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# Incidence of *Clostridium-difficile*-associated disease: first results of CDAD-KISS as component of the German nosocomial infection surveillance system

## Summary

**Background:** First results of the surveillance component 'CDAD-KISS' of the German National Reference Center for surveillance of nosocomial infections are available.

**Method:** CDAD- KISS started in January 2007 with a systematic recording of CDAD cases according to the surveillance protocol. Data from a total of 34 hospitals were included for the calculation of incidence densities and were distinguished between community acquired and nosocomial cases and severe cases.

**Results:** Incidence density of CDAD cases per 1000 patient days was 0.66, nosocomial incidence density of CDAD cases per 1000 patient days 0.48, incidence density of severe cases 0.06 per 1000 patient days and prevalence of cases known on admission was 0.13.

**Conclusion:** This was a much higher incidence level compared to previously published German data based on discharge diagnoses, but comparable with other international data determined by active surveillance systems. These data are providing a first reference level of nosocomial CDAD cases in Germany.

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and even fatal toxic megacolon. In the past five years there has been a rapid rise in the incidence of disease and mortality attributed to this bacterium in middle European countries and in North America [1,2,3]. A dramatic increase has also been observed in Germany [4].

To gain a clear overview of the epidemiological situation of CDAD nosocomial infections in Germany, the National Reference Centre (NRZ), which is responsible for surveillance of nosocomial infections, launched the CDAD-KISS module (KISS: German acronym for Hospital Infection Surveillance System) to record the number of CDAD cases, while requesting hospitals to make available their CDAD data on a voluntary basis that assured confidentiality. Also those hospitals that are interested in this topic, but do not make available their data, can record their CDAD cases as per the definitions and specifications given in the protocol and then compare these data with the "reference data" made available by the NRZ, so as to identify any infection problems related to CDAD within their institution. Already in 2007 participants recorded data retrospectively for 2006 as a pilot project. This paper presents this new surveillance module, together with the first data for 2007.

## Introduction

*Clostridium difficile* is the most common aetiological agent of nosocomial (health-care-associated) infections caused by anaerobic bacteria. It causes not only *Clostridium difficile*-associated disease (CDAD), but also pseudomembranous enterocoli-

## Method

Surveillance is conducted on the basis of the criteria set out in the CDAD-KISS registration protocol. CDAD data are recorded for the entire hospital, but only for in-

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patients. The registration protocol as well as registration sheet can be downloaded from the internet at [www.nrz-hygiene.de](http://www.nrz-hygiene.de)

### Definitions

A CDAD case must meet one or several of the following criteria:

1. Diarrhoea or toxic megacolon and detection of *C. difficile* toxins or culture-based proof of toxin-producing *C. difficile* in stools;
2. Pseudomembranous colitis diagnosed on endoscopy;
3. Histopathological proof of *C. difficile* infection (with or without diarrhoea) on endoscopy, colectomy or autopsy (case definition as per the European Centre for Disease Prevention and Control (ECDC) [5]).

A distinction is made between nosocomial infections and those contracted outside the hospital (imported cases) on the basis of the temporal association between CDAD detection and patients' admission and discharge data [6] (Figure 1):

CDAD case contracted outside the hospital

- CDAD had already been diagnosed at the time of admission to hospital or
- CDAD symptoms occurred within 48 hours of admission to hospital or
- CDAD symptoms occurred at least four weeks after discharge from hospital.

Cases contracted outside the hospital are subdivided into those contracted in an ambulatory setting vs. those contracted in another healthcare institution.

### Nosocomial CDAD case

CDAD symptoms occurred

- at least 48 hours after admission to hospital or
- within four weeks of discharge from hospital.

### Severe courses of a CDAD case

The definition of severe CDAD cases corresponds to the examples given by the Robert Koch Institute (RKI) for notification of severe cases [7] and is described as follows:

A case is deemed to be severe if at least one of the following criteria is met:

- if the patient must be re-admitted for treatment of recurrent CDAD or
- if the patient must be admitted to an intensive care unit (ICU) for treatment of CDAD or associated complications or

– if the patient undergoes surgery because of toxic megacolon, perforation or colitis or

– if the patient dies within 30 days of diagnosis of CDAD and CDAD was the cause of death or contributed to death.

### Patient days and patient number

To calculate CDAD incidence densities, the hospital's patient days are needed for the period of one year. The "patient days" represent the sum of all days spent by all patients in hospital. To that effect, the difference between the discharge date and admission date is calculated for each hospital stay (example: Pat. A was hospitalised from 1 to 10 January, this thus means nine patient days) and the differences for all patients are added.

