

Bloodstream Infections in Patients with COVID-19 Admitted to Intensive Care Units in Europe: A Literature Review and Meta-Analysis

António Martins¹, David Reid²

¹Department of Infectious Diseases, Unidade Local de Saúde de São João, Porto, Portugal

²Department of Public Health Environments and Society, London School of Hygiene and Tropical Medicine, London, UK

Email: antonio.rm626@gmail.com, david.reid@lshtm.ac.uk

How to cite this paper: Martins, A. and Reid, D. (2026) Bloodstream Infections in Patients with COVID-19 Admitted to Intensive Care Units in Europe: A Literature Review and Meta-Analysis. *Advances in Infectious Diseases*, 16, 541-557.

<https://doi.org/10.4236/aid.2026.163038>

Received: August 14, 2026

Accepted: September 27, 2026

Published: September 30, 2026

Copyright © 2026 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Patients with COVID-19 admitted to intensive care unit (ICU) have an increased risk of bloodstream infections (BSI), compared to patients without COVID-19. To date, no literature review and meta-analysis of the incidence rate of BSI in these patients is available. A literature review was performed based on a systematic search from January 2020 to December 2023. Eligible studies had to address the incidence rate of BSI in adult patients with COVID-19 admitted to ICU within Europe. Data on incidence and mortality rates was collected. A meta-analysis was conducted to estimate the pooled incidence rate. Twelve studies met eligibility criteria. The incidence rate of BSI in patients with COVID-19 admitted to ICU varied between 6.4 and 92/1000 patient-days with a mortality rate between 25% and 54%. The pooled incidence rate was 29.5/1000 patient-days (95% CI 12.1 - 71.6) with substantial heterogeneity observed. Compared to non-COVID-19 patients admitted to ICU during the pandemic, the incidence rate of BSI was higher. According to this literature review and meta-analysis, the incidence rate of BSI in patients with COVID-19 admitted to ICU is two-fold higher. Clinical teams taking care of these patients should adapt BSI prevention protocols and antimicrobial treatments.

Keywords

Bloodstream Infections, COVID-19, Intensive Care Unit

1. Introduction

Intensive care units (ICU) are the hospital wards with the highest prevalence of

hospital-acquired infections (HAI), with bloodstream infections (BSI) being among the most common [1]. Patients with COVID-19 admitted to ICU have an increased risk of BSI, compared to patients without COVID-19 [2]. The immunopathogenesis of SARS-CoV-2, the critical illness features of COVID-19 and the use of immunomodulatory therapies in these patients are potential explanatory factors.

In several observational studies, the proportion of these patients who developed BSI has been variably described, including rates lower than 1% and higher than 50% [3] [4]. A single meta-analysis of BSI in hospitalized patients with COVID-19, including both ICU and non-ICU patients, estimated a pooled occurrence rate of 7.3% [5]. However, the authors limited their analysis to data published until April 2021. To date, no literature review and meta-analysis of the incidence rate of BSI in patients admitted to ICU with COVID-19 is available.

The aim of the present study was to assess and characterize BSI in adult patients with COVID-19 admitted to ICU within Europe and two objectives were pursued. The first objective was to evaluate the incidence and mortality rates and to estimate a pooled incidence rate. The second objective was to identify risk factors, etiologic pathogens and antimicrobial resistance (AMR) rates.

2. Methods

A literature review was performed based on a systematic search across the EMBASE, Medline and CINAHL databases from January 2020 to December 2023. This study was structured according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) 2020 checklist (Table S1). A search strategy was developed for the systematic search based on the key concepts “bloodstream infection”, “intensive care unit” and “coronavirus disease 2019”. The search strategy was adapted to each database according to database-specific search terms (Table S1). Search records were screened by one reviewer and relevant records were identified from titles and abstracts. Duplicate studies were removed. Studies selected as relevant were evaluated through full text analysis.

Eligibility was assessed by one reviewer and eligible studies had to address the incidence rate of BSI in adult patients admitted to ICU with COVID-19 within Europe. BSI incidence rate was the primary outcome of the study and was defined as the ratio between the number of new events and the total patient-time at risk. New events corresponded to BSI defined by the positivity of at least one blood culture for a recognized pathogen, including bacterial, fungal and polymicrobial agents, or two positive blood cultures for a common skin contaminant.

