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ORIGINAL ARTICLE

High Level of Gastrointestinal Nosocomial Infections in the German Surveillance System, 2002–2008

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OBJECTIVE. Surveillance of nosocomial infections (NIs) is well established in many countries but often does not include gastrointestinal infections. We sought to determine the proportion of NIs among all hospitalized cases for the 4 most prevalent types of gastrointestinal infections in Germany.

METHODS. We analyzed all notifications of laboratory-confirmed or epidemiologically linked gastrointestinal infections due to norovirus, rotavirus, *Salmonella* species, and *Campylobacter* species reported to the Robert Koch Institute in Berlin, Germany, from 2002 through 2008. Infections were considered nosocomial if disease onset was more than 2 days after hospitalization for norovirus, rotavirus, and *Salmonella* infection and more than 5 days after hospitalization for *Campylobacter* infection.

RESULTS. During the study period, 710,725 norovirus, 394,500 rotavirus, 395,736 *Salmonella,* and 405,234 *Campylobacter* gastrointestinal infections were reported. Excluding cases for which nosocomial status could not be determined, we identified 39,424 (49%) of 80,650 norovirus, 11,592 (14%) of 83,451 rotavirus, 3,432 (8%) of 43,348 *Salmonella,* and 645 (2%) of 33,503 *Campylobacter* gastrointestinal infections as definite nosocomial cases. Multivariate analysis confirmed higher risk of gastrointestinal NIs for patients aged more than 70 years (relative risk [RR], 7.0 [95% confidence interval {CI}, 6.7–7.2]; $P < .001$) and residents of western states (RR, 1.3 [95% CI, 1.2–1.3]; $P < .001$) and lower risk for female patients (RR, 0.9 [95% CI, 0.9–0.9; $P < .001$). Yearly NI proportions remained stable except for norovirus.

CONCLUSIONS. The investigated gastrointestinal NIs in Germany do not show a clear trend, but they are at high level, revealing potential for public health action and improvement of hospital infection control mainly among older patients. National prevalence studies on gastrointestinal NIs would be of additional value to give more insight on how and where to improve hospital infection control.

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A nosocomial infection (NI) is an infection acquired by a patient in a hospital or other healthcare facility.[1,2] NIs are a substantial burden both for the patient and for public health.[1] The estimated prevalence of NIs among hospitalized patients in Germany in 1994 was 3.5%.[3] To our knowledge, only 3 published studies on the prevalence of NIs also address gastrointestinal NIs: the prevalence of gastrointestinal NIs in general hospitals was found to be 0.4% in Italy,[4] 4.1% in Greece,[5] and 3.5% on average (stratified by ward, 0%–13%) in a point-prevalence study performed in France.[6] We therefore aimed to investigate the role of NIs among the 4 most prevalent types of gastrointestinal infections captured within the notifiable disease surveillance system in Germany from 2002 through 2008 and to identify changes over time and possible risk groups, which might lead to improved prevention of gastrointestinal NIs.

METHODS

Local health departments receive notifications from laboratories or clinicians, verify the cases according to the national case definitions, and forward them electronically to the Robert Koch Institute in Berlin, Germany, via the state health departments on a single-case basis with information on the patient's age, sex, laboratory diagnosis, hospitalization status, and so forth.[7] Data transfer within the German surveillance system is anonymous.

We included all cases of norovirus, rotavirus, *Salmonella,* and *Campylobacter* infection reported to the Robert Koch Institute from 2002 through 2008 for which information on hospitalization status was available. According to the national case definition, a case of acute gastroenteritis was either confirmed by a laboratory or epidemiologically linked to a laboratory-confirmed case.[8]

We determined that a case was nosocomial by taking into account the time between admission to the hospital and disease onset with reference to the mean incubation period[9-13] of the pathogen, according to definitions of NI used by the Centers for Disease Control and Prevention and the World Health Organization.[1,2] Norovirus, rotavirus, and *Salmonella* infections with disease onset more than 2 days after hospital

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TABLE 1. Characteristics of Study Population and Proportion of Nosocomial Infections (NIs) for the 4 Most Prevalent Types of Gastrointestinal Infection (GI) in Germany, 2002–2008