In addition, the total number of all inpatients (= case number) in the hospital from 1 January to 31 December of the year for which data is recorded is needed. Both numbers can be obtained from the hospital's administrative or controlling departments.

The patient days and case numbers are, furthermore, subdivided for subsequent stratification as per the following disciplines and different specialist departments: intensive medicine, internal medicine, surgery, other surgical disciplines and other conservative disciplines

The CDAD-KISS protocol defines assignment to the groups in the individual case. The CDAD cases are classified accordingly.

### Calculation

The following data are calculated for the individual hospitals as well as as a reference value for all institutions:

Total CDAD incidence density: number of all CDAD cases in the hospital per 1,000 patient days

Incidence density of nosocomial CDAD cases in the hospital: nosocomial CDAD cases per 1,000 patient days.

The incidence densities were also compiled for the subgroups: intensive medicine, internal medicine, other surgical disciplines and other conservative disciplines.

CDAD on admission: number of CDAD cases contracted outside the hospital per 100 patients admitted to hospital.

## Results

For 2007, 34 hospitals participated in the CDAD-KISS module: 16 hospitals with up to 300 beds, 9 hospitals with between 301 and 600 beds, 9 hospitals with over 601 beds.

As such, it was mainly smaller hospitals that reported data for 2007.

In these hospitals a total of 3,033 CDAD cases occurred involving a total of 652,971 patients (46.5 CDAD cases / 10,000 patients).

820 CDAD cases (27.04 %) were contracted outside the hospital, of which 619 (20.41 %) were contracted in an ambulatory setting and 201 (6.63 %) in other healthcare institutions.

The total incidence density was 0.66 CDAD cases / 1,000 patient days. The incidence density of nosocomial CDAD cases was 0.48 nosocomial CDAD cases / 1,000 patient days, and that of severe CDAD cases 0.06 CDAD cases / 1,000 patient days.

The distribution of hospitals based on the total incidence density showed that the majority of hospitals (14) had an incidence density between 0.25–0.5 cases per 1000 patient days. Two hospitals were conspicuous for their high incidence density of almost two cases per 1,000 patient days (Table 1, Figure 2).

In statistical terms, CDAD was seen in 0.13 cases per 100 patients admitted to hospital.

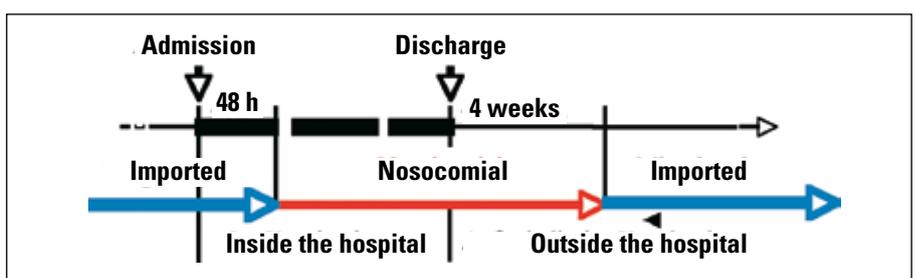


Figure 1: Time frame for making a distinction between nosocomial / imported CDAD cases (based on ECDC recommendations [5]).

Table 1: Distribution of incidence density of 34 hospitals per 1,000 patient days.

	Mean value	Q1	Median	Q3
Incidence density: total CDAD cases	0.66	0.32	0.56	0.92
Incidence density: nosocomial CDAD cases	0.48	0.17	0.35	0.67

Table 2: CDAD cases and incidence based on specialist departments.

Dept.	CDAD cases	Patient days	CDAD cases per 1,000 patient days	Nosocomial cases	Nosocomial cases per 1,000 patient days	Imported cases	
						Ambulatory setting	Contracted in other healthcare institution
Intensive care unit	193	212,783	0.91	160	0.75	24	9
Internal medicine	1,687	1,392,385	1.21	1,112	0.80	446	129
Surgery	394	985,525	0.41	331	0.35	55	8
Other surgical departments	187	1,044,303	0.18	159	0.15	28	0
Other conservative departments	572	983,732	0.58	451	0.46	66	55
ALL	3,033	4,591,728	0.66	2,213	0.48	619	201

### Distribution of CDAD incidences based on specialist departments

The highest CDAD incidences were recorded for the internal medicine departments, followed by intensive care units and the other conservative departments (Table 2).