Additionally, eligible studies were published in English and were randomized trials or observational studies. Studies were excluded if they had less than 10 patients, BSI caused by a specific pathogen only or BSI occurring in a specific sub-population only.

Studies underwent a critical appraisal and quality assessment based on the

JBIC's Critical Appraisal Tools appropriate for study type (**Table S1**). After quality assessment, the included studies were reviewed for content. For the first objective, extracted data included author, year, type of study, study period, country, sample size, incidence rate, comparators, and mortality rate. For the second objective, extracted data included risk factors, etiologic pathogens and AMR rates.

Statistical analysis was performed using Stata software. For the meta-analysis, studies reporting raw new events with ICU patient-time or incidence rates with corresponding 95% confidence interval (CI) were included. Incidence rates were log-transformed and pooled using inverse-variance weighting under a random-effects model, accounting for between-study heterogeneity. Between-study variance was estimated using restricted maximum likelihood. Studies reporting central line-associated BSI were excluded due to differing exposure definitions. Sensitivity analysis was performed by additionally including the studies that did not report ICU patient-time or 95% CI. In these, ICU patient-time was approximated using the product of sample size and median ICU length of stay, acknowledging this may not accurately reflect total exposure time.

3. Results

After screening based on title and abstract followed by text assessment of study eligibility, 12 studies were selected for data extraction and analysis (**Figure 1**) [6]–[17].

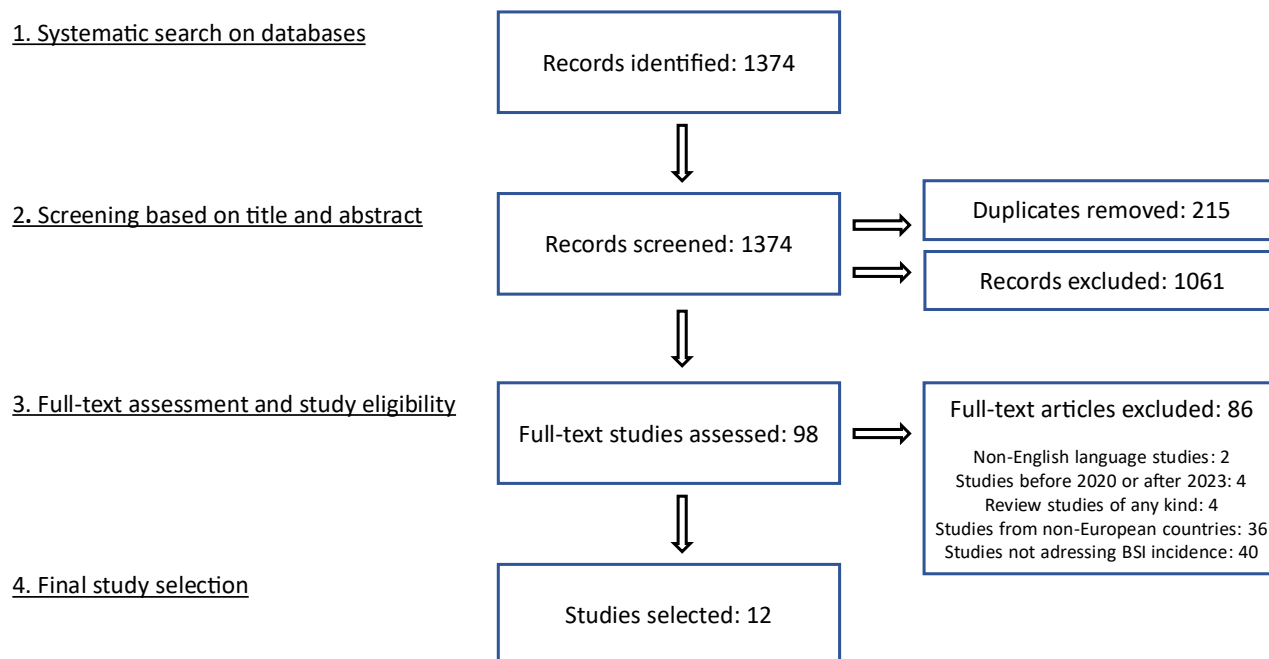


Figure 1. Flowchart of the screening and selection of studies.

