Update

Clostridioides difficile

Franz Allerberger
15.00 – 15.30
Lawson PA, Citron DM, Tyrrell KL, SM Findegold
Reclassification of Clostridium difficile as Clostridioides difficile (Hall and O'Toole 1935) Prévot 1938.
Anaerobe 2016 (Aug.) 40: 95–99

The recent proposal by Lawson and Rainey (2015) to restrict the genus Clostridium to Clostridium butyricum and related species has ramifications for the members of the genera that fall outside this clade that should not be considered as Clostridium sensu stricto. One such organism of profound medical importance is Clostridioides difficile that is a major cause of hospital-acquired diarrhea and mortality in individuals. Based on 16S rRNA gene sequence analysis, the closest relative of Clostridium difficile is Clostridium mangenotii with a 94.7% similarity value and both are located within the family Peptostreptococcaceae that is phylogenetically far removed from C. butyricum and other members of Clostridium sensu stricto. Clostridium difficile as Clostridium mangenotii each produce abundant H2 gas when grown in PYG broth and also produce a range of straight and branched chain saturated and unsaturated fatty acids with C16:0 as a major product. The cell wall peptidoglycan contains meso-DAP as the diagnostic diamino acid. Based on phenotypic, chemotaxonomic and phylogenetic analyses, novel genus Clostridioides gen. nov. is proposed for Clostridium difficile as Clostridioides difficile gen. nov. comb. nov. and that Clostridium mangenotii be transferred to this genus as Clostridioides mangenotii comb. nov. The type species of Clostridioides is Clostridioides difficile
In 2013, the Wilhelminenspital (Vienna, Austria), a large tertiary care community hospital with 1,081 beds and 357,892 patient days, was affected by a CDI-outbreak [32]. While their CDI-numbers were stable at <200 patients per year from 2009 to 2011 (0.56, 0.51, and 0.50 per 1,000 patient days, respectively), an increase to 313 patients was observed in 2012 (0.88/1,000 patient days). In the first 5 months of 2013, a further increase in CDI patients was detected (n = 294; 1.98/1,000 patient days). Severe disease was recorded for 31% of the patients, and in 131 (25%) of the cases, the patient died within 30 days of diagnosis. Of the cases in which the patient died, 57 (43.4%) involved ribotype 027.
HAIs are a major public health problem in the Member States (according to figures compiled by the European Centre for Disease Prevention and Control (ECDC), 1 in 20 hospital in-patients on average suffer from an HAI in the EU, that is to say, 4.1 million patients annually, and every year 37,000 people in the EU die as a result of an HAI, although 20 to 30% of those infections are considered to be preventable by intensive hygiene and control programmes), and this places a heavy burden on limited health service budgets.
Burden of CDI in Europe and US

US
- 453,000 CDI/year\(^1\)
- 29,500 deaths
- 1\(^{st}\) agent responsible for HAI (12.5\%)\(^2\)
- Urgent threat (CDC)

Europe
- 172,000 CDI/year
- 9\% mortality (direct or indirect)
- 8\(^{th}\) agent responsible for HAI (5.4\%)

Österreich:
11.360 CDI-Fälle
740 †

US (319 Mill.)
- 453 000 CDI/year\(^1\)
- 29 500 deaths
- 1\(^{st}\) agent responsible for HAI (12.5%) \(^2\)
- Urgent threat (CDC)

2.709 CDI-Fälle
244 †

• Europe (508 Mill.)
  - 172 000 CDI/year
  - 9% mortality (direct or indirect)
  - 8\(^{th}\) agent responsible for HAI (5.4%)

\(^1\)Lessa , NEJM 2015, 372, 825; \(^2\) Magill SS, NEJM 2014; 370, 1198-208:
Hot Topic: Laboratory Diagnosis of Clostridium difficile: Why So Difficult? Mayo Medical Laboratories

An: franz.allerberger 06.03.2017 21:08

*Clostridium difficile* has received a lot of attention in the last 2 decades due to the increasing burden it has been placing on our patients and our healthcare system. *C difficile is the most commonly reported pathogen causing healthcare-associated infections in US hospitals*, recently surpassing methicillin-resistant *Staphylococcus aureus*, or MRSA. Since 2013, the National Healthcare Safety Network (NHSN) has mandated reporting of *C difficile* infections (CDI) for hospitals participating in the Centers for Medicare and Medicaid Services (CMS) program.

