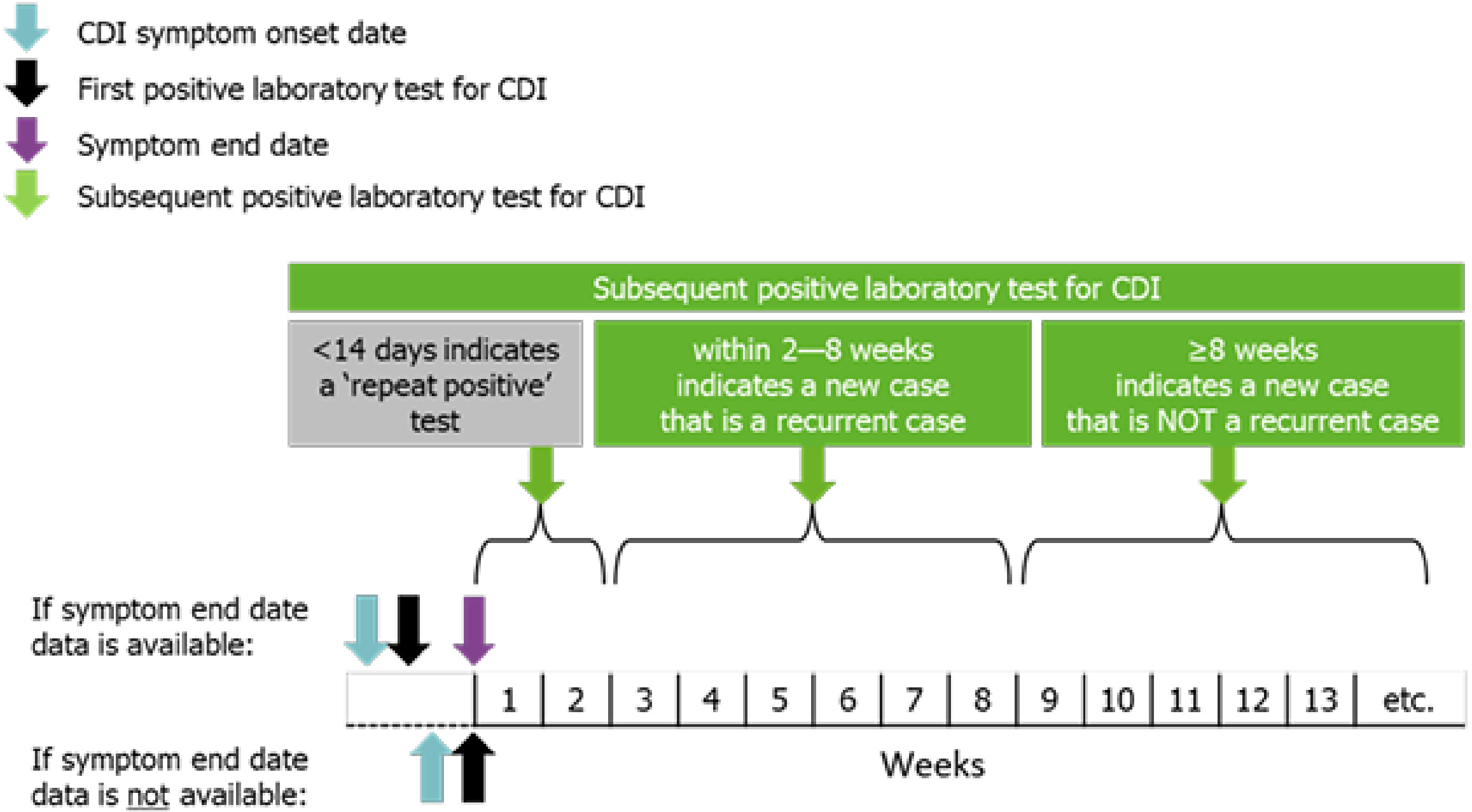
YES

< 2 weeks since current RX
= REPEAT / DO NOT REPORT

Symptomatic
= REPEAT / DO NOT REPORT

2-8 weeks since current treatment

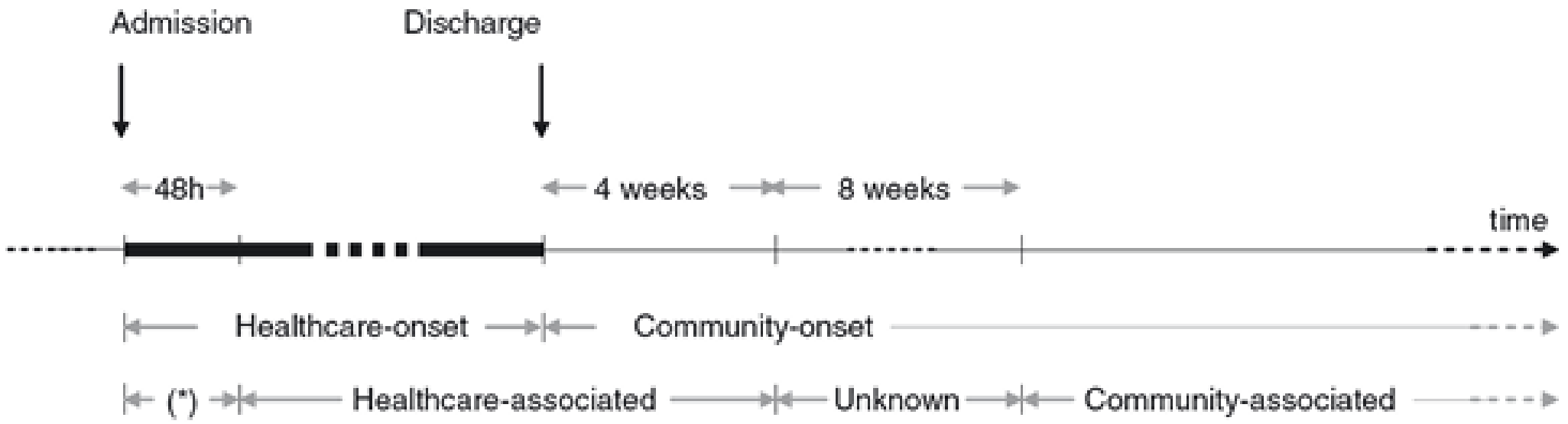
SYMPTOMS RESOLVED BUT RETURNED
= RECURRENT CDI CASE



:www.ecdc.europa.eu/sites/default/files/documents/clostridium-difficile-infections-EU-surveillance-protocol-vers2.4.pdf

ONSET = *WHERE WAS THE PERSON WHEN THEY DEVELOPED SYMPTOMS?*

ORIGIN (ASSOCIATED = *WHERE DID THEY ACQUIRE CDI?*



CDI ORIGIN

Healthcare ASSOCIATED CDI

ADMITTED AS AN INPATIENT

48 HOURS + AFTER ADMISSION

UP TO 4 WEEKS AFTER DISCHARGE

CDI ORIGIN

COMMUNITY ASSOCIATED CDI

NOT ADMITTED

0- 48 HOURS ADMISSION

ADMITTED AS AN INPATIENT

12 WEEKS + AFTER DISCHARGE

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Notifiable since May 2008: Infectious Diseases (Amendment) Regulations 2022

- **Outbreaks**
- **Weekly CDI case reports published**
- **Case type (new/recurrent)**

DATA: *C. DIFFICILE* IN IRELAND

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- **Voluntary national enhanced CDI programme since 2009**
  - **97% of all tertiary and general hospitals participating**
  - **Quarterly CDI reports: Case type / Origin & onset / Severity**
  - **HA-CDI reduction with concurrent rise in community-associated (CA) CDI**

