Surveillance of *Clostridium difficile* infection (CDI) in Belgium

Working group Meeting June 24 2015
Hosted by WIV-ISP
Dr Fiona Neely
Dr Marie-Laurence Lambert
Objectives of Meeting

• Results from Surveillance Report 2015
• Update on new research / guidelines / international surveillance protocols
• Discussion of potential new changes / actions
• CDIF research projects WIV-ISP & NRC
Annual Report 2015

• Hospital epidemiological & Reference Laboratory surveillance data 2008 - 2014

• Hospital stay data (RCM/ MZG) & CDI test billing - hospitalised pts (INAMI / RIZIV) 1999 – 2012

• Death registrations 1998 - 2012
Surveillance data

Mandatory 2007-2014*

- Acute hospitals, 1 semester/yr
- Case based – NSIHweb1
- Reference lab – samples from 5 consec pts / hosp / sem
  Confirmation & Ribotyping

*Ref: Arrêté Royal 19 Jun 2007
Surveillance data

• Change in legislation – July 2014*
  1/4 mandatory surveillance progs:
  - Surgical site infection
  - Vancomycin resistant enterococci
  - Pneumonia or septicaemia in ICU
  - *Clostridium difficile* infection

*Ref: Arrêté Royal 8 Jan 2015*
Hospital case-based surveillance 2008-2014

- NSIHweb1

- High participation
  2014: 141 hospitals at least 1 semester
  108 hospitals 2 semesters
Trends in incidence of hospital associated episodes (HA*) and all episodes, 2008-2014

*Definition of hospital associated infection: onset of symptoms 2 days or more after admission in the declaring hospital (onset date – admission date ≥2)
Characteristics of cases 2014

N episodes = 2,431
N patients = 2,325

**Age at diagnosis, patients**

- Age 0-2: 2%
- Age 3-64: 27%
- Age 65-79: 29%
- Age >=80: 42%

**Median age of**

Hospital associated (HA) cases > other cases
79 yrs > 72 yrs
Characteristics of cases 2014

Department (top 5) of diagnosis HA*-CDI

*Definition of hospital associated CDI: onset of symptoms 2 days or more after admission in the declaring hospital
Characteristics of CDI cases 2014

Recurrence
% episodes recurrent

- Unknown: 17%
- Recurrent: 9%
- Non-Recurrent: 74%

Complications
% patients with complications

- Death (direct or indirect result of CDI) within 30 days: 3% of pts
- Complications (pmcol, ICU, surgery): 3% of pts
- Complic or death: 5% of pts
Trends in proportion of CA* & HA* CDI

*Definition of hospital associated (HA) CDI: onset of symptoms 2 days or more after admission in the declaring hospital

*Definition of community associated (CA) CDI: onset of symptoms less than 2 days after admission to hospital when there is no other known admission to a healthcare facility in the previous 12 weeks
Incidence HA-CDI*: Variation between hospitals (acute only)

*Definition of hospital associated infection: onset of symptoms 2 days or more after admission in the declaring hospital (onset date – admission date ≥2)
Incidence HA* CDI – Regional variation (acute hospitals)

*Definition of hospital associated infection: onset of symptoms 2 days or more after admission in the declaring hospital (onset date – admission date >2)
Incidence CDI (moving average)
Seasonal variation

*Definition of hospital associated infection: onset of symptoms 2 days or more after admission in the declaring hospital (onset date – admission date ≥2)
Reference Laboratory data 2009-2014

- Part of surveillance programme
- Samples from 5 consecutive cases
- Confirmation of *C. difficile* & ribotyping
Laboratory surveillance participation

- Huge diversity – 121 ribotypes
  - 66 only isolated once
- Widespread across regions

### N isolates received, typable & included in the surveillance programme
<table>
<thead>
<tr>
<th>Year</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>389</td>
<td>505</td>
<td>462</td>
<td>648</td>
<td>585</td>
<td>616</td>
</tr>
</tbody>
</table>

