



# EU-wide surveillance of *Clostridium difficile* provides opportunity to assess outcomes of *C. difficile* ribotype 027 infections

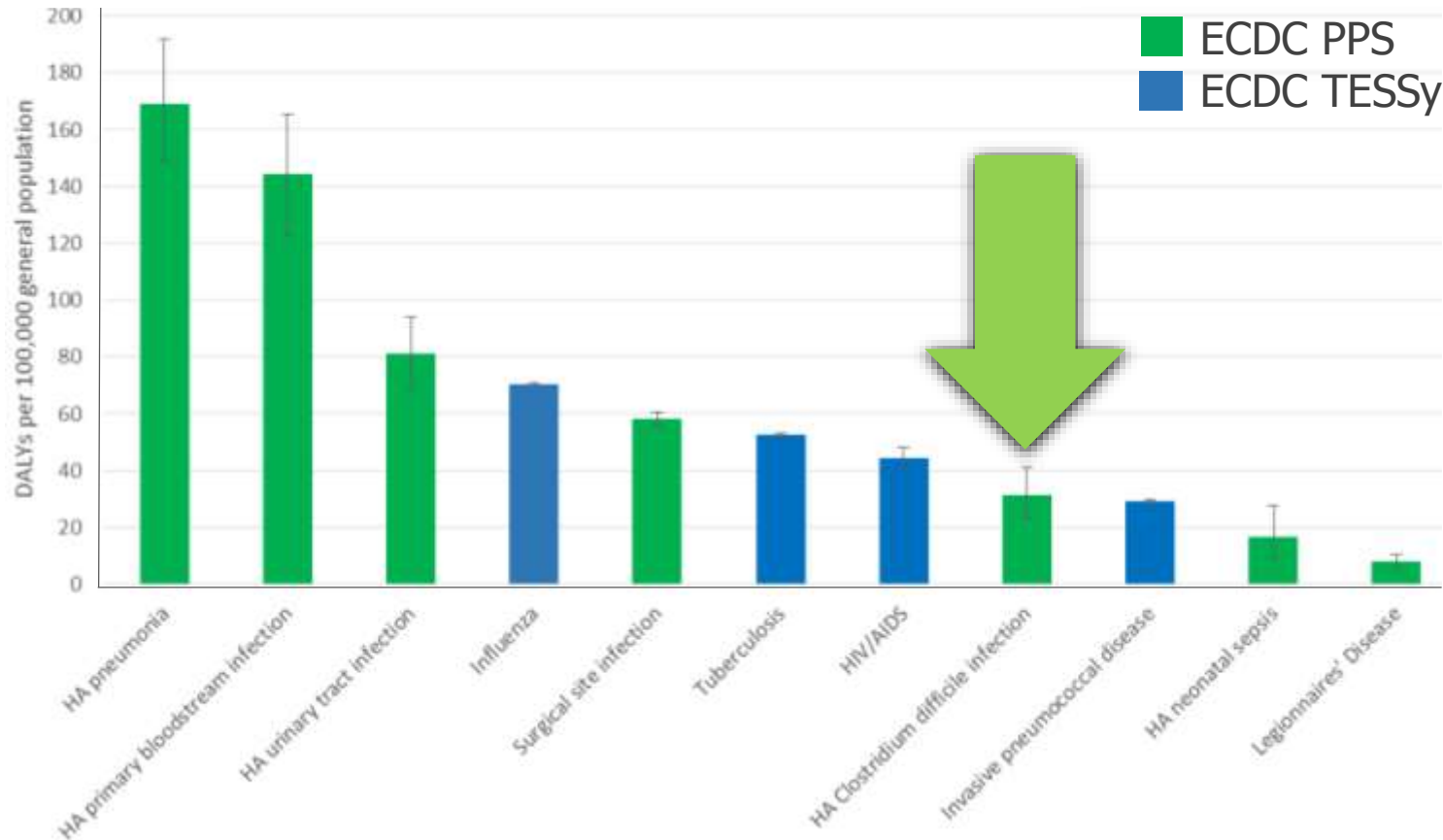
**Pete Kinross**

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ECCMID; Vienna, Austria; 22 April 2017

