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Original article

Effectiveness of a hospital-wide infection control programme on the incidence of healthcare-associated infections and associated severe sepsis and septic shock: a prospective interventional study

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ABSTRACT

Objectives: To evaluate whether a hospital-wide infection control programme (ICP) is effective at reducing the burden of healthcare-associated infections (HAIs) and associated severe sepsis/septic shock or death (severe HAIs).

Methods: Prospective, quasi-experimental study with two surveillance periods (September 2011 to August 2012; May 2013 to August 2014). Starting October 2012, the ICP included hand hygiene promotion and bundle implementation for common HAIs. We applied segmented mixed-effects Poisson regression and multi-state models. We reported adjusted incidence rate ratios (aIRR) and adjusted hazard ratios (aHR) with 95% confidence intervals (CI).

Results: Overall, 62 154 patients were under surveillance, with 1568 HAIs identified in 1170 patients (4.3 per 100 admissions) in the first and 2336 HAIs identified in 1711 patients (4.9 per 100 admissions) in the second surveillance period. No differences were found in the overall HAI incidence rates between the periods in the general wards (aIRR 1.29, 95% CI 0.78–2.15) and intensive care units (ICUs) (aIRR 0.59, 95% CI 0.27–1.31). However, the HAI incidence rate was declining in the ICUs after starting the ICP (aIRR 0.98, 95% CI 0.97–1.00 per 1-week increment), in contrast to general wards (aIRR 1.01, 95% CI 1.00–1.02). A reduction in severe HAIs (aIRR 0.13, 95% CI 0.05–0.32) and a lower probability of HAI-associated in-hospital deaths (aHR 0.56, 95% CI 0.31–0.99) were observed in the second period in the ICUs.

Conclusions: There was no overall reduction in HAIs after implementation of the ICP. However, there was a significant reduction in severe HAIs in ICUs. Whether this difference was a consequence of the ICP or improvement in HAI case management is not clear. **S. Hagel, Clin Microbiol Infect 2019;25:462**

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Introduction

Healthcare-associated infections (HAIs) are among the leading complications in hospitalized patients, and they are associated with increased morbidity and mortality, and excess costs [1,2]. In a recent prevalence survey by Magill et al. [3], 4% of inpatients in 183 US acute-care hospitals had at least one HAI. An even higher prevalence of 6% was reported by the European Centre for Disease Prevention and Control based on data from 947 European acute-care hospitals [4]. Increasing prevention efforts is imperative for decreasing this burden. However, it remains unclear whether hospital-wide infection control programmes (ICPs) aimed at a wide array of HAIs and organisms are more efficacious than control strategies targeting only specific hospital sectors, certain types of infections or specific pathogens [5].

Hence, the primary aim of this study was to examine the effectiveness of a hospital-wide ICP for reducing the overall burden of HAIs without targeting specific pathogens, types of HAIs or hospital wards. The secondary aim was to characterize the intervention effect on severe HAIs causing severe sepsis/septic shock or death.

Methods

Study design and setting

This prospective, quasi-experimental, intervention study was performed at the Jena University Hospital. The Jena University Hospital is a 1350-bed tertiary-care hospital with approximately 50 000 annual admissions. Until the beginning of the study, infection control professionals focused primarily on non-patient-centred hospital hygiene (for details see the Supplementary material). The study was performed in 32 wards consisting of 27 general wards and 5 intensive care units (ICUs) (see Supplementary material, Table S1). Overall, 817 hospital beds were included. All other departments were situated at a separate geographical location and excluded. The study was performed from September 2011 to August 2014. In the first surveillance period (period 1; September 2011 to August 2012), the baseline incidence rate of HAIs was assessed. Thereafter, a multifaceted ICP was launched to complement the basic but unstructured infection control measures already in place (see below and Supplementary material, Table S2). A second surveillance period (period 2; May 2013 to August 2014) was included to evaluate the effectiveness of the intervention. Approval by higher hospital management, including the nursing director and management, had been secured in advance so that the programme was considered a hospital-wide priority. The data protection commissioner and institutional review board approved the study with a waiver of informed consent for individual patients (ID: 3139-05/11). The trial has been registered at the German Clinical Trials Register (DRKS00003166).

