Global Healthcare-Associated Bloodstream Infection among Inpatients: A Systematic Review and Meta-Analysis

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Abstract

Background: Healthcare-associated or nosocomial infections are among the most common infections and potential threats to patients and remain a significant problem for healthcare workers. Similarly, healthcare-associated bloodstream infections are the most common healthcare-associated infection. Therefore, this review aimed to determine the global and regional prevalence of healthcare-associated bloodstream infection among inpatients.

Methods: This systematic review and meta-analysis followed the PRISMA guidelines. Studies were retrieved from databases and other search engines such as PubMed, Scopus, Web of Science, Google Scholar, and MedNar using Boolean operators, MeSH terms, and relevant keywords. Data was extracted using an Excel form created by the authors. Data analysis was performed using comprehensive meta-analysis software version 4 with random effects. The quality of articles was assessed using the Joanna Briggs Institute Critical Appraisal Tool. Heterogeneity was evaluated using the I^2 statistic. Publication bias was evaluated using funnel plots. Sensitivity analysis was conducted to examine the impact of extreme values on overall estimates.

Results: A total of 1681 studies were searched from the included electronic databases and other search engines. Finally, 36 articles conducted on 937,412 inpatients were included in the current study. The findings from the current review revealed that the global prevalence of blood-stream infection was 1.2% (95% CI: 0.8%, 1.70 %). Based on the World Health Organization's region and survey period, the highest prevalence of healthcare-associated blood-stream infection reported between 2019 and 2023 was 4.2% (95% CI: 1.2%, 13.4%) and in the African region (3.5%: 95% CI: 1.1%, 10.6%).

Conclusions: This review found that at least one in 100 patients is infected with a healthcare-associated bloodstream infection. The prevalence varies in different regions of the world, with the highest prevalence reported in the African region. The findings from the current review indicate the need to implement effective infection prevention and control to prevent healthcare-associated bloodstream infections.

***Keywords*: ** Bloodstream Infections; Hospital Acquired Infections; Patient safety; Inpatients

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Introduction

Healthcare-associated or Hospital acquired infections (HAIs) pose potential threats to patients across the world and remain a significant challenge for healthcare workers (WHO, 2016). HAIs is the major cause of morbidity and mortality related with diagnostic, clinical, and therapeutic procedures (CDC, 2020; OASH, 2020). They affect hundreds of millions of patients each year, causing high mortality rate and significant financial and service losses. Currently, there is no region free from HAIs problems (WHO, 2016).Globally, about three million health professionals are affected by HAI annually (WHO, 2004, Endalew *et al*, 2022).Blood stream infection among HAIs remain a growing public health concern across the world (Goto and Al-Hasan, 2013). Blood stream infection (BSIs) accounted for about 15.0% of nosocomial infections and it affects about 1.0% of all inpatients (Exline *et al*, 2013; Bharadwaj *et al*, 2014). Increasing in HA-BSIs mortality is mainly associated with delayed or inappropriate treatment (Loonen et al., 2014; Opota et al., 2015). They are a major cause of mortality, with a significant increase in incidence and severity (Peker *et al*., 2018). Each year an estimate of

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1,200,000 episodes of BSIs in Europe represents a rising public health problem (Goto and Al-Hasan, 2013).

Furthermore, an increase in BSIs is associated with multiple co-occurring conditions, other infection, neutropenia, prolonged use of various immunosuppressive drugs, and extended duration of indwelling intravenous catheters (Yamin *et al*, 2021) as well as inappropriate antimicrobial treatment (Islas-Muñoz *et al*., 2018).

Healthcare associated BSIs mainly caused by different pathogenic microorganisms, including *Escherichia coli, Staphylococcus species, Klebsiella species,* coagulase-negative staphylococci, *Pseudomonas aeruginosa, and Salmonella enterica* (Kern and Rieg, 2020). These pathogens are associated with antimicrobial resistance, and reducing utilization expensive third-line agents, such as daptomycin, ceftaroline, tigecycline, and ceftazidime-avibactam (Pfaller *et al*., 2020). They mainly related to severe diseases associated with a significant morbidity and mortality across the world (Opota *et al*., 2015; Rutanga and Nyirahabimana, 2016; Loonen *et al*., 2014) and significantly increased length of hospital stay (Goto and Al-Hasan, 2013; Vrijens *et al.,* 2010; Umscheid *et al.,* 2011) as well as compromise patient prognosis (Rosenthal, 2009; Olaechea *et al*., 2013).

Even though HA-BSIs is a global public health problem, the problems are high in developing countries, including sub-Saharan Africa, and likely increase mortality (Lester *et al.,* 2020). Currently, there is limited data or evidence across the world particularly, on the prevalence of healthcare associated BSI. However, beside this gap, there was no other systematic review and meta-analysis that provided regional and global pooled prevalence of healthcare associated BSIs among patients. The previous reviews were done on community onset BSIs (Marchello *et al.,* 2019), in some African countries (Reddy *et al*., 2010), and BSI among adults related to peripherally inserted catheters (Chopra *et al*., 2013). Another study was conducted on the attributable mortality of central line BSIs (Ziegler *et al.,* 2015).

The current review aimed to provide the global and regional pooled prevalence of HA-BSIs among inpatients. The findings from this review can help national and international agencies as an evidence for effective prevention and control of healthcare-associated BSIs.

Materials and Methods

The review was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher *et al.,* 2015).

Eligibility Criteria

For the current study, research published without restrictions on the publication year, in English with full-text access, and presenting clear objectives and methodologies were included. Eligible studies consisted of cross-sectional studies reporting the frequency, prevalence, or magnitude of healthcare-associated bloodstream infections (BSIs), utilizing both primary and secondary data. Studies published in languages other than English, those that did not present clear objectives or methodologies, and those limited to abstracts or lacking relevant data on the outcome of BSIs were excluded. Additionally, studies from healthcare facilities of any type or level, regardless of geographic location, were considered.

Information Sources

The studies were retrieved from PubMed, Web of Science, SCOPUS, Google Scholar, and MedNar, from October 01, 2023 to November 26, 2023. A combination of Boolean operators (AND, and OR), Medical Subject Headings (MeSH), and keywords (e.g., healthcare facility, nosocomial infection, BSIs, patients, hospital-acquired infection, healthcare-associated infection) was employed to search the selected databases. The primary keywords and index terms were verified across these databases, and references from eligible articles were also reviewed to identify additional relevant studies.