# Burden of *C. difficile* infections in EU/EEA countries, 2011–2012

- 8<sup>th</sup> most frequent microorganism in HAIs in ECDC PPS, 2011-2012 (1<sup>st</sup> in US CDC PPS, 2011)
- 124 000 (95% CI 61 000 – 285 000) healthcare-associated (HA) CDI cases/year in EU/EEA
- 3–6% attributable mortality, 3 700 attributable deaths/year






# Overview of the ECDC CDI surveillance protocol

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	Minimal surveillance	Light surveillance	Enhanced surveillance	Form
Collected information				<b>Form H</b> (aggregated numerator and denominator data) 
				<b>Form C</b> (case-based numerator data) 
				<b>Form M</b> (one form for each <i>C. difficile</i> isolate) 

## Definitions (ESCMID-aligned\*):

- Case definition
- Subsets, e.g. HA CDI
- Complicated course of infection

## Denominators:

- Beds, patient-days, discharges, stool tests

## Surveillance period:

- 3–12 months/year

## Microbiol. data (Form M):

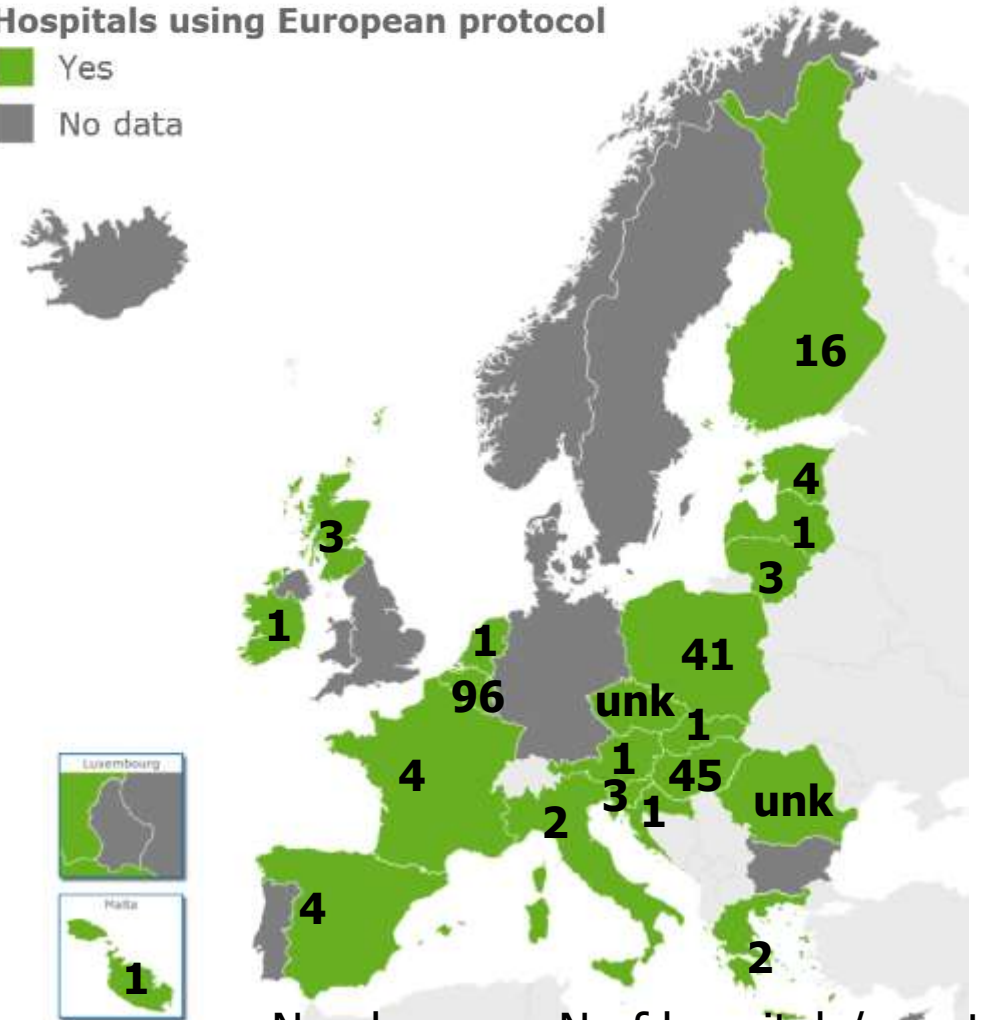
- PCR ribotype
- Toxin production
- MIC & SIR (EUCAST):  
Metronidazole, vancomycin, moxifloxacin