Surveillance and definitions

The HAIs were diagnosed according to the methodology of the German national surveillance system (Krankenhaus Infektions Surveillance System) [6], which uses the CDC's definition of HAI [7]. The clinical study team consisted of two physicians and three study nurses. All were externally trained and validated by the German National Reference Centre for the Surveillance of HAIs. Patients in general wards were pre-screened based on the initiation of antimicrobial therapy (excluding antimicrobial prophylaxis for any reason) because antimicrobial therapy has been demonstrated to be a sensitive proxy indicator for HAIs (sensitivity 95%–100%) [8–10]. For all patients in ICUs and patients from general wards who fulfilled the criteria in the pre-screening, the medical records were screened retrospectively to identify potential HAIs. In patients with an identified HAI, the clinical parameters within 5 days after the diagnosis of HAI were documented to identify possible progressions to severe sepsis/septic shock. For all patients under surveillance, demographic data were extracted from the hospital information system.

Interventions

The ICP was initiated in October 2012 and continued throughout the second surveillance period. The programme consisted of the promotion of hand hygiene and implementation of bundles for the prevention of the most common types of HAIs (i.e. central line-associated bloodstream infections, ventilator-associated pneumonia, catheter-associated urinary tract infection and surgical-site infections). Each bundle combined interventions recommended by the best practice evidence at the time of study initiation (see Supplementary material, Table S2). The hand hygiene promotion programme was based on the recommendations of the WHO Multimodal Hand Hygiene Improvement Strategy [11].

Outcomes

The incidence rate of HAIs was the primary outcome. The HAI incidence rates were calculated from the number of HAIs divided by the person-time at risk (i.e. the number of days a patient stays in the hospital) during the respective surveillance period. Similarly, the incidence rates were calculated for the combined secondary end point related to severe HAIs. We defined severe HAIs as HAIs with progression towards severe sepsis/septic shock or death caused by an underlying HAI. Severe sepsis and septic shock were defined according to published criteria at the time of study planning [12].

Sample size calculation

Based on hospital administrative data, we expected about 25 000 inpatients who would fulfil the inclusion and exclusion criteria for the first surveillance period of 12 months. According to literature, 5% to 10% of inpatients were expected to develop an HAI. To detect a clinically relevant, relative reduction of HAIs of 15% with a statistical power of 0.9 at a two-sided significance level of 0.05, the second surveillance phase should recruit 14 092 inpatients in case of an HAI incidence rate of 5%, 7822 in case of a rate of 7.5% and 5328 in case of a rate of 10%.

Statistical analysis

Patients at risk were inpatients with a hospital stay $\geq$48 hours and staying on a ward under observation during one of the two surveillance periods. Patient characteristics in the two surveillance periods were initially compared by applying the chi-squared, Wilcoxon–Mann–Whitney and rate ratio tests depending on the variable scale. To calculate the patient-days at risk, any part of a day counted as a whole day. We performed analyses stratified by general wards and ICUs. Consequently, the HAIs were assigned to the ward where they were most likely acquired (excluding HAIs with unknown origin: 68 in period 1 and 134 in period 2). To analyse the relationship between the infection control programme (intervention) and (the primary and secondary) outcomes, we applied multiple segmented mixed-effect Poisson regression models with a random slope (for details see the Supplementary material). We reported the adjusted incidence rate ratios (aIRR) together with the 95% confidence intervals (CI) and corresponding p-values (unadjusted for multiple testing). As an exploratory sensitivity analysis,

Table 1
Incidence and distribution of healthcare-associated infections (HAI) for patients with HAIs acquired on general wards (left columns) and intensive care units (ICUs, right columns)

