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Published in:
Clinical Microbiology and Infection

DOI (link to publication from Publisher):
10.1016/j.cmi.2022.09.004

Publication date:
2023

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Mortensen, V. H., Mygind, L. H., Schønheyder, H. C., Staus, P., Wolkewitz, M., Kristensen, B., & Søgaard, M. (2023). Excess length of stay and readmission following hospital-acquired bacteraemia: A population-based cohort study applying a multi-state model approach. *Clinical Microbiology and Infection*, *29*(3), 346-352. Advance online publication. https://doi.org/10.1016/j.cmi.2022.09.004

Clinical Microbiology and Infection 29 (2023) 346–352

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Excess length of stay and readmission following hospital-acquired bacteraemia: a population-based cohort study applying a multi-state model approach

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ARTICLE INFO

Article history:
Received 13 March 2022
Received in revised form
1 September 2022
Accepted 9 September 2022
Available online 20 September 2022

Editor: Jesus Rodriguez-Baño

Keywords:
Hospital-acquired bacteraemia
Length of stay
Multi-state model
Population-based
Readmission

ABSTRACT

Objectives: Population-based estimates of excess length of stay after hospital-acquired bacteraemia (HAB) are few and prone to time-dependent bias. We investigated the excess length of stay and readmission after HAB.

Methods: This population-based cohort study included the North Denmark Region adult population hospitalized for ≥48 hours, from 2006 to 2018. Using a multi-state model with 45 days of follow-up, we estimated adjusted hazard ratios (aHRs) for end of stay and discharge alive. The excess length of stay was defined as the difference in residual length of stay between infected and uninfected patients, estimated using a non-parametric approach with HAB as time-dependent exposure. Confounder effects were estimated using pseudo-value regression. Readmission after HAB was investigated using the Cox regression.

Results: We identified 3457 episodes of HAB in 484 291 admissions in 205 962 unique patients. Following HAB, excess length of stay was 6.6 days (95% CI, 6.2–7.1 days) compared with patients at risk. HAB was associated with decreased probability of end of hospital stay (aHR, 0.60; 95% CI, 0.57–0.62) driven by the decreased hazard for discharge alive; the aHRs ranged from 0.30 (95% CI, 0.23–0.40) for bacteraemia stemming from 'heart and vascular' source to 0.72 (95% CI, 0.69–0.82) for the 'urinary tract'. Despite increased post-discharge mortality (aHR, 2.76; 95% CI, 2.38–3.21), HAB was associated with readmission (aHR, 1.42; 95% CI, 1.31–1.53).

Conclusion: HAB was associated with considerably excess length of hospital stay compared with hospitalized patients without bacteraemia. Among patients discharged alive, HAB was associated with increased readmission rates. **Viggo Holten Mortensen, Clin Microbiol Infect 2023;29:346**

Introduction

Hospital-acquired bacteraemia (HAB) is a serious and increasing clinical challenge [1]. Beside severe clinical consequences, HAB is an economic concern [2]. Many studies have estimated attributable costs and length of stay due to hospital infections, including HAB, with length of stays attributed to HAB ranging from 6.7 to 30 days [3–15]. Most of these estimates have been derived from matched

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https://doi.org/10.1016/j.cmi.2022.09.004
1198-743X/

case-control or cohort studies, largely without considering the temporal nature of admission, infection, and discharge [3,4,6–14]. In these studies, the attributable length of stay is often estimated as the difference in total length of stay, comparing patients who eventually become infected with those who were not. This runs the risk of time-dependent (immortal time) bias, as prolonged hospital stay in itself is a risk factor for HAB [16].

Few studies have applied a cohort design with matched risk-set or exposure density sampling of controls to handle time-dependent bias [5,15]. However, this introduces challenges with matching and lack of comparable controls. Multi-state models may handle the temporal dynamics to avoid time-dependent bias without limiting data by the matching of controls [17].

Using population-based data and a multi-state model approach, we investigated the excess of length of stay in patients with HAB and readmission rates in patients who were discharged alive.