Searching Databases and Strategies

The initial search for articles in PubMed was conducted using the following terms: "Prevalence" [Mesh Terms] OR "Prevalence" [All Fields], "Incidence" [Mesh Terms] OR "Incidence" [All Fields], "Proportion" [Mesh Terms] OR "Proportion" [All Fields], combined with ("Nosocomial" [Mesh Terms] OR "Nosocomial" [All Fields], "Hospital Acquired" [All Fields] OR "Hospital Acquired" [Mesh]) AND ("Bloodstream Infection" [All Fields] OR "Bloodstream Infection" [Mesh]). Additional terms included

("Infection" [Mesh Terms] OR "Hazards" [Mesh]) AND ("Patient" [All Fields], "Patients" [All Fields], OR "Service Users" [All Fields]). The same terms were employed to retrieve the articles from other databases with a modification in search strategies.

Study Selection

The study selection process was carried out using the PRISMA flow chart, which outlined the number of articles included and excluded, along with the reasons for exclusion. After searching relevant electronic databases, duplicate articles were removed using ENDNOTE software (version X5, Thomson Reuters, USA). Once duplicates were removed, the authors (DAM, EMA, MD, AT, DD, FA, AM, and TG) independently screened the articles based on titles and abstracts to assess their eligibility according to the inclusion criteria. Subsequently, the full texts of the relevant articles were independently reviewed by the authors (DAM, MD, AT, DD, FA, AM, and TG). Any disagreements regarding study inclusion were resolved through consensus following discussion. Finally, studies that met the inclusion criteria were included in the review.

Data Extraction

All authors (DAM, EMA, MD, AT, DD, FA, AM, and TG) independently extracted the necessary data for the study from the selected articles. A pre-determined Microsoft Excel template (Excel 2016) was used to record data, such as the publication year, study period, country of study, sample size, WHO region, and primary outcomes, including the prevalence of healthcare associated BSI among inpatients. Disagreements between the authors regarding the data extraction were resolved through discussion.

Selection and Quality Assessment

The authors (DAM, MD, DD, AT, FA, AM, and TG) conducted a quality appraisal of all included articles using the Joanna Briggs Institute (JBI) Critical Assessment Tools for prevalence studies (JBI, 2019). Based on the appraisal results, each article was evaluated for its relevance or eligibility by the authors (DAM, EMA, MD, AT, DD, FA, AM, and TG).

The JBI critical appraisal tools has nine criteria: appropriate sampling frame, proper sampling technique, adequate sample size, study subject and setting description, sufficient data analysis, valid methods for identified conditions, valid measurements for all participants, appropriate statistical analysis, and adequate response rate. Each criterion was scored as 1 for "Yes" and 0 for "No." Articles were categorized based on their total score: those scoring 85% or above were classified as low risk of bias, those between 60% and 85% as moderate risk, and those below 60% as high risk of bias. Only articles with low and moderate risk of bias were included in the review. Any disagreements among the authors regarding the quality assessment were resolved through discussion after repeating the evaluation process.

Outcome Measures

In this review HA-BSIs was measured based on definitions from the National Healthcare Safety Network (NHSN) and Centers for Disease Control and Prevention (CDC) (Garner *et al*., 1988, CDC, 2024). Based on the above and other references, the outcome used in the current review is determined by identifying the number of central line-associated BSIs (CLABSIs) in each unit (the numerator) and dividing this by the number of catheter day in the unit (denominator), both based on NHSN definitions (Garner *et al.,* 1988, Buetti *et al.,* 2022, Ranji *et al*., 2010).

Data Processing and Analysis

The data were analysis using Comprehensive Meta-Analysis version 4.0 statistical software. A forest plot and random-effects model were employed to visualize the pooled prevalence of HA-BSIs, including the 95% confidence interval. The heterogeneity between the included studies was assessed using the I^2 statistic, which measures the proportion of total variability due to true differences in effect sizes. Heterogeneity was categorized as none (0%), low (25–50%), moderate (50–75%), or high (>75%) based on Ades *et al.,* 2005). Additionally, subgroup analysis was performed based on survey period, WHO region, and study locations.

Publication bias was assessed using funnel plots and met regression analysis. Sensitivity analysis was done to determine the differences in pooled prevalence HA-BSIs by dropping findings that expected to influence the overall estimates.

Ethical Consideration
Not applicable

Result

Description of Studies

A total of 1,681 articles were initially retrieved from the selected electronic databases and manual searches Google. After removing 800 duplicated articles, 259 articles were excluded based on their titles and abstracts. An additional 622 full-text studies were assessed for eligibility, resulting in the exclusion of 220 articles. Furthermore, 402 articles were further evaluated based on the objectives, methods, and outcomes. Finally, 36 articles were included in the systematic review and meta-analysis (Figure 1).