All studies were designed as observational studies, including three as prospec-

tive and nine as retrospective. Five studies were classified as high-quality according to critical appraisal [10]-[12] [14] [16]. The studies with the largest sample size were performed by Massar, N. *et al.* (n = 4010) and Lepape, A. *et al.* (n = 4465). Two studies reported central line-associated BSI [7] [10]. The incidence rate of BSI in patients with COVID-19 admitted to ICU varied between 6.4 and 92 episodes per 1000 patient-days (**Table 1**).

Table 1. Summary of the data collected from the selected studies.

Study	Year	Type	Period	Country	Sample size	BSI incidence	Clinical outcome	Non-COVID BSI incidence	Pre-COVID BSI incidence
Pozza, G. <i>et al.</i>	2023	Retrospective single centre	2020-2022	Italy	404 patients	87/1000 patient-days	---	---	---
Verberk, J. D. M. <i>et al.</i>	2023	Retrospective multicentre	2020	Netherlands	350 patients	7.8/1000 central line-days	---	4.8/1000 central line-days	0.7/1000 central line-days
Giacobbe, D. R. <i>et al.</i>	2020	Retrospective single centre	2020	Italy	78 patients	47/1000 patient-days	Mortality rate 25%	---	---
Ramos, R. <i>et al.</i>	2021	Retrospective single centre	2020	Spain	213 patients	13.1/1000 patient-days	---	---	---
Hlinkova, S. <i>et al.</i>	2023	Retrospective single centre	2020-2022	Slovakia	207 patients	10.2/1000 central line-days	---	4.3/1000 central line-days	2.8/1000 central line-days
Szabó, B. G. <i>et al.</i>	2023	Prospective single centre	2020-2022	Hungary	379 patients	12.1/1000 patient-days	---	---	---
Lepape, A. <i>et al.</i>	2022	Retrospective multicentre	2020	France	4465 patients	6.4/1000 patient-days	---	3.9/1000 patient-days	3.4/1000 patient-days
Bonazzetti, C. <i>et al.</i>	2022	Retrospective multicentre	2020-2021	Italy	537 patients	92-27/1000 patient-days	Mortality rate 54%	---	---
Bloch, N. <i>et al.</i>	2023	Prospective single centre	2021-2022	Switzerland	64 patients	9.4/1000 patient-days	---	5.6/1000 patient-days	---
Torrecillas, M. <i>et al.</i>	2022	Retrospective single centre	2020	Spain	220 patients	32.7/1000 patients-days	Mortality rate 47%	---	10.1/1000 patients-days
Massart, N. <i>et al.</i>	2021	Prospective multicentre	2020	France, Belgium, Switzerland	4010 patients	10.3/1000 patient-days	Mortality rate 39%	---	---
Cataldo, M. A. <i>et al.</i>	2020	Retrospective single centre	2020	Italy	57 patients	37.3/1000 patient-days	Mortality rate 32%	---	---

The high-quality studies reported an incidence rate between 6.4 and 12.1 per 1000 patient-days and the large-scale studies between 6.4 and 10.3 per 1000 patient-days [10]-[12] [14] [16]. Only five studies described the clinical outcome of the patients, reporting ICU mortality rates ranging from 25% to 54% [8] [11] [15]-[17].

The pooled incidence rate was 29.5 per 1000 patient-days (95% CI 12.1 - 71.6) (Figure 2). Substantial between-study heterogeneity was observed, and the 95% prediction interval ranged from approximately 2.8 to 307 per 1000 patient-days. In the Bonazzetti study, there were two mutually exclusive cohorts that were included as different cohorts in the primary analysis.

