Clostridioides difficile
– Healthcare transmission in a Swedish setting

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About me

MD, resident physician, VGR

- Infection Protection and Control
- Clinical Microbiology

PhD student, GU

- *Clostridioides difficile*: preventive strategies
- Main supervisor: Gunnar Jacobsson

Course leader, Nordic master programme, GU

- 3rd course (15 hp), Infection Protection and Control (“Smittskydd & Vårdhygien”)

Background

KLINIK & VETENSKAP VÅRDUTVECKLING

Citera som: Läkartidningen. 2014;111:CIIL

Lömskt och omfattande utbrott av Clostridium difficile

Ändrade städrutiner och täta utvärderingar halverade infektionerna

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SVENSKA DAGBLADET

Fjärde dödsfallet av ny tarmbakterie i Växjö

Ytterlig
aggress
misstär

Ystads lasarett höll dödsorsaken hemlig

Publicerad 19 jun 2014 kl 06.34

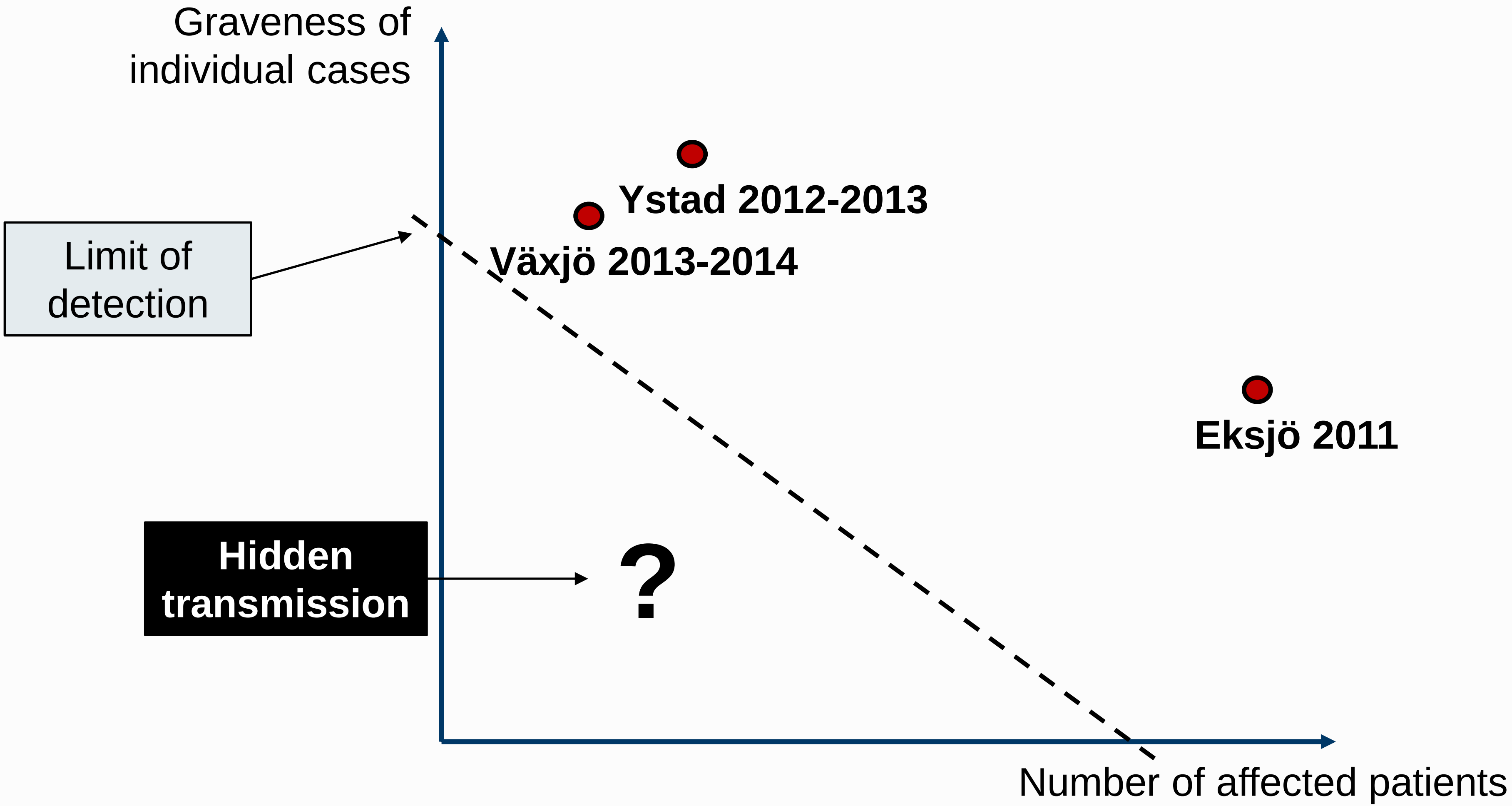
Tio patienter avled i sviterna av den aggressiva tarmbakterien på Ystads lasarett.

Men ledningen för sjukhuset valde att dölja den verkliga dödsorsaken för de anhöriga. Det gjordes inte ens någon Lex Maria-anmälan om händelserna.

– Jag är otroligt besviken. Det är ett flagrant misstag och jag vill verkligen be alla anhöriga om ursäkt, säger regiondirektören Jonas Rastad.