Characteristic	Norovirus	Rotavirus	*Salmonella*	*Campylobacter*
All reported GIs	710,725	394,500	395,736	405,234
All reported GIs with known hospitalization status (% of all reported GIs)	699,463/710,725 (98)	391,167/394,500 (99)	391,302/395,736 (99)	401,195/405,234 (99)
Cases involving hospitalization (% of all reported GIs with known hospitalization status)	179,941/699,463 (26)	158,578/391,167 (41)	91,497/391,302 (23)	52,662/401,195 (13)
Study population after exclusions (% of cases involving hospitalization)	90,849/179,941 (50)	90,335/158,578 (57)	46,955/91,497 (51)	35,896/52,662 (68)
Non-NIs (% of study population)	41,226/90,849 (45)	71,859/90,335 (80)	39,916/46,955 (85)	32,858/35,896 (92)
Probable NIs (% of study population)	10,199/90,849 (11)	6,884/90,335 (8)	3,607/46,955 (8)	2,393/35,896 (7)
Definite NIs (% of study population)	39,424/90,849 (43)	11,592/90,335 (13)	3,432/46,955 (7)	645/35,896 (2)
Final study population without probable NIs (% of cases involving hospitalization)	80,650/179,941 (45)	83,451/158,578 (53)	43,348/91,497 (47)	33,503/52,662 (64)
Definite NIs (% of final study population)	39,424/80,650 (49)	11,592/83,451 (14)	3,432/43,348 (8)	645/33,503 (2)

NOTE. Data are proportion (%) of cases, unless otherwise indicated.

admission and *Campylobacter* infections with disease onset more than 5 days after admission were considered to have been acquired nosocomially. Norovirus, rotavirus, and *Salmonella* infections with disease onset 1–2 days after admission and *Campylobacter* infections with disease onset 2–5 days after admission were considered probable NIs.

The study population included only cases with known hospitalization status and dates of hospitalization and disease onset. We excluded the following cases for which the patient was hospitalized long before or after the gastrointestinal infection, which would probably have been community acquired: cases with (1) disease onset more than 3 days before hospitalization for norovirus, *Salmonella,* and rotavirus gastrointestinal infections and more than 6 days before hospitalization for *Campylobacter* gastrointestinal infections, because those are community acquired and not related to hospitalization; (2) disease onset later than 25.5 days after hospitalization, because these cases would be highly unlikely nosocomial, taking into account the mean length of hospitalization in Germany; or (3) disease onset more than 3 days after hospital discharge for norovirus, *Salmonella,* and rotavirus gastrointestinal infections and more than 6 days after hospital discharge for *Campylobacter* gastrointestinal infections, because these cases again would not be nosocomial, taking into account the incubation periods of the pathogens. Furthermore, we excluded probable NIs, because their nosocomial status could not be proven, so the final study population contained only all cases that were definitely nosocomial or definitely not nosocomial (Table 1). Within the final study population, we calculated proportions of definite NIs for each pathogen and also stratified by sex, age group (less than 1, 1, 2, 3, 4, 5–9, 10–14, 15–19, 20–24, 25–29, 30–39, 40–49, 50–59, 60–69, and more than 69 years), and yearly and geographical distribution. For multivariate analysis, we used a quartile distribution of age groups. For geographical distribution, we stratified between eastern states (Berlin, Brandenburg, Mecklenburg-Vorpommern, Sachsen, Sachsen-Anhalt, and Thüringen) and western states (Baden-Württemberg, Bayern, Bremen, Hamburg, Hessen, Niedersachsen, Rheinhard-Pfalz, Saarland, and Schleswig-Holstein). Multivariate analysis was performed to analyze risk factors and to control for confounding factors.

For the evaluation of the data, we used Excel (Microsoft), and statistical analyses (forward logistic regression including all variables) were performed in SPSS, version 15 (SPSS). All *P* values are 2-sided, and a *P* value of less than .05 was considered to reveal a significant difference using the Wald test.