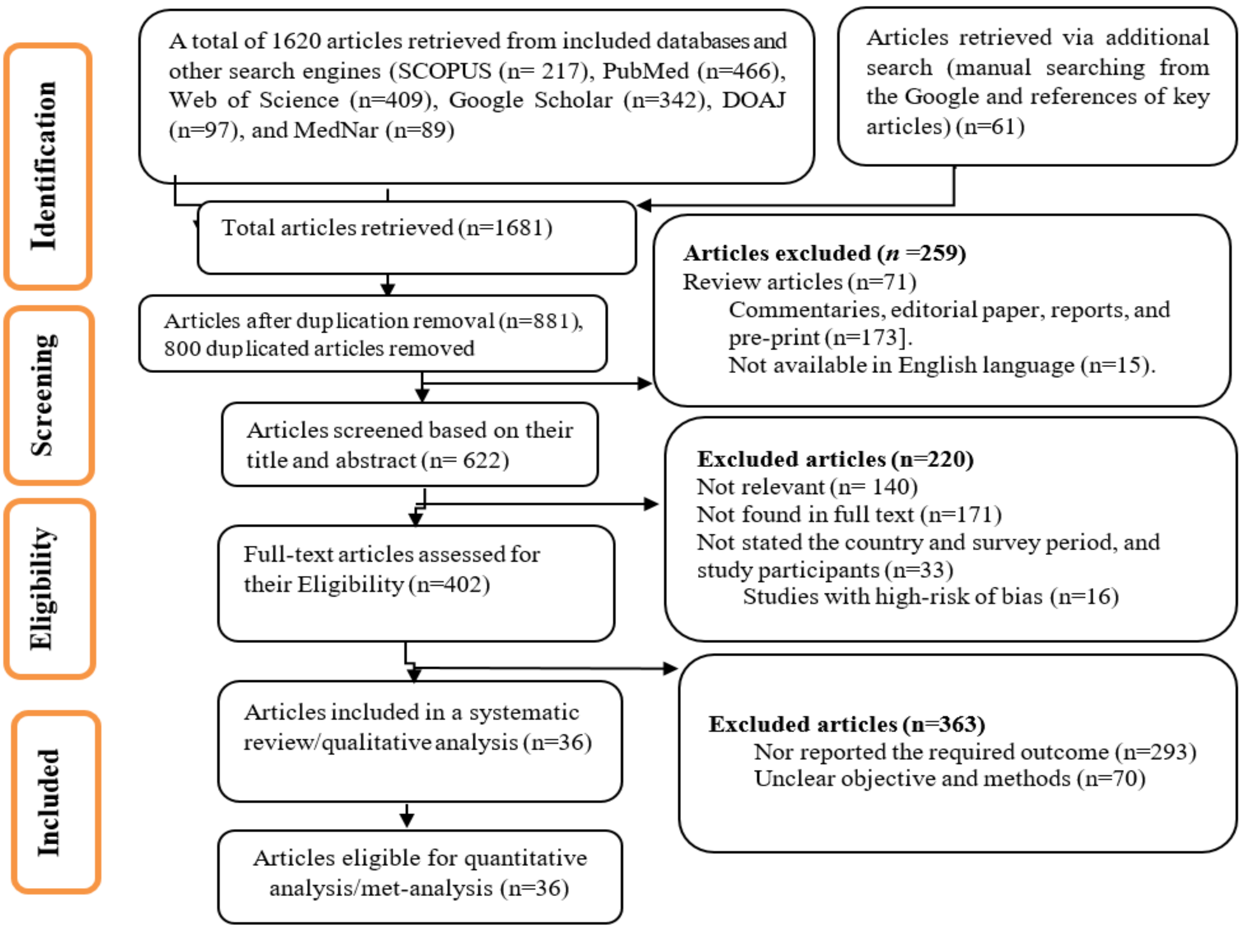

Figure 1: Studies selection process of included studies in the systematic review and meta-analysis., 2023.

Study Characteristics

This systematic review and meta-analysis analyzed 36 studies involving a total of 937,412 inpatients, with study participant numbers ranging from 105 (Bunduki*t al*., 2021) to 633,990 (Zhang *et al*., 2019). Among the studies, 9 were conducted in China (Huang *et al*, 2020; Lee *et al*., 2007; Zhao *et al*., 2020; Zhong *et al.,* 2021; Zhang *et al.,* 2016; Zhang *et al*., 2019; Wang *et al*., 2019; Jiang *et al*., 2020; Zhu *et al.,* 2019), 3 in the USA (Nash et al., 2006; Magill et al., 2012; Toor *et al*., 2022), and 2 each in Switzerland (Pittet et al., 1999; Miihlemann *et al*., 2011) and Iran (Askarian et al., 2012; Heydarpour et al., 2017). One study each was selected from Benin (Ahoyo *et al*., 2014), Italy (Gentili *et al*., 2020), Cuba (Izquierdo-Cubas et al., 2008), Thailand (Danchaivijitr *et al.,* 2007), Albania (Faria *et al.,* 2007), Malawi (Bunduki *et al.,* 2021), Saudi Arabia (Balkhy *et al*., 2006), Ghana (Labi *et al*.,2019), Argentina (Durlach *et al.,* 2012), Nigeria (Abubakar, 2020), Ethiopia (Motbainor *et al*., 2020), South Africa (Strasheim *et al.,* 2015), Tunisia (Ghali *et al.,* 2021), Nepal (Shrestha *et al*., 2022), Kuwait (Alfouzan *et al*., 2021), Germany (Arefian *et al*., 2019), Australia (Russo *et al*., 2019), Herzegovina (Custovic *et al*., 2014), Bahrain (Al-Khawaja *et al*., 2021), and India (Sahu *et al.,* 2016). All studies were included in the systematic review and underwent qualitative analysis. The studies included cross sectional or prevalence studies (Table 1).

Table 1: Overall characteristics of included articles in the systematic review and meta-analysis, 2024

Author/s	Sample size	Survey Year	Publication Year	Prevalence of BSI	Country	WHO region	Risk of bias
Pittet *et al*., 1999	1,349	1996	1999	1.7	Switzerland	EuR	Moderate
Faria *et al*., 2007	968	2003	2007	0.3	Albania	EuR	Low
Miihlemann *et al*., 2011	520	2000	2004	2.5	Switzerland	EuR	Moderate
Bunduki *et al*., 2021	105	2020	2021	2.86	Malawi	AfR	Low
Labi *et al*., 2019	2107	2016	2019	1.71	Ghana	AfR	Low
Abubakar, 2020	321	2019	2020	0.059	Nigeria	AfR	Low
Ahoyo *et al*., 2014	3130	2012	2014	0.5	Benin	AfR	Moderate
Motbainor *et al*., 2020	238	2018	2020	5.64	Ethiopia	AfR	Low
Strasheim *et al*., 2015	332	2013	2015	17.16	South Africa	AfR	Low
Huang *et al*., 2020	6717	2014-2018	2020	0.25	China	WpR	Low
Gentili *et al*., 2020	6263	2013-2018	2020	1.04	Italy	EuR	Low
Custovic *et al*., 2014	834	2010	2014	0.72	Herzegovina	EuR	Moderate
Arefian *et al*., 2019	62,154	2011-2014	2019	0.77	Germany	EuR	Low
Zhao *et al*., 2015	134637	2015-2017	2015	0.02	China	WpR	Low
Lee *et al*., 2007	1021	2005	2007	0.9	China	WpR	Low
Zhong *et al*., 2021	686	2019	2021	19.24	China	WpR	Low
Zhu *et al*., 2019	5046	2013-2017	2019	0.031	China	WpR	Low
Russo *et al*., 2019	2767	2018	2019	1.1	Australia	WpR	Low
Zhang *et al*., 2016	4,029	2012-2014	2016	0.22	China	WpR	Low
Zhang *et al*., 2019	633990	2013-2017	2019	0.58	China	WpR	Low
Wang *et al*., 2019	1347	2013-2015	2019	1.56	China	WpR	Low
Jiang *et al*., 2020	13695	2013-2019	2020	0.36	China	WpR	Low
Nash *et al*., 2006	11879	2006	2011	2.6	USA	AmR	Low
Durlach *et al*., 2012	4249	2008	2012	1.5	Argentina	AmR	Low
Izquierdo-Cubas *et al*., 2008	4240	2004	2008	0.7	Cuba	AmR	Moderate
Toor *et al*., 2022	1125	2020	2022	1.15	USA	AmR	Low
Magill *et al*., 2012	851	2009	2012	0.94	USA	AmR	Moderate
Shrestha *et al*., 2022	300	2016	2022	2.67	Nepal	SeAR	Low
Sahu *et al*., 2016	6,864	2013-2014	2016	0.35	India	SeAR	Low
Danchaivijitr *et al*., 2007	9,865	2006	2007	0.6	Thailand	SeAR	Moderate
Al-Khawaja *et al*., 2021	1634	2015-2018	2021	2.1	Bahrain	EmR	Low
Balkhy *et al*., 2006	562	2003	2006	2.49	Saudi Arabia	EmR	Low
Askarian *et al*., 2012	3450	2008-2009	2012	2.5	Iran	EmR	Low
Ghali *et al*., 2021	2729	2012-2020	2021	1.06	Tunisia	EmR	Low
Alfouzan *et al*., 2021	1408	2018-2019	2021	2.77	Kuwait	EmR	Low
Heydarpour *et al*., 2017	6,000	2011-2014	2017	0.02	Iran	EmR	Moderate