- **National KPI since April 2014: Hospital-acquired CDI rates/10,000 BDU**

	2016	2017	2018	2019	2020	2021
***C. difficile* infection CIDR events notified**	1871	1763	2056	2288	1733	1766
Crude Incidence Rate*/100,000 population	35.7	32.4	38.7	48.4	31.8	32.8
C. difficile infection enhanced cases reported	1877	1906	2030	2185	1707	1774
Rate hospital-acquired** cases/10,000 BDU	2.2	2.2	2.4	2.8	2.3	2.1

Limited ribotyping data: 078 (n=58; 16%), 002 (n=33; 9%), 014 (n=32; 9%), 020 (n=29; 8%) and 005 (n=24; 7%) most common

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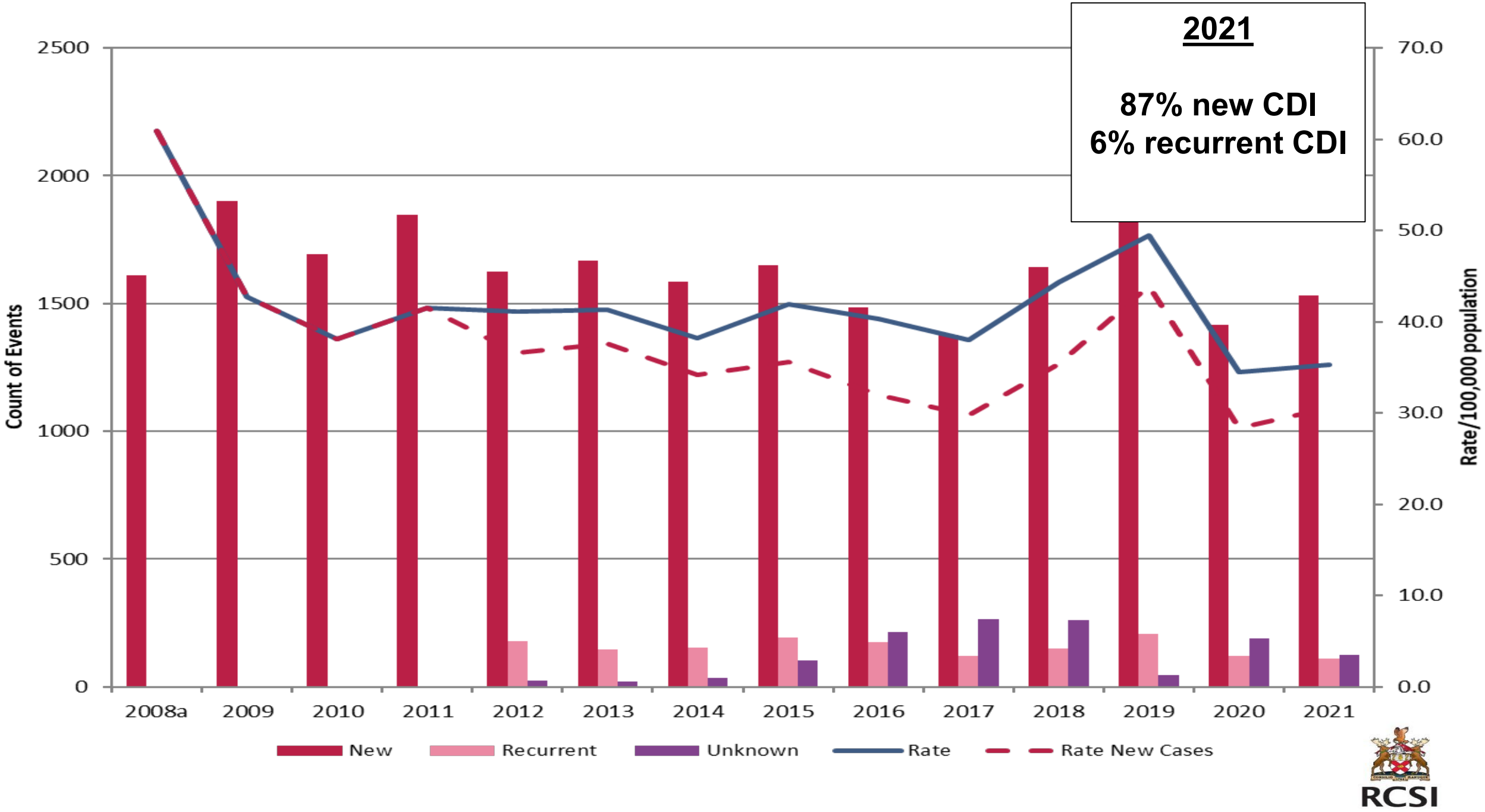
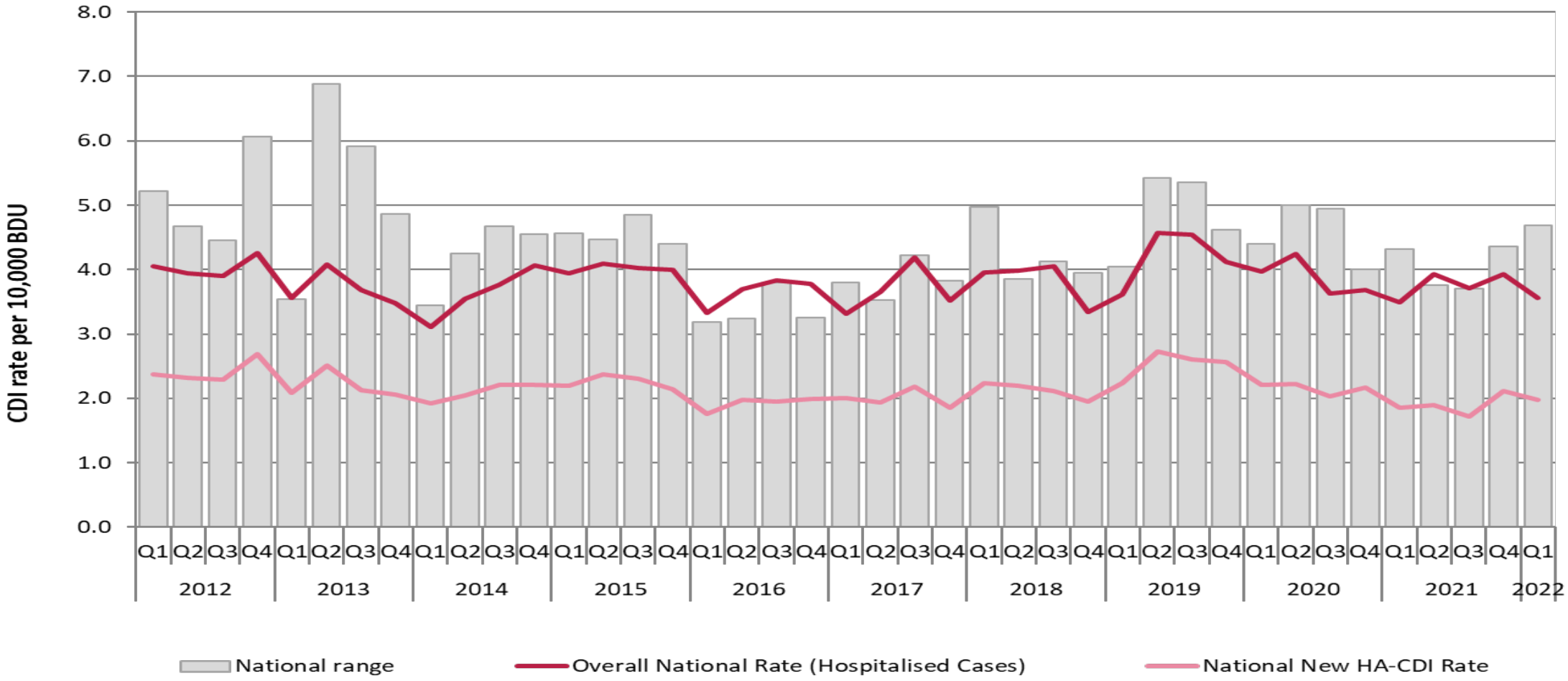