### Diagnostic criteria

The principle criterion is criterion 1, according to which symptoms must be evidenced and proof furnished of toxin or of toxin-producing *Clostridium*.

### Severe courses

In the participating hospitals a total of 260 (8.75 %) severe cases were observed.

## Discussion

Initial evaluation of the data of the CDAD-KISS module highlighted the fact that CDAD is a serious problem in German hospitals. Based on discharge diagnoses (Diagnoses-Related Group – DRG – codes) the number of cases of enterocolitis caused by *C. difficile* in 2006 was 97.5 cases per 100,000 discharges [8], whereas the number for 2007 based on the CDAD-KISS data available was 465 CDAD cases per 100,000 patients.

The somewhat fourfold increase in the number of CDAD cases is attributable, inter alia, to prospective active CDAD-KISS data registration. The high CDAD

incidence rates may also be suggestive of the fact that it was mainly hospitals with an awareness of the problems associated with this infection which participated in the CDAD-KISS module, and could thus lead to selection bias.

Overall, the incidence densities differed greatly among the participating hospitals. The possible reasons for that were e.g. different CDAD diagnostic methods and a difference in frequency of requests for testing, as well as the use of microbiology

tests of varying sensitivity for diagnostic purposes in the laboratory.

In an initial survey conducted among CDAD-KISS participants, 57 % of interviewees stated that they had initiated measures for diagnosis of CDAD immediately after onset of nosocomial diarrhoea. Other hospitals took diagnostic measures only after the patient had received antibiotics.

Likewise, the different approaches to antibiotic therapy (choice of antibiotic and duration of use) can result in different

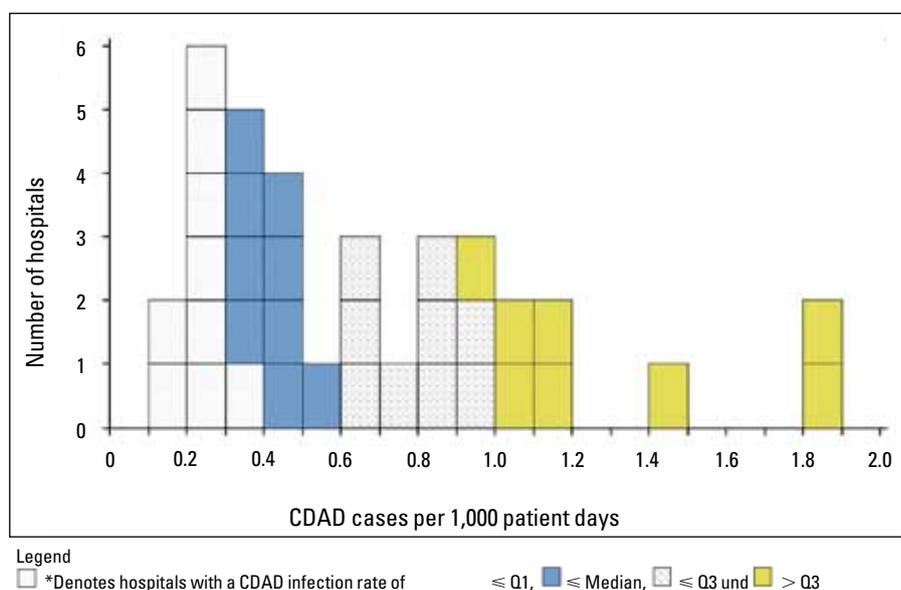


Figure 2: Distribution of the participating hospitals based on incidence densities (CDAD cases per 1,000 patient days). Q1 = 25 % percentile; Q3 = 75 % percentile, with Q1 = 0.32 / median = 0.56 / Q3 = 0.92.

Table 3: Distribution of cases based on diagnostic criteria (Criterion 1: Diarrhoea or toxic megacolon and detection of *C. difficile* toxins or culture-based evidence of toxin-producing *C. difficile* in stools; Criterion 2: Pseudomembranous colitis diagnosed on endoscopy; Criterion 3: Histopathology evidence of *C. difficile* infection (with or without diarrhoea) on endoscopy, colectomy or autopsy (ECDC case definition).

Dept.	CDAD cases	Criterion 1	Criterion 2	Criterion 3
ALL*	3,033	2,880	111	16

\* It was not possible to make any assignment for 26 patients.