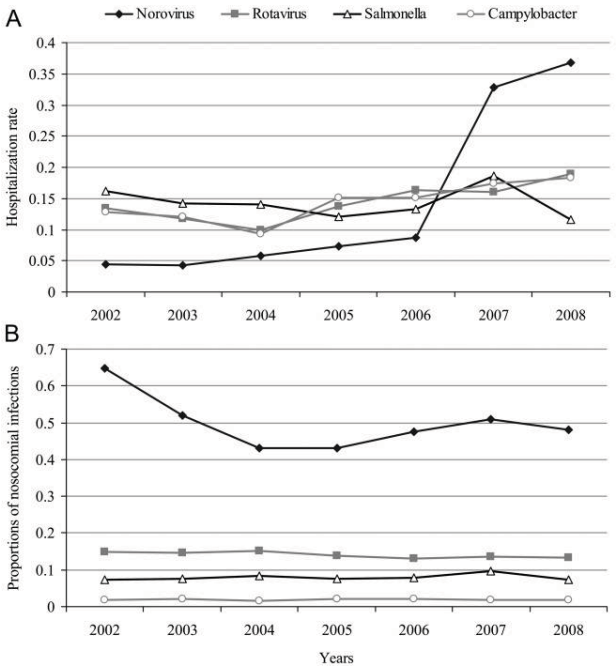

FIGURE 1. Hospitalization rates of all reported cases *(A)* and proportions of definite nosocomial infections *(B)* in the final study population for the 4 most prevalent types of gastrointestinal infection in Germany according to year, 2002–2008.

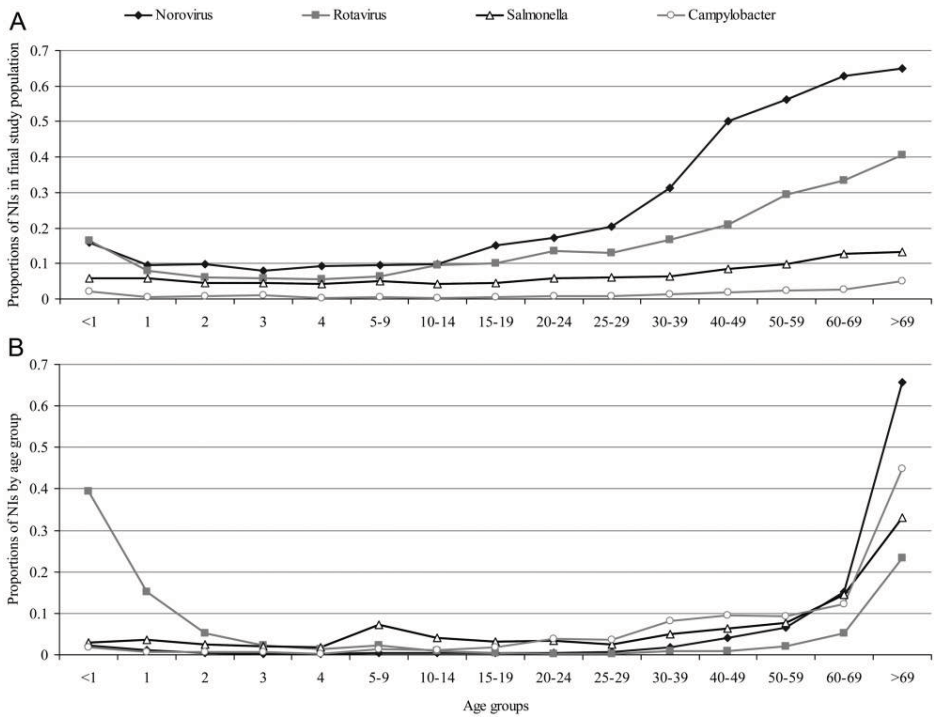

FIGURE 2. Proportions of cases of infection in each age group of the final study population that were definitely nosocomial (*A*) and age distribution of definite nosocomial infections (*B*) for the 4 most prevalent types of gastrointestinal infection in Germany, 2002–2008.

RESULTS

A total of 710,725 cases of norovirus gastrointestinal infection, 394,500 cases of rotavirus gastrointestinal infection, 395,736 cases of *Salmonella* gastrointestinal infection, and 405,234 cases of *Campylobacter* gastrointestinal infection were reported from 2002 through 2008 in Germany, resulting in annual incidences of 123.2, 68.4, 68.6, and 70.3 cases per 100,000 population, respectively (Table 1). Hospitalization status was known for 98% of norovirus infections and for 99% of rotavirus, *Salmonella,* and *Campylobacter* infections. Among those cases with known hospitalization status, 26% of norovirus cases, 41% of rotavirus cases, 23% of *Salmonella* cases, and 13% of *Campylobacter* cases involved hospitalization (Table 1). The hospitalization rate among all reported cases increased during the observed time period, especially for norovirus infection (from 4% to 37%); slightly increasing trends are also seen for rotavirus (from 13% to 19%) and *Campylobacter* (from 13% to 18%), whereas the rate of hospitalization for *Salmonella* infection was stable (Figure 1*A*).