Methods

Study design and setting

We conducted a population-based cohort study in the North Denmark Region from 2006 to 2018, linking the North Denmark Bacteraemia Research Database [18] and Danish national health registries. All Danish citizens at birth or immigration are given a unique personal identifier that allows individual-level linkage of research databases and nationwide registries [19]. Residents are offered tax-supported healthcare free of charge. Hospital uptake is defined by geographic catchment area, with few exceptions for highly specialized treatment (e.g. solid organ transplant, allogeneic bone marrow transplant), which is centralized nationally. The North Denmark Region (approximately 582 000 inhabitants) has one referral hospital, Aalborg University Hospital (approximately 800 beds), and several public hospitals (7 in 2006, 6 in 2018). Outpatient treatment with i.v. antibiotics was not routinely available during the study. The Department of Clinical Microbiology provides bacteriological services, including blood cultures, for all hospitals and general practitioners in the region. Blood culture procedures have been described previously [20]. The study was approved by the Danish Patient Safety Authority (record number 3-3013-2954/1) and the Data Protection Agency through institutional registration (record number 2019-50).

Population

The cohort comprised adult patients (≥18 years) hospitalized for ≥48 hours in a hospital in the North Denmark Region**.** Patients were identified using the Danish National Patient Registry [19]. Readmission within the first 48 hours of discharge was considered a continuation of the admission.

Definition of HAB

We defined bacteraemia as 'a clinical entity associated with the presence of viable bacteria or fungi in the bloodstream evidenced by blood cultures in which contamination had been ruled out' [18]. Coagulase-negative staphylococci, *Corynebacterium spp.*, and *Cutibacterium acnes* were regarded as contaminants unless isolated from two or more separate blood culture sets [21]. Time of venepuncture of the first positive blood culture was used to categorize an episode as hospital-acquired if it occurred within a time window of 48 hours after admission to 48 hours after discharge. The source of bacteraemia was determined by the clinical microbiologist who supervised the blood culture analyses.

Comorbidities

Comorbidities were captured using diagnoses recorded in the Danish National Patient Registry using a 5-year look-back period. Diagnoses were categorized according to the updated Charlson Comorbidity Index (CCI) [22], with the CCI scores categorized as low (0 points), medium (1–2 points), and high (≥3 points) levels of comorbidity (Table S1).

Outcomes

The main outcomes were the relative daily probability of end of stay, the excess length of stay in days, and the relative daily probability of readmission between 48 hours and 30 days of discharge. We estimated the probabilities for combined endpoint of all-cause end of stay and for discharge alive and in-hospital mortality as separate endpoints. Patients transferred to post-acute care units were treated as discharged alive. A low daily probability of discharge indicated a prolonged stay. Accordingly, the excess length of stay describes the number of additional days a patient with HAB stays in hospital compared with patients without HAB [16]. Dates of admission, discharge, and readmission were captured from the National Danish Patient Registry. Information on vital status at discharge was retrieved from the Civil Registration System [23].

Statistical analysis

We adopted a multi-state approach, considering the patients' admission as a transition through various states. We used an illness-discharge multi-state model without recovery, including all admissions of ≥48 hours (Fig. 1). Patients were observed until the end of stay or for 45 days (administrative censoring). An intermediate state 'HAB' was achieved if the patient developed HAB during admission. If discharge and HAB occurred on the same day, time of discharge was pushed forward 1 day as venepuncture logically occurred before discharge. Using the Cox regression, transition-specific hazard ratios were calculated for 'all-cause end of stay' and 'discharge alive' while censoring patients discharged because of death. HAB was treated as a time-dependent variable.

Covariates for adjustment were chosen on the basis of the disjunctive cause criterion [24] and included the following baseline covariates: sex, age group (20-year intervals), number of previous admissions in the past year (continuous), admission type ('surgical' or 'non-surgical'), urgency of admission ('acute' or 'elective'), and predisposing conditions (dichotomous).