Accurate and rapid diagnosis of CDI is important for the patient and the healthcare environment. Upon diagnosis, providers begin therapy with an appropriate antimicrobial agent such as metronidazole or oral vancomycin and discontinue antimicrobial agents that may be predisposing to CDI. Infection control precautions are instituted in order to curb spread of the spores.
Severe *Clostridium difficile infection* is a notifiable disease in Germany, according to the Infection Prevention Law (Infektionsschutzgesetz). With May 1, 2016 the legal framework for notification and the reporting entities changed. From now on outpatient cases which are hospitalized because of CDI are defined as severe cases and thus notifiable.
Stockholm/Wien (APA) - Pro Jahr kommt es in Europa (EU/AEEA) zu rund 2,6 Millionen Fällen von bakteriellen Spitalsinfektionen. **Das ist eine größere Krankheitslast als jene durch Influenza, HIV und Tuberkulose zusammen und führt zu rund 91.000 Todesfällen.** Das geht aus einer Studie europäischer Experten hervor, die in PLOS Medicine veröffentlicht worden ist.


Anschaulicher als die DALYS als epidemiologischer Rechenwert ist das Faktum, dass laut den Wissenschaftlern jährlich rund 91.000 Todesfälle im EU/EEA-Raum auf solche Infektionen zurückzuführen sind. Das entspricht in etwa den Todesfällen durch Pankreaskarzinome in der EU. Es handelt sich dabei um Sepsisfälle, Clostridium difficile-Infektionen, Blutvergiftungen bei Neugeborenen im Spital, Pneumonien, Wundinfektionen nach chirurgischen Eingriffen und Harnwegsinfektionen.
RESEARCH ARTICLE

Burden of Six Healthcare-Associated Infections on European Population Health: Estimating Incidence-Based Disability-Adjusted Life Years through a Population Prevalence-Based Modelling Study

Alessandro Cassini1,2,*, Diamantis Plachouras1,2,*, Tim Eckmanns3, Muna Abu Sin3, Hans-Peter Blank2, Tanja Ducomble3, Sebastian Haller3, Thomas Harder3, Anja Klingeberg3, Madlen Sixtensson3, Edward Velasco3, Bettina Weiß3, Piotr Kramarz1, Dominique L. Monnet1, Mirjam E. Kretzschmar2,4, Carl Suetens1

1 European Centre for Disease Prevention and Control, Stockholm, Sweden, 2 Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands, 3 Robert Koch Institute, Berlin, Germany, 4 Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands

* These authors contributed equally to this work.

Open Access


Abstract

Background

Estimating the burden of healthcare-associated infections (HAIs) compared to other com-
Blue = years lived with disabilities (YLDs)
Red = years of life lost due to pre-mature mortality (YLLs)
DALY = disability-adjusted life years (One DALY can be thought as one lost year of "healthy life")
“The restriction of fluoroquinolone prescribing should be a cornerstone in the control of epidemic C. difficile infections in the UK and worldwide” Lancet Infect Dis 2017; 17:411-21
Fig. 1A Mandatory incidence of *Clostridium difficile* infections corresurs to all infections reported for individuals older than 2 years (from 2004 to 2007, infections were only reported for individuals older than 65 years, and were upweighted to provide similar estimates in individuals older than 2 years). Since mandatory reporting was only introduced in 2004, we have also included voluntary-reported *Clostridium difficile* infections to give an indication of trends before that date.