C. difficile outbreaks in Sweden during the 2010s described in the media:

- Insidious and extensive outbreak
- Fourth death from new gut bacterium
- The hospital kept the cause of death secret



Graveness of individual cases

Limit of detection

Hidden transmission

?

Ystad 2012-2013

Växjö 2013-2014

Eksjö 2011

Number of affected patients

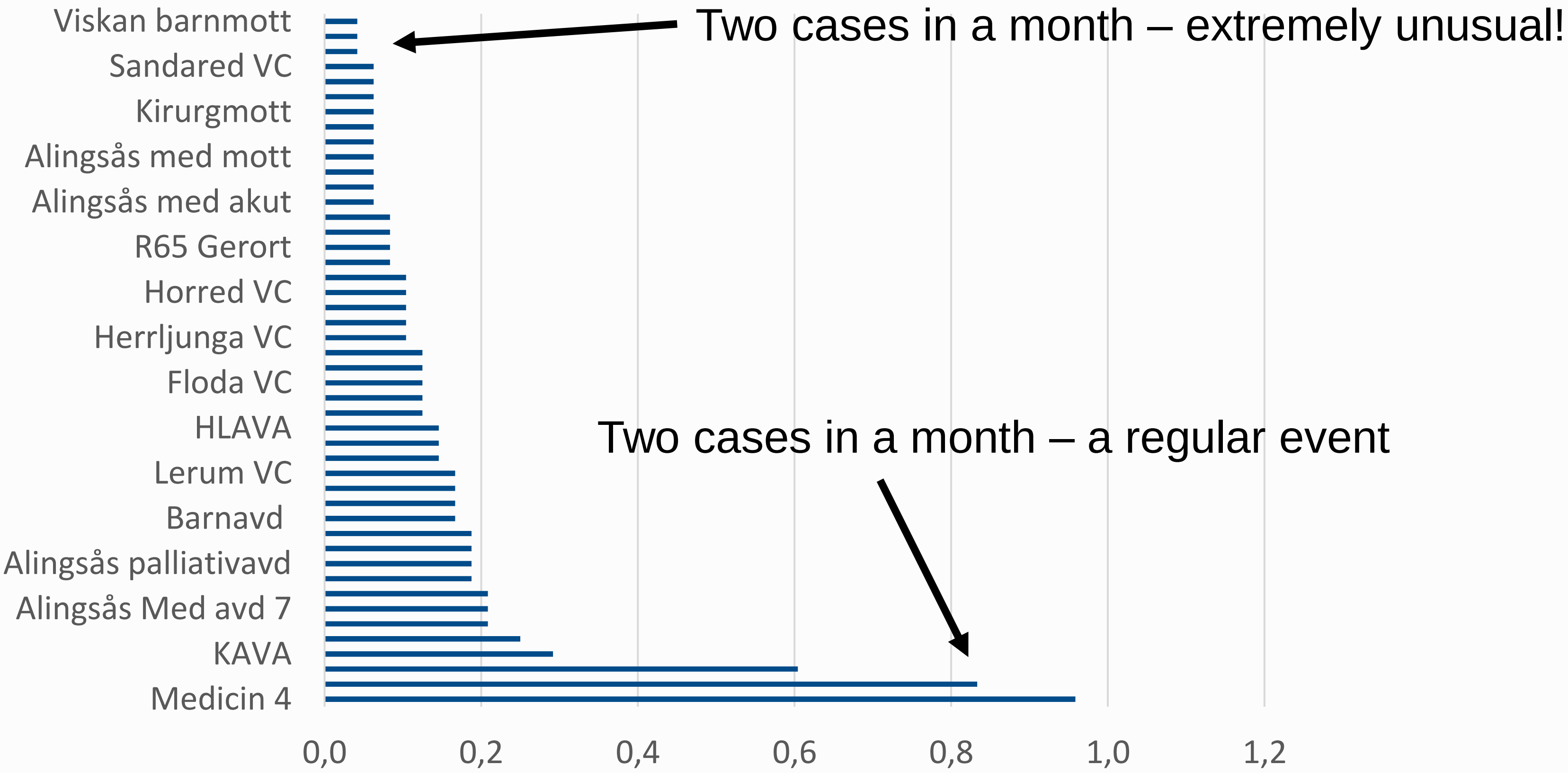
How to detect outbreaks early enough?

Classic definition of a suspected outbreak: two cases with a suspected connection

In practice: two cases from the same ward within the same month?

This algorithm seemed to result in a lot of false alarms on certain wards.