Source: Tara Mitchell HPSC

NATIONAL & HOSPITAL-ACQUIRED CDI RATES
Q1 2012 – Q1 2022



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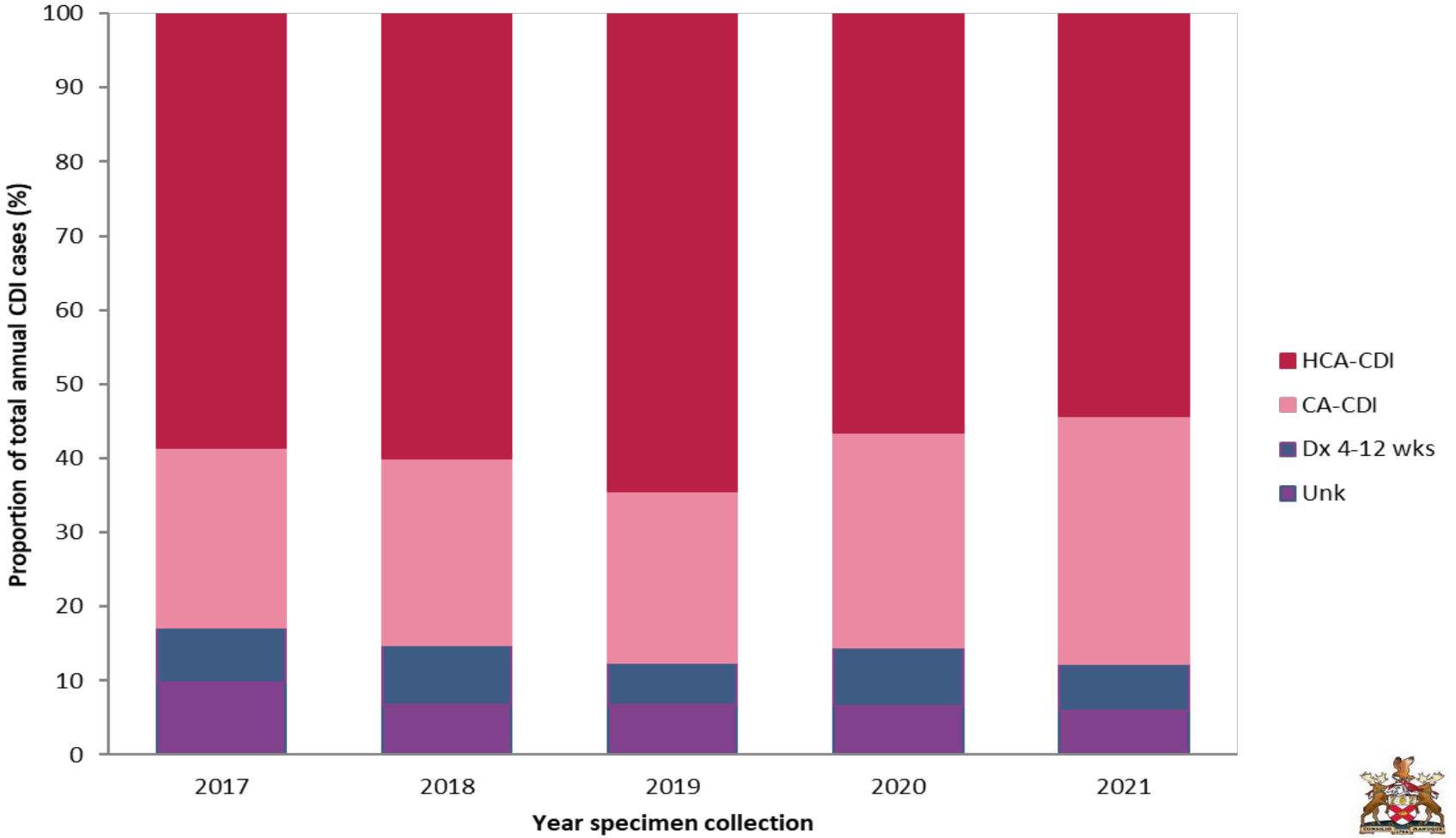
Source: Tara Mitchell HPSC

CDI ORIGIN 2021:
33% COMMUNITY & 54% HEALTHCARE

2013:
- **18% CA**
- **64% HCA**

2019:
National hospital acquired 002 outbreak

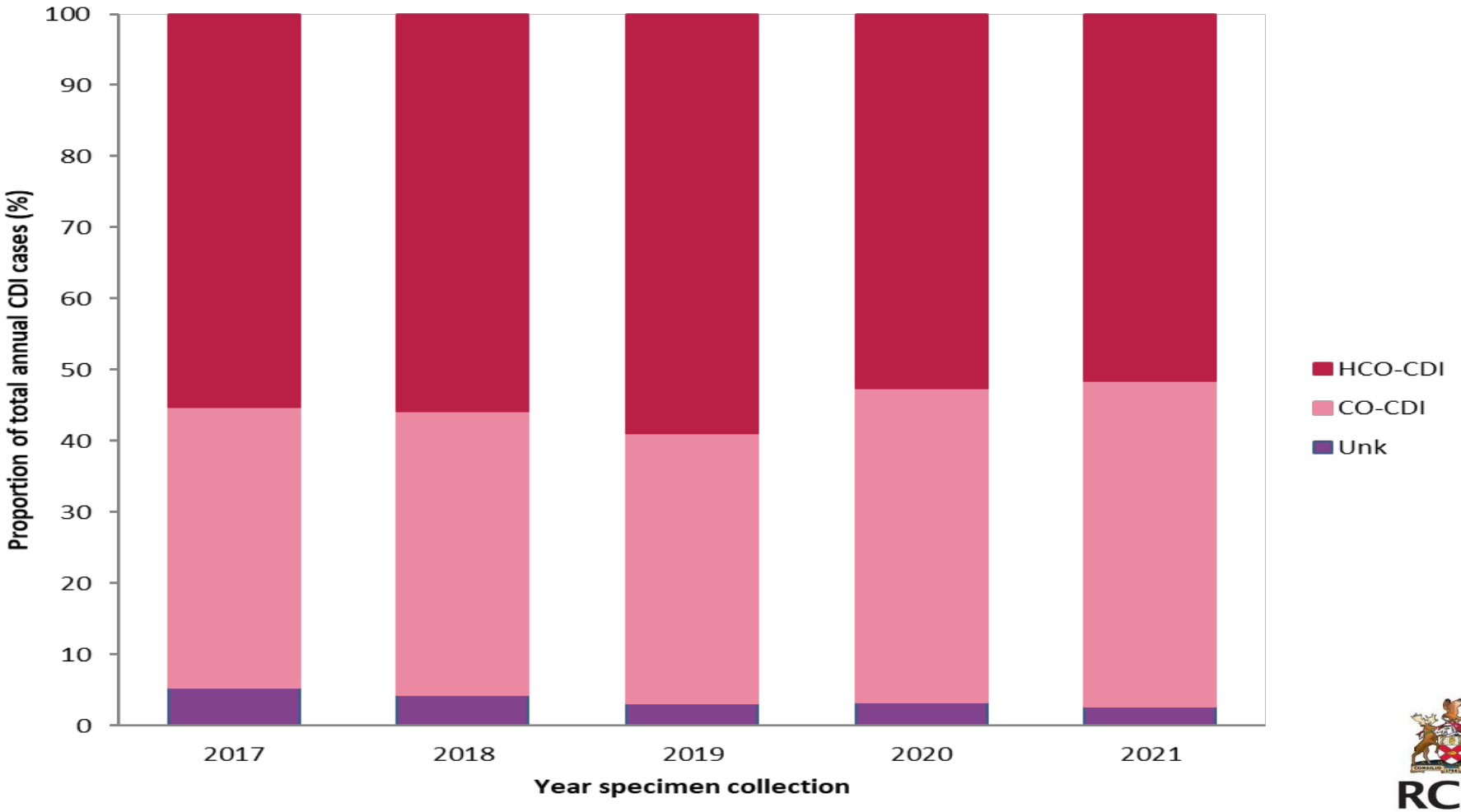


Source: Tara Mitchell HPSC

CDI ONSET 2021:
46% COMMUNITY & 52% HEALTHCARE

2013:
- **29% CO**
- **61% HCO**

2019:
National hospital acquired 002 outbreak



Source: Tara Mitchell HPSC

HOW DOES THIS COMPARE?