Effects of control interventions on *Clostridium difficile* infection in England: an observational study

Kate E Dingle, Xavier Didelot, T Phuong Quan, David W Eyre, Nicole Stoesser, Tanya Golubchik, Rosalind M Harding, Daniel I Wilson, David Griffiths, Alison Vaughan, John M Finney, David H Wylie, Sarah J Oakley, Warren N Fawley, Jane Freeman, Kirsti I Morris, Jessica Martin, Philip Howard, Sherwood Gorbach, Ellie J C Goldstein, Diane M Citron, Susan Hopkins, Russell Hope, Alan P Johnson, Mark H Wilcox, Timothy E A Peto, A Sarah Walker, Darrick W Crook, the Modernising Medical Microbiology Informatics Group.*

Summary

**Background** The control of *Clostridium difficile* infections is an international clinical challenge. The incidence of *C. difficile* in England declined by roughly 80% after 2006, following the implementation of national control policies; we tested two hypotheses to investigate their role in this decline. First, if *C. difficile* infection declines in England were driven by reductions in use of particular antibiotics, then incidence of *C. difficile* infections caused by resistant isolates should decline faster than that caused by susceptible isolates across multiple genotypes. Second, if *C. difficile* infection declines were driven by improvements in hospital infection control, then transmitted (secondary) cases should decline regardless of susceptibility.

**Methods** Regional (Oxfordshire and Leeds, UK) and national data for the incidence of *C. difficile* infections and antimicrobial prescribing data (1998–2014) were combined with whole genome sequences from 4045 national and international *C. difficile* isolates. Genotype (multilocus sequence type) and fluoroquinolone susceptibility were determined from whole genome sequences. The incidence of *C. difficile* infections caused by fluoroquinolone-resistant and fluoroquinolone-susceptible isolates was estimated with negative-binomial regression, overall and per genotype. Selection and transmission were investigated with phylogenetic analyses.

**Findings** National fluoroquinolone and cephalosporin prescribing correlated highly with incidence of *C. difficile* infections (cross-correlations >0.88), by contrast with total antibiotic prescribing (cross-correlations >0.50). Regionally, *C. difficile* decline was driven by elimination of fluoroquinolone-resistant isolates (approximately 67% of Oxfordshire infections in September, 2006, falling to approximately 3% in February, 2013; annual incidence rate ratio 0.52, 95% CI 0.48–0.56 vs fluoroquinolone-susceptible isolates: 1.02, 0.97–1.08). *C. difficile* infections caused by fluoroquinolone-resistant isolates declined in four distinct genotypes (p<0.01). The regions of phylogenies containing fluoroquinolone-resistant isolates were short-branched and geographically structured, consistent with selection and rapid transmission. The importance of fluoroquinolone restriction over infection control was shown by significant declines in inferred secondary (transmitted) cases caused by fluoroquinolone-resistant isolates with or without hospital contact (p<0.0001) versus no change in either group of cases caused by fluoroquinolone-susceptible isolates (p<0.2).

**Interpretation** Restricting fluoroquinolone prescribing appears to explain the decline in incidence of *C. difficile* infections, above other measures, in Oxfordshire and Leeds, England. Antimicrobial stewardship should be a central component of *C. difficile* infection control programmes.
Abbildung 5: Ergebnisse der in vitro Empfindlichkeitstestung von 53 C. difficile-Isolaten. R: resistent; I: intermediär; S: sensibel

Nationale Referenzzentrale für Clostridium difficile - Jahresbericht 2016
ICD-10 Daten: A04.7
Enterokolitis durch Clostridium difficile

CDI-Meldedaten Österreich 2010-2016
Meldepflicht von Erkrankungsfällen an einer schwer verlaufenden *Clostridium difficile* assoziierten Erkrankung und Todesfällen