### N hospitals (different sites) sending samples for typing
<table>
<thead>
<tr>
<th>Year</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>104</td>
<td>103</td>
<td>84</td>
<td>111</td>
<td>103</td>
<td>112</td>
</tr>
</tbody>
</table>

Source: UCL-ST Luc – Pr Delmée, J. Van Broeck
Ribotype trends 2009-2014

Percentage of ribotypes belonging to the most common ribotypes in Belgian hospitals

Source: UCL-ST Luc – Pr Delmée, J. Van Broeck
Epidemiological + Lab data linkage

- Able to match since 2011 using automatic code
- Improved matching each year

2014
- 96% of 678 total ref lab specimens matched
- 27% of 2470 cases on NSIHweb1 matched
# Ribotype, patient characteristics and outcome (1/2)

## Top 7 ribotypes 2011-2015

<table>
<thead>
<tr>
<th>Ribotype (BR)</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>014</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>020</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>002</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>078</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>027</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>106</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>001</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Other Ribotypes</td>
<td>56%</td>
<td></td>
</tr>
<tr>
<td>All ribotypes</td>
<td>2509</td>
<td>100</td>
</tr>
</tbody>
</table>

*BR: Brazier European classification*
Ribotype, patient characteristics and outcome*

ref: all other ribotypes

- **Ribotype 106**
  - Younger (<80)  
    - RR 0.8 [0.6-1.0]

- **Ribotype 027**
  - Older (≥80)  
    - RR 1.4 [1.2-1.6]
  - Less likely to have HAI  
    - RR 0.8 [0.7-1.0]
  - More complications  
    - RR 1.9 [1.0-3.5]
Hospital stay data 1999-2012

- Source: Service Fédéral Santé Publique / Federale Overheidsdienst
- RHM / MZG
- ICD-9-CM 008.45: “Intestinal infection due to C. difficile”
Trends in incidence CDI
$1^0$ or $2^0$ diagnostic code \textit{C.difficile}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{trends_cdi.png}
\caption{Trends in incidence CDI $1^0$ or $2^0$ diagnostic code \textit{C.difficile}}
\end{figure}

\textit{Source: FOD – Hospital stay data RHM/MZG, ICD-9-CM 008.45}
Billed testing vs. cases identified*

*Source: billing data INAMI/RIZIV and hospital stay data FOD RHM/ MZG
Death registration data 1998-2012

- Source: DGSIE ("Statistics Belgium")
- ICD-10 code A04.7 as underlying cause of death: "death due to a *Clostridium difficile* related enterocolitis"
Age standardized CDI mortality rate, by region

Source deaths: DGSIE ICD-10 code A04.7; Population data: https://www.wiv-isp.be/epidemio/spma/index.htm 2014-2005 Belgian population, deaths standardized according to age groups 0-64, 65-79, >80
Summary (1/2)

- Peak incidence 2008, declining
- Trends not attributable to changes in testing rates
- Increase in the proportion of community cases
- Incidence of hospital associated infection very variable between hospitals and regions - potentially important area for prevention
Summary (2/2)

- Mortality rates decreased after peak 2004-2005
- Decreasing severity until 2010, now stable

- Reference laboratory data - large variety of strains
  - Decline since 2009 ribotype 027
  - Predominant strain in Belgium now 014/020
  - Emergence of ribotype 106 & 87
Report 2015 now available


- Main report – English
- Résumé – FR
- Samenvattung - NL
New research / guidelines / protocols
Point prevalence survey 2011-2013
Largest in Europe: 20 countries

Europe

- 482 hospitals, 7000+ specimens
- Incidence since 2008 – increasing
- Diversity of strains – high
- Most prevalent ribotype – 027 (18%) – increasing trend
- Missed cases++ samples not sent for testing or false negatives
- Optimal testing methods – 48% hospitals

Belgium

- 10 hospitals, 156 specimens
- Decreasing
- High
- Decreasing ribotype 027 (3%)
- No missed cases
- 60% hospitals

Source: Lancet Infect Dis 2014 Dec;14(12):1208-19
National Belgian recommendations for prevention and control of *Clostridium difficile* infection