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HONG KONG

Crude incidence of *Clostridioides difficile* infections, by epidemiologic category, Hong Kong, China, 2015–2019*

†No. cases/100,000 adults.

		No. cases			Incidence†		
Year	Adult population	Overall	HA-CDI	CA-CDI	Overall	HA-CDI	CA-CDI
2015	6,247,460	3,160	2,921	181	50.6	46.8	2.9
2016	6,301,560	3,303	3,058	185	52.4	48.5	2.9
2017	6,357,420	3,618	3,303	231	56.9	52.0	3.6
2018	6,410,080	3,557	3,248	223	55.5	50.7	3.5
2019	6,481,000	3,467	3,187	205	53.5	49.2	3.2

Guo CLT et al Trends in Incidence and Clinical Outcomes of Clostridioides difficile Infection, Hong Kong. Emerg Infect Dis. 2021 Dec;27(12):3036–44. doi: 10.3201/eid2712.203769. PMID: 34812719; PMCID: PMC8632188.

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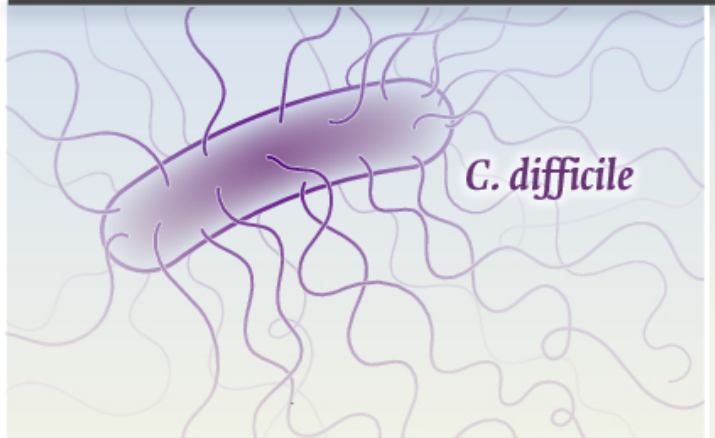
The NEW ENGLAND JOURNAL of MEDICINE

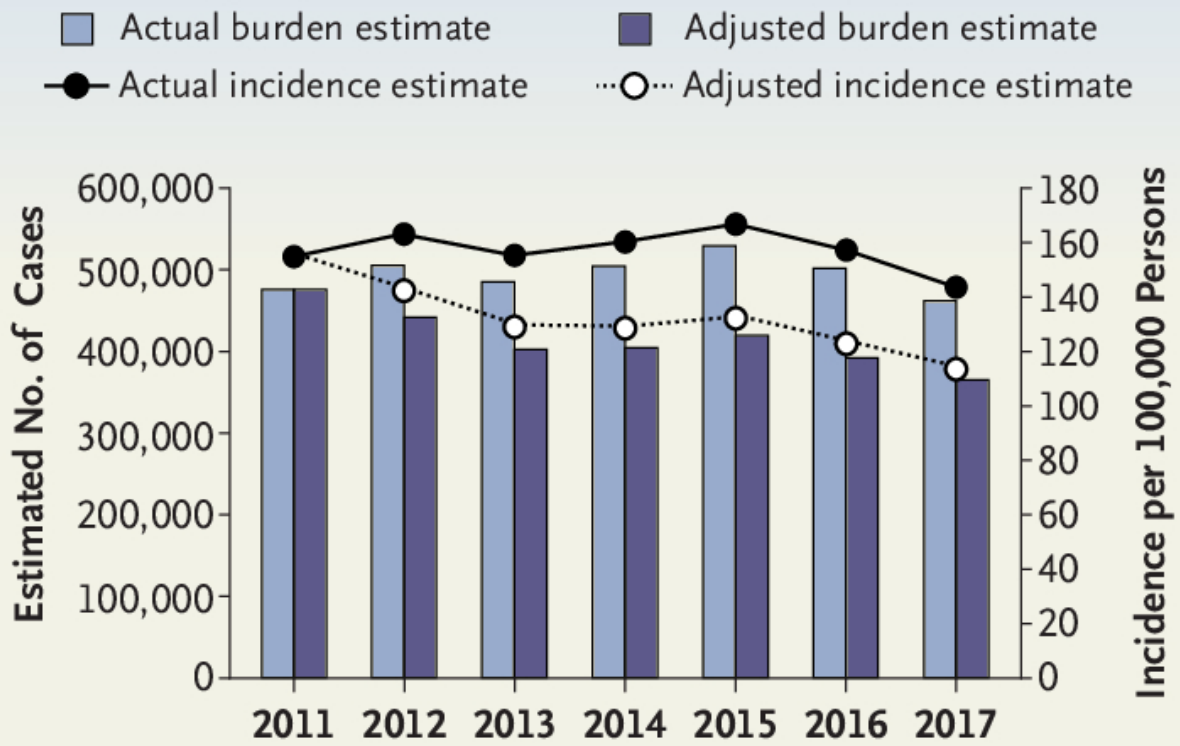
Trends in U.S. Burden of *Clostridioides difficile* Infection

ESTIMATES BASED ON SURVEILLANCE IN 10 U.S. SITES, 2011–2017



Estimates are based on nucleic acid amplification test use adjusted for age, sex, and race.

Adjusted estimates are further adjusted to 2011 nucleic acid amplification test use.



Decreased U.S. infection burden reflected a decline in health care–associated infections

A.Y. Guh et al. 10.1056/NEJMoa1910215

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CDC: POPULATION-BASED SURVEILLANCE: 10 EMERGING INFECTIONS PROGRAM SITES

- **Crude incidence 2021 110.2 /100,000 persons:**
  - **Community associated (55.9/100,000 persons)**
  - **Healthcare-associated cases (54.3/100,000 persons)**
- **Severe CDI rare**

Table 2 – Diagnostic Assay Results of CDI Cases (N=13348)

Diagnostic assay	N	%
Toxin positive	4140	31
Nucleic acid amplification test (NAAT) positive/toxin negative	4465	33
NAAT positive/toxin result unknown[a]	4742	36
Unspecified assay	1	<1

[a] Includes cases diagnosed mainly by NAAT or multiplex PCR panel (i.e., toxin enzyme immunoassay or cell cytotoxicity assay was not performed) or by NAAT as part of a multistep algorithm where the toxin result was not readily known