# Data acquired using the European CDI protocol since its launch on 1<sup>st</sup> January 2016, n=20 EU/EEA countries\*

- **Current data are mostly 'start-up phase':**  
Jan-Feb 2016,  $\geq 1$  month,  $\geq 1$  hospital
- Data from **20 countries:**
  - 13/20 used ECDC software (HelicsWin.Net)
  - 1 not compatible
- Included: **235 hospitals** from 19 countries, **>8 million patient-days:**
  - 2 'minimal' protocol option
  - 95 'light' (case-based) option
  - 138 'enhanced' (+ microbiological data)
- **2797 case records**
  - 649 cases' microbiological data
    - **525 cases' PCR ribotype data**
  - **371 (13%) died**, of which  $\geq 79$  (21%) CDI-related

## Hospitals using European protocol

- Yes
- No data

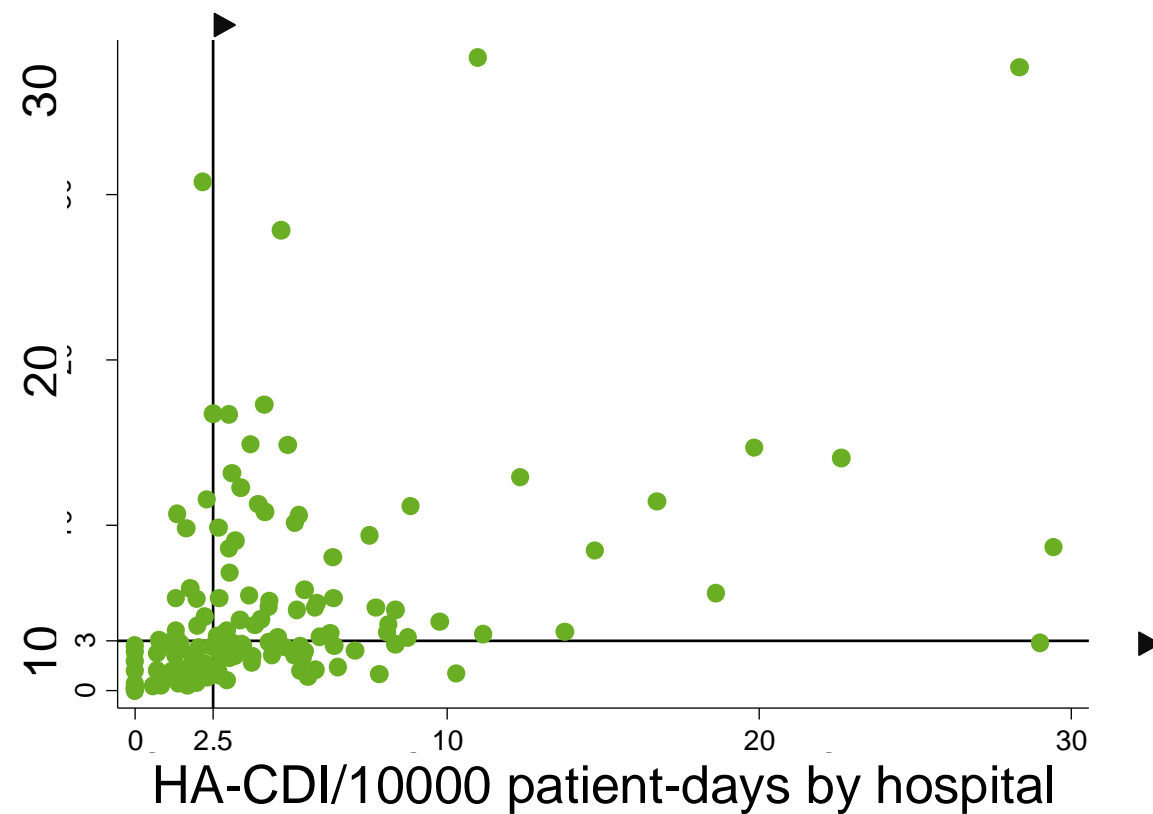
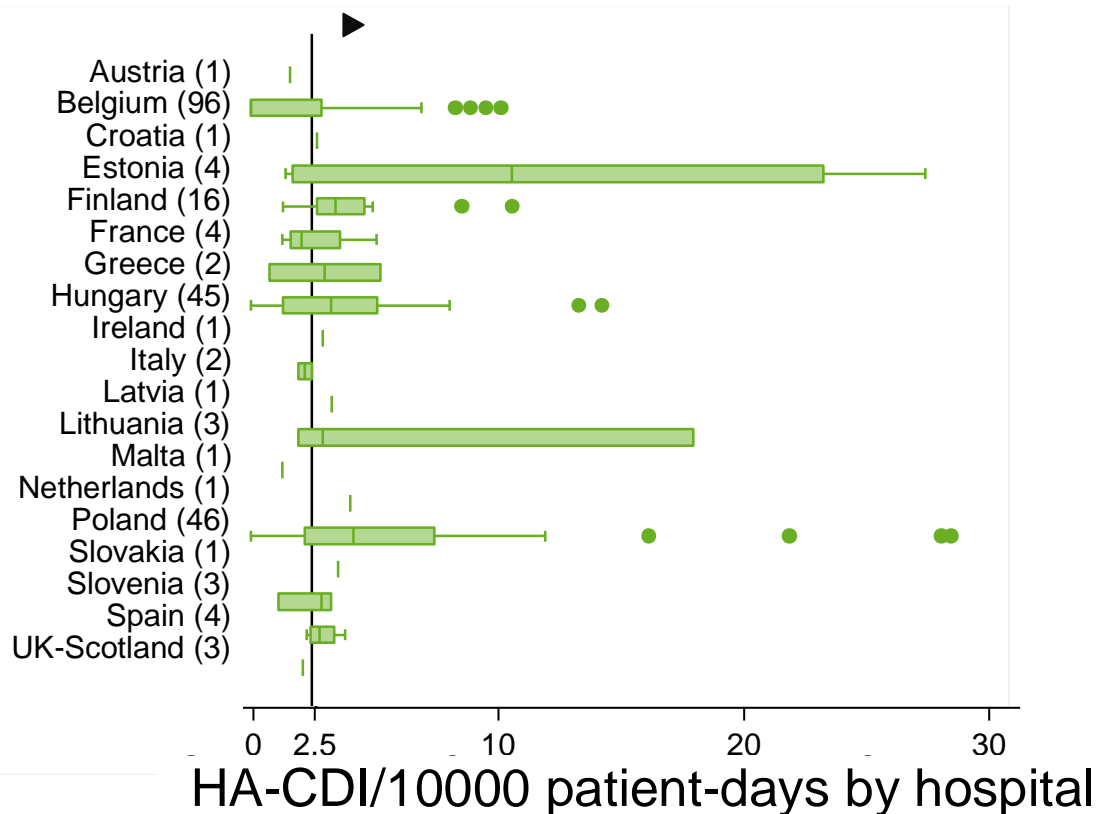