Excess length of stay was estimated through a non-parametric approach that included several steps. First, a matrix of transition probabilities was calculated based on the Aalen-Johansen estimator for all admission days [25]. Second, using these matrices of daily probabilities, we calculated the excess length of stay as the daily difference in residual length of stay in patients with HAB compared with the patients currently at risk of bacteraemia [26]. Third, a weighted average of the excess length of stay was computed using weights based on the probability of acquiring HAB each day. Moreover, CIs were derived by bootstrap resampling with 200 iterations.

To explore the contribution of possible confounders, a pseudo-value regression model was applied [27], with estimates for t covariates reflecting their effect on excess length of stay given the baseline excess length of stay.

The relative rate of readmission in patients discharged alive after admission with HAB compared with patients without HAB was estimated using the Cox regression. In this analysis, the date of discharge was considered day 0, and patients were considered at risk of readmission from day 2 to until readmission, death, or day

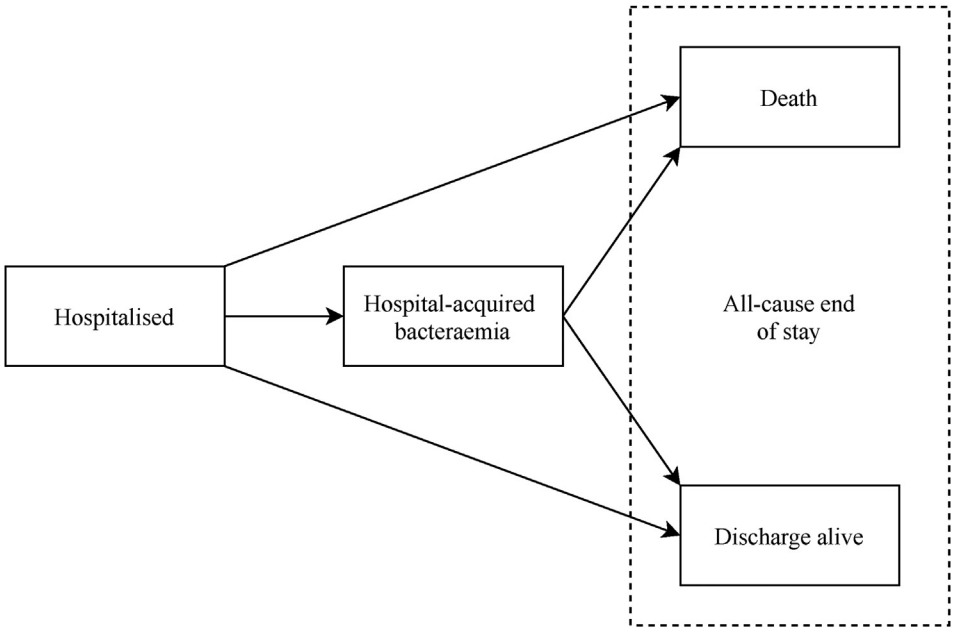

Fig. 1. Illness-discharge model without recovery to investigate the excess length of hospital stay attributable to hospital-acquired bacteraemia. 'Death' and 'Discharge alive' were aggregated to a single state: all-cause end of stay.

Table 1
Baseline characteristics of the hospital population and patients with hospital-acquired bacteraemia