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<tr>
<td>2017*</td>
<td>11*</td>
<td>208*</td>
</tr>
</tbody>
</table>

*as of 21. April 2017*
Conclusions

- Two distinct patterns of *C. difficile* spread
- Ribotypes 027, 001, 018/356, 176 had evidence of country-specific clustering, consistent with reports of these as healthcare-associated
- By contrast, 078, previously associated with pig-farming, and 015, 002, 014 and 020 had evidence of Europe-wide dissemination, consistent with spread via other routes/sources, e.g. possibly via the food chain
- Within-country clustering, i.e. probable healthcare-adaptation, was associated with fluoroquinolone resistance

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Nationale Referenzzentrale für *Clostridium difficile* - Jahresbericht 2016
Transmissibility of *Clostridium difficile* Without Contact Isolation: Results From a Prospective Observational Study With 451 Patients

Andreas F. Widmer,1 Reno Frei,2 Stefan Erb,1 Anne Stranden,1 Ed J. Kuijper,3 Corneliis W. Knetsch,3 and Sarah Tschudin-Sutter1

Divisions of 1Infectious Diseases and Hospital Epidemiology and 2Clinical Microbiology, University Hospital Basel, University of Basel, Switzerland; and 3Section of Experimental Microbiology, Department of Medical Microbiology, Center of Infectious Diseases, Leiden University Medical Center, The Netherlands

**Background.** Contact precautions are recommended by health authorities in Europe and the United States for patients with *Clostridium difficile* infection (CDI). Recently, the significance of nosocomial transmission has been challenged by screening on admission studies and whole-genome sequencing, providing evidence for an endogenous source of *C. difficile*. We discontinued contact precautions for patients with CDI, except for patients infected with hypervirulent ribotypes or with stool incontinence, to determine the rate of transmission.

**Methods.** From January 2004 to December 2013, contacts of each index case with CDI were screened for toxigenic *C. difficile* by culturing rectal swabs. Transmission was defined as possible if toxigenic *C. difficile* was detected in contacts, as probable if the identical polymerase chain reaction ribotype was identified in index–contact pairs, and as confirmed if next-generation sequencing (NGS) revealed clonality of strains.

**Results.** Four hundred fifty-one contacts were exposed to 279 index patients nursed in 2- to 4-bed rooms. Toxigenic *C. difficile* was detected in 6.0% (27/451) after a median contact time of 5 days. Identical ribotypes were identified in 6 index–contact pairs, accounting for probable transmission in 1.3% (6/451). NGS was performed for 4 of 6 pairs with identical strains, and confirmed transmission in 2 contact patients.

**Conclusions.** The rate of transmission of toxigenic, predominantly nonhypervirulent *C. difficile*, was low and no outbreaks were recorded over a 10-year period after discontinuing contact precautions for patients with CDI who were not severely incontinent and who used dedicated toilets. As contact precautions may lead to lower levels of care, their implementation needs to be balanced against the risk of nosocomial transmission.

**Keywords.** *C. difficile*; transmission; contact precautions; screening; acute care hospital.
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

See ECDC website for ECDC protocol v2.3
European surveillance of Clostridium difficile infections - surveillance protocol version 2.3

Available as PDF in the following languages

→ EN

This document is free of charge.


Abstract

ECDC publishes a protocol developed for the surveillance Clostridium difficile infections (CDI) to address the lack of standardised surveillance of CDI in EU Member States. This updated protocol prescribes the methodology, and provides the data collection tools required to achieve the objectives of European surveillance of CDIs.