- CDI section currently in draft
  To replace 2008 guidance*
- Part of MDRO guidelines
- Superior Health Council – CSS / HGR
- Changes:
  - Diagnostics
  - New outbreak section
  - Prevention

*Source: Conseil Supérieur de la Santé, Belgian Infection Control Society, Institut Scientifique de Santé Publique. Recommandations belges pour le contrôle et la prévention des infections à Clostridium difficile dans les hôpitaux aigus et dans les maisons de repos et de soins. 2008 May. Report No.: 8365
European surveillance protocol 2015

The future

Research projects
SURVEILLANCE OF CLOSTRIDIUM DIFFICILE: THE FUTURE
Surveillance of CDI: the future

• Changes in protocol?
  • ECDC surveillance recommendations, May 2015
  • Other suggestions

• New platform – health data
  • Data collection
  • Individualised feed-back
Surveillance of CDI: ECDC vs Belgium (1) Objectives

**ECDC**
- estimate incidence (local/national)

At local level: focus on **INTER-** hospital comparisons

**Belgium**
- estimate incidence (local/national)
- At local level: focus on **INTRA-** hospital comparisons (monitoring trends to evaluate prevention measures)
## Surveillance of CDI: ECDC vs Belgium (2)

### Definitions - CDI

<table>
<thead>
<tr>
<th>ECDC</th>
<th>Belgium</th>
</tr>
</thead>
<tbody>
<tr>
<td>- diarrheal stools or toxic megacolon</td>
<td>- diarrhea (at least 3 liquid stools/24h) or toxic megacolon</td>
</tr>
<tr>
<td>- AND positive lab assay for toxin A and/or B in stools</td>
<td>- AND positive lab assay for toxin A and/or B in stools</td>
</tr>
<tr>
<td>- or a toxin-producing <em>C. difficile</em> organism detected in stools via culture or other means <strong>eg PCR</strong></td>
<td>- or a toxin-producing <em>C. difficile</em> organism detected in stools via culture or other means</td>
</tr>
<tr>
<td>- CPM, histopathology</td>
<td>- CPM, histopathology</td>
</tr>
</tbody>
</table>
Surveillance of CDI: ECDC vs Belgium (3)
Definitions – CDI - recurrence

**ECDC**
Episode of CDI

- More than 2 weeks, less than 8 weeks
- ... following onset of a previous episode

**Belgium**
Episode of CDI

- Less than 8 weeks
- ... following onset of previous episode
  (Provided symptoms subsided after first episode)
Surveillance of CDI: ECDC vs Belgium (4)

Definitions: CDI case origin

ECDC, Belgium

Community associated:

Onset of symptoms
- outside of health-care facilities OR
- day of admission to HC facility or following day

AND
- no stay in HC facility within 12 weeks
Surveillance of CDI: ECDC vs Belgium (4)
Definitions: CDI case origin

ECDC

Health-care (HC) associated
Onset of symptoms
- >=2 days after admission in HC facility
OR
- In the community within 4 weeks of discharge from a HC facility

Best for epidemiological objective at national level

Belgium

Hospital-associated
Onset of symptoms
- >=2 days after admission in declaring hospital

(nb: HC-associated can be computed from available data)

Best for operational objective at hospital level
Surveillance of CDI: ECDC

Data collection

Aggregated denominators AND

**Minimal**

- Aggregated numerators
  - N health-care associated CDI
  - N community-associated CDI
- Algorithms used for CDI diagnosis
- N tests

**Light**

- Case-based numerator

**Enhanced**

- Case-based + additional information + microbiology
Surveillance of CDI: ECDC
Algorithm used for data collection

**Important:** All wards/units should be included for the surveillance of CDI. If despite this recommendation certain wards/units were excluded, it is crucial that the aggregated denominator data are provided for the included wards/units only.

**Algorithm used for CDI diagnosis:**
The diagnostic algorithms below are categorised in decreasing order of expected test validity (maximised sensitivity and specificity). If none of the algorithms below is adequate, indicate the test algorithm which is the closest to the one that you apply. If you apply multiple algorithms, please indicate the most frequently applied algorithm(s), that is/are used for >80% of the samples tested for *C. difficile*.