Cases/month, Borås hospital dec 2013 - nov 2017



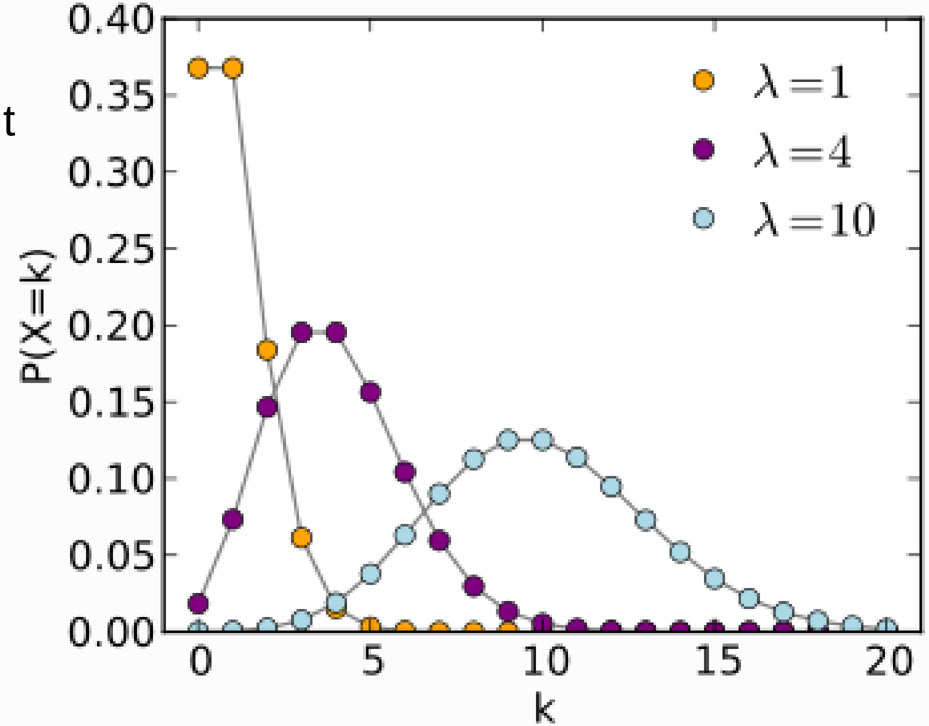
Two cases in a month – extremely unusual!