BSIs: Bloodstream Infections; USA: United States of America; EuR: European Region; AfR: African Region; EmR: Eastern Mediterranean Region; AmR: American Region; SeAR: South-East Asia Region; WpR: Western Pacific Region; WHO: World Health Organization

Prevalence of Bloodstream Infections

The global pooled prevalence of HA-BSIs among in-patients is estimated to be 1.2% (95% CI: 0.8% to1.7%), with a p-value of < 0.001 and I^2 value of 85.0% (Figure 2).

Study name	Prevalence	Lower limit	Upper limit	Z-Value	p-Value
Pittet *et al*, 1999	0.017	0.011	0.025	-19.264	0.000
Ahoyo *et al*, 2014	0.005	0.003	0.008	-20.888	0.000
Izquierdo-Cubas *et al*, 2008	0.007	0.005	0.010	-26.899	0.000
Danchaivijitr *et al*, 2007	0.006	0.005	0.008	-39.196	0.000
Al-Khawaja *et al*, 2021	0.021	0.015	0.029	-22.268	0.000
Faria *et al*, 2007	0.003	0.001	0.009	-9.879	0.000
Nash *et al*, 2006	0.026	0.023	0.029	-62.844	0.000
Bunduki *et al*, 2021	0.029	0.009	0.085	-6.021	0.000
Huang *et al*,2020	0.003	0.002	0.004	-24.511	0.000
Balkhy *et al*, 2006	0.025	0.015	0.042	-13.548	0.000
Labi *et al*, 2019	0.017	0.012	0.024	-24.110	0.000
Askarian *et al*, 2012	0.025	0.020	0.031	-33.596	0.000
Abubakar, 2020	0.059	0.038	0.091	-11.691	0.000
Gentili *et al*, 2020	0.010	0.008	0.013	-36.574	0.000
Durlach *et al*, 2012	0.015	0.012	0.019	-33.156	0.000
Mühlemann *et al*, 2004	0.025	0.015	0.043	-13.043	0.000
Lee *et al*, 2007	0.009	0.005	0.017	-14.188	0.000
Motbainor *et al*, 2020	0.056	0.033	0.094	-10.026	0.000
Strasheim *et al*, 2015	0.172	0.135	0.216	-10.815	0.000
Zhao *et al*, 2015	0.000	0.000	0.000	-38.523	0.000
Zhong *et al*, 2021	0.192	0.165	0.224	-14.810	0.000
Toor *et al*, 2022	0.012	0.007	0.020	-15.928	0.000
Zhu *et al*, 2019	0.031	0.027	0.036	-42.380	0.000
Ghali *et al*, 2021	0.011	0.007	0.015	-24.268	0.000
Shrestha *et al*, 2022	0.027	0.013	0.052	-10.041	0.000
Alfouzan *et al*, 2021	0.028	0.020	0.038	-21.912	0.000
Magill *et al*, 2012	0.009	0.005	0.019	-13.111	0.000
Arefian *et al*, 2019	0.008	0.007	0.008	-105.884	0.000
Russo *et al*, 2019	0.011	0.008	0.016	-24.683	0.000
Zhang *et al*, 2016	0.002	0.001	0.004	-18.192	0.000
Zhang *et al*, 2019	0.006	0.006	0.006	-311.028	0.000
Custovic *et al*, 2014	0.007	0.003	0.016	-12.029	0.000
Wang *et al*, 2019	0.016	0.010	0.024	-18.851	0.000
Heydarpou *et al*, 2017	0.000	0.000	0.001	-9.329	0.000
Jiang *et al*, 2020	0.004	0.003	0.005	-39.412	0.000
Sahu *et al*, 2016	0.004	0.002	0.005	-27.652	0.000
Overall	**0.012**	**0.008**	**0.017**	**-23.318**	**0.000**