Characteristic	General wards				Intensive care units			
	Period 1 & 2 (28 months)	Period 1 (12 months)	Period 2 (16 months)	p value	Period 1 & 2 (28 months)	Period 1 (12 months)	Period 2 (16 months)	p value
All patients								
Number of patients	60 938 (100)	26 456 (100)	34 482 (100)		11 654 (100)	4647 (100)	7007 (100)	
Days at risk [day]	658 315	282 305	376 010		225 469	90 032	135 437	
Age at admission (year); median (Q_1–Q_3)	65 (52–75)	65 (52–74)	65 (52–75)	0.003[a]	68 (56–76)	68 (55–75)	69 (57–76)	<0.001[a]
Females	28 606 (46.9)	12 329 (46.6)	16 277 (47.2)	0.142	4533 (38.9)	1817 (39.1)	2716 (38.8)	0.728
Charlson's comorbidity index; median (Q_1–Q_3)	3 (2–4)	3 (1–4)	3 (2–5)	<0.001 [a]	4 (2–5)	4 (2–5)	4 (2–5)	0.418 [a]
In-hospital deaths	1711 (2.8)	735 (2.8)	976 (2.8)	0.717	1469 (12.6)	644 (13.9)	825 (11.8)	0.001
HAI incidence rate (per 100 000 patient-days at risk)	348.6	346.4	350.3	0.812 [d]	713.6	655.3	752.4	0.008 [d]
Patients with HAIs								
Patient-level (patients with at least one HAI)								
Number of patients (cumulative incidence)	1910 (3.1)	818 (3.1)	1092 (3.2)	0.615	1130 (9.7)	412 (8.9)	718 (10.2)	0.015
Age at admission [year]; median (Q_1–Q_3)	69 (56–77)	69.5 (56–77)	69 (57–76)	0.548 [a]	68 (57–75)	66 (54.5–74)	70 (58.25–76)	<0.001 [a]
Females	901 (47.2)	401 (49.0)	500 (45.8)	0.175	404 (35.8)	143 (34.7)	261 (36.4)	0.624
Charlson's comorbidity index; median (Q_1–Q_3)	4 (3–5)	4 (3–5)	4 (3–5)	0.507 [a]	4 (3–6)	4 (2–5)	4 (3–6)	0.051 [a]
Based on infections								
Number of infections	2295 (100)	978 (100)	1317 (100)		1609 (100)	590 (100)	1019 (100)	
Site of infection [c]				<0.001				0.032
Primary bloodstream infection	303 (13.2)	129 (13.2)	174 (13.2)		177 (11.0)	73 (12.4)	104 (10.2)	
Urinary tract infection	364 (15.9)	133 (13.6)	231 (17.5)		107 (6.7)	29 (4.9)	78 (7.7)	
Respiratory tract infection	379 (16.5)	143 (14.6)	236 (17.9)		688 (42.8)	242 (41.0)	446 (43.8)	
(VAP [e] (% of RTI))	—	—	—		95 (13.8)	38 (15.7)	57 (12.8)	
Surgical site infection	731 (31.9)	307 (31.4)	424 (32.2)		342 (21.3)	141 (23.9)	201 (19.7)	
Clostridium difficile infection	240 (10.5)	134 (13.7)	106 (8.0)		99 (6.2)	29 (4.9)	70 (6.9)	
Other	278 (12.1)	132 (13.5)	146 (11.1)		196 (12.2)	76 (12.9)	120 (11.8)	
Incidence rates per 1000 patient-days at risk								
All combined	3.486	3.464	3.503	0.812 [d]	7.136	6.553	7.524	0.008 [d]
Primary bloodstream infection	0.460	0.457	0.463	0.962	0.785	0.811	0.768	0.776
Urinary tract infection	0.553	0.471	0.614	0.016	0.475	0.322	0.576	0.008
Respiratory tract infection	0.576	0.507	0.628	0.047	3.051	2.688	3.293	0.012
(VAP[e] (% of RTI) among factors)					0.421	0.422	0.421	1.000
Surgical site infection	1.110	1.087	1.128	0.656	1.517	1.566	1.484	0.662
Clostridium difficile infection	0.365	0.475	0.282	<0.001	0.439	0.322	0.517	0.037
Other	0.422	0.468	0.388	0.137	0.869	0.8444	0.886	0.801
Incidence rates per 1000 device days								
Primary bloodstream infection					4.016	3.689	4.282	0.367
Urinary tract infection					2.281	1.439	2.915	0.001
VAP					4.005	3.233	4.763	0.078
Severe HAIs								
Severe sepsis/septic shock due to HAI [c]								
Number of patients	256 (13.4)	115 (14.1)	141 (12.9)	0.509	566 (50.1)	252 (61.2)	314 (43.7)	<0.001
Number of infections	283 (12.3)	125 (12.8)	158 (12.0)	0.616	727 (45.2)	339 (57.5)	388 (38.1)	<0.001
In-hospital deaths caused by HAI [c]								
Number of patients	121 (6.3)	49 (6.0)	72 (6.6)	0.660	166 (14.7)	68 (16.5)	98 (13.6)	0.223
Number of infections	129 (5.6)	51 (5.2)	78 (5.9)	0.525	187 (11.6)	82 (13.9)	105 (10.3)	0.037
Severe HAIs [b, c]								
Number of patients	296 (15.5)	126 (15.4)	170 (15.6)	0.973	576 (51.0)	254 (61.7)	322 (44.8)	<0.001
Number of infections	329 (14.3)	137 (14.0)	192 (14.6)	0.745	743 (46.2)	342 (58.0)	401 (39.4)	<0.001
Incidence rates per 1000 patient-days at risk								
All combined[f]	0.450	0.446	0.452	0.962 [d]	2.555	2.821	2.377	0.046 [d]
Primary bloodstream infection	0.062	0.060	0.064	0.985	0.430	0.511	0.377	0.162
Urinary tract infection	0.023	0.032	0.016	0.281	0.106	0.100	0.111	0.984
Respiratory tract infection	0.173	0.177	0.170	0.904	1.495	1.611	1.418	0.270
(VAP [d,e] among factors)					0.213	0.244	0.192	0.489
Surgical site infection	0.176	0.156	0.191	0.325	0.705	0.911	0.583	0.006
Clostridium difficile infection	0.003	0.004	0.003	1.000	0.00	0.000	0.000	1.000
Other	0.058	0.057	0.059	1.000	0.448	0.533	0.391	0.147
Incidence rates per 1000 device days								
Primary bloodstream infection					2.201	2.325	2.100	0.689
Urinary tract infection					0.512	0.447	0.561	0.746
VAP					2.024	1.872	2.172	0.712