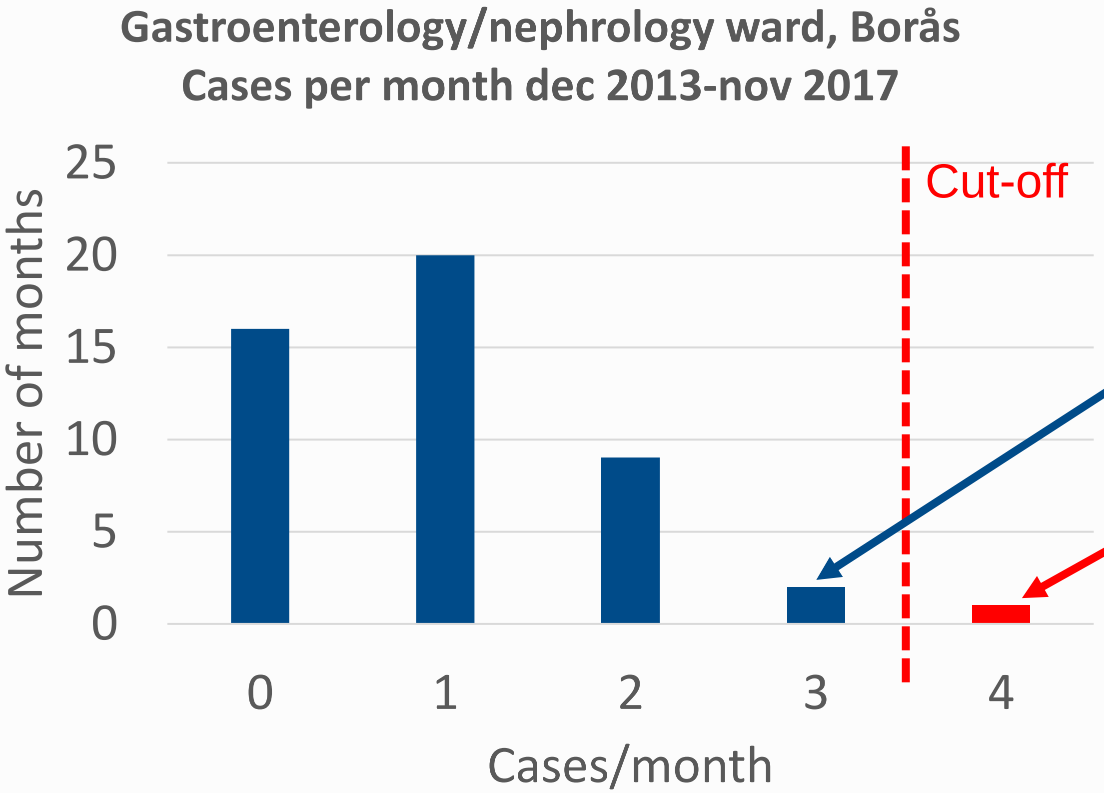
Two cases in a month – a regular event

Poisson distribution

Lambda = expected frequency/time unit

Variance = lambda



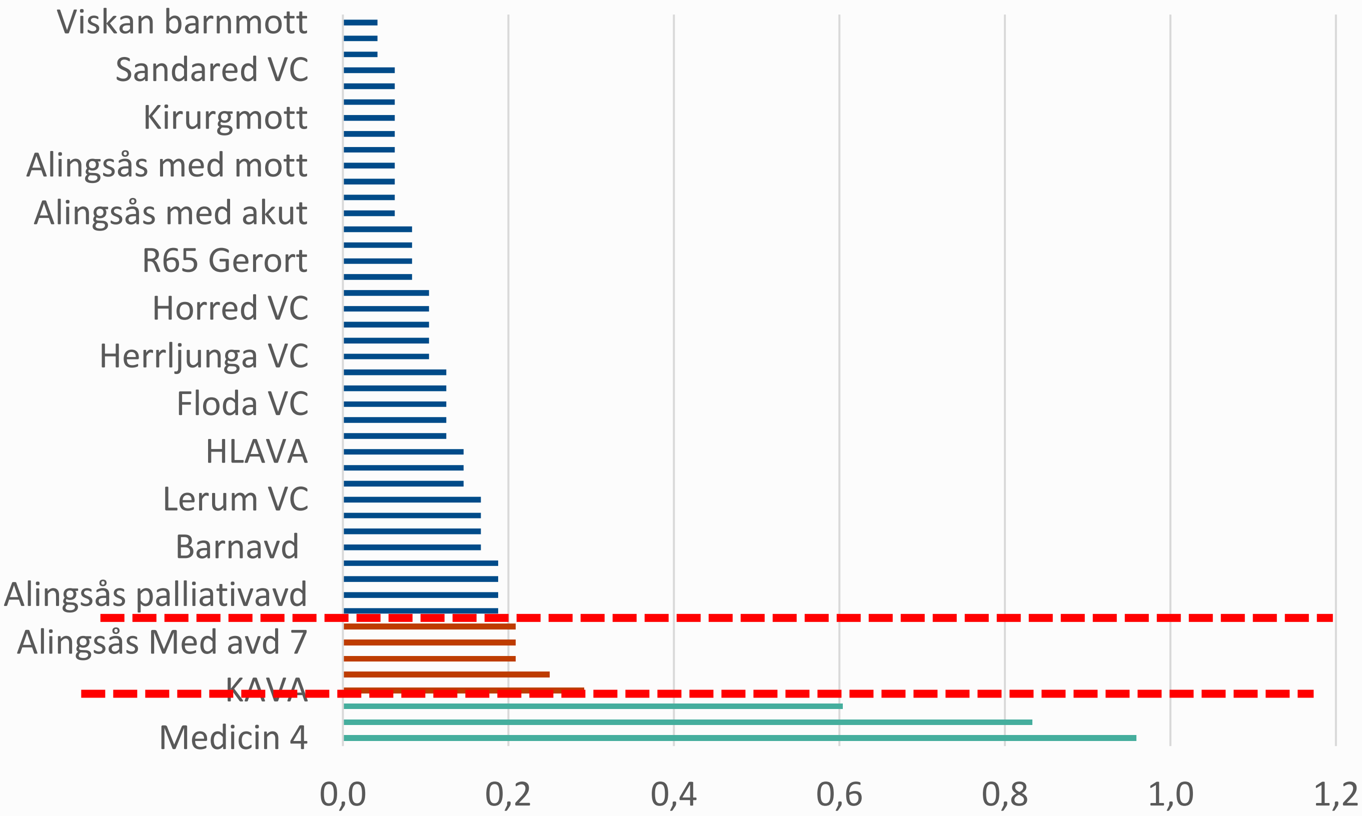


Gastroenterology/nephrology ward, Borås
Cases per month dec 2013-nov 2017

Expected to happen every 15 months

Expected to happen every five years

Cases/month, dec 2013-nov 2017



2 cases/month ->
measures taken

3 cases/month ->
measures taken

4 cases/month ->
measures taken

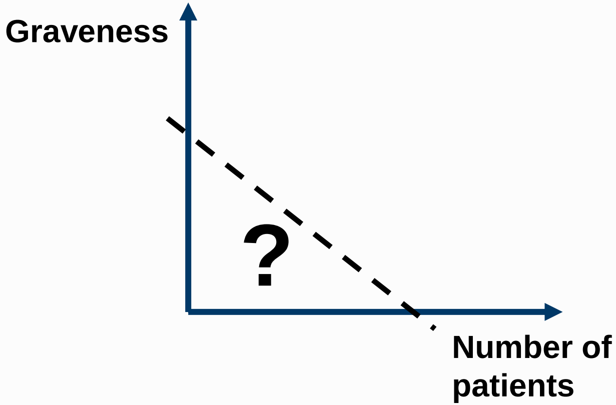
Measures taken

- Chart review (when/where did the patient get symptoms? How severe are the symptoms?
- Have the patients been in the same room?
- Inform unit manager – remind them of CDI routines
- Consider ribotyping
- Consider initiating an outbreak group

Aim

Study aims

1. Hidden transmission: how common is it?



2. Evaluate ward-specific cut-off

(and the simpler two-case algorithm)