Heterogeneity I^2=85%, p-value <0.01

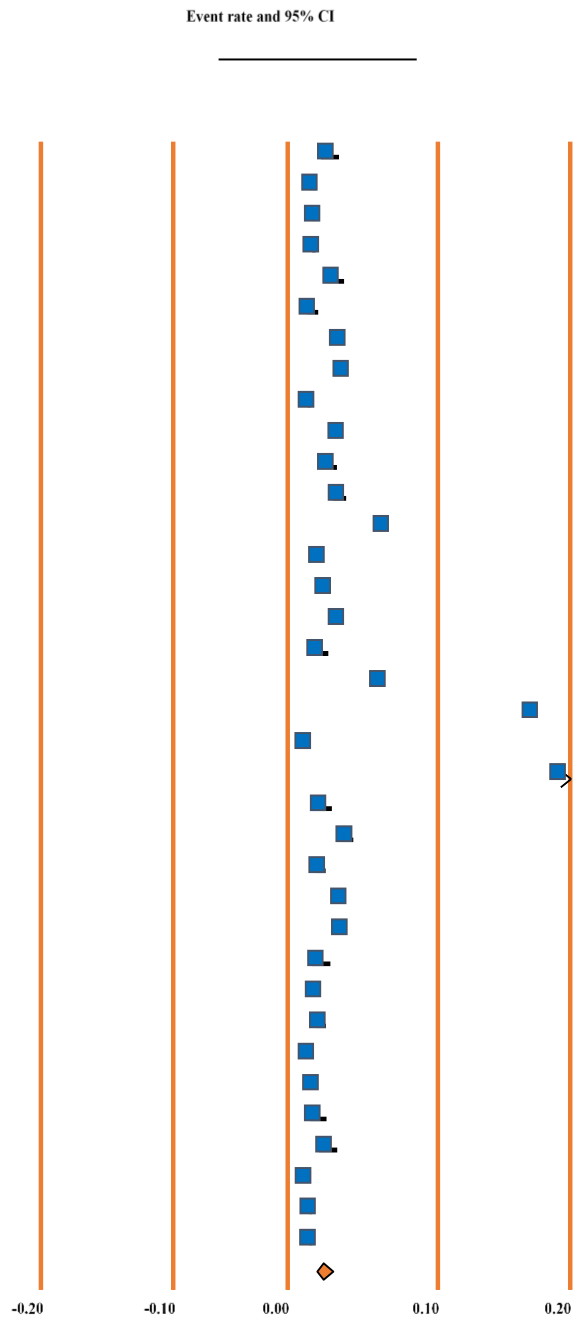

Figure 2: The forest plot shows an overall pooled prevalence of healthcare associated bloodstream infection among patients, 2023

According to the subgroup analysis based on the year of the survey, studies conducted between 2008 and 2013 showed the lowest prevalence of HA-BSIs among inpatients accounted for 0.8% (95% CI: 0.4, 1.8%). In contrast, studies conducted between 2019 and 2023 had the highest prevalence, accounting for 4.2% (95% CI: 1.2%, 13.4%). The findings suggest a decline in HA-BSIs prevalence from 2% in the period 1996-2001 to 0.9% from 2014 to 2018. However, there was an increase in prevalence from 0.9% (2014-2018) to 4.2% (2019-2023) (Figure 3).

Group by Survey period	Study name	Prevalence	Lower Limit	Upper Limit	Z-Value	P-Value
			Statistics for each study			
1996 -2001	Pittet *et al*, 1999	0.017	0.011	0.025	-19.264	0.000
1996 -2001	Mühlemann *et al*, 2004	0.025	0.015	0.043	-13.043	0.000
1996 -2001	**Pooled**	**0.020**	**0.014**	**0.029**	**-20.338**	**0.000**
2002-2007	Izquierdo-Cubas *et al*, 2008	0.007	0.005	0.010	-26.899	0.000
2002-2007	Danchaivijitr *et al*, 2007	0.006	0.005	0.008	-39.196	0.000
2002-2007	Faria *et al*, 2007	0.003	0.001	0.009	-9.879	0.000
2002-2007	Nash *et al*, 2006	0.026	0.023	0.029	-62.844	0.000
2002-2007	Balkhy *et al*, 2006	0.025	0.015	0.042	-13.548	0.000
2002-2007	Lee *et al*, 2007	0.009	0.005	0.017	-14.188	0.000
2002-2007	**Pooled**	**0.010**	**0.005**	**0.021**	**-11.825**	**0.000**
2008-2013	Ahoyo *et al*, 2013	0.005	0.003	0.008	-20.888	0.000
2008-2013	Askarian *et al*. 2012	0.025	0.020	0.031	-33.596	0.000
2008-2013	Durlach *et al*, 2012	0.015	0.012	0.019	-33.156	0.000
2008-2013	Strasheim *et al*, 2015	0.172	0.135	0.216	-10.815	0.000
2008-2013	Magill *et al*, 2012	0.009	0.005	0.019	-13.111	0.000
2008-2013	Arefian *et al*, 2019	0.008	0.007	0.008	-105.884	0.000
2008-2013	Zhang *et al*. 2016	0.002	0.001	0.004	-18.192	0.000
2008-2013	Custovic *et al*. 2014	0.007	0.003	0.016	-12.029	0.000
2008-2013	Heydarpou *et al*, 2017	0.000	0.000	0.001	-9.329	0.000
2008-2013	Sahu *et al*, 2016	0.004	0.002	0.005	-27.652	0.000
2008-2013	**Pooled**	**0.008**	**0.004**	**0.018**	**-11.968**	**0.000**
2014-2018	Al-Khawaja *et al*, 2021	0.021	0.015	0.029	-22.268	0.000
2014-2018	Huang *et al*, 2020	0.003	0.002	0.004	-24.511	0.000
2014-2018	Labi *et al*, 2016	0.017	0.012	0.024	-24.110	0.000
2014-2018	Gentili *et al*, 2020	0.010	0.008	0.013	-36.574	0.000
2014-2018	Motbainor *et al*, 2020	0.056	0.033	0.094	-10.026	0.000
2014-2018	Zhao *et al*, 2015	0.000	0.000	0.000	-38.523	0.000
2014-2018	Zhu *et al*, 2019	0.031	0.027	0.036	-42.380	0.000
2014-2018	Ghali *et al*, 2021	0.011	0.007	0.015	-24.268	0.000
2014-2018	Shrestha *et al*, 2022	0.027	0.013	0.052	-10.041	0.000
2014-2018	Russo *et al*, 2019	0.011	0.008	0.016	-24.683	0.000
2014-2018	Zhang *et al*, 2019	0.006	0.006	0.006	-311.028	0.000
2014-2018	Wang *et al*, 2019	0.016	0.010	0.024	-18.851	0.000
2014-2018	Jiang *et al*, 2020	0.004	0.003	0.005	-39.412	0.000
2014-2018	**Pooled**	**0.009**	**0.005**	**0.016**	**-16.156**	**0.000**
2019-2023	Bunduki *et al*, 2021	0.029	0.009	0.085	-6.021	0.000
2019-2023	Abubakar, 2020	0.059	0.038	0.091	-11.691	0.000
2019-2023	Zhong *et al*, 2021	0.192	0.165	0.224	-14.810	0.000
2019-2023	Toor *et al*, 2022	0.012	0.007	0.020	-15.928	0.000
2019-2023	Alfouzan *et al*, 2021	0.028	0.020	0.038	-21.912	0.000
2019-2023	**Pooled**	0.042	0.012	0.134	-4.871	0.000
Overall	**Pooled**	**0.014**	**0.011**	**0.019**	**-31.145**	**0.000**