Numbers are N of hospitals/country

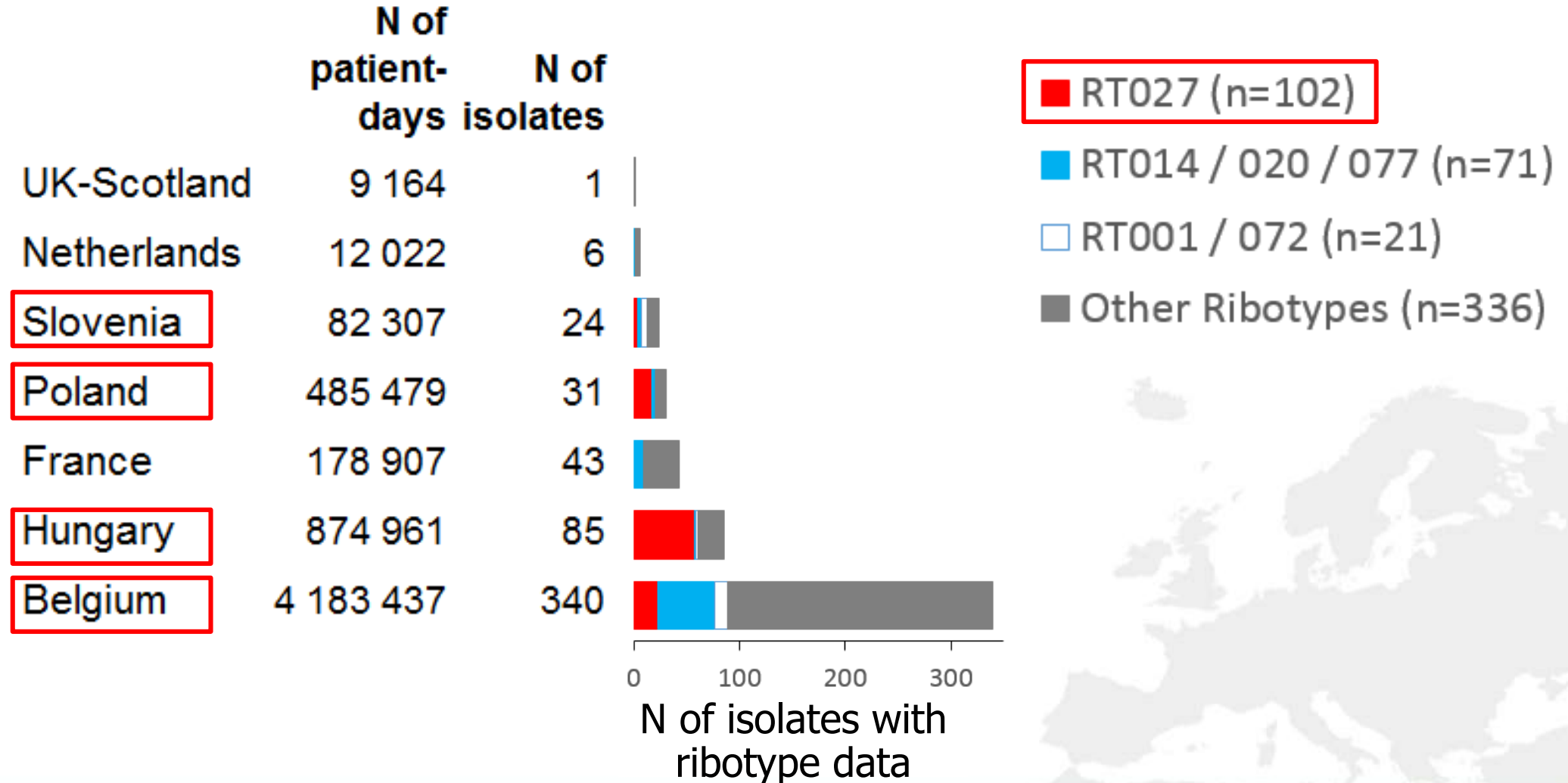
# CDI incidence in EU/EEA hospitals, Jan 2016 – Nov 2016



Incidence (cases/10,000 patient-days)	Pooled mean (crude)	Median (IQR)
Healthcare-associated (HA) CDI	3.5 (2.7)	2.5 (0.5 – 4.5)
Total (HA + community-associated) CDI	4.3 (3.4)	3.1 (1.3 – 5.2)
Recurrent CDI	0.5 (0.3)	0.0 (0.0 – 0.5)



# Most commonly reported *C. difficile* PCR ribotypes, EU/EEA countries (n=7\*), Jan–Nov 2016



\* 7/20 countries reported PCR ribotype data



# Multivariable analysis of factors associated with most common PCR ribotypes, EU/EEA, Jan–Nov 2016



**Objective:** Identify outcomes/factors associated with PCR ribotypes (RT027)

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**Inclusion criteria:** Country reporting  $\geq 1$  RT027

**Model:** Multi-level mixed-effects logistic regression models (STATA 14.0)

- Cluster levels: Hospitals, within countries
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## **Assessed characteristics/outcomes:**

- Outcomes of infection: Recurrence, complicated course of infection, death
- General risk factors: Age, gender
- Risk factors for outcome: McCabe score, hospital ward type, origin of infection
- Susceptibility: Metronidazole-R\*, vancomycin-R, moxifloxacin-R