This technical document is an update of the 'European Surveillance of Clostridium difficile infections. Surveillance protocol version 2.2', published in November 2016.
Table 1. Information collected for different CDI surveillance options

<table>
<thead>
<tr>
<th>Collected Information</th>
<th>Minimal surveillance</th>
<th>Light surveillance</th>
<th>Enhanced surveillance</th>
<th>Form</th>
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<tbody>
<tr>
<td>Hospital data for each hospital (aggregated numerator data)</td>
<td>Minimum CDI surveillance for each hospital (aggregated numerator data)</td>
<td>Minimum CDI surveillance for each hospital (aggregated numerator data)</td>
<td>Minimum CDI surveillance for each hospital (aggregated numerator data)</td>
<td>Form H (aggregated numerator and denominator data)</td>
</tr>
<tr>
<td>Hospital data for each hospital (aggregated denominator data)</td>
<td>Information on each CDI case (case-based numerator data)</td>
<td>Information on each CDI case (case-based numerator data)</td>
<td>Information on each CDI case (case-based numerator data)</td>
<td>Form C (case-based numerator data)</td>
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<tr>
<td>Microbiological data (for the first 5 consecutively detected cases in each participating healthcare facility: characterisation, susceptibility testing and typing of each C. difficile isolate)</td>
<td>Form M (one form for each C. difficile isolate)</td>
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</table>

**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.

Note that on average, a 300-bed European hospital (with 100% bed occupancy) can expect seven CDI cases every three months, or 28 cases per year, for an incidence of three CDI cases per 10 000 patient-days.

*The pilot study demonstrated that completion of Form H is made much easier by starting surveillance on the first day of a month.*
**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.

Note that on average, a 300-bed European hospital (with 100% bed occupancy) can expect seven CDI cases every three months, or 28 cases per year, for an incidence of three CDI cases per 10 000 patient-days.
EU.LabCap indicator 1.33

Total number of Clostridium difficile diagnostic tests* performed/1000 hospital-inpatient days, based on national estimate**.

* A test = a stool sample tested by one or more diagnostic Clostridium difficile assays including toxin immunoassay, toxin cytotoxic cell-culture assay, PCR, or culture

** Estimate can be determined using a (representative) sample of a survey”

Number of tests performed =
Number of hospital-inpatient days =
## mikrobiologische Untersuchungen im Jahr 2015

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<th>KRANKENANSTALT</th>
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<th>Belegstage im Jahr 2015</th>
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5.4/1.000 Belagstage
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<tr>
<th>KRANKENANSTALT</th>
<th>mikrobiologische Untersuchungen im Jahr 2016</th>
<th>Belegstage im Jahr 2016</th>
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Results 2: Prevalence

• HOD point prevalence 3.57% (95% CI 3.13 – 4.03%)

<table>
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<tr>
<th>Hospital type</th>
<th>Point prevalence of HOD (%)</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>District general (DGH)</td>
<td>2.2</td>
<td>1.56, 2.86</td>
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<tr>
<td>Teaching</td>
<td>4.79</td>
<td>3.77, 5.69</td>
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</tbody>
</table>

• Odds ratio for teaching hospital versus DGH 2.21 (1.57 – 3.12)

• Prevalence unaffected by specialty, ward characteristics (number of beds or side rooms) and season
Results 3: Potential causes of HOD

- 97% patients had ≥1 potential cause of HOD
- 85% multiple possible causes (median 3; range 2–13)

<table>
<thead>
<tr>
<th>Potential Cause</th>
<th>No. of patients (%; n = 230)</th>
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<td>Underlying condition</td>
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<td>Antimicrobials</td>
<td>125 (54)</td>
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<tr>
<td>Other medication</td>
<td>195 (85)</td>
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<tr>
<td>CDI</td>
<td>9 (4)</td>
</tr>
<tr>
<td>Norovirus</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>
Recurrent CDI cases are patients meeting the CDI case definition with an episode of CDI (return of diarrhoeal stools with a positive laboratory test after the end of treatment) more than two weeks and less than eight weeks following the onset of a previous episode (no matter where that previous episode occurred). ECDC v3.2 21042017
FDA Approves Merck’s ZINPLAVA™ (bezlotoxumab) to Reduce Recurrence of Clostridium difficile Infection (CDI) in Adult Patients Receiving Antibacterial Drug Treatment for CDI Who Are at High Risk of CDI Recurrence

KENILWORTH, N.J.—(BUSINESS WIRE)—

Merck (MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has approved ZINPLAVA™ (bezlotoxumab) Injection 25 mg/mL. Merck anticipates making ZINPLAVA available in first quarter 2017.