Heterogeneity I^2=78.9 %, p-value <0.01

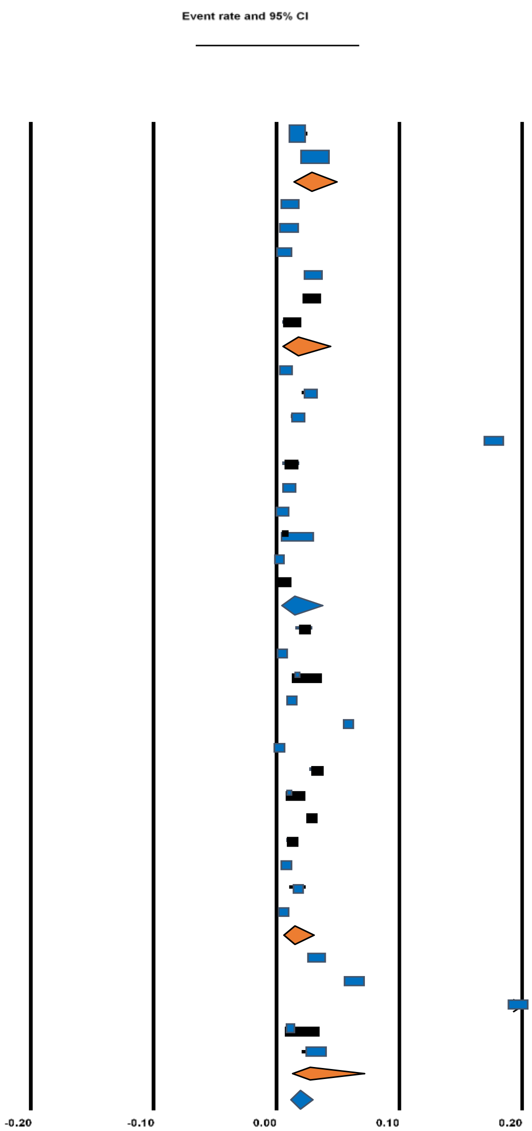

Figure 3: The forest plot shows the subgroup analysis of the pooled prevalence of healthcare associated bloodstream infections among inpatients based on the survey period, 2023.

The overall pooled prevalence of HA-BSIs was 1.2% (95% CI: 0.8% to 1.7%), which remained almost consistent even after subgroup analysis was done based on WHO's region which accounted for 1.4% (95% CI: 1.1% to 1.9%). The highest prevalence of HA-BSIs was observed in the African Region, with a rate of 3.5% [95% CI: 1.1, 10.6%]. In contrast, the lowest prevalence was found in the Western Pacific Region at 0.7% [95% CI: 0.2, 2.0%]. The South East Asian and European Regions had HA-BSIs prevalence of 1.0% [95% CI: 0.1, 6.7%] and 1.0% [95% CI: 0.7, 1.4%], respectively (Figure 4).

Grouped by WHO region	Authors name	Statistics for each study: Prevalence	Lower Limit	Upper limit	Z-Value	p-Value
African Region	Ahoyo *et al*, 2014	0.005	0.003	0.008	-20.888	0.000
African Region	Bunduki *et al*,2021	0.029	0.009	0.085	-6.021	0.000
African Region	Labi *et al*,2019	0.017	0.012	0.024	-24.110	0.000
African Region	Abubakar, 2020	0.059	0.038	0.091	-11.691	0.000
African Region	Motbainor *et al*, 2020	0.056	0.033	0.094	-10.026	0.000
African Region	Strasheim *et al*, 2015	0.172	0.135	0.216	-10.815	0.000
African Region	**Pooled**	**0.035**	**0.011**	**0.106**	**-5.447**	**0.000**
American Region	Danchaivijitr *et al*, 2012	0.006	0.005	0.008	-39.196	0.000
American Region	Nash *et al*, 2006	0.026	0.023	0.029	-62.844	0.000
American Region	Durlach *et al*, 2012	0.015	0.012	0.019	-33.156	0.000
American Region	Toor *et al*, 2022	0.012	0.007	0.020	-15.928	0.000
American Region	Magill *et al*, 2012	0.009	0.005	0.019	-13.111	0.000
American Region	**Pooled**	**0.012**	**0.006**	**0.024**	**-12.936**	**0.000**
Eastern Mediterranean Region	Al-Khawaja *et al*, 2021	0.021	0.015	0.029	-22.268	0.000
Eastern Mediterranean Region	Balkhy *et al*, 2006	0.025	0.015	0.042	-13.548	0.000
Eastern Mediterranean Region	Askarian *et al*, 2012	0.025	0.020	0.031	-33.596	0.000
Eastern Mediterranean Region	Ghali *et al*, 2021	0.011	0.007	0.015	-24.268	0.000
Eastern Mediterranean Region	Alfouzan *et al*, 2021	0.028	0.020	0.038	-21.912	0.000
Eastern Mediterranean Region	Heydarpou *et al*, 2017	0.000	0.000	0.001	-9.329	0.000
Eastern Mediterranean Region	**Pooled**	**0.016**	**0.010**	**0.026**	**-16.766**	**0.000**
European Region	Pittet *et al*, 199	0.017	0.011	0.025	-19.264	0.000
European Region	Izquierdo-Cubas *et al*, 2008	0.007	0.005	0.010	-26.899	0.000
European Region	Faria *et al*, 2007	0.003	0.001	0.009	-9.879	0.000
European Region	Gentili *et al*, 2020	0.010	0.008	0.013	-36.574	0.000
European Region	Mühlemann *et al*, 2004	0.025	0.015	0.043	-13.043	0.000
European Region	Arefian *et al*, 2019	0.008	0.007	0.008	-105.884	0.000
European Region	Custovic *et al*, 2014	0.007	0.003	0.016	-12.029	0.000
European Region	**Pooled**	**0.010**	**0.007**	**0.014**	**-27.372**	**0.000**
South East Asian Region	Shrestha *et al*, 2022	0.027	0.013	0.052	-10.041	0.000
South East Asian Region	Sahu *et al*, 2016	0.004	0.002	0.005	-27.652	0.000
South East Asian Region	**Pooled**	**0.010**	**0.001**	**0.067**	**-4.520**	**0.000**
Western Pacific Region	Huang *et al*, 2020	0.003	0.002	0.004	-24.511	0.000
Western Pacific Region	Lee *et al*,2007	0.009	0.005	0.017	-14.188	0.000
Western Pacific Region	Zhao *et al*, 2015	0.000	0.000	0.000	-44.192	0.000
Western Pacific Region	Zhong *et al*, 2021	0.192	0.165	0.224	-14.810	0.000
Western Pacific Region	Zhu *et al*,2019	0.031	0.027	0.036	-42.380	0.000
Western Pacific Region	Russo *et al*, 2019	0.011	0.008	0.016	-24.683	0.000
Western Pacific Region	Zhang *et al*, 2016	0.002	0.001	0.004	-18.192	0.000
Western Pacific Region	Zhang *et al*, 2019	0.006	0.006	0.006	-311.028	0.000
Western Pacific Region	Wang *et al*, 2019	0.016	0.010	0.024	-18.851	0.000
Western Pacific Region	Jiang *et al*, 2020	0.004	0.003	0.005	-39.412	0.000
Western Pacific Region	**Pooled**	**0.007**	**0.002**	**0.020**	**-9.310**	**0.000**