\* Decreased susceptibility, i.e.  $2\text{mg/L} < \text{MIC} < 8\text{mg/L}$

# Multi-level mixed effects model of association of *C. difficile* RT027 with characteristics and outcome of CDI

n=4\*\* EU/EEA countries, Jan–Nov 2016



Characteristic/Outcome	PCR Ribotype				Univariate analysis		Multivariable analysis	
	RT027 (n=102)		non-RT027 (n=102)		Odds Ratio ( 95%CI )	p-value	Odds Ratio ( 95%CI )	p-value
	n / N	(%)	n / N	(%)				
Age (years)	102	70.5*	102	67.2*	1.01 (0.99 – 1.03)	0.4	1.02 (0.99 – 1.05)	0.14
Gender (Male)	50/102	(49)	41/102	(40)	1.96 (0.89 – 4.33)	0.094	2.28 (0.75 – 6.92)	0.15
Metronidazole (Resistant) <sup>X</sup>	6/53	(11)	1/60	(2)	2.43 (0.27 – 21.5)	0.4		
Moxifloxacin (Resistant)	53/55	(96)	11/60	(18)	61.8 (11.2 – 340)	<b>&lt;0.001</b>		
Vancomycin (Resistant)	0/55	(0)	0/60	(0)	NA	NA		
Recurrent Case	13/79	(16)	12/94	(13)	1.91 (0.50 – 7.29)	0.3	1.83 (0.36 – 9.41)	0.5
Healthcare-associated case	88/102	(86)	82/102	(80)	2.05 (0.69 – 6.06)	0.20	2.18 (0.55 – 8.73)	0.3
High incidence hospital (i.e. >75th percentile)	32/102	(31)	4/102	(4)	5.74 (1.63 – 20.1)	<b>0.006</b>	6.69 (1.42 – 31.6)	<b>0.016</b>
Complicated course	14/88	(16)	8/96	(8)	1.91 (0.50 – 7.29)	0.3	5.94 (1.08 – 32.7)	<b>0.041</b>
Dead (all causes)	23/99	(23)	16/96	(17)	1.23 (0.45 – 3.38)	0.7	5.63 (1.16 – 27.4)	<b>0.032</b>

\*: mean; \*\*: Belgium, Poland, Hungary, Slovenia; <sup>X</sup>: decreased susceptibility, i.e. 2mg/L < MIC <8mg/L



# Limitations

## ❖ **Non-standard nomenclature for PCR ribotypes**

- 63% ribotypes were 'other', i.e. a local/national nomenclature.
- *Insufficient statistical power:* for similar analyses of RT001/072 and RT014/020/077 (data not shown)

## ❖ **Data currently not representative of Europe or most EU/EEA countries**

- 1 month of data from 1 hospital from many countries
- *Insufficient statistical power:* for multivariable identification of risk factors for outcome(s) of CDI, e.g. death (data not shown)

## ❖ **Definition of 'complicated course'**

- i.e. ICU stay, surgery, died or hospitalisation of community cases
- Some countries hospitalise community cases more frequently

## Conclusions

- ECDC surveillance protocol acquires comparable CDI data in most of Europe, to focus local, national and EU-level actions.
- Current data suggest that PCR ribotype 027 is associated with higher transmissibility, morbidity and mortality.

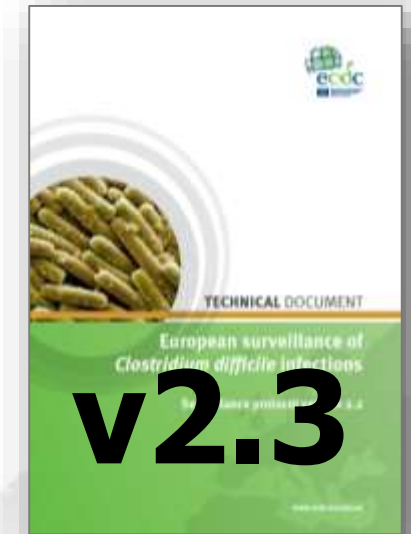
## Recommendations

Member States should consider recommending that

- hospitals collect data as described in the ECDC surveillance protocol, and
- laboratories use a standardised methodology to acquire ribotype data.