Of cases involving hospitalization, 45% of norovirus, 53% of rotavirus, 47% of *Salmonella,* and 64% of *Campylobacter* cases were included in the final study population. The proportions of definite NIs were 49%, 14%, 8%, and 2%, respectively (Table 1).

Our results show that the proportions of rotavirus, *Salmonella,* and *Campylobacter* NIs in the final study population remained stable over time, whereas the proportions of norovirus NIs showed fluctuating patterns (Figure 1*B*). In the final study population, there was no sex difference in the proportions of definite NIs for infections due to rotavirus, *Salmonella,* and *Campylobacter,* but for infections due to norovirus, the proportion of NIs was 47% (16,391 of 34,907) among male patients and 50% (23,003 of 45,663) among female patients. The geographical distribution of definite NIs within the final study population showed higher proportions for norovirus, rotavirus, and *Salmonella* NIs in western states (50% [22,423 of 45,056], 15% [7,446 of 50,590], and 10% [3,055 of 31,600], respectively) than in eastern states (48% [16,995 of 35,582], 13% [4,146 of 32,858], and 3% [376 of 11,745], respectively), whereas *Campylobacter* NIs did not show any geographical difference. The age distribution of definite NIs due to norovirus and rotavirus in the final study population shows a U-shaped allotment—infections due to these pathogens were most often definitely nosocomial among patients aged less than 1 year (16% [906 of 5,729] for norovirus and 16% [4,576 of 27,941] for rotavirus) or more than 69 years (65% [25,933 of 39,992] for norovirus and 41% [2,699 of 6,642] for rotavirus). The proportions of *Salmonella* and *Campylobacter* NIs slowly increased with age—infections due to these pathogens were most often definitely nosocomial in patients aged more than 69 years (13% [1,137 of 8,555] and 5% [289 of 5,775], respectively) (Figure 2*A*). We also

TABLE 2. Multivariable Analysis of Definite Nosocomial Infections for 4 Most Prevalent Types of Gastrointestinal Infection and Their Risk Factors in Germany, 2002–2008

	All pathogens (n = 240,952)		Norovirus (n = 80,650)		Rotavirus (n = 83,451)		*Salmonella* (n = 43,348)		*Campylobacter* (n = 33,503)	
Variable	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
Sex distribution										
Male	Reference		Reference		Reference					
Female	0.9 (0.9–0.9)	<.001	0.9 (0.9–0.9)	<.001	1.0 (0.9–1.0)	.03				
Geographic distribution										
East	Reference				Reference		Reference			
West	1.3 (1.2–1.3)	<.001			1.3 (1.3–1.4)	<.001	3.3 (3.0–3.7)	<.001		
Age[a]										
Quartile 1	Reference		Reference		Reference		0.3 (0.3–0.4)	<.001	Reference	
Quartile 2	0.6 (0.6–0.6)	<.001	8.5 (8.1–8.9)	<.001	0.5 (0.4–0.5)	<.001	0.3 (0.3–0.3)	<.001	1.7 (1.2–2.4)	.004
Quartile 3	3.9 (3.8–4.1)	<.001	14.3 (13.5–15.0)	<.001	0.3 (0.3–0.4)	<.001	0.6 (0.6–0.7)	<.001	3.3 (2.4–4.5)	<.001
Quartile 4	7.0 (6.7–7.2)	<.001	13.0 (12.4–13.6)	<.001	1.6 (1.5–1.7)	<.001	Reference		7.5 (5.6–10.0)	<.001
Yearly incidence										
2002	Reference		Reference		Reference		0.8 (0.7–0.9)	.004		
2003	0.9 (0.8–0.9)	<.001	0.6 (0.5–0.7)	<.001	1.0 (0.9–1.1)	.95	0.8 (0.7–0.9)	.004		
2004	0.8 (0.8–0.9)	<.001	0.5 (0.5–0.6)	<.001	1.0 (0.9–1.1)	.48	0.9 (0.8–1.0)	.23		
2005	0.8 (0.7–0.8)	<.001	0.5 (0.4–0.5)	<.001	0.9 (0.9–1.0)	.054	0.8 (0.7–0.9)	.004		
2006	0.8 (0.7–0.8)	<.001	0.6 (0.5–0.7)	<.001	0.9 (0.8–0.9)	<.001	0.8 (0.7–0.9)	.002		
2007	0.8 (0.8–0.8)	<.001	0.6 (0.5–0.6)	<.001	0.9 (0.8–0.9)	<.001	Reference			
2008	0.7 (0.7–0.7)	<.001	0.5 (0.5–0.6)	<.001	0.8 (0.6–0.9)	<.001	0.7 (0.7–0.8)	<.001		

NOTE. CI, confidence interval; RR, relative risk.