Heterogeneity I^2=80.1 %, p-value <0.01

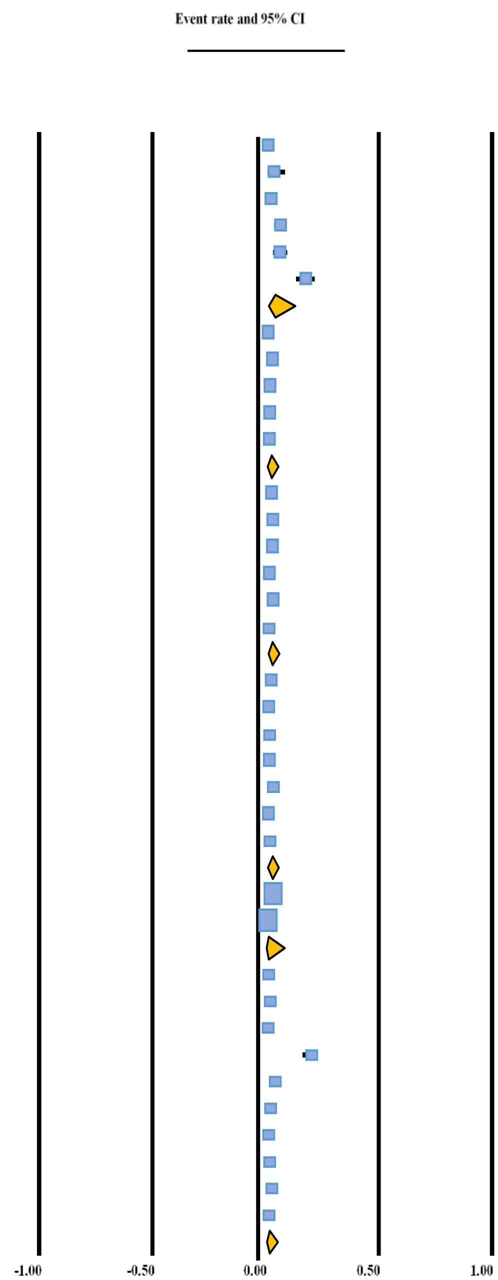

Figure 4: The forest plot shows the subgroup analysis of the pooled prevalence of stream bloodstream infections among inpatients based on the World Health Organization's Region of the world

Publication Bias

Publication bias was evaluated using a funnel plot, which visually represents the distribution of study results. The findings were largely symmetrically distributed around the overall effect size, suggesting minimal publication bias. To address a few outliers, a sensitivity analysis was performed to determine their impact on the overall HA-BSIs prevalence (Figure 5)

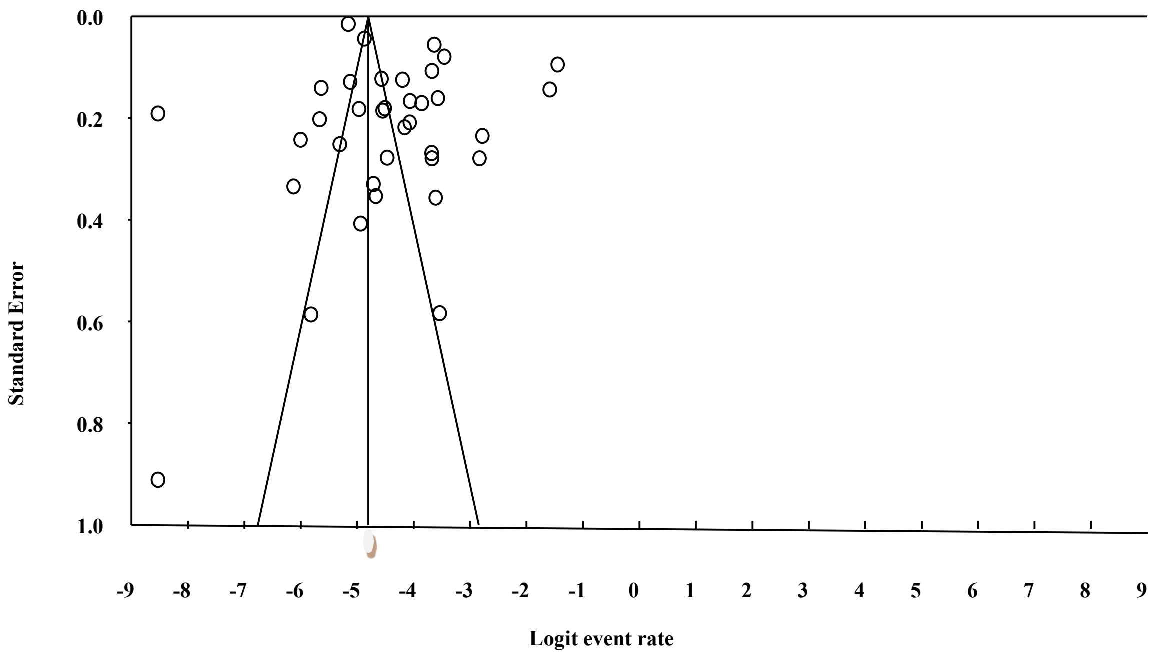

Figure 5: Funnel plot showing the distribution of study findings, healthcare associated bloodstream infections among inpatients

Meta Regression

The finding from meta-regression, based on a random-effects model shows a coefficient of -4.4367 + 0.192 (SE) with a 95% confidence interval (-4.8124, -4.061, Z-value of -23.15 and p-value of < 0.001), with minimal random variation.