## Next steps

- **ECDC contracted outputs:** Consortium lead by Leiden University Medical Centre (NL) generating guidance document for diagnostics, CE-PCR ribotyping, and ribotype acquisition, e.g. WebRibo (Vienna workshop, May 2017); typing non-typeable strains.
- **EU/EEA data:** Full national 2016 data expected by Jul–Sep 2017
  - ➔ Further multivariable analyses, burden calculations and trend analyses



# Thanks to:



## **ECDC**

- Carl Suetens and the HAI-Net team
- ECDC Microbiology

## **ECDIS-Net coordination team**

- Leiden Univ. Medical Centre (NL): Ed Kuijper & Sofie van Dorp
- Charite Berlin (DE): Petra Gastmeier, Alexander Kola
- RIVM (NL); University of Leeds (UK)

## **HAI-Net CDI network**

- Particularly National Focal Points for HAIs in Belgium, Hungary and Poland
- All participating hospitals and public health institutes



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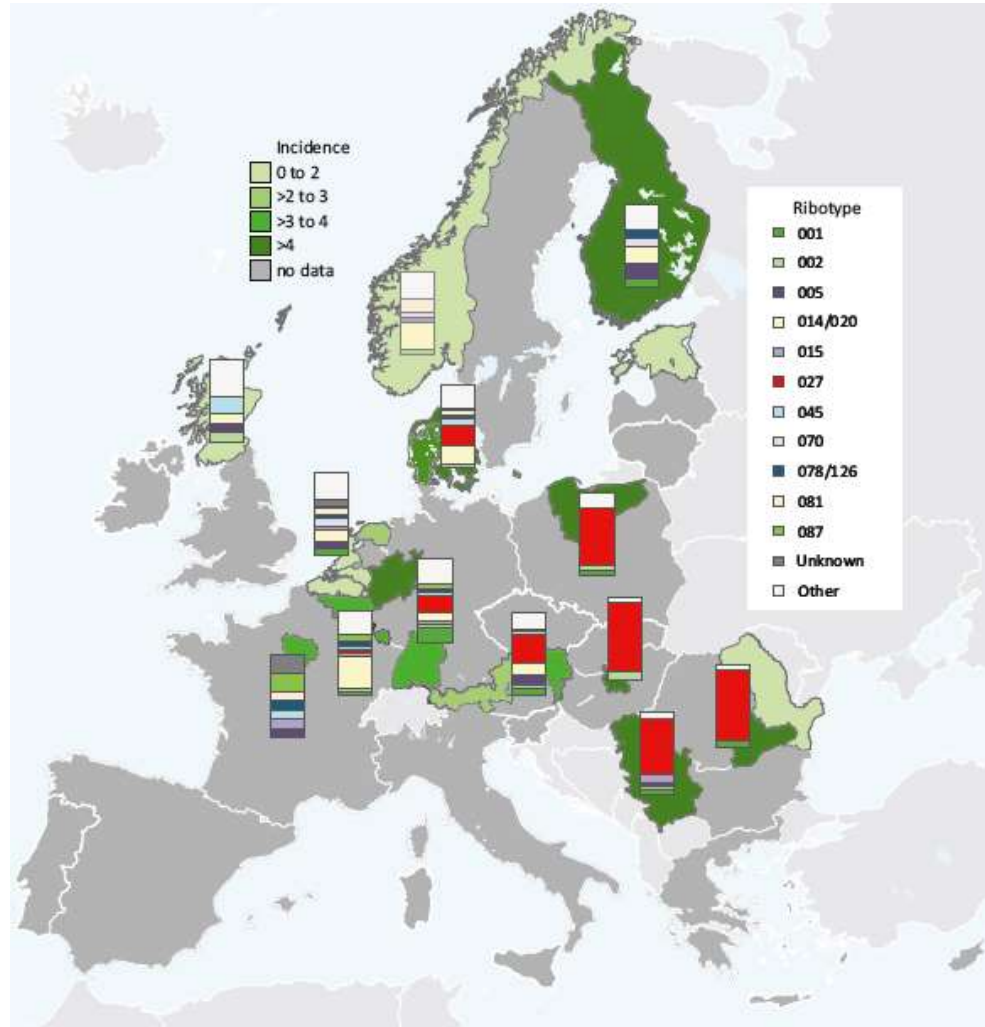
# Standardised surveillance of *Clostridium difficile* infection in European acute care hospitals: a pilot study, 2013



**Systematic survey of EU surveillance activities:**  
2011 onwards

**Protocol development:**  
Feb 2012 – Apr 2013

**Protocol finalisation:**  
Jan 2014, Leiden



**Pilot survey:**  
May–November 2013  
N=37 hospitals  
N=14 countries  
Workload: 6 person-days/hosp.