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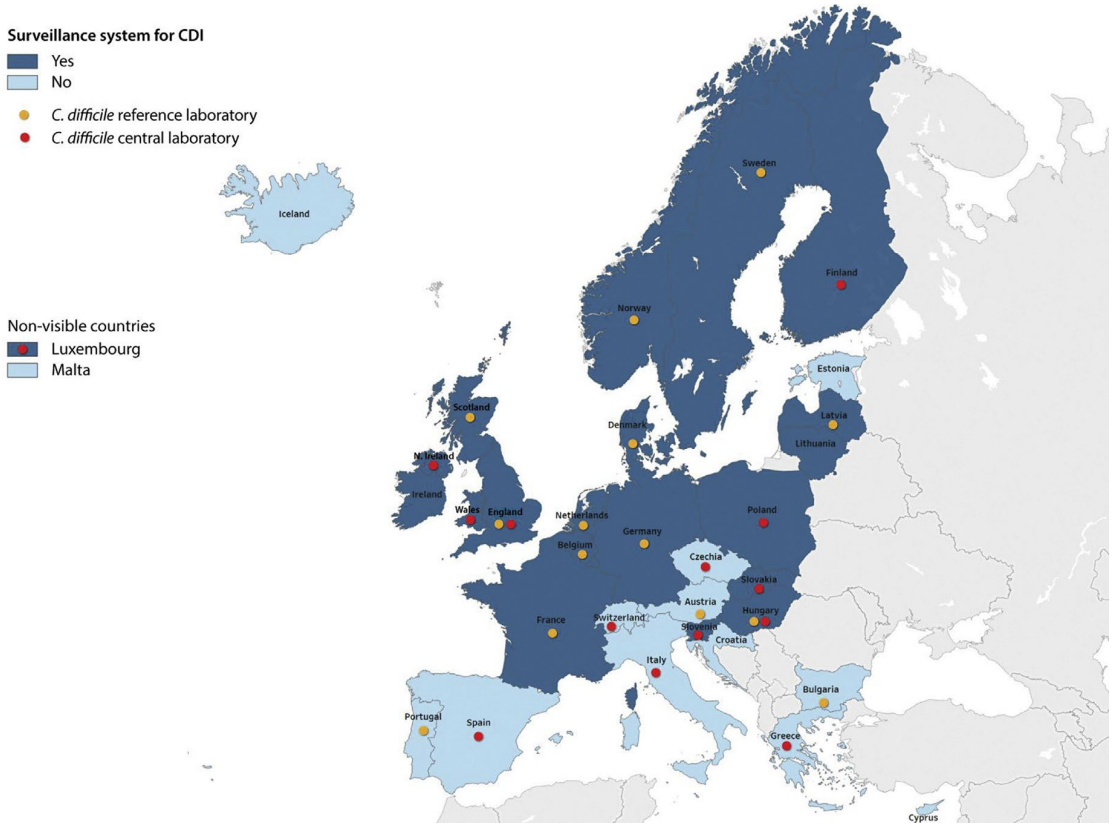
https://www.cdc.gov/hai/eip/Annual-CDI-Report-2021.html

ECDC CDI surveillance in acute care hospitals in EU/EEA countries since 2016

2016-2017 crude incidence in 23 European countries = 3.48 /10,000 patient days

- Healthcare associated (60.9%)
- Community associated or unknown association (32.7%)



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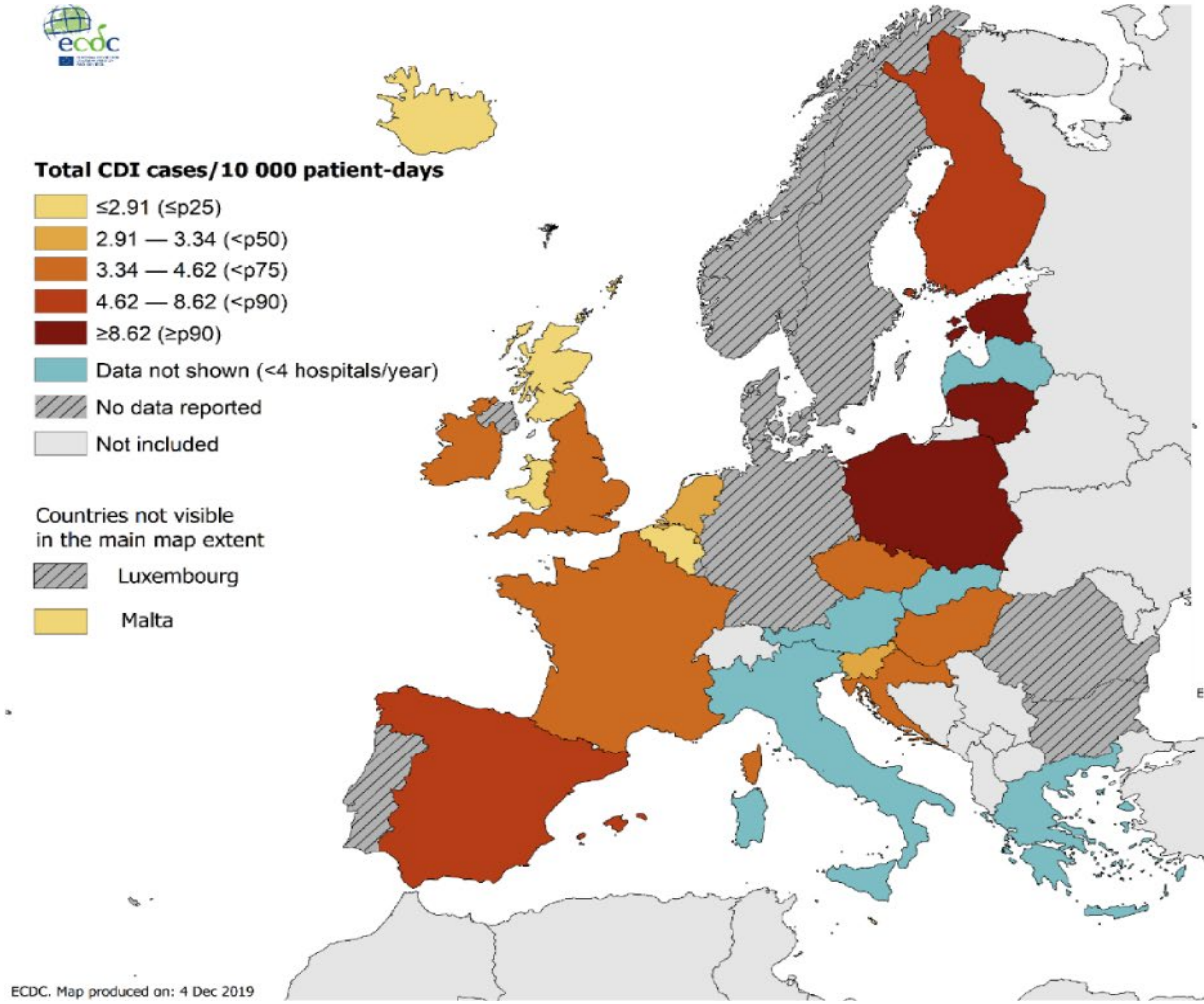