**Category 1:**
- 0 Screening test with NAAT, confirmation with EIA toxin detection
- 0 Screening test with both GDH and toxin detection, confirmation with NAAT
- 0 Screening test with both GDH and toxin detection, confirmation with toxigenic culture

**Category 2:**
- 0 Screening test with GDH, confirmation with NAAT
- 0 Screening test with GDH, confirmation with toxigenic culture
- 0 NAAT alone

**Category 3:**
- 0 Screening with toxin detection, confirmation with NAAT or toxigenic culture
- 0 Toxigenic culture alone
- 0 EIA for toxins alone
- 0 Stool cytotoxicity assay alone
- 0 Multiple methods for the same stool specimen
- 0 Other, please specify: ..........................
Surveillance of CDI: ECDC vs Belgium (4)

Data collection

ECDC – « enhanced »

- severity of underlying condition using (Mc Cabe score categories
  - Rapidly/ ultimately/ not fatal

- + AM susceptibility testing
  - Metronidazole
  - Vancomycin
  - Moxifloxacin

Belgium – « enhanced »

(minor differences in phrasing)
Surveillance of CDI: ECDC vs Belgium
Minimal surveillance period

**ECDC**

- Min
  - 3 consecutive months (based on expected incidence 3/10 000)
  - oct-dec or jan – march
  - Recommended: all year

**Belgium**

- Min
  - 6 months (Observed incidence 1.2/10 000)

Recommended: all year

**NB:** All year needed for operational objectives
### Surveillance of CDI: ECDC vs Belgium (4)

**Data collection – reference laboratory**

<table>
<thead>
<tr>
<th></th>
<th>ECDC</th>
<th>Belgium</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ribotyping</strong></td>
<td>10 first cases (over 3 mo) (+susceptibility testing)</td>
<td>5 first cases (over 6 mo)</td>
</tr>
</tbody>
</table>


## Surveillance of CDI: ECDC vs Belgium

<table>
<thead>
<tr>
<th>ECDC</th>
<th>Belgium</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Focus:</strong> Epidemiology at national level</td>
<td><strong>Focus:</strong> Prevention at hospital level</td>
</tr>
<tr>
<td>Option for a « minimal protocol »</td>
<td></td>
</tr>
<tr>
<td>(aggregated numerator data only)</td>
<td></td>
</tr>
<tr>
<td>Min: 3 mo, 10 first cases to ribotype, susceptibility testing</td>
<td>Min 6 mo, 5 first cases to ribotype,</td>
</tr>
</tbody>
</table>
## Surveillance of CDI: ECDC vs Belgium

### Summary (2)

<table>
<thead>
<tr>
<th>ECDC</th>
<th>Belgium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea: no def</td>
<td>Diarrhea: 3 loose stools/day</td>
</tr>
<tr>
<td>Def recurrence: (min: 2 weeks, max 8 weeks after first onset)</td>
<td>No min</td>
</tr>
<tr>
<td>Diagnosis algorithms</td>
<td>Included but rarely done</td>
</tr>
<tr>
<td>N diagnostic tests</td>
<td></td>
</tr>
<tr>
<td>Severity of underlying condition (Mc Cabe)</td>
<td></td>
</tr>
</tbody>
</table>
Surveillance of CDI: ECDC vs Belgium - Decisions (1)

??? develop option « minimal » protocol » aggregated data only
European surveillance of *Clostridium difficile* infections

Form H: Hospital-based data (All types of surveillance)

Hospital code: __________________________

Hospital type:
- Primary
- Secondary
- Specialised hospital (please specify) ______________

Surveillance period: From ___ / ___ / 20___ (dd/mm/yyyy) to ___ / ___ / 20___ (dd/mm/yyyy)

For the above surveillance period, specify:

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of beds</td>
<td></td>
</tr>
<tr>
<td>No. of discharges/admissions</td>
<td></td>
</tr>
<tr>
<td>No. of patient-days</td>
<td></td>
</tr>
<tr>
<td>No. of HA* CDI cases</td>
<td></td>
</tr>
<tr>
<td>No. of CA* CDI cases or CDI cases of unknown origin</td>
<td></td>
</tr>
<tr>
<td>No. of recurrent CDI cases</td>
<td></td>
</tr>
<tr>
<td>No. of stool specimen tested for CDI</td>
<td></td>
</tr>
<tr>
<td>No. of stool specimen that tested positive for CDI</td>
<td></td>
</tr>
</tbody>
</table>

*HA*: healthcare-associated; *CA*: community-associated; ‘recurrent cases excluded

Exclusion of wards/units:
- No (recommended)
- Yes (just recommended)

If some wards/units were excluded, specify which wards/units were excluded:

Important: All wards/units should be included for the surveillance of CDI. If despite this recommendation certain wards/units were excluded, it is crucial that the aggregated denominator data are provided for the included wards/units only.

Algorithm used for CDI diagnosis:

The diagnosis algorithms below are categorised in decreasing order of expected test validity (normalised sensitivity and specificity). If none of the algorithms below is adequate, indicate the test algorithm which is closest to the one that you apply. If you apply multiple algorithms, please indicate the most frequently applied algorithm(s), that is, are used for ≥80% of the samples tested for C. difficile.

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- Screening test with GDH, confirmation with toxigenic culture
- NAAT alone

Category 3:
- Screening with toxin detection, confirmation with NAAT or toxigenic culture
- Toxigenic culture alone
- EIA for toxins alone
- Stool cytotoxicity assay alone
- Multiple methods for the same stool specimen
- Other, please specify: __________________________
Surveillance of CDI: ECDC vs Belgium - Decisions (2)

Minimal surveillance period:
3 mo vs 6 mo vs 12 mo

Proposal:
Keep 6 mo, recommend whole year
Surveillance of CDI: ECDC vs Belgium - Decisions (3)

Ref lab: 5 vs 10 samples / surveillance period?

Susceptibility testing?

(NB: cultures!)
## Surveillance of CDI: ECDC vs Belgium Decisions (4)

<table>
<thead>
<tr>
<th>ECDC</th>
<th>Belgium</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Def recurrence:</strong> (min: 2 wks, max 8 wks after first onset)</td>
<td>Adjust to ECDC ?</td>
</tr>
<tr>
<td>Diagnosis algorithms</td>
<td>Add?</td>
</tr>
<tr>
<td>N tests</td>
<td>Enforce?</td>
</tr>
</tbody>
</table>
Surveillance of CDI in Belgium

- Changes in protocol?
  - ECDC surveillance recommandations, May 2015
  - Other suggestions?
Surveillance of CDI in Belgium

- **Changes in protocol?**
  - *ECDC surveillance recommendation, May 2015*
  - *Other suggestions?*

- **New platform**
  - Data collection
  - Individualised feed-back
Surveillance of CDI in Belgium

New platform: Health data

- We have a dream…
  - User friendly, reliable, flexible…etc

- Explicit vision of avoiding duplication

- 2015-2016
SURVEILLANCE OF CLOSTRIDIUM DIFFICILE IN BELGIUM: RESERCH PROJECTS
Ongoing / planned research projects (1)

- Characteristics of different ribotypes
  - Exploiting linkage between reflag and epidemiological data
Ongoing / planned research projects (2)

Transmission of CDI in Belgian hospitals

Objective:
• to measure the % of CDI attributable to local transmission in Belgian hospitals

Methods
36 (27) hospitals participating to surveillance for an entire year + ribotyping of ALL episodes
Ongoing / planned research projects (3)

Association between *Clostridium difficile* infection rates and antimicrobial use patterns in Belgian hospitals

**Objectives**

- To quantify variation in rate of CDI with hospital onset in Belgian hospitals that can be attributed to variation in antimicrobial use
- To identify AM use patterns associated with higher/ lower CDI rates.

**Methods**

- Use of RHM/RFM data
Thank you!