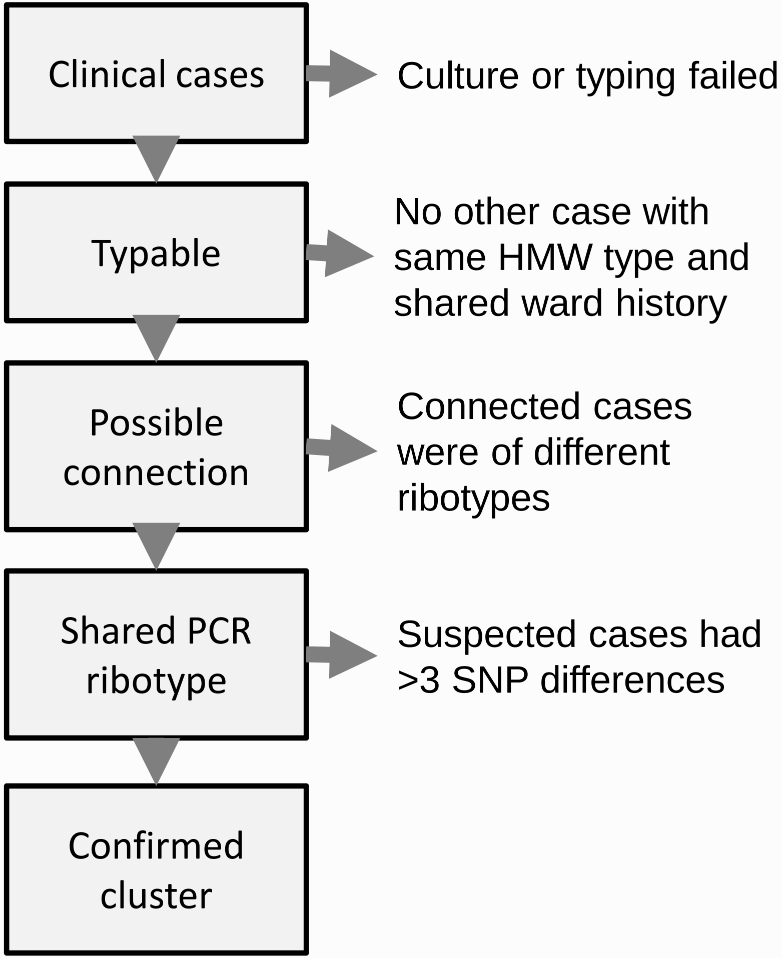
Methods

All positive toxin PCR at two hospitals during two years (2020 & 2021) were studied

Culture -> High Molecular Weight typing by MALDI-TOF

Medical records studied – shared ward + shared *C. difficile* type?

Ribotyping and Whole Genome Sequencing of isolates in suspected clusters



Clinical cases

Culture or typing failed

Typable

No other case with same HMW type and shared ward history

Possible connection

Connected cases were of different ribotypes

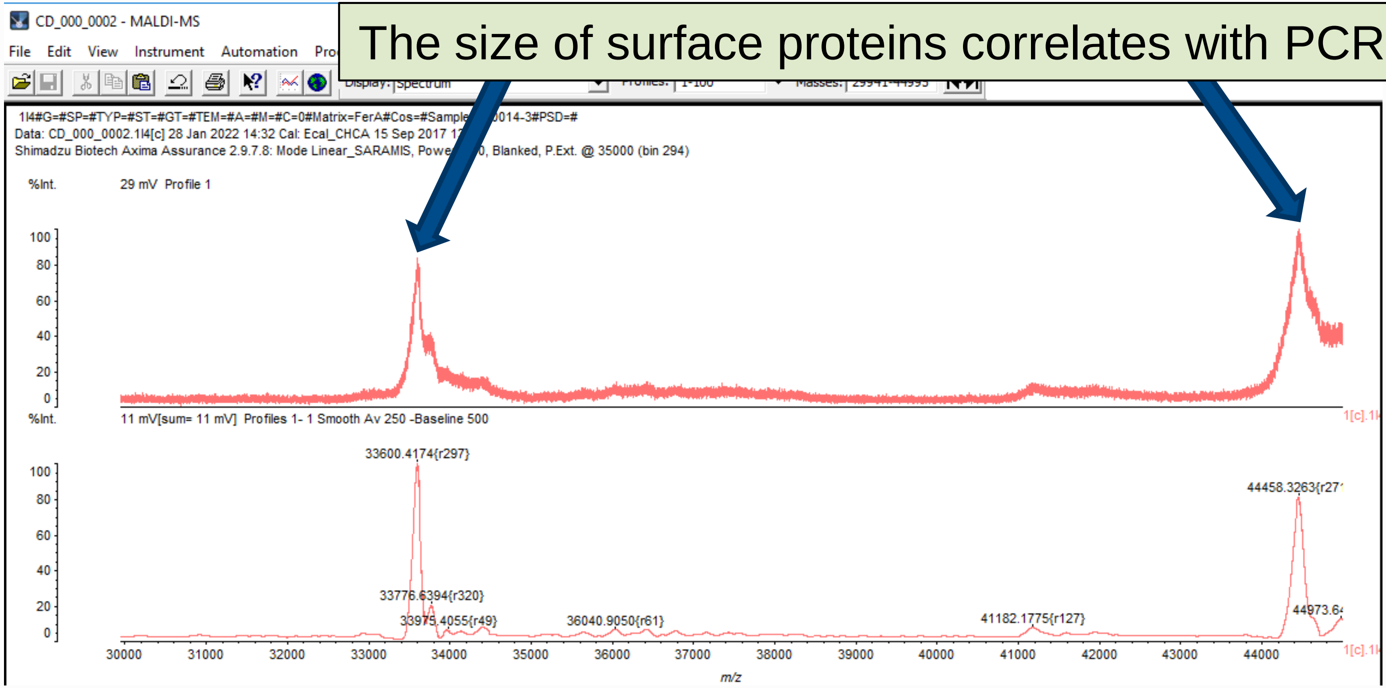
Shared PCR ribotype

Suspected cases had >3 SNP differences

Confirmed cluster

HMW typing

(High Molecular Weight typing using MALDI-TOF)