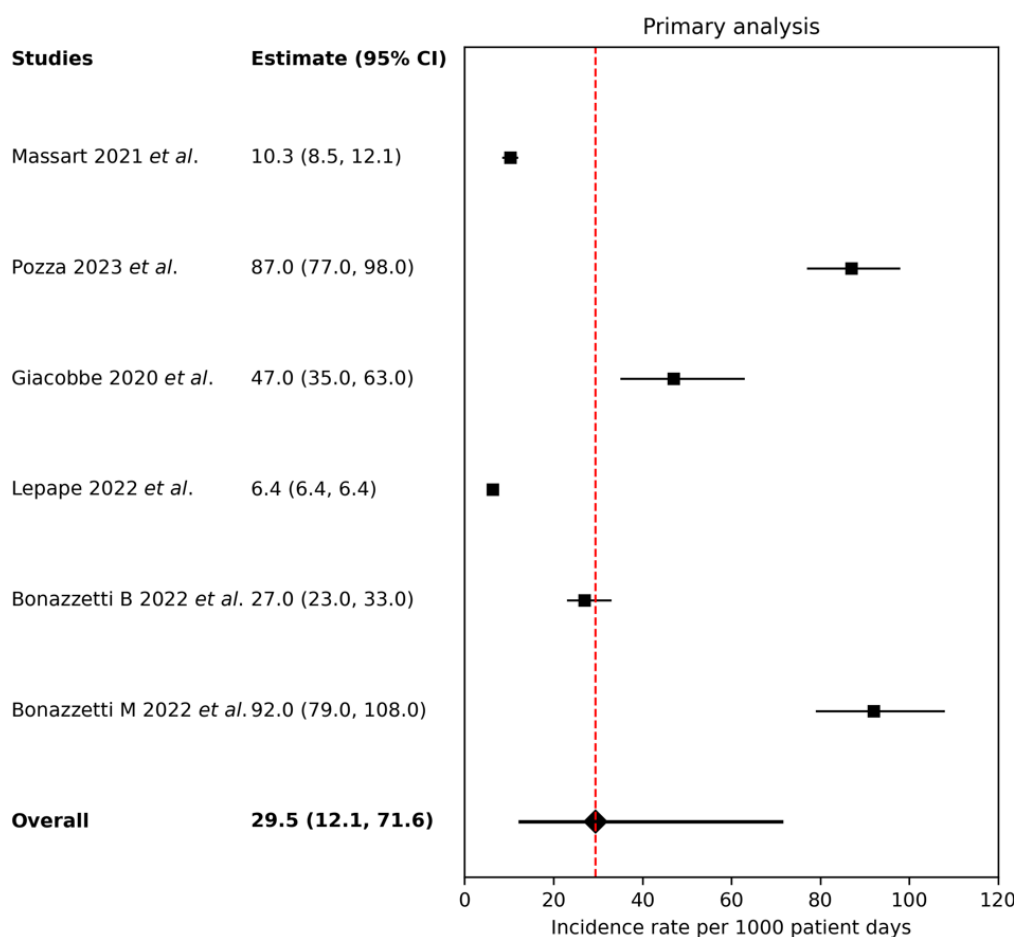


Figure 2. Forest plot for the primary analysis of pooled incidence rate.

In sensitivity analysis, the pooled incidence rate was 26.8 per 1000 patient-days (95% CI 14.7 - 48.6) (Figure 3). The corresponding prediction interval remained wide (4.2 - 172 per 1000 patient-days).

Comparison between the incidence rate of BSI in COVID-19 and non-COVID-19 patients during the pandemic years showed a higher incidence rate of BSI in COVID-19 patients in all four studies (6.4 to 9.4 vs. 3.9 to 5.6/1000 patient-days (two studies) and 7.8 to 10.2 vs. 4.3 to 4.8/1000 central line-days (two studies)) [7] [10] [12] [14]. Additionally, in studies which used historical data, the incidence

rate of BSI in COVID-19 patients was also superior to non-COVID-19 patients admitted to ICU before the pandemic [7] [10] [12] [15].