ZINPLAVA is indicated to reduce recurrence of Clostridium difficile infection (CDI) in patients 18 years of age or older who are receiving antibacterial drug treatment of CDI and are at high risk for CDI recurrence. ZINPLAVA is not indicated for the treatment of CDI. ZINPLAVA is not an antibacterial drug. ZINPLAVA should only be used in conjunction with antibacterial drug treatment of CDI.

CDI is caused by bacteria that produce toxins, including toxin B. Symptoms of CDI include mild-to-severe diarrhea, abdominal pain and fever. The incidence of recurrent CDI is higher in certain patient populations, including people 65 years of age or older and those with compromised immune systems.

“For generations, Merck has been steadfast in its commitment to fighting infectious diseases – and that commitment continues today. ZINPLAVA is a human monoclonal antibody that binds to C. difficile toxin B and neutralizes its effects,” said Dr. Nicholas Kartsonis, vice president of clinical development, infectious diseases, Merck Research Laboratories.

Selected safety information about ZINPLAVA
Prävention einer rekurrrierende CDI

Rezidivrate mit Bezlotoxumab
Humanisierter Antikörper gegen Toxin B

Rezidivrate mit Fidaxomicin im Vergleich zu Vancomycin – Initiales Ansprechen gleichwertig

Pooled Data

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Recurrence

There are only a limited number of antimicrobials for treating severe *Clostridium difficile* infection (sCDI). Tigecycline shows significant *in vitro* effect against *C. difficile* and is approved for management of complicated intra-abdominal infections. Our aim was to analyse the efficacy of tigecycline compared with standard therapy (oral vancomycin plus intravenous metronidazole) in adults treated for sCDI. A retrospective cohort study of such patients hospitalized at our department from January 2014 to December 2015 was performed. Patients receiving tigecycline monotherapy were compared with patients treated with standard therapy alone. Diagnosis and severity of CDI were determined according to guidelines of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). Primary outcome was clinical recovery, secondary outcomes were in-hospital and 90-day all-cause mortality and relapse, colectomy, and complication rates. Of the 359 patients hospitalized for sCDI, 90 (25.0%) were included, 45 in each group. Patients treated with tigecycline had significantly better outcomes of clinical cure (34/45, 75.6% vs. 24/45, 53.3%; p 0.02), less complicated disease course (13/45, 28.9% vs. 24/45, 53.3%; p 0.02), and less CDI sepsis (7/45, 15.6% vs. 18/45, 40.0%; p 0.009) compared with patients receiving standard therapy. Tigecycline usage was not associated with adverse drug reactions or need for colectomy. Rates of ileus, toxic megacolon, mortality, and relapse were similar between the two groups. Favourable outcomes suggest that tigecycline might be considered as a potential candidate for therapeutic use in cases of sCDI refractory to standard treatment.
Conclusion: No firm conclusions can be drawn regarding the effectiveness of antibiotic treatment in severe CDI as most studies excluded these patients. The lack of any ‘no treatment’ control studies does not allow for any conclusions regarding the need for antibiotic treatment in patients with mild CDI beyond withdrawal of the antibiotic that caused CDI. Nonetheless, moderate quality evidence suggests that vancomycin is superior to metronidazole and fidaxomicin is superior to vancomycin. The differences in effectiveness between these antibiotics were not too large and the advantage of metronidazole is its far lower cost compared to the other antibiotics. The quality of evidence for teicoplanin is very low. Larger studies are needed to determine if teicoplanin performs as well as the other antibiotics. A trial comparing the two cheapest antibiotics, metronidazole and teicoplanin would be of interest.