The size of surface proteins correlates with PCR ribotype

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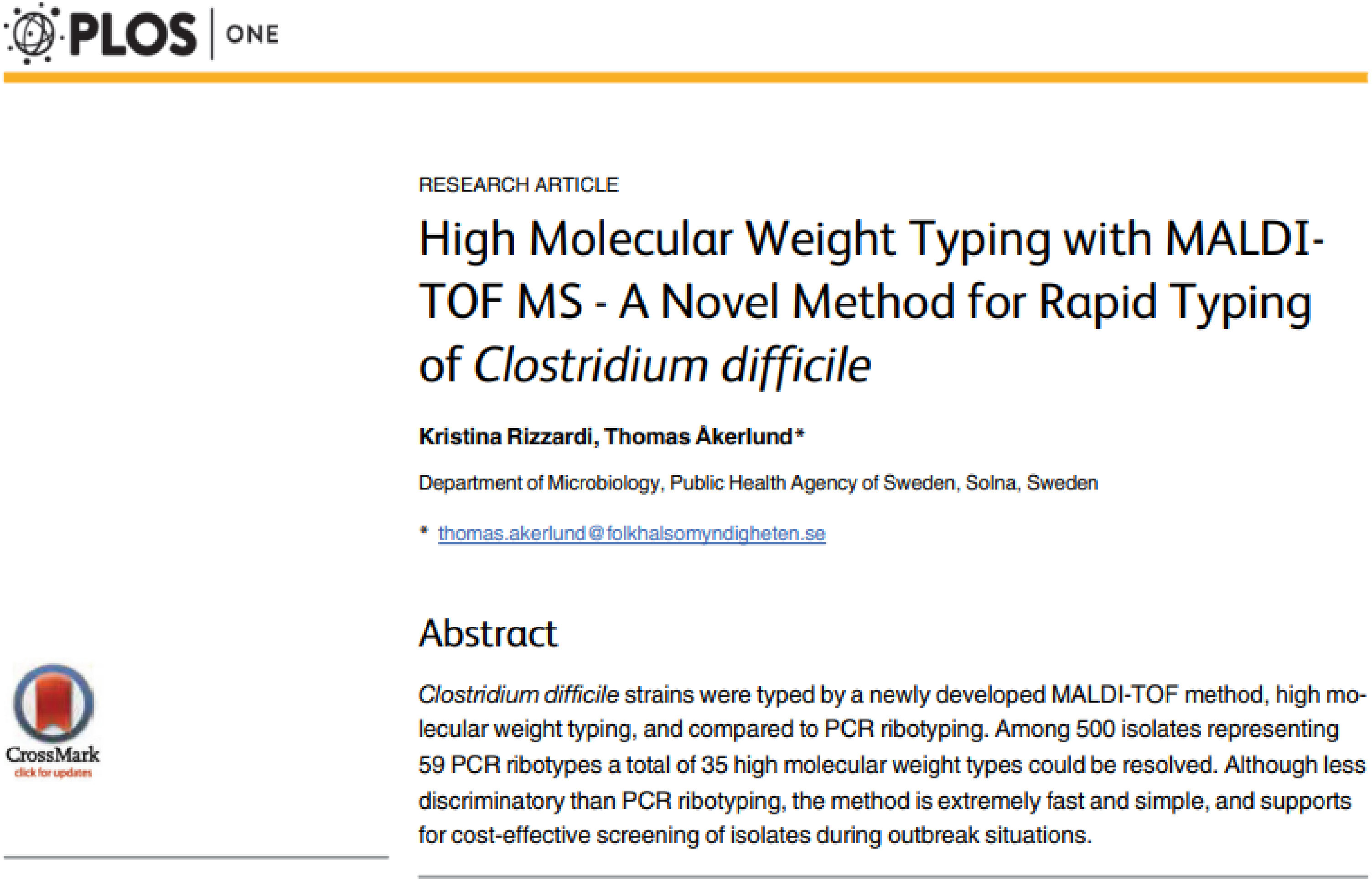
1I4#G=#SP=#TYP=#ST=#GT=#TEM=#A=#M=#C=0#Matrix=FerA#Cos=#Sample 0014-3#PSD=#
Data: CD_000_0002.1I4[c] 28 Jan 2022 14:32 Cal: Ecal_CHCA 15 Sep 2017 1
Shimadzu Biotech Axima Assurance 2.9.7.8: Mode Linear_SARAMIS, Powe 0, Blanked, P.Ext. @ 35000 (bin 294)
```



PLOS | ONE

RESEARCH ARTICLE

High Molecular Weight Typing with MALDI-TOF MS - A Novel Method for Rapid Typing of *Clostridium difficile*

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Abstract

Clostridium difficile strains were typed by a newly developed MALDI-TOF method, high molecular weight typing, and compared to PCR ribotyping. Among 500 isolates representing 59 PCR ribotypes a total of 35 high molecular weight types could be resolved. Although less discriminatory than PCR ribotyping, the method is extremely fast and simple, and supports for cost-effective screening of isolates during outbreak situations.

HMW typing

(High Molecular Weight typing using MALDI-TOF)

Once set up, it is easy to perform and cheap, using regular lab equipment

Excellent for ruling out suspected transmission

Not high-res enough to confirm transmission

Used in conjunction with Whole Genome Sequencing at Swedish national reference labs (Örebro University Hospital, Public Health Agency of Sweden

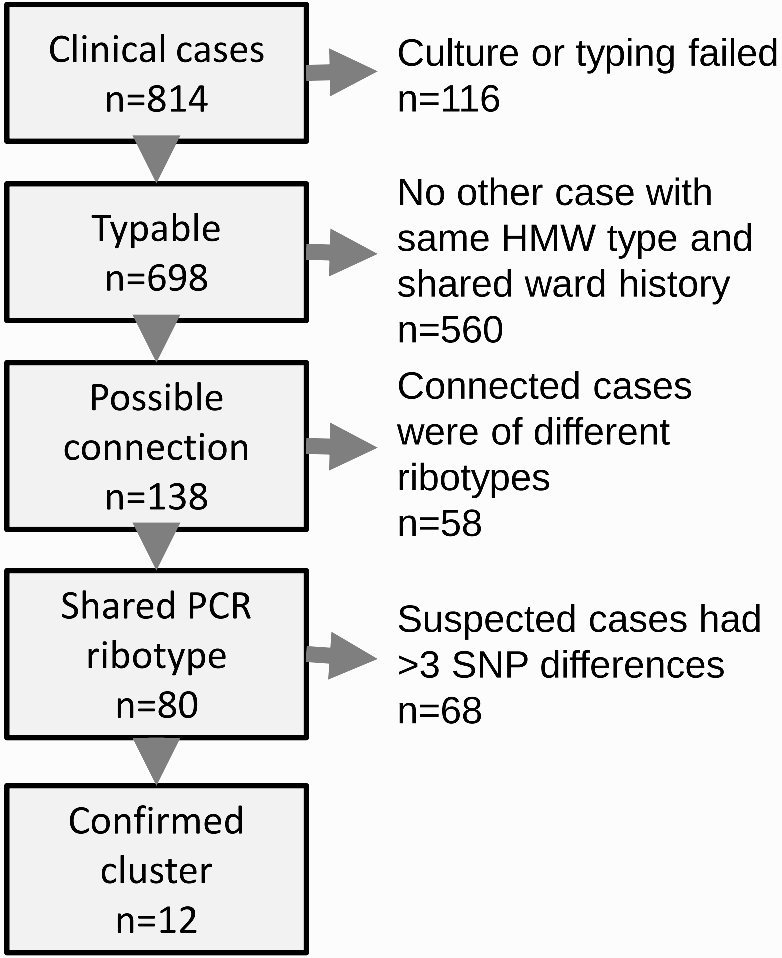
Results