	Overall hospital population		Patients with hospital-acquired bacteraemia	
	Count	%	Count	%
Number of patients	205 962		3239	
Number of admissions/episodes	484 291		3457	
Female[a]	267 498	55.3	1290	37.3
Age (y), median (interquartile range)	66 (49–77)		70 (60–78)	
Type of hospital department				
Non-surgical	285 913	59.0	2223	64.3
Surgical	198 378	41.0	1234	35.7
Urgency of admission				
Acute	360 112	74.4	2755	79.7
Elective	124 179	25.6	702	20.3
Number of admissions the previous year				
0	312 516	64.5	1627	47.1
1	94 251	19.5	785	22.7
≥2	77 524	16.0	1045	30.2
Charlson Comorbidity Index				
Low (0)	265 564	54.8	1170	33.8
Medium (1–2)	142 214	29.4	1291	37.3
High (≥3)	76 513	15.8	996	28.8
Diabetes mellitus without complications	30 304	6.3	303	8.9
Diabetes mellitus with complications	26 871	5.5	328	9.5
Rheumatic disease	16 954	3.5	129	3.7
Leukaemia	4818	1.0	164	4.7
Lymphoma	9231	1.9	198	5.7
Localized cancer	68 252	14.1	744	21.5
Metastatic cancer	21 031	4.3	283	8.2
Chronic pulmonary disease	69 566	14.4	508	14.7
Renal disease	21 087	4.4	334	9.7
Cerebrovascular disease	55 054	11.4	389	11.3
Dementia	9258	1.9	45	1.3
Mild liver disease	7229	1.5	100	2.9
Severe liver disease	4480	0.9	82	2.4
Human immunodeficiency virus infection and AIDS	573	0.1	8	0.2
Congestive heart failure	41 717	8.6	429	12.4
Peripheral vascular disease	32 810	6.8	399	11.5
Ischaemic heart disease	24 120	5.0	167	4.8
Inflammatory bowel disease	9428	1.9	68	2.0
Days from admission to venipuncture, median (interquartile range)	—	—	9 (4–16)	—

Statistics are reported by admission; patients could be included multiple times if multiple admissions occurred.
[a] Sex for 261 patients was not recorded (none had an episode of hospital-acquired bacteraemia).

30 (administrative censoring), whichever occurred first, considering death before readmission as a competing event.

Missing values are reported in the corresponding tables. Individuals with missing information on any cofounders were excluded from adjusted analyses, as they were few and assumed missing at random and, therefore, not expected to affect the estimates.

For data management and analyses, we used the R statistical software version 4.1.0 [28] using the etm package version 1.1.1, the geepack package version 1.3.2, and the survival package version 3.2.11.

Results

Characteristics

From 2006 to 2018, 205 962 unique patients were admitted at least once with a hospital stay of ≥48 hours, yielding 484 291 admissions in total (Table 1). During these admissions, 3457 episodes of HAB occurred in 3239 patients. Patients with HAB were slightly older than the overall hospitalized population (median age, 70 vs. 66 years), were less likely to be women (37.3% vs. 55.3%), and had higher level of comorbidity (CCI score ≥3; 28.8% vs. 15.8%). Aetiology according to the source of HAB is reported in Table S2.

Probability of end of stay

HAB was associated with lower adjusted hazard for all-cause end of stay (adjusted hazard ratio [aHR], 0.60; 95% CI, 0.57–0.62), with aHRs ranging from 0.30 (95% CI, 0.23–0.40) for heart and vascular sources to 0.72 (95% CI, 0.69–0.82) for urinary tract sources. Fungi were associated with the lowest aHR for all-cause end of stay (Table S3). Hazard ratios for all-cause end of stay were driven by significantly lower probability of discharge alive among patients with HAB than in patients without bacteraemia: the overall aHR for discharge alive was 0.46 (95% CI, 0.44–0.48) and ranged from 0.21 (95% CI, 0.15–0.30) for heart and vascular to 0.72 (95% CI, 0.66–0.79) for urinary tract sources (Table 2).

Excess length of stay

Fig. 2(a) illustrates the relationship between excess length of stay in days and time of acquisition (days since admission). Infections early during hospitalization contributed most to the excess length of stay, whereas the effect of HAB diminished throughout hospitalisation. Based on the relative incidence of HAB, Fig. 2(b) depicts the weights used to calculate the average excess length of stay presented in Table 2. Most episodes occurred around day 4 of hospitalization. Overall, patients with HAB experienced an excess length of stay of 6.6 days (95% CI, 6.2–7.1 days), with substantial variation by source of bacteraemia, from 3.8 days (95% CI, 3.3–4.2 days) for bacteraemia originating in the urinary tract to 18.3 days (95% CI, 17.9–18.7 days) for heart and vascular sources. The mean excess length of stay following HAB was slightly lower in the most recent years (5.9 days in 2013–2018 vs. 7.5 days in 2006–2012) (Table S4).