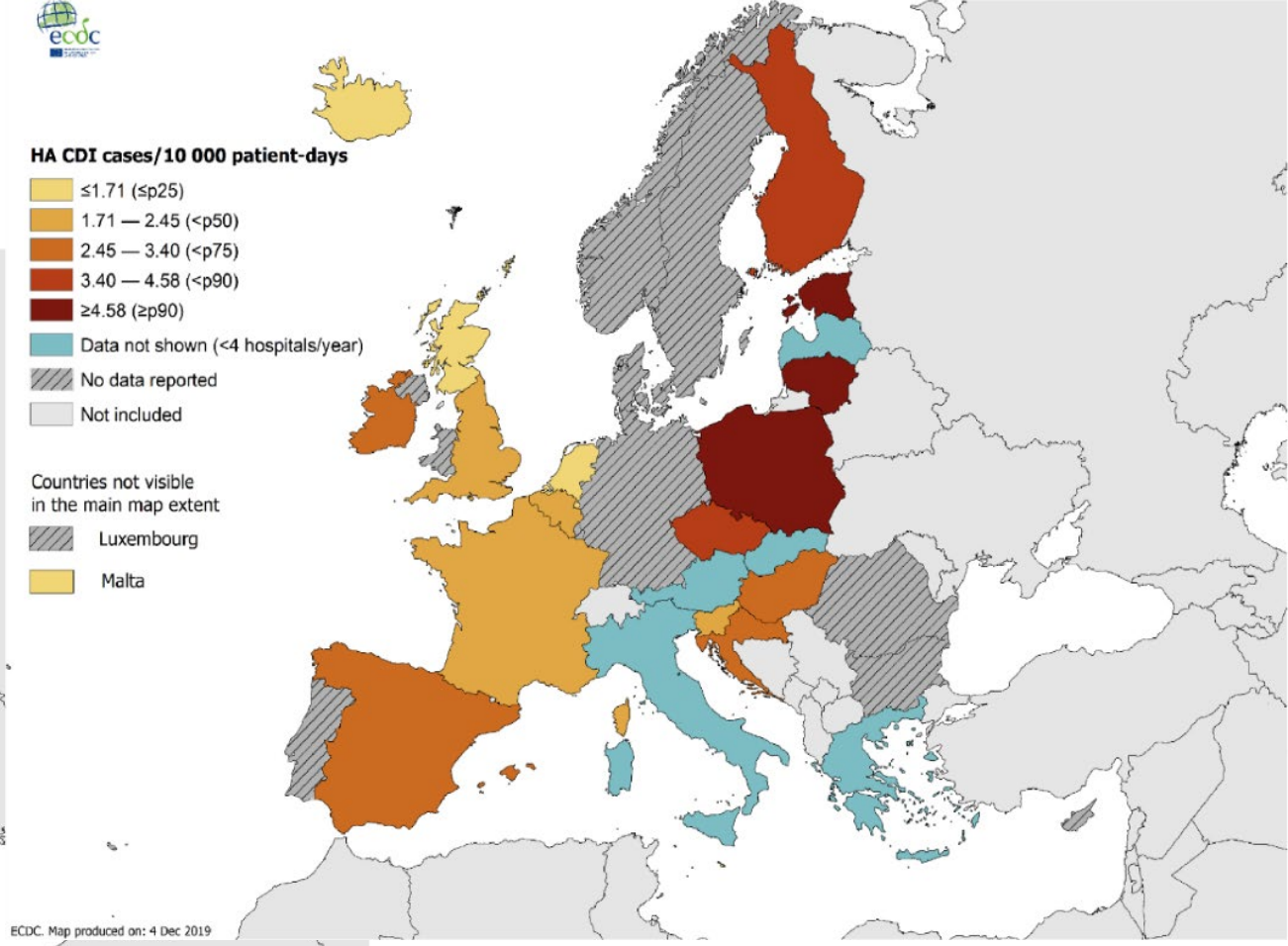

https://atlas.ecdc.europa.eu/public/index.aspx

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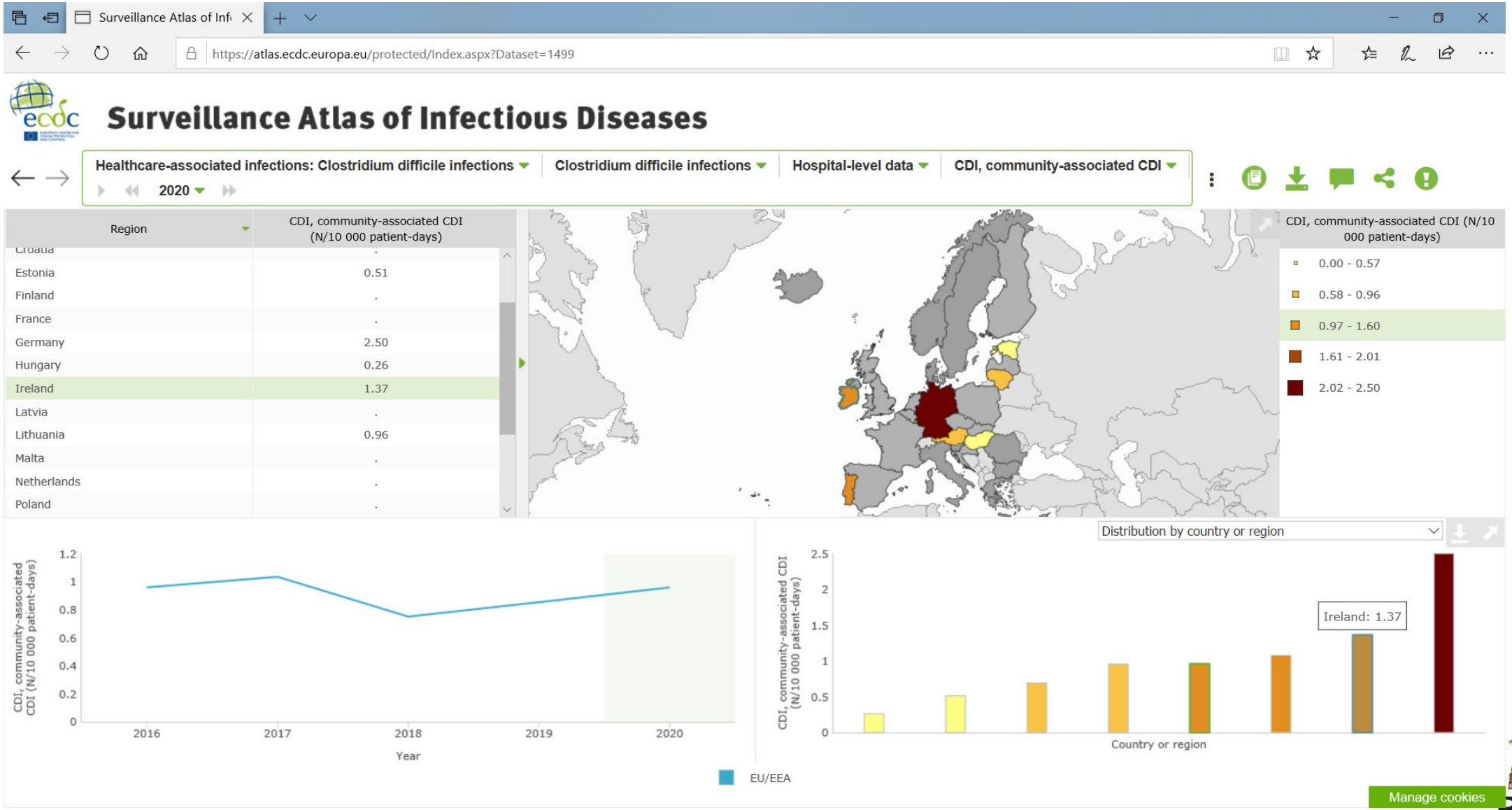
COMMUNITY-ASSOCIATED CDI IN EU, 2020



CDI – NOT JUST HEALTHCARE-ASSOCIATED

Increasing proportion of community-acquired CDI

- **US 2011-2017: adjusted healthcare-associated (HA) CDI decreased X 36%, community-associated (CA)-CDI unchanged**

- **UK GP study 1994-2004: Increase in CDI <1 to 22/100,000**
- **Finland 2008-2013: Increase in CA-CDI from 30.8/100,000 to 37.5/100,000**

Guh AY *et al. NEJM* 2020;382:1230-1330
Dial *et al. JAMA* 2005;294:2989-2995;
Kotila *et al. EID* 2016;22:1747-1753;