[a] Age quartiles consist of the following ranges: all pathogens: ⩽1, 1–20, 21–70, and >70 years; norovirus: ⩽25, 26–69, 70–81, and >81 years; rotavirus: prenatal, 0–1, 2–3, and >3 years; *Salmonella:* ⩽6, 7–25, 26–65, and >65 years; *Campylobacter:* ⩽19, 20–34, 35–62, and >62 years.

calculated the age distribution of definite NIs due to each pathogen and determined that the highest load of norovirus, *Salmonella,* and *Campylobacter* NIs also occurred in patients aged more than 69 years (66% [25,933 of 39,424], 33% [1,137 of 3,432], and 45% [289 of 645], respectively), but the highest load of rotavirus NIs occurred in patients aged less than 1 year (39% [4,576 of 11,592]) or 1 year (15% [1,762 of 11,592]) (Figure 2*B*).

Multivariate analysis of definite NIs (Table 2) confirmed higher risk of NI with increasing age, especially for patients aged more than 70 years (relative risk [RR], 7.0 [95% confidence interval {CI}, 6.7–7.2]; $P < .001$), and higher risk of NI in western states (RR, 1.3 [95% CI, 1.2–1.3]; $P < .001$). In comparison with NI due to norovirus, the risks of NI due to rotavirus (RR, 0.4 [95% CI, 0.4–0.5]; $P < .001$), *Salmonella* (RR, 0.1 [95% CI, 0.1–0.1]; $P < .001$), and *Campylobacter* (RR, 0.02 [95% CI, 0.02–0.02]; $P < .001$) were lower. In contrast to the results of the descriptive analysis, the risk of NI due to all pathogens was slightly lower for female patients (RR, 0.9 [95% CI, 0.9–0.9]; $P < .001$) than for male patients.

DISCUSSION

To our knowledge, this analysis is the first population-based assessment of gastrointestinal NIs. The proportions of NIs in Germany are high (49% of norovirus, 14% of rotavirus, 8% of *Salmonella,* and 2% of *Campylobacter* gastrointestinal infections). In Europe, mainly rotavirus infections have been studied in this sense: the median proportion of rotavirus NIs among all hospital admissions in Europe ranges from 0.3% to 27.7%[14] and among rotavirus-associated hospitalizations from 21% to 27%.[15,16]

Our results show that NIs are particularly prevalent in the very young and the very old. Ford-Jones et al[17] found that in children, gastrointestinal infections usually account for 17%–20% of NIs, whereas in adults, NIs occur less often in the gastrointestinal tract.[3,4] Our estimates for NIs as a proportion of the final study population in patients aged less than 1 year were higher for norovirus and rotavirus infections (16% for each) and lower for *Salmonella* and *Campylobacter* infections (6% and 2%, respectively). In the elderly population, we observed NI proportions as high as 65% for norovirus gastrointestinal infections and 41% for rotavirus gastrointestinal infections, whereas the proportion of NIs among *Salmonella* and *Campylobacter* gastrointestinal infections were much lower (13% and 5%, respectively).

For norovirus infections, the elderly and immunocompromised patients are more often[18,19] and more severely affected, whereas, unlike with rotavirus infections, neonates and very young children are rarely affected.[20] This is supported by our study, in which 66% of all norovirus NIs occurred among the elderly, whereas only 0.5% occurred among children aged less than 9 years. These age-related differences suggest that patients with more intensive care during hospitalization may be more exposed to nosocomial transmission.

Interestingly, the proportions of NIs due each pathogen did not show much yearly shift in Germany, except norovirus.