If not otherwise specified, the absolute and relative frequencies and p-values for period comparison from chi-squared tests are reported.
Abbreviations: Q_1–Q_3, first and third quartile for the interquartile range; VAP, ventilator-associated pneumonia.
[a] Wilcoxon–Mann–Whitney test.
[b] Severe sepsis/septic shock or in-hospital death caused by an HAI.
[c] Percentages refers to number of HAIs/number of patients with HAIs.
[d] Rate ratio test.
[e] Definition of VAP: ≥48 h mechanical ventilation AND Clinical Pulmonary Infection Score ≥6 AND new/worsening pulmonary infiltrates.
[f] Patients with at least one severe HAI are counted.

we performed a regression analysis using patient-level data. Each patient was assigned to the ward under observation that the patient first visited. For patients with at least one HAI, the date of the first HAI was derived. A multistate model with five states was used to address competing events in the course of hospitalization (hospital admission, HAI acquisition, discharge alive, death due to HAI, death due to other cause) [13]. We reported the adjusted hazard ratios (aHR) with 95% CI. The Poisson regression analyses were conducted via the STATA parallel edition 13.1, and R version 3.0.2 was used for all other analyses. For the multistate model, we applied the msm R-package [14].

Results

Overall, 62 154 patients were at risk of acquiring an HAI, including 26 943 patients in the first period (12 months) and 35 211 patients in the second period (16 months). In all, 35.6% of all patients under surveillance were assessed for HAIs individually by the study team during both surveillance periods (see Supplementary material, Fig. S1). In total, 1568 HAIs were identified in 1170 patients (4.3 per 100 admissions) in the first surveillance period, and 2336 HAIs were identified in 1711 patients (4.9 per 100 admissions) in the second surveillance period. The cumulative incidence was 3.1 per 100 admissions in patients in general wards and 9.7 per 100 admissions in patients in ICUs (Table 1).