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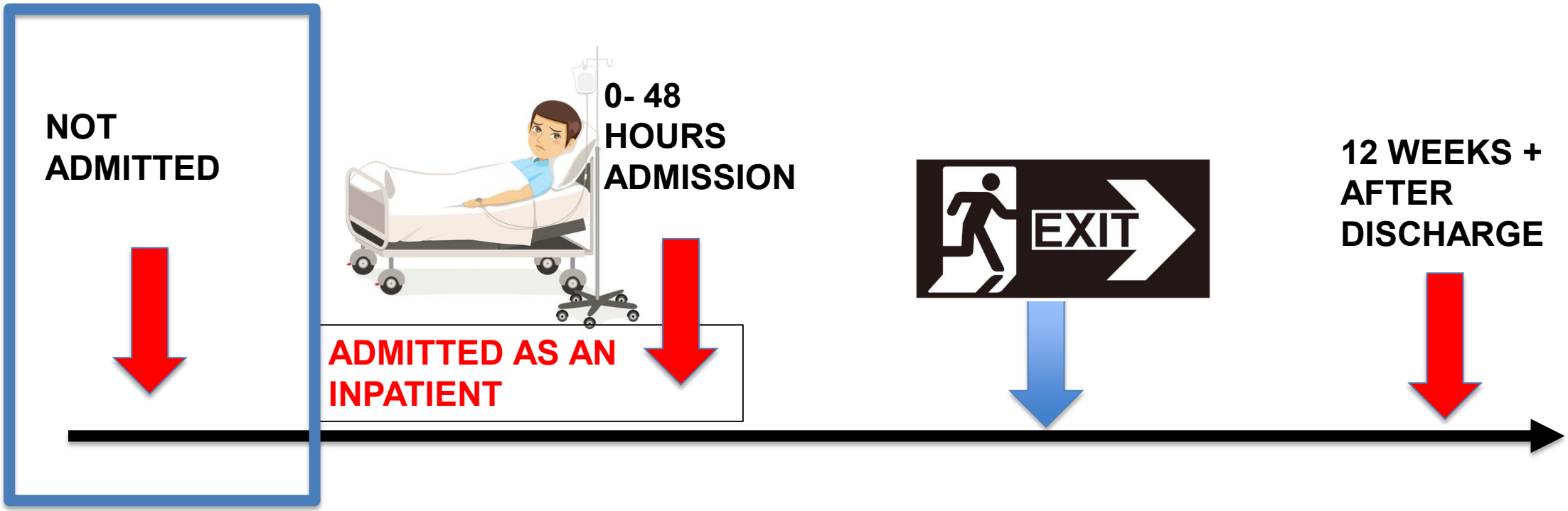
THE PROBLEM WITH "COMMUNITY-ASSOCIATED CDI"



‘COMMUNITY’-ASSOCIATED CDI

- **Patients who live in their own homes + not admitted prior to CDI onset**
- **Patients utilising healthcare day services and live in their own homes**
  - **In our hospital outpatient activity increasing X 21% over ten years**
  - **Day surgery, day wards (e.g., oncology and renal dialysis) etc**

i.e. NO overnight hospital admission but still exposed to healthcare services, professionals and the hospital environment

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Beaumont
Hospital

Department of
Clinical Microbiology &
Infection Prevention and Control

Clean Care is Safer Care

WHAT WOULD HAPPEN IF WE SEPARATED THESE OUT?

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CDI TESTING

RCSI Beaumont Hospital

- 800 bed, tertiary referral teaching hospital: Seven day service – onsite lab
- All stool samples which take the shape of the container, irrespective of clinician request
- 2-step testing
  - From Q1 2015: *C. difficile tcdB* PCR /enzyme immunoassay (EIA) for *C. difficile* toxin
  - Prior (since 2008): glutamate dehydrogenase / *C. difficile tcdB* PCR testing.
- Positive results are phoned daily by the clinical microbiologist
- First positive sample per patient, irrespective of case type, prospectively sent to Leeds Regional Public Health Laboratory

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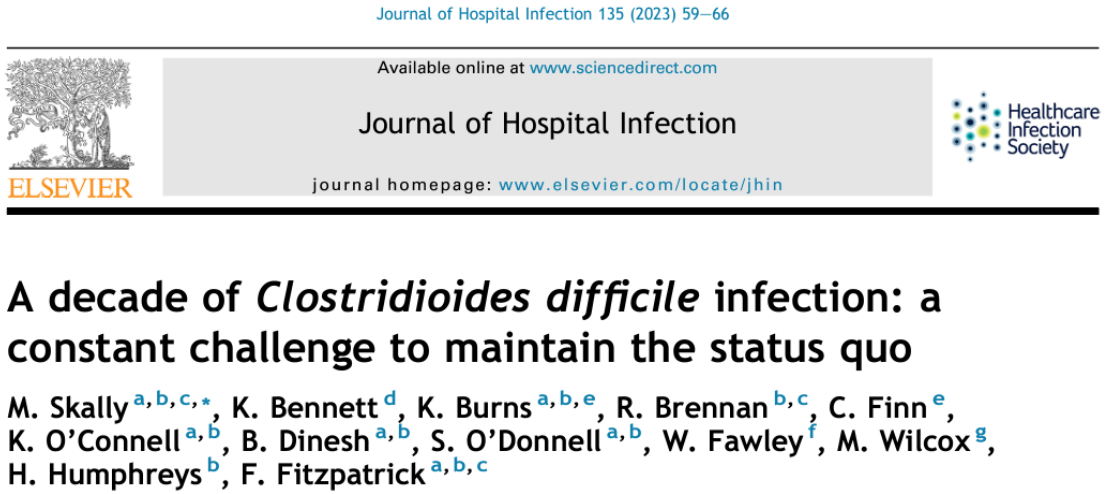
CDI 1ST JANUARY 2012 AND 31ST DECEMBER 2021

- 1,047 new-onset CDI: 205 (20%) CA-CDI


Journal of Hospital Infection 135 (2023) 59–66

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

ELSEVIER

Healthcare Infection Society

A decade of *Clostridioides difficile* infection: a constant challenge to maintain the status quo

M. Skally[a,b,c,*], K. Bennett[d], K. Burns[a,b,e], R. Brennan[b,c], C. Finn[e], K. O'Connell[a,b], B. Dinesh[a,b], S. O'Donnell[a,b], W. Fawley[f], M. Wilcox[g], H. Humphreys[b], F. Fitzpatrick[a,b,c]

CA-CDI vs HA-CDI

- Younger (< 65 yrs: 50% vs 30% p<0.01)
- More females (68% vs 54% p<0.01)
- Shorter median length of stay (9 vs 31 days p<0.01)

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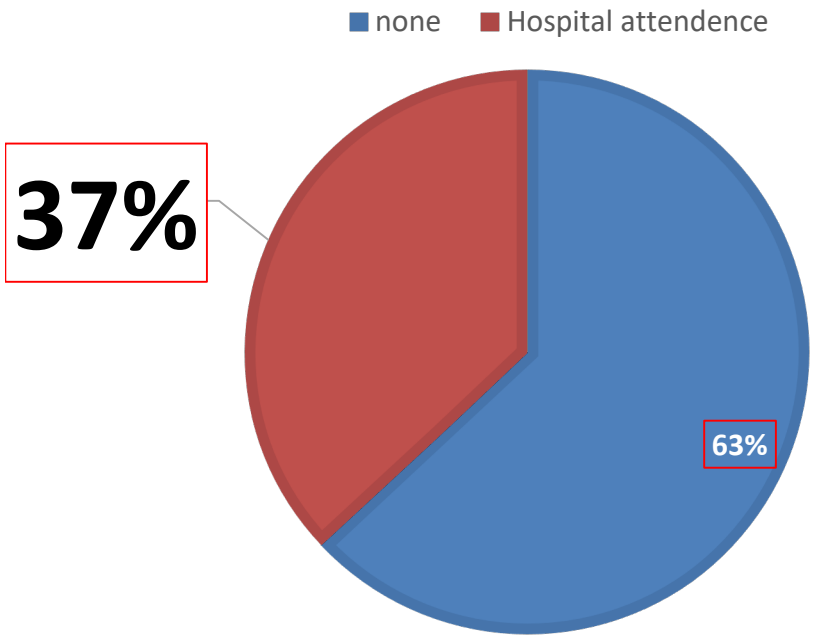
HOSPITAL ATTENDANCE IN PREVIOUS 12 WEEKS (N=205)