Inappropriate Antibiotic Use Often Leads to *Clostridium difficile* Infection

- 126 Fälle mit *Clostridium difficile* Infektionen
- In 74% 1 Episode inadäquater antibiotischer Therapie
- 45% aller Antibiotikatherapien inadäquat

PD Norma JUNG, Uni.-Klinik Köln
Antibiotikaverbrauch (in kg Wirksubstanz) in Österreich von 2010-2016, getrennt nach niedergelassenem Bereich und stationärem Bereich (©AGES)
Während in der tierischen Lebensmittelproduktion bereits ein Rückgang des Antibiotikaeinsatzes belegbar ist (Rückgang von 50,9 Tonnen im Jahr 2011 auf 45,7 Tonnen im Jahr 2015) [= -10,2%] ist die Menge des Antibiotikaverbrauchs in der Humanmedizin [alle unter den ATC-Code "J01 zur systemischen Applikation" fallenden Substanzen] bislang nicht gesunken (Gesamtverbrauch 2011: 66,9 t; 2016: 72 t). [= +7,6%]

Mit einem Antibiotikaverbrauch (in kg Wirksubstanz) von 72.020 kg fand sich im Jahr 2016 leider ein neuer Spitzenwert: 67% vom Gesamtwert gelangten im niedergelassenen Bereich zur Anwendung, 33% im stationären Bereich).
Prevention of Clostridium difficile infection in acute care hospitals – updated ESCMID guideline

Infection control measures
Sarah Tschudin Sutter (Basel)

Surveillance and screening
Markus Hell (Salzburg)

Antibiotic stewardship
Charis Marwick (Dundee)

**Clostridium difficile**

*C. difficile* is a Gram-positive, spore-forming, anaerobic bacillus that was first identified in 1935\(^1\). *C. difficile* is the leading cause of nosocomial diarrhoea in industrialised countries\(^2\). *C. difficile* passes through a life cycle where it exists in two forms, as vegetative cells and as spores\(^3\).

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The disease cycle of *Clostridium difficile* infection (CDI)

1. Ingestion of spores transmitted from other patients, via hands of healthcare personnel and the environment

2. Germination into growing (vegetative) cells

3. Disruption of normal colonic microflora allows colonisation and overgrowth of *C. difficile* in the colon

4. Toxin production leads to inflammation and damage to intestinal cells

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TABLE 3. Clinical pictures compatible with Clostridium difficile infection.

**Diarrhoea** Loose stools, i.e. taking the shape of the receptacle or corresponding to Bristol stool chart types 5–7, plus a stool frequency of three stools in 24 or fewer consecutive hours or more frequently than is normal for the individual.

**Ileus** Signs of severely disturbed bowel function such as vomiting and absence of stool with radiological signs of bowel distension.

**Toxic megacolon** Radiological signs of distension of the colon (>6 cm in transverse width of colon) and signs of a severe systemic inflammatory response.
Klinische Verlaufsformen

• Asymptomatischer Trägerstatus
• *Clostridium difficile* Infektion mit Diarrhoe und mit/ohne Colitis (CDI)
• Schwere *Clostridium difficile* Infektion
  – Fulminante *Clostridium difficile* Infektion (Notfallskolektomie zu erwägen)
• Rezidivierende *Clostridium difficile* Infektion

http://www.oeggh.at/images/downloads/Clostridien_Slides%20NEU_OEGGH%2022%202010%202013.pdf
CDI-Rezidiv:

Eine Episode, die innerhalb von 2 Monaten gegenüber einer früheren Episode auftritt (Rückkehr der Symptome weniger als 2 Monaten nach Besserung des klinischen Bildes), wird als ein Rückfall der anfänglichen Erkrankung angesehen.
Definition of recurrent Clostridium difficile infection

Recurrence is present when CDI re-occurs within 8 weeks after the onset of a previous episode, provided the symptoms from the previous episode resolved after completion of initial treatment.
Pathogenesis: CdC and progression to CdI

Determinants for colonisation

C. difficile spores

Colonisation
Intact intestinal cells and microbiome

Determinants for infection

Infection
Damaged intestinal cells and microbiome

sollte man basierend auf den neuen daten zu infection control und c. difficile

Effects of control interventions on Clostridium difficile infection in England: an observational study.