For the primary end point, we did not observe differences in the HAI incidence rates between the periods in the general wards (aIRR 1.29, 95% CI 0.78–2.15, p = 0.31) and ICUs (aIRR 0.59, 95% CI 0.27–1.31, p = 0.20). However, the HAI incidence rate was declining in the ICUs after starting the ICP (aIRR 0.98, 95% CI 0.97–1.00 per 1-week increment, p = 0.04), in contrast to the general wards (aIRR 1.01, 95% CI 1.00–1.02 per 1-week increment, p = 0.02) (see Table 2, see Supplementary material, Table S3 and Fig. S2).

For the secondary end point, we observed fewer severe HAIs in ICUs during the second surveillance period (aIRR 0.13, 95% CI 0.05–0.32, p < 0.001, see Table 2, see Supplementary material, Table S4 and Fig. S2), and this decrease was observed for all types of HAIs (see Table 3). Furthermore, we observed a decrease in the incidence rate for severe HAIs in ICUs after the start of the intervention (aIRR 0.85, 95% CI 0.82–0.88 per 1-month increment, p < 0.001, Table 2), which was both not observed in the general wards (aIRR 0.86, 95% CI 0.35–2.10, p = 0.74, aIRR 1.10, 95% CI 1.03–1.18, p = 0.006, Table 2).

In the patient-level analyses, there were no differences in the risk of HAI acquisition between the two surveillance periods in patients in general wards (aHR 1.08, 95% CI 0.99–1.18, see Supplementary material, Table S5) or patients in ICUs (aHR 1.05, 95% CI 0.89–1.23, see Supplementary material, Table S5). The probability of in-hospital death caused by HAI was significantly lower in the ICU patients in the second surveillance period (aHR 0.56, 95% CI 0.31–0.99) but not in the general ward patients (aHR 1.27, 95% 0.94–1.72, see Supplementary material, Table S5, Fig. 1).

At least one pathogen was detected in 1738 of 2295 (75.7%) HAIs acquired in the general wards and in 1275 of 1609 (79.2%) HAIs acquired in the ICUs (see Supplementary material, Table S6). In the ICUs, fewer multidrug-resistant and extensively drug-resistant *Pseudomonas* spp. and extensively drug-resistant *Enterobacteriaceae* were detected in the second surveillance period (Table 4).

Compliance with hand hygiene improved from 41.0% (2235 of 5453 hand hygiene opportunities) at baseline to 50.5% (3246 of 6428 hand hygiene opportunities) after the intervention (+23.2%, χ^2 test p < 0.001). Differences were not observed in the baseline and post-intervention compliance between the general wards and ICUs. The mean consumption of alcohol-based handrub solution in ICUs increased from 101.3 mL per patient-day (range 78.3–115.2 mL) in 2011 to 143.1 mL per patient-day (range 112.8–168.3 mL) in 2014, representing a +41.3% change. In general wards the mean consumption increased from 37.0 mL per patient-day (range 18.0–97.8 mL) in 2011 to 42.7 mL per patient-day (range 15.3–95.4 mL) in 2014, representing a +15.4% change.

Discussion

The primary aim of this study, to reduce the overall incidence of HAIs, was not achieved. However, we observed a decline in the incidence of overall HAIs and fewer severe HAIs after the ICP was

Table 2
Segmented mixed Poisson regression analyses from model V for the adjusted incidence rate ratios (aIRRs) of healthcare-associated infections (HAIs, upper panels) and of severe HAIs (lower panels) on general wards (left panels) and intensive care units (right panels) comparing the (surveillance) periods. aIRRs are listed with the 95% confidence intervals (CI) and corresponding p values.