Sensitivity Analysis Results

The sensitivity analysis was conducted to evaluate the impact of extreme values on the overall prevalence of HA-BSIs. After the removal of the identified outliers or extreme values, the results showed no substantial difference in the prevalence of BSI among inpatients (Table 2).

Table 2: Sensitivity analysis based on sample size and study outcomes expected to affect the pooled prevalence of healthcare associated bloodstream infection.

Criteria	Pooled prevalence after applying criteria	p-value
After dropping the two largest and two smallest outcomes	1.2 (95% CI: 0.9, 1.6%)	<0.001
After dropping four largest sample size	1.3 (95% CI: 0.9, 2.1%)	<0.001
After dropping two smallest sample size	1.1(95% CI: 0.7, 1.6%)	<0.001

Discussion

This study aimed to assess the global prevalence of HA-BSIs among inpatients, as well as the prevalence across different WHO regions. The systematic review found the overall HA-BSIs prevalence accounted for 1.2% (95% CI: 0.8, 1.7%), which was lower compared to the finding from previous systematic reviews that reported 3.4% prevalence of BSIs (O'Horo *et al.,* 2014) and 6.4% (Ista *et al.,* 2016). The variation in BSI prevalence observed across studies can be attributed to several factors, including differences in participant demographics (such as age, health status, and underlying conditions), the types of healthcare-associated BSIs being studied, and the geographical or institutional scope of each study

The current study found the highest prevalence of HA-BSIs in the African region, with a prevalence of 3.5% (95% CI: 1.1, 10.6%). This finding is lower than the finding reported by WHO accounted for 4.27% prevalence in developing countries (WHO, 2011). Several factors may contribute to this variation, including differences in healthcare infrastructure, infection prevention and control practices, and the burden of infectious diseases. Poorly resourced healthcare systems, limited medical supplies, and inadequate infection control measures in some regions may increase the risk of HA-BSIs. Additionally, socioeconomic challenges, such as poverty and limited access to healthcare, can elevate the vulnerability to infections. Furthermore, variations in data collection methods, differences in regional healthcare policies, and the diversity in study populations could all influence the observed discrepancies in prevalence rates.

The finding of the current study was notably lower than those reported in previous systematic review conducted by Droz *et al*. (2019), which identified a prevalence of positive blood cultures at 19.1%, with 15.5% reported in Africa and 28.0% in Asia. This discrepancy in rates of HA-BSIs can be attributed to several factors, including the scope of the studies, types and number of BSIs examined. For example, the Droz *et al*. study included both community-acquired and pediatric BSIs, which could lead to higher reported rates. Moreover, the socioeconomic factors in the region, such as poor economic conditions and limited healthcare resources, play a significant role in the persistence of BSIs (Cekin *et al*, 2023; Timsit *et al,* 2020). These constraints can impair the effectiveness of infection prevention and treatment strategies, further contributing to the disparity in prevalence (Ekane *et al*., 2014).

The study results showed a decline in the prevalence of HA-BSIs, from 2% (95% CI: 1.4, 2.9%) between 1996 and 2001 to 0.9% (95% CI: 0.5, 1.6%) between 2014 and 2018. However, the prevalence rose again from 0.9% (95% CI: 0.5, 1.6%) in 2014–2018 to 4.2% (95% CI: 1.2, 13.4%) in 2019–2023. The initial decline in HA-BSIs may be attributed to the implementation of infection prevention and patient's safety measures, such as training and targeted intervention programs, while the increase in BSIs could be due to factors such as improved reporting systems, or differences in study characteristics (Garcia *et al,* 2022).

In general, the current study highlights global variations in the prevalence of HA-BSIs, with the highest prevalence observed in African region. This underscores the need for enhanced health and safety measures, especially in low- and middle-income countries, to better protect patient health. Strengthening healthcare systems in these countries is crucial, which can be achieved through education and skill development (Danwang *et al*., 2020). Implementing quality improvement interventions has been shown to help prevent central line-associated BSIss (Blot *et al*., 2014). Additionally, prioritizing the continuous enhancement of the BSI diagnostic process, including improvements in sampling quality and time to result, is essential to improve patient outcomes and reducing unnecessary antibiotic use (Lamy *et al*., 2020).

Strength and Limitations

This review was conducted following PRISMA guidelines and focused on healthcare-associated BSIs in various regions worldwide, providing both global and regional prevalence. Multiple electronic databases were used to retrieve relevant studies. There was an uneven distribution of studies globally, resulting in a limited number of articles. Additionally, many countries' HA-BSIs prevalence data were not included due to the absence of studies that met the eligibility criteria. Variations in surveillance systems across regions may contribute to differences in BSI prevalence. The authors were unable to determine specific risk factors for HA-BSIs prevalence due to inconsistencies in measurement units. Furthermore, the scarcity of studies on BSI prevalence limits the ability to adequately compare the current findings with previous research.

Conclusions

This review found that at least one in 100 patients is infected with a healthcare-associated infection. There is also variation in prevalence in different regions of the world, with the highest prevalence reported in the African region. The findings from the current review indicate the need to implement effective infection prevention and control to prevent healthcare-associated bloodstream infections

Competing Interests

The authors declare that they have no competing interests.

Funding Statement

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Authors' Contributions

DAM initiated the concept and played a central role in the review process, data extraction, analysis, writing, drafting, and manuscript editing. All authors (DAM, MD, AT, DD, FA, AM, and TG) contributed to data extraction, analysis, and manuscript revisions. In the final stage, the authors (DAM, MD, AT, DD, FA, AM, and TG) reviewed and approved the manuscript for publication and agreed upon all aspects of the work.

List of Abbreviations

BSIs: Bloodstream Infections; CDC: Centers for Disease Control and Prevention; CMA: Comprehensive Meta-Analysis; HAI: Healthcare-Associated Infections; HA-BSIs: Healthcare-Associated Bloodstream Infections; JBI: Joanna Briggs Institute; OASH: Office of Disease Prevention and Health Promotion; PRISMA: Preferred Reporting Items for Systematic Review and Meta-Analysis; WHO: World Health Organization; MeSH: Medical Subject Headings.

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