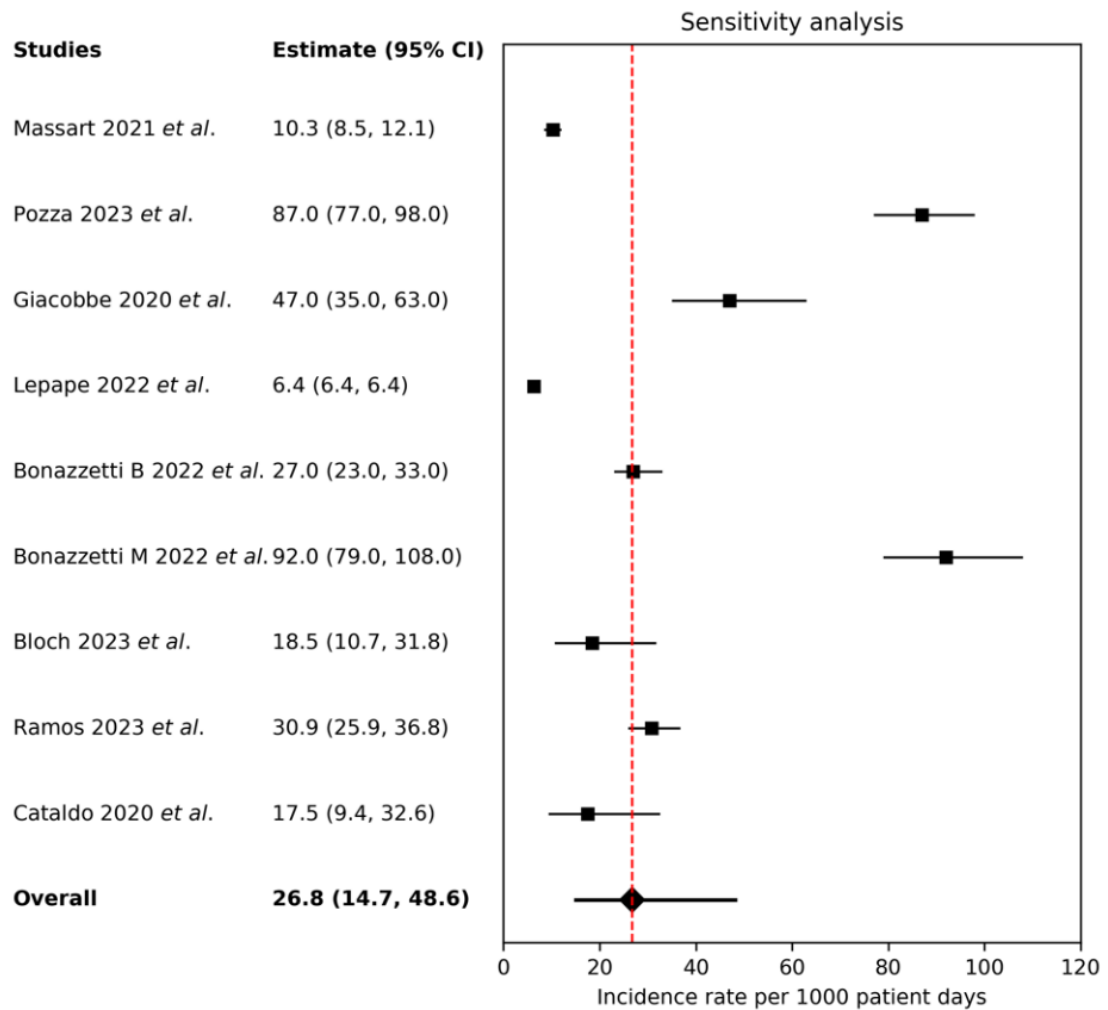


Figure 3. Forest plot for the sensitivity analysis of pooled incidence rate.

Regarding risk factors, three studies performed multivariable analysis to identify risk factors for BSI in patients with COVID-19 admitted to ICU (Table 2). In the first, after multivariable analysis, only the use of anti-inflammatory therapy retained an independent association with BSI (Table 2) [8]. The risk was the lowest with tocilizumab (HR 1.07, 95% CI 0.38 - 3.04) and the highest with combination of methylprednisolone plus tocilizumab (HR 10.69, 95% CI 2.71 - 42.17). In the second study, factors independently associated with BSI included the sequential organ failure assessment (SOFA) and the Charlson comorbidity index scores [13]. In the third, risk factors included male gender, antiviral therapy before admission, simplified acute physiology score (SAPS) II score, longer time from hospital admission to ICU and tracheal intubation during the period at risk for BSI [15]. In the last two studies, no association between immunosuppressive therapy and BSI was found.

Table 2. Data on risk factors, etiologic pathogens and AMR rates.

Study	Risk factors	Etiologic pathogens	AMR rates
Pozza, G. <i>et al.</i>	---	<i>Enterococcus spp</i> (43.1%) CoNS (27.8%) <i>Enterobacterales</i> (40%) <i>P. aeruginosa</i> (10.4%) <i>Enterobacter spp</i> (9.6%)	VRE (4.9%) ESBL (4.7%) MRSA (3.1%) CPE (2.9%) MDR <i>P. aeruginosa</i> (2.9%)
Giacobbe, D. R. <i>et al.</i>	Anti-inflammatory treatment (HR 1.07-10.69)	CoNS (24%) <i>