Variables included in the regression model	General wards				Intensive care units			
	aIRR	95% CI		p value	aIRR	95% CI		p value
Healthcare-associated infections								
Period (ref.: period 1)	1.296	0.784	2.145	0.312	0.592	0.267	1.310	0.196
Time after intervention (week)	1.009	1.002	1.017	0.018	0.983	0.967	0.999	0.037
Time since study initiation (week)	0.994	0.986	1.001	0.079	1.014	1.000	1.029	0.057
Mean Charlson comorbidity index	1.127	1.030	1.232	0.009	1.062	0.992	1.136	0.084
Ratio male:female	1.157	0.965	1.388	0.116	0.961	0.856	1.079	0.500
Mean age (year)	0.990	0.954	1.027	0.591	0.983	0.944	1.024	0.415
Season (ref.: summer)				0.069				0.006
Autumn	1.111	0.960	1.286	0.158	0.917	0.810	1.038	0.168
Winter	1.211	1.042	1.408	0.013	0.939	0.877	1.006	0.074
Spring	1.078	0.952	1.221	0.235	0.592	0.267	1.310	0.196
Number of blood cultures	1.000	0.999	1.001	0.570	0.983	0.967	0.999	0.037
Severe healthcare-associated infections								
Period (ref.: period 1)	0.862	0.353	2.102	0.744	0.125	0.049	0.315	<0.001
Time after intervention (month)	1.100	1.027	1.177	0.006	0.847	0.815	0.880	<0.001
Time since study initiation (month)	0.959	0.905	1.016	0.152	1.176	1.112	1.244	<0.001
Mean Charlson comorbidity index	1.040	0.888	1.219	0.627	1.250	1.046	1.493	0.014
Ratio male:female	1.365	1.126	1.656	0.002	0.976	0.773	1.232	0.838
Mean age (year)	0.999	0.966	1.032	0.930	0.870	0.833	0.909	<0.001
Season (ref.: summer)				0.013				<0.001
Autumn	1.795	1.251	2.577	0.001	1.286	1.115	1.484	0.001
Winter	1.946	1.187	3.190	0.008	1.396	1.248	1.561	<0.001
Spring	1.483	1.063	2.069	0.020	1.017	0.831	1.246	0.868
Number of blood cultures	1.002	1.000	1.004	0.065	0.999	0.998	1.001	0.422

Table 3
Absolute and relative frequencies of patients with severe healthcare-associated infections stratified by focus of infection and place of acquisition

Focus of infection	General ward		Intensive care unit	
	Period 1 (12 months)	Period 2 (16 months)	Period 1 (12 months)	Period 2 (16 months)
Surgical site infection	44 (14.4)	72 (17.3)	82 (60.7)	79 (41.6)
Respiratory tract infection	50 (35.2)	64 (27.6)	145 (61.4)	192 (44.2)
Among them VAP[a]	—	—	22 (57.9)	26 (45.6)
Urinary tract infection	9 (6.9)	6 (2.6)	9 (31.0)	15 (19.5)
Primary bloodstream infection	17 (14.0)	24 (14.3)	46 (67.6)	51 (50.5)
Other infection	16 (13.0)	22 (15.6)	48 (69.6)	53 (47.7)
Clostridium difficile infection	1 (0.8)	1 (1.0)	0 (0.0)	0 (0.0)

The proportion of patients with healthcare-associated infection (HAI) that progressed to severe HAI (severe sepsis/septic shock or in-hospital death caused by HAI) is indicated in parentheses (%). Multiple infections per patient were possible.

[a] Definition of ventilator-associated pneumonia (VAP): ≥48 hours mechanical ventilation AND Clinical Pulmonary Infection Score ≥ 6 AND new/worsening pulmonary infiltrates.

initiated in the ICUs. This observation was supported by the individual patient data analysis, which indicated that fewer in-hospital deaths caused by HAIs occurred in the ICUs. Whether this was a consequence of the ICP or of improvements in HAI case management is not clear because during the study period, several activities were performed to improve the management of patients with infections. The most notable finding was that after the ICP was implemented, the HAI incidence rate decreased over time in ICUs but increased over time in general wards, although there was no difference in its overall incidence between the surveillance periods. A variety of reasons for this observation is available.

The main focus of the infection control campaign was the improvement of hand hygiene behaviour. Previous studies demonstrated a reduction of HAIs through improved hand hygiene