Transmissibility of Clostridium difficile Without Contact Isolation: Results From a Prospective Observational Study With 451 Patients.
Widmer AF, Frei R, Erb S, Stranden A, Kuijper EJ, Knetsch CW, Tschudin-Sutter S.

die sehr strikte anordnung zur einzelzimmerisolierung auflockern oder etwas mehr spezifizieren?
danke und liebe grüße, .....
Overcoming barriers to effective recognition and diagnosis of CDI

“Many clinicians still believe that a majority of CDI cases occur endogenously, with patients already harbouring *C. difficile* on admission to hospital and CDI developing following subsequent antibiotic therapy. This is a common misconception, as asymptomatic carriers of toxigenic *C. difficile* are significantly less likely than non-carriers to develop CDI”¹,²

Prevalence of *C. difficile* colonisation at hospital admission

707/6,855 patients admitted to 1 of 5 participating departments at a 2000-bed University Hospital in Vienna between July 2013–July 2014 were included.

Prevalence of colonisation at admission was 3.5% (25/707; 95% CI: 2.4–5.2).

Out of the 707 study patients, 202 were available for follow-up examination at discharge.

Of the 177 patients negative for *C. difficile* at admission, two developed CDI and one became colonised.

None of the 25 patients already colonised at admission developed CDI during stay.

One hundred twelve healthy and asymptomatic staff members from 9 departments and the medical school were screened for C difficile. All stool samples tested negative by primary inoculation of the selective plate. Enough material (1 g) to perform testing by broth enrichment technique was available for 45 of the 112 samples (40.2%). Broth enrichment technique yielded negative results for all stool samples tested. Also, 67 stool samples provided by administrative staff of a major Austrian groceries chain proved negative when tested (parallel to our study) using both methods (data not shown). Our finding of absence of fecal carriage in Austrian hospital staff was surprising but in accordance with results reported by Carmeli et al, who showed absence of intestinal carriage of C difficile among 55 hospital staff in Israel.
Among 128 healthcare workers, 77% were female, of mean age 43 years, and the majority were nursing staff (73%). Nineteen HCWs (15%) reported diarrhoea, and 12 (9%) had taken antibiotics in the previous six weeks. Over 40% of participants reported having contact with a patient with known or suspected CDI in the 6 weeks before the stool was collected. *C. difficile* was not isolated from the stool of any participants.
CDI more likely to kill than other types of infective diarrhoea

- Recent study in Austria
- Patients with CDI twice as likely to die while in hospital than patients with other types of infective diarrhoea
- All-cause mortality in CDI patients pre-discharge 20.0% versus 7.2% in non-CDI diarrhoea patients

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Hygienemaßnahmen

• Übertragung von *C. difficile* durch Sporen
  – Tragen von Einweghandschuhen und Einmalschürzen (zumindest bis zum Abklingen der Diarrhoe)
  – Händewaschen mit Seife und Wasser
    • Alkohol tötet Sporen nicht ab
• Isolierung von Patienten mit *C.difficile* assoziierten Diarrhoe ist nach Möglichkeit anzustreben
  – Keine Isolierung von asymptomatischen Trägern
  – Mikrobiologische Kontrolle nach erfolgreicher Therapie nicht sinnvoll – daher ist Aufhebung der Isolierung nicht davon abhängig
  – Bei leichten Verlaufsformen ambulante Behandlung anstreben
• Flächendesinfektion mit sporozoiden Desinfektionsmittel