The proportion of norovirus NIs among all norovirus-associated hospitalizations was high (49% overall), and it decreased substantially from 2002 to 2004 but then increased again in 2007. This fact is interesting in combination with the finding that the rate of hospitalization for norovirus infection increased sharply in 2007 (33%) and 2008 (37%) in comparison with 2002–2003 (4%). We believe that the decreasing trend might be partly explained by improved hospital hygiene since 2002. The new increase of norovirus NIs after 2006 is probably due to the global spread of GII.4 strains that triggered winter epidemics in 2006–2007, 2007–2008, and 2008–2009[21-23] and overwhelmed the hospitals' capacity to stop further spread of the disease within the facilities.

We have difficulty explaining why the proportions of rotavirus and *Salmonella* NIs were significantly higher in western Germany (RR, 1.3 [95% CI, 1.3–1.4]; $P < .001$; and RR, 3.3 [95% CI, 3.0–3.7]; $P < .001$, respectively) than in eastern Germany: generally, surveillance sensitivity for gastrointestinal infections is higher in eastern than in western Germany,[24] which could result in a higher denominator when proportions of NIs are calculated. We did not find any significant geographical difference in hospitalization length of stay. Furthermore, geographical differences may reflect not only surveillance differences but also different management styles, thus revealing potential for general improvement.

The high proportion of NIs among the 4 types of gastrointestinal infections in Germany indicates a need for improvement in hospital infection control. Although it is known that hand hygiene is an effective means of preventing NIs, adherence among patients, patients' visitors, and healthcare workers might be poor.[25] Therefore, we suggest additional support for hospital-wide programs promoting hand hygiene and other control measures for the prevention of NIs.[1,10,26-31]

Our study had some limitations. Data on hospitalization were not available for all patients, but we do not expect that the factors leading to incomplete capture of hospitalization data would bias the analysis. Our definition of NI was based simply on the incubation period for each pathogen; nonetheless, these differ according to infectious dose and health status of the host. For the NI analysis, we used a very specific definition of NI to ensure that only definite NIs were analyzed. We also did not account for infections occurring after hospital discharge. For these reasons, the true proportion of NIs is likely to be even larger than that described here.

Gastrointestinal NIs do not show a clear trend but are frequent in Germany. This indicates that hospital infection control needs to be improved and suggests that gastrointestinal infections should be addressed by surveillance and infection control programs in hospitals. National prevalence studies on gastrointestinal NIs and analysis of outbreaks caused by these pathogens would complete the data presented and would help to specify the improvements needed in hospital infection control in Germany.

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REFERENCES

1. Ducel G, Fabry J, Nicolle L, eds. Prevention of hospital-acquired infections: a practical guide. 2nd ed. WHO document WHO/CDS/CSR/EPH/2002.12. World Health Organization (WHO) website. http://www.who.int/csr/resources/publications/whocdscsreph200212.pdf. Published 2002. Accessed October 28, 2010.
2. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988 [published correction appears in *Am J Infect Control* 1988;16(4):177]. *Am J Infect Control* 1988;16(3):128–140.
3. Gastmeier P, Kampf G, Wischnewski N, et al. Prevalence of nosocomial infections in representative German hospitals. *J Hosp Infect* 1998;38(1):37–49.
4. Lizioli A, Privitera G, Alliata E, et al. Prevalence of nosocomial infections in Italy: result from the Lombardy survey in 2000. *J Hosp Infect* 2003;54(2):141–148.
5. Starakis I, Marangos M, Gikas A, Pediaditis I, Bassaris H. Repeated point prevalence survey of nosocomial infections in a Greek university hospital. *J Chemother* 2002;14(3):272–278.
6. Prevalence of nosocomial infections in France: results of the nationwide survey in 1996. *J Hosp Infect* 2000;46(3):186–193.
7. Faensen D, Claus H, Benzler J, et al. SurvNet@RKI: a multistate electronic reporting system for communicable diseases. *Euro Surveill* 2006;11(4):100–103.
8. Krause G, Brodhun B, Altmann D, Claus H, Benzler J. Reliability of case definitions for public health surveillance assessed by round-robin test methodology. *BMC Public Health* 2006;6:129.
9. Kaplan JE, Gary GW, Baron RC, et al. Epidemiology of Norwalk gastroenteritis and the role of Norwalk virus in outbreaks of acute nonbacterial gastroenteritis. *Ann Intern Med* 1982;96(6 pt 1):756–761.
10. Hedberg CW, Osterholm MT. Outbreaks of food-borne and waterborne viral gastroenteritis. *Clin Microbiol Rev* 1993;6(3):199–210.
11. Gray J, Vesikari T, Van DP, et al. Rotavirus. *J Pediatr Gastroenterol Nutr* 2008;46 (suppl 2):S24–S31.
12. Glynn JR, Palmer SR. Incubation period, severity of disease, and infecting dose: evidence from a *Salmonella* outbreak. *Am J Epidemiol* 1992;136(11):1369–1377.
13. Skirrow MB. *Campylobacter.* Lancet 1990;336(8720):921–923.
14. Gleizes O, Desselberger U, Tatochenko V, et al. Nosocomial rotavirus infection in European countries: a review of the epidemiology, severity and economic burden of hospital-acquired rotavirus disease. *Pediatr Infect Dis J* 2006;25(suppl 1):S12–S21.
15. The Paediatric Rotavirus European Committee (PROTECT). The paediatric burden of rotavirus disease in Europe. *Epidemiol Infect* 2006;134(5):908–916.
16. Fischer TK, Bresee JS, Glass RI. Rotavirus vaccines and the prevention of hospital-acquired diarrhea in children. *Vaccine* 2004;22(suppl 1):S49–S54.
17. Ford-Jones EL, Mindorff CM, Gold R, Petric M. The incidence of viral-associated diarrhea after admission to a pediatric hospital. *Am J Epidemiol* 1990;131(4):711–718.
18. Rockx B, De WM, Vennema H, et al. Natural history of human calicivirus infection: a prospective cohort study. *Clin Infect Dis* 2002;35(3):246–253.