All positive toxin PCR at two hospitals during two years (2020 & 2021) were studied

Culture -> High Molecular Weight typing by MALDI-TOF

Medical records studied – shared ward + shared *C. difficile* type?

Ribotyping and Whole Genome Sequencing of isolates in suspected clusters



Clinical cases
n=814

Culture or typing failed
n=116

Typable
n=698

No other case with same HMW type and shared ward history
n=560

Possible connection
n=138

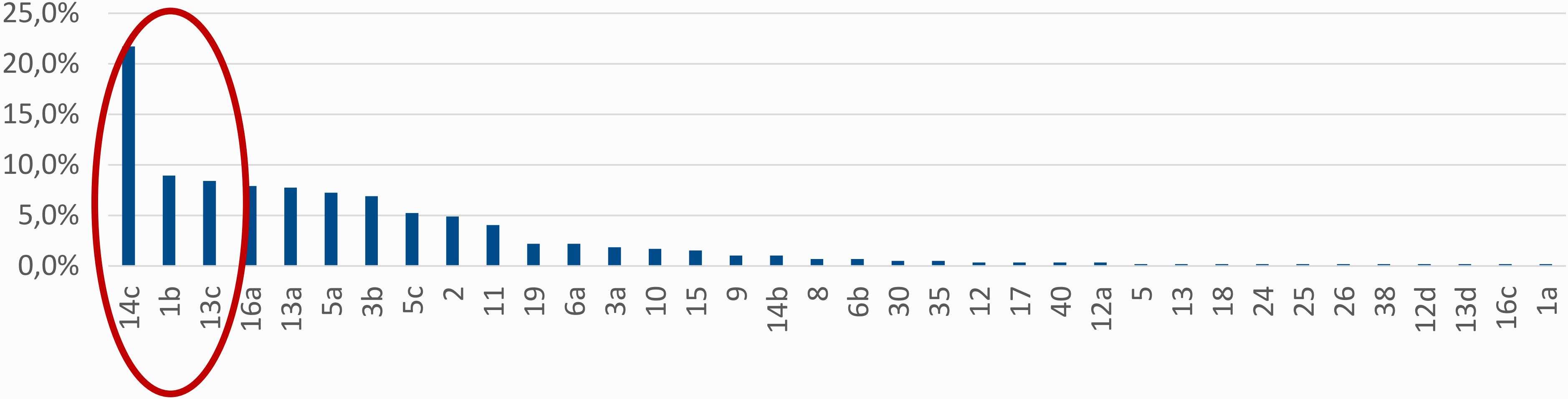
Connected cases were of different ribotypes
n=58

Shared PCR ribotype
n=80

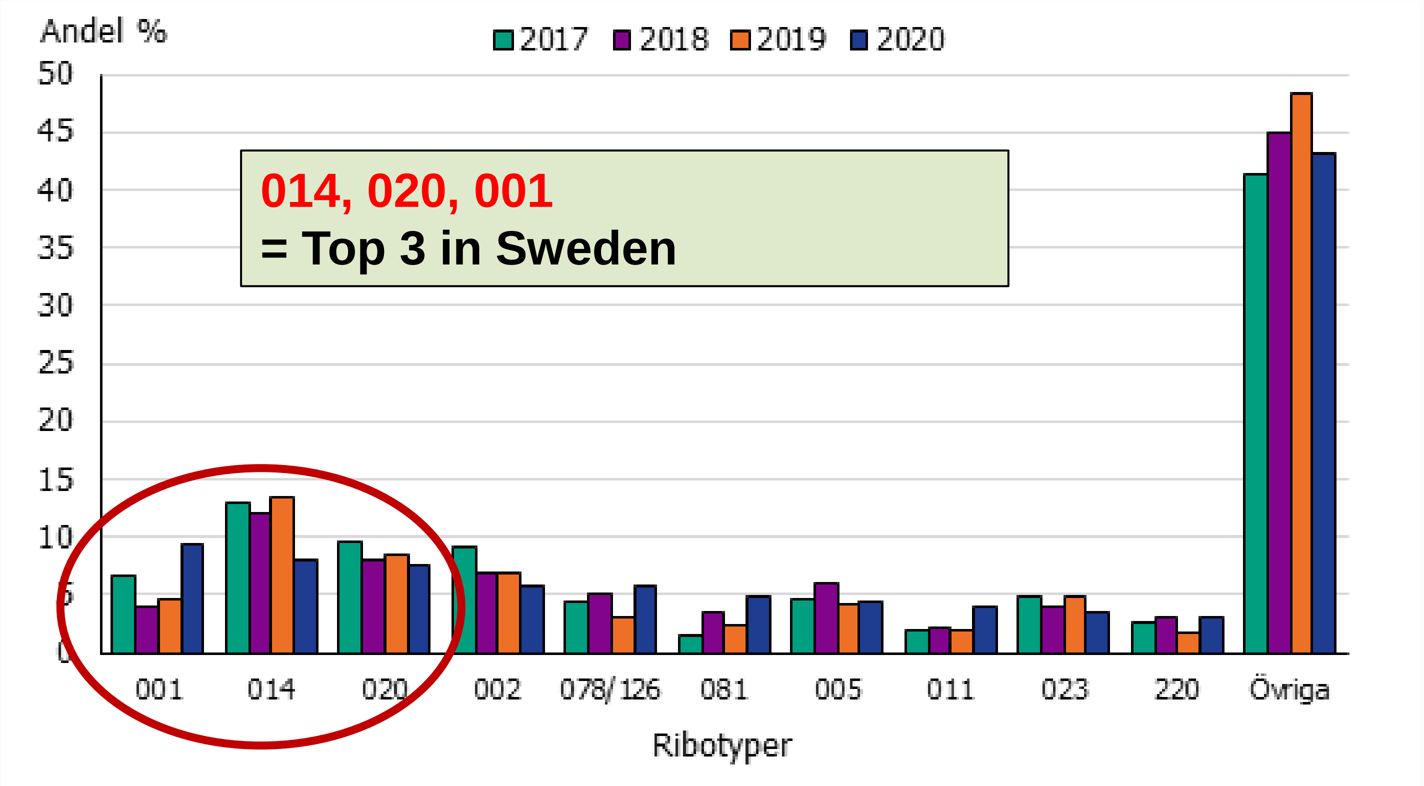
Suspected cases had >3 SNP differences
n=68

Confirmed cluster
n=12

Distribution of HMW types



HMW type	PCR ribotypes
14c	**014**, 077, **020**, 095, 106, 220
1b	**001**, 015, 032, 087, 104, 062, 251, 403
13c	029, 043, 097, 248, 353



014, 020, 001

= Top 3 in Sweden

Cluster (ribotype)	SNP diff	Shared ward	Ward where test was taken	Poisson alert	Two-case alert
A (014)	0-1	Surgical (general)	Surgical (gastrointestinal)	-	-
			Medical ward	-	-
			Infectious diseases (outpatient)	-	-
B (020)	0	Medical (cardiology)	Medical (kidney)	Medical (kidney)	Medical (kidney)
			Medical (general)	-	Medical (emergency)
C (001)	0	Medical (kidney)	Infectious diseases	Infectious diseases	Infectious diseases
			Medical (kidney)	Medical (kidney)	Medical (kidney)
		-	Neurology (stroke)	-	-
D (x231)	1	Surgical ward 2	Medical (lung)	-	Medical (lung)
			Medical (general)	-	-