Based on pseudo-value regression, the baseline patient (male, aged 41–60 years, without prior admission and comorbidity with a non-acute admission to a surgical ward) could expect an excess length of stay of 10.3 days (95% CI, 8.6–12.0 days) (Table S5). The excess length of stay was shorter for older patients, especially those aged 81–100 years (6.08 days shorter than at reference age). The excess length of stay following HAB declined with increasing number of previous admissions (−0.64 days per previous admission; 95% CI, −1.25 to −0.03 days), and the impact was lower in non-surgical patients (−2.1 days; 95% CI, −3.6 to −0.61 days). The effect of predisposing conditions ranged from −10.6 days (95% CI, −33.22 to 12.13 days) for human immunodeficiency virus

Table 2
Relative rates of all-cause end of hospital stay, discharge alive, and extended length of stay attributed to hospital-acquired bacteraemia

		All-cause end of stay HR (95% CI)		Discharged alive HR (95% CI)		In-hospital mortality HR (95% CI)		Excess length of stay Days (95% CI)
	Count	Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]	Unadjusted	Adjusted[b]	Non-parametric approach[c]
Overall hospital-acquired bacteraemia	3457	0.59 (0.57–0.62)	0.60 (0.57–0.62)	0.46 (0.44–0.48)	0.46 (0.44–0.48)	2.56 (2.37–2.76)	2.35 (2.19–2.53)	6.6 (6.2–7.1)
Source of infection								
Thoracic, including pneumonia	124	0.50 (0.40–0.61)	0.48 (0.39–0.59)	0.30 (0.23–0.40)	0.30 (0.23–0.39)	3.12 (2.29–4.26)	3.07 (2.25–4.20)	9.9 (9.5–10.3)
Heart and vascular	78	0.27 (0.20–0.36)	0.30 (0.23–0.40)	0.19 (0.13–0.27)	0.21 (0.15–0.30)	1.43 (0.89–2.29)	1.17 (0.73–1.88)	18.3 (17.9–18.7)
Abdomen	314	0.46 (0.40–0.52)	0.42 (0.37–0.48)	0.34 (0.30–0.40)	0.31 (0.27–0.37)	2.08 (1.65–2.63)	2.11 (1.67–2.66)	10.4 (9.9–10.9)
Liver and biliary system	365	0.61 (0.54–0.68)	0.58 (0.52–0.65)	0.54 (0.48–0.62)	0.52 (0.46–0.59)	1.54 (1.16–2.03)	1.39 (1.05–1.83)	6.1 (5.7–6.6)
Urinary tract	574	0.71 (0.65–0.78)	0.75 (0.69–0.82)	0.68 (0.62–0.74)	0.72 (0.66–0.79)	1.32 (1.01–1.71)	1.02 (0.78–1.32)	3.8 (3.3–4.2)
Skin, soft-tissue, and bone	121	0.51 (0.42–0.62)	0.51 (0.42–0.62)	0.46 (0.37–0.57)	0.46 (0.37–0.57)	1.32 (0.80–2.19)	1.33 (0.80–2.21)	7.0 (6.6–7.4)
Intravenous catheter	259	0.57 (0.50–0.66)	0.55 (0.48–0.64)	0.54 (0.46–0.63)	0.52 (0.45–0.61)	1.03 (0.69–1.56)	1.24 (0.82–1.86)	8.0 (7.6–8.4)
Miscellaneous[a]	43	0.54 (0.39–0.76)	0.43 (0.31–0.60)	0.56 (0.40–0.79)	0.43 (0.30–0.60)	0.26 (0.04–1.85)	0.76 (0.10–5.40)	6.2 (5.8–6.6)
Unknown	1579	0.63 (0.60–0.66)	0.65 (0.62–0.69)	0.41 (0.38–0.44)	0.42 (0.40–0.46)	3.79 (3.47–4.15)	3.42 (3.12–2.74)	6.2 (5.8–6.6)

HR, hazard ratio.