19. Dedman D, Laurichesse H, Caul EO, Wall PG. Surveillance of small round structured virus (SRSV) infection in England and Wales, 1990–5. *Epidemiol Infect* 1998;121(1):139–149.
20. Greenberg HB, Valdesuso J, Kapikian AZ, et al. Prevalence of antibody to the Norwalk virus in various countries. *Infect Immun* 1979;26(1):270–273.
21. Infektionsepidemiologisches Jahrbuch meldepflichtiger Krankheiten für 2008. Berlin, Germany: Robert Koch–Institute, 2009. Available at: http://www.gapinfo.de/gesundheitsamt/alle/technik/dowload/seuche/allg/infepi_jb/Jahrbuch_2008.pdf. Accessed October 29, 2010.
22. Siebenga JJ, Vennema H, Zheng DP, et al. Norovirus illness is a global problem: emergence and spread of norovirus GII.4 variants, 2001–2007. *J Infect Dis* 2009;200(5):802–812.
23. Kroneman A, Vennema H, Harris J, et al. Increase in norovirus activity reported in Europe. *Euro Surveill* 2006;11(12):E061214.
24. Koch J, Schneider T, Stark K, Schreier E. Norovirus infections in Germany [in German]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2006;49(3):296–309.
25. Ward RL, Bernstein DI, Knowlton DR, et al. Prevention of surface-to-human transmission of rotaviruses by treatment with disinfectant spray. *J Clin Microbiol* 1991;29(9):1991–1996.
26. Zerr DM, Allpress AL, Heath J, Bornemann R, Bennett E. Decreasing hospital-associated rotavirus infection: a multidisciplinary hand hygiene campaign in a children's hospital. *Pediatr Infect Dis J* 2005;24(5):397–403.
27. Ebnöther C, Tanner B, Schmid F, La Rocca V, Heinzer I, Bregenzer T. Impact of an infection control program on the prevalence of nosocomial infections at a tertiary care center in Switzerland. *Infect Control Hosp Epidemiol* 2008;29(1):38–43.
28. Chadwick PR, Beards G, Brown D, et al. Management of hospital outbreaks of gastro-enteritis due to small roundstructured viruses. *J Hosp Infect* 2000;45(1):1–10.
29. Barker J, Vipond IB, Bloomfield SF. Effects of cleaning and disinfection in reducing the spread of norovirus contamination via environmental surfaces. *J Hosp Infect* 2004;58(1):42–49.
30. Gallimore CI, Cubitt D, du PN, Gray JJ. Asymptomatic and symptomatic excretion of noroviruses during a hospital outbreak of gastroenteritis. *J Clin Microbiol* 2004;42(5):2271–2274.
31. Koopmans M. Noroviruses in healthcare settings: a challenging problem. *J Hosp Infect* 2009;73(4):331–337.