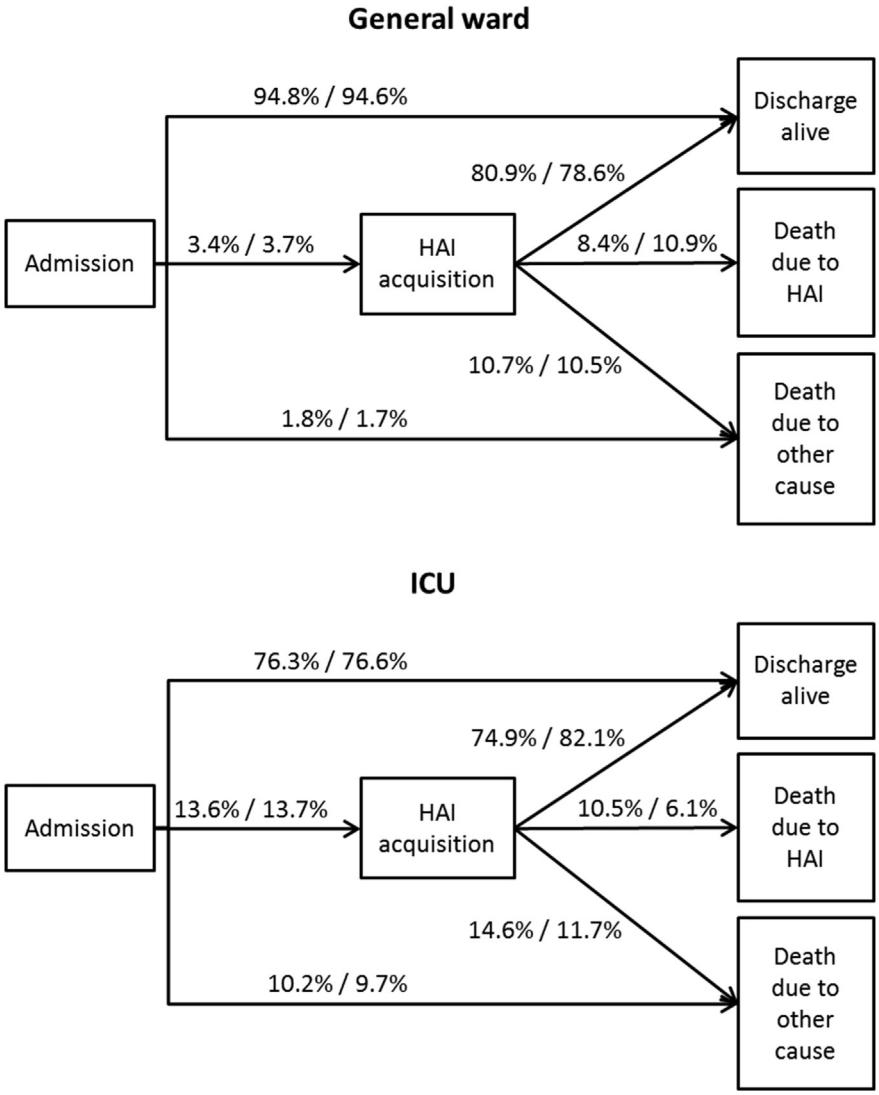

Fig. 1. Multistate model with transition probabilities for period 1/period 2 for both general wards (upper panel) and intensive care units (ICUs; lower panel). For general wards, we excluded one outlier (a patient with a healthcare-associated infection (HAI) that was diagnosed extremely late) because the computations could not be run otherwise.

Table 4
Microbial testing and antimicrobial resistance for selected pathogens

Pathogen	Period 1		Period 2		p value
	No. of isolates tested	Resistance (%)	No. of isolates tested	Resistance (%)	
General wards					
Staphylococcus aureus, resistance to methicillin	100	21.0	127	14.2	0.239
Enterococcus faecium, resistance to vancomycin	97	26.8	172	28.5	0.877
Pseudomonas spp.					
MDR[a]	56	19.6	75	10.7	0.233
XDR[b]	56	5.4	75	0.0	0.076[e]
Enterobacteriaceae					
MDR[c]	362	10.8	606	10.7	1.000
XDR[d]	362	0.3	606	0.3	1.000[e]
Intensive care units					
Staphylococcus aureus, resistance to methicillin	49	18.4	90	10.0	0.255
Enterococcus faecium, resistance to vancomycin	115	31.3	160	40.6	0.146
Pseudomonas spp.					
MDR[a]	64	23.4	98	7.1	0.006
XDR[b]	64	17.2	98	6.1	0.047
Enterobacteriaceae					
MDR[c]	223	9.9	409	9.0	0.845
XDR[d]	223	4.5	409	0.7	0.002[e]

p-value for chi-squared test is given if not otherwise indicated.
MDR, multi-drug resistant; XDR, extensively drug resistant.
[a] Sensitive to either ceftazidime OR carbapenems OR piperacillin OR fluoroquinolones (only one group).
[b] Resistant to carbapenems AND ceftazidime AND piperacillin AND aminoglycosides.
[c] Resistant to carbapenems OR resistant to cephalosporins AND fluoroquinolones.
[d] Resistant to cephalosporins AND fluoroquinolones AND carbapenems AND aminoglycosides.
[e] Fisher's exact test.