[a] Miscellaneous includes patients with bacteraemia with the following foci: oral (4 patients), central nervous system (10 patients), female genitalia (25 patients), and transfusion or i.v.-misuse related (4 patients).

[b] Adjustments were made for the following covariates: sex, age groups (20-year intervals), number of previous admissions in the past year (continuous), type of admission (surgical or non-surgical), urgency of admission (acute or elective), and the following predisposing conditions (dichotomous): diabetes mellitus with and without complications, rheumatic disease, leukaemia, lymphoma, localized cancer, metastatic cancer, chronic pulmonary disease, renal disease, cerebrovascular disease, dementia, mild and severe liver disease, human immunodeficiency virus infection and AIDS, congestive heart failure, peripheral vascular disease, ischaemic heart disease, and inflammatory bowel disease. Observations with missing values for sex (261 patients) were excluded from the adjusted analysis.

[c] CIs achieved by the means of bootstrapping.

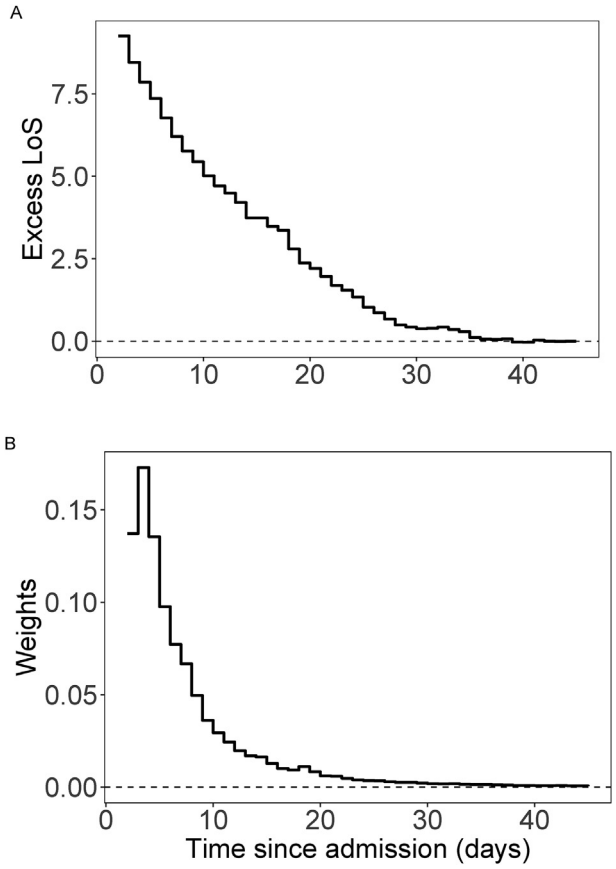

Fig. 2. Results of a multi-state model to estimate the excess LoS after the patient contracted a hospital-acquired bacteraemia compared with hospitalized patients at risk of hospital-acquired bacteraemia. (a) The relationship between excess LoS and time of hospital-acquired bacteraemia acquisition (computed daily by subtracting the residual LoS for a patient who had not experienced hospital-acquired bacteraemia from those who had). (b) The weights used to calculate the average excess LoS (i.e. the relative frequency of hospital-acquired bacteraemia each day). LoS, length of stay.

infection and AIDS to 20.6 days (95% CI, 9.9–21.3 days) for leukaemia (Table S5).

Readmission rates

Despite the increased post-discharge mortality (i.e. death before readmission) among patients with HAB (aHR, 2.76; 95% CI, 2.38–3.21), HAB was associated with increased readmission rates (aHR, 1.42; 95% CI, 1.31–1.53) (Table 3). Depending on the source of infection, readmission rates in patients with HAB ranged from 7.3 (heart and vascular) to 16.3 (i.v. catheters) readmissions per 1000 person-days. In comparison, the readmission rate per 1000 person-days was 7.1 in patients without HAB. The relative rates of readmission varied from an aHR of 0.78 (95% CI, 0.35–1.74) in HAB originating from the heart and vascular sources to 1.80 (95% CI, 0.86–3.77) for bacteraemia from 'miscellaneous' sources.