E (045)	3	-	Medical (general)	-	-
			Infectious diseases (outpatient)	-	-

Testing of the Poisson model

	Confirmed transmission	No confirmed transmission
Possible transmission according to Poisson model	a	b
No transmission according to Poisson model	c	d

Sensitivity:
a/(a+c)

Specificity:
d/(b+d)

PPV:
a/(a+b)

NPV:
c/(c+d)

Conclusions

Question	Answer
Hidden transmission: how common is it?	It happens regularly in our setting, but not very often (~2 %) Caveat: only symptomatic cases with transmission at a shared ward within 30 days were identified! Not included: asymptomatic donor, asymptomatic receiver, transmission between wards, transmission over longer time periods…

Question	Answer
Evaluate ward-specific cut-off **(and the simpler two-case algorithm)**	The ward-specific cut-off **does not** work, at least in absence of an overt outbreak. A two-case algorithm also **does not** work in this setting. The main reason: patients are generally **not tested at the same** ward as the ward where the bacteria were transmitted.

So, what to do?

HMW typing of all cases is feasible (but requires culturing)

The typing must be combined with each patient´s ward history – not only the ward ordering the test

A hard work to do manually, but IT solutions can help!
- Patients and their current and previous wards connected to lab data including typing results -> **automatized algorithm** for alert

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Thank you for listening!