Table 4: Comparison of total CDAD incidence rates of other countries.

Country	Incidence of CDAD cases per 10,000 patients
Germany	46.5 (2007)
Canada	47.4 (January-April 2007) [12]
Netherlands	16 (Surveillance Study 2005) [13]

CDAD incidence rates. A more restrictive approach to using antibiotics reduces the occurrence of CDAD [9,10].

Hospitals often differ in terms of their patient populations. For example, there are hospitals with infectious or gastroenterology departments which, alone because of the nature of their specialisms, have a high CDAD incidence, as well as departments treating a high number of elderly patients (patients older than 65 years).

Another main reason for the divergent CDAD incidences is, of course, the differences in hygiene practices. For example, certain studies have clearly revealed that infection control measures can effectively reduce high CDAD incidences [11].

Based on data already published for 2007, CDAD incidence densities are similar in Canada [12]. The incidence in the Netherlands with 16 cases per 10,000 patients (data from 2005) [13] is markedly lower.

## Conclusion

CDAD is a serious problem in German hospitals. The data available for 2007 mean that for the first time ever, CDAD "reference data" are available to hospitals and after comparing their own data with the reference data it is possible to identify any specific infection control problems related to CDAD. Thirty-four hospitals reported data for 2007, and 67 hospitals are currently participating in CDAD-KISS. It is possible at all times to sign up to CDAD-KISS so as to be better able to assess the situation in one's own hospital by comparing one's data with the reference data.

## Conflict of Interest

The authors declare that there is no conflict of interest as understood by the International Committee of Medical Journal Editors.

## References

- McDonald LC, Owings M, Jernigan DB. *Clostridium difficile* infection in patients discharged from US short-stay hospitals, 1996-2003. *Emerging infectious diseases* 2006;12:409-415
- Kuijper EJ, Coignard B, Brazier JS, et al. Update of *Clostridium difficile*-associated disease due to PCR ribotype 027 in Europe. *Euro Surveill* 2007;12:E1-2
- Barbut F, Mastrantonio P, Delmee M, et al. Prospective study of *Clostridium difficile* infections in Europe with phenotypic and genotypic characterisation of the isolates. *Clin Microbiol Infect* 2007;13:1048-1057
- Vonberg RP, Schwab F, Gastmeier P. *Clostridium difficile* in discharged inpatients, Germany. *Emerging infectious diseases* 2007;13:179-180
- Kuijper EJ, Coignard B, Tull P. Emergence of *Clostridium difficile*-associated disease in North America and Europe. *Clin Microbiol Infect* 2006;12 Suppl 6:2-18
- McDonald LC, Coignard B, Dubberke E, et al. Recommendations for surveillance of *Clostridium difficile*-associated disease. *Infect Control Hosp Epidemiol* 2007;28:140-145
- [http://www.rki.de/cln\\_100/nn\\_717602/DE/Content/InfAZ/C/Clostridium\\_\\_difficile/Meldetatbestaende.html](http://www.rki.de/cln_100/nn_717602/DE/Content/InfAZ/C/Clostridium__difficile/Meldetatbestaende.html)
- Vonberg RP. *Clostridium difficile*: Zum Stand der Meldungen schwer verlaufender Infektionen in Deutschland. *RKI - Epidemiologisches Bulletin* 2008;Nr.15
- Baxter R, Ray GT, Fireman BH. Case-control study of antibiotic use and subsequent *Clostridium difficile*-associated diarrhea in hospitalized patients. *Infect Control Hosp Epidemiol* 2008;29:44-50.
- Dubberke ER, Reske KA, Yan Y, et al. *Clostridium difficile*-associated disease in a setting of endemicity: identification of novel risk factors. *Clin Infect Dis* 2007;45:1543-1549.

- Muto CA, Blank MK, Marsh JW, et al. Control of an outbreak of infection with the hypervirulent *Clostridium difficile* BI strain in a university hospital using a comprehensive "bundle" approach. *Clin Infect Dis* 2007;45:1266-1273.
- Canada PHA. [www.phac-aspc.gc.ca/nois-sinp/survprog-eng.php](http://www.phac-aspc.gc.ca/nois-sinp/survprog-eng.php)
- Paltansing S, van den Berg RJ, Guseinova RA, et al. Characteristics and incidence of *Clostridium difficile*-associated disease in The Netherlands, 2005. *Clin Microbiol Infect* 2007;13:1058-1064.