Discussion

Using a modern multi-state approach, this population-based cohort study of hospitalized adults revealed decreased probability of all-cause end of stay and discharge alive after HAB, leading to an excess length of stay of 6.6 days. The hazard ratio for all-cause end of stay and estimates of excess length of stay varied by the source of infection, with a particularly high excess length of stay for bacteraemia originating from heart and vascular sources (18.3 days). The excess length of stay was lower in the older and non-surgical patients, likely reflecting the higher mortality in these groups. Patients with leukaemia had the highest excess length of stay, likely attributed to immunosuppression, causing lengthy recovery. Among patients discharged alive, rates of readmission were significantly higher in patients who previously had HAB.

Interestingly, HAB occurring shortly after admission was associated with the longest excess length of stay. This likely reflects differing severity of the underlying illness among comparisons, as patients with late onset, HAB are compared with patients still admitted, who are likely to be in a severe condition.

Previous studies have an estimated increased length of stays attributed to HAB ranging from 6.7 to 30 days [3–15]. However, ten of these studies used the difference in the total length of stay as a measure of excess length of stay, disregarding the time-dependency of hospital-acquired infections [4–8,10–14], and only few considered confounding properly. More comparable to our results, two studies applied a form of risk-set sampling and found an excess length of stay of 8.4 [9] and 16.9 days [15], respectively. However, these two studies were limited to patients with major traumatic injuries in a single hospital in Canada [9] and patients from a single hospital in China [15]. Using inverse probability-weighted survival curves, another study of intensive care unit (ICU)–acquired bacteraemia estimated that 3.7 ICU-days per bacteraemia were attributable to HAB [29]. However, the interpretation of this method is slightly different from that of our study, as it estimates how many days shorter the hospitalization would have been in a hypothetical population had these patients not developed HAB [16].

It is important to note the severe burden carried by HAB. As shown in our study, HAB was associated with lower probability of being discharged alive, prolonged length of stay, and high rates of readmission. HAB had the largest effect on the probability of being discharged alive compared with the effect on all-cause end of stay, which combined with the high in-hospital mortality associated with HAB [1], suggests that a decrease in mortality may lead to more hospital bed-days and argues strongly for preventive initiatives to reduce cost. The slight reduction in excess length of stay in recent years may reflect increasing the use of outpatient i.v. therapy.

As this study is observational in nature, its main limitation lies in various factors that influence the length of hospital stay. Procedures during hospitalization will inevitably affect the length of stay while also being the possible risk factors for HAB [30]. We lacked data on the severity of illness and hospital procedures (e.g. intravascular access, haemodialysis, and mechanical ventilation), and it was not possible to model these dynamics. This might have led to unmeasured confounding.

Universal healthcare coverage with easy access to the healthcare system and population-wide registers strengthens the generalizability of our findings to societies with similar healthcare systems. However, the length of stay and readmission are influenced by both administrative and cultural factors, including the incidence of HAB, distribution of sources and aetiologies, and the level of advanced care and threshold for ICU admission, which may affect the generalizability.