	Day attendance (n=75)	Number of day attendences (n=348)		
	N %	N %	Median	IQR[a]
Day ward	30 (40%)	64 (18 %)	1	1 - 3
Haematology day services	5 (7%)	74 (21%)	12	11 - 21
Oncology day services	4 (5%)	22 (6 %)	4	3 - 8
Haemodialysis (2 +)	4 (5%)	144[b] (41 %)	N/A	N/A
Emergency Dept (2 +)	24 (32%)	35 (10%)	1	1 - 2
Radiology	8 (11%)	9 (3%)	1	1 - 1

Accessible Version: https://www.cdc.gov/hai/eip/Annual-CDI-Report-2021.html

MEANWHILE IN THE US 2021:

Emerging Infections Program
Healthcare-Associated Infections–Community Interface Report
***Clostridioides difficile* Infection Surveillance, 2021**

Table 8 – Selected Healthcare Exposures and Risk Factors of Incident CDI Cases in the 12 Weeks Before the Date of Incident Specimen Collection by Epidemiologic Classification (N=6558)

Healthcare Exposure[a]	CA (N=4292), N	CA (N=4292), %	COHCFA (N=1773), N	COHCFA (N=1773), %	HCFO (N=493), N	HCFO (N=493), %
Acute care hospitalization	0	0	1734	98	244	49
Long-term care facility residence	0	0	187	11	178	36
Long-term acute care hospitalization	0	0	7	<1	9	2
Surgery	196	5	491	28	125	25
Emergency room	881	21	740	42	142	29
Observation unit	69	2	103	6	17	3
Chronic dialysis	106	2	163	9	51	10

[a] Healthcare exposure categories are not mutually exclusive.

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DO WE NEED A NEW CASE DEFINITION TO CAPTURE THESE PATIENTS? HEALTHCARE EXPOSURE (HE)

- **Discharged from a healthcare facility between 4 & 12 weeks before the onset of symptoms**

AND

- **One + day case, oncology day ward, haematology day ward or haemodialysis attendances**

or

- **Two + radiology or emergency department attendances**

within the previous 12 weeks

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WHY IS THIS IMPORTANT?

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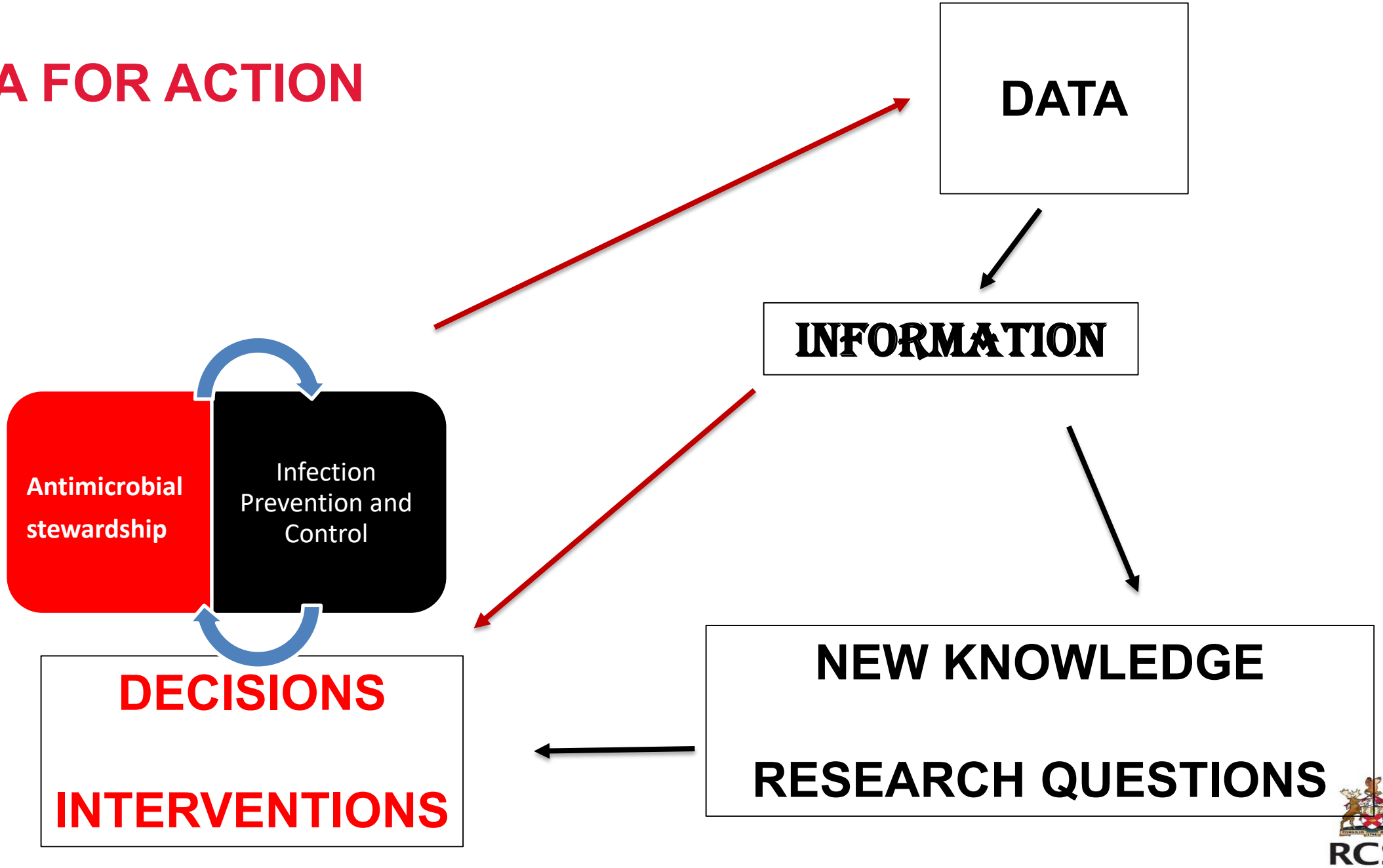
DATA FOR ACTION



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WE NEED TO TEASE OUT SUBGROUPS OF CA-CDI

Significant burden of disease

- **Patients tend to be younger**
- **Many have no recent history of antibiotic treatment**
- **By definiton = Lack of recent admission to HCF but not lack of healthcare contact**

What does this mean?

- **We may need to modify our CDI control strategies to each subgroup**
- **What additional reservoirs and routes of transmission are important?**

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ACKNOWLEDGEMENTS

- **Mairead Skally, Beaumont Hospital and RCSI**
- **Tara Mitchell, HPSC**
- **Staff and colleagues Microbiology and Infection Prevention and Control Beaumont Hospital and Clinical Microbiology RCSI**

ESGCD
ESCMID STUDY GROUP FOR CLOSTRIDIUM DIFFICILE
European Society of Clinical Microbiology and Infectious Diseases

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