behaviour alone. For example, Sickbert-Bennett et al. [15] observed that a 10% improvement in hand hygiene compliance was associated with a 6% reduction of HAIs. Pittet et al. [16] demonstrated a reduction of HAIs from 17% to 10% after implementation of a hospital-wide hand hygiene programme. The post-intervention hand hygiene compliance in both studies, which was >95% in the study of Sickbert-Bennett et al. [15] and 66% in the study by Pittet et al. [16], was markedly higher than that in our study (51%), which might have reduced the effect of hand hygiene on the HAI incidence in our study. However, whether direct observations of hand hygiene compliance represent a valid instrument for assessing hand hygiene behaviour is debatable [17,18]. An analysis of alcohol-based handrub solution consumption as a marker of hand hygiene behaviour indicated that a remarkable increase in consumption occurred in the ICUs while a less pronounced increase occurred in the general wards. This finding might explain the observed decline in the HAI incidence after starting the campaign in the ICUs, which was not observed on the general wards.

In addition to improving hand hygiene, implementing bundles was part of the ICP. However, a majority of recommended measures were already implemented in daily care before initiating the study. For example, perioperative antibiotic prophylaxis was administered within 60 minutes before incision in 95% of patients undergoing surgery and chlorhexidine was already part of daily oral care in ventilated patients. In the context of the study, the previously implemented items were precised and implemented as a bundle. Considering the aforementioned points, the additional effect of the bundle strategy on HAI prevention remains unclear and may potentially vary between ICUs and general wards.

In addition to the varying effectiveness of the ICP, several confounding factors that influenced the incidence of HAIs must be considered. As a consequence of the improvement in HAI management, the number of collected blood culture sets nearly doubled hospital-wide from 13 126 to 25 805 per annum between 2011 and 2014, which probably undermined our study objective [19].

Besides that, the study provides unique data on the hospital-wide incidence of HAIs over a long observation period. Studies assessing the burden of HAIs usually perform prevalence surveys. Puhto and Syrjälä recently published a study using a hospital-wide electronic surveillance system for assessing the incidence of HAIs in a tertiary-care hospital in Finland [8]. The 3-year incidence of HAI was 4.9%, which was comparable to our observations. In addition, our study provides data on the severity of different types of HAIs in both ICU and general ward patients for the first time. This can help when determining where to most effectively use limited resources for future prevention and control interventions.

Our study has several limitations in addition to those already addressed. First, infections treated without antimicrobials may have remained unnoticed because the initiation of antimicrobial therapy was one criterion for pre-screening in the general wards. Second, surveillance was performed retrospectively; so, incomplete documentation might have biased the HAI surveillance and influenced assessments of progression to severe sepsis/septic shock. Third, only a few process parameters were recorded. In addition, the observation period for assessing the effectiveness of the infection control programme may have been too short to realize the full effect of the ICP.

Conclusion

Compared with previous studies that typically focused on certain HAIs or were limited to high-risk settings, our study evaluated the effectiveness of a hospital-wide ICP. Although the primary aim of the study of reducing the overall incidence of HAIs was not achieved, the study demonstrated a decline of severe HAIs in patients in ICUs in the second surveillance period. Whether this result was a consequence of the ICP or a general improvement in HAI management remains unclear.

Transparency declaration

The authors have no conflicts of interest to declare.

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Author contributions

S. Harbarth, PG, FB and S. Hagel designed the study. MW, MK, S. Hagel and AS analysed the data. SH, KL, JF and AM performed the surveillance. S. Hagel, PG, S. Harbarth, MP, MK and AS wrote the manuscript.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.cmi.2018.07.010.

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