In conclusion, our findings show that after contracting HAB, patients have a lower daily probability of being discharged alive, leading to a considerable prolongation of their hospital stay, compared with patients at risk of bacteraemia. The excess stay was lower in older and non-surgical patients and varied with various predisposing conditions. Excess length of stay, combined with the increased readmission rates, poses a serious challenge for our healthcare system because prolonged hospitalization

Table 3
Rates of readmission and the competing outcome of death before readmission among patients discharged alive with versus without an episode of HAB

	Readmission					Death before readmission			
	Number of episodes	Count (%)	Readmissions per 1000 person-days	Hazard ratio (95% CI)	Adjusted hazard ratio[b] (95% CI)	Count (%)	Deaths per 1000 person-days	Hazard ratio (95% CI)	Adjusted hazard ratio[b] (95% CI)
Non-HAB	459 027	86 471 (19)	7.07	Reference		10 392 (2)	0.9	Reference	
Overall HAB	2021	664 (33)	14.1	1.99 (1.84–2.15)	1.42 (1.31–1.53)	175 (9)	3.7	4.22 (3.63–4.90)	2.76 (2.38–3.21)
Thoracic, including pneumonia	53	11 (21)	8.0	1.14 (0.63–2.06)	0.93 (0.52–1.68)	<5 (<9)	2.9	3.40 (1.28–9.07)	3.09 (1.16–8.23)
Heart and vascular	31	6 (19)	7.3	1.04 (0.47–2.31)	0.78 (0.35–1.74)	0 (0)	0	Na	Na
Abdomen	165	59 (36)	16.1	2.27 (1.76–2.94)	1.71 (1.33–2.21)	17 (10)	4.6	5.22 (3.24–8.40)	3.68 (2.29–5.93)
Liver and biliary system	265	88 (33)	14.6	2.06 (1.67–2.94)	1.45 (1.18–1.79)	34 (13)	5.7	6.37 (4.55–8.92)	3.70 (2.64–5.19)
Urinary pathway	452	120 (27)	10.8	1.52 (1.27–1.82)	1.19 (1.00–1.42)	31 (7)	2.8	3.21 (2.25–4.56)	1.83 (1.28–2.60)
Skin, soft-tissue, and bone	82	28 (34)	14.5	2.05 (1.41–2.97)	1.72 (1.19–2.50)	5 (6)	2.6	2.94 (1.22–7.06)	2.27 (0.94–5.46)
Intravenous catheter	163	63 (39)	16.3	2.31 (1.80–2.95)	1.43 (1.12–1.83)	5 (3)	1.3	1.47 (0.61–3.53)	1.43 (0.59–3.43)
Miscellaneous[a]	33	7 (21)	7.9	1.12 (0.53–2.34)	1.80 (0.86–3.77)	0 (0)	0	Na	Na
Unknown	777	282 (36.3)	16.2	2.29 (2.03–2.57)	1.50 (1.33–1.68)	79 (10)	4.5	5.10 (4.09–6.37)	3.23 (2.58–4.03)

HAB, hospital-acquired bacteraemia; Na, Not applicable.
[a] Miscellaneous includes bacteraemia patients with the following foci; oral (4 patients), central nervous system (10 patients), female genitalia (25 patients), and transfusion or i.v. misuse related (4 patients).
[b] Adjustments were made for the following covariates: sex, age groups (20-year intervals), number of previous admissions in the past year (continuous), type of admission (surgical or non-surgical), urgency of admission (acute or elective), and the following predisposing conditions (dichotomous): diabetes mellitus with and without complications, rheumatic disease, leukaemia, lymphoma, localized cancer, metastatic cancer, chronic pulmonary disease, renal disease, cerebrovascular disease, dementia, mild and severe liver disease, human immunodeficiency virus infection and AIDS, congestive heart failure, peripheral vascular disease, ischaemic heart disease, and inflammatory bowel disease. Observations with missing values for sex (261 patients) were excluded from the adjusted analysis.

increases the risk of additional complications and is associated with substantial costs.

Author contributions

Writing: original draft: V.H.M.; review and editing: V.H.M., L.H.M., H.C.S, P.S., M.W., B.K., and M.S. Conceptualisation: V.H.M., H.C.S., M.W., B.K., and M.S. Resources: H.C.S.; data curation: V.H.M. and H.C.S. Methodology: V.H.M., M.S., P.S., and M.W. Formal analysis: V.H.M.

Transparency declaration

M.S. reports personal fees from Bayer, outside the submitted work. The other authors declare that they have no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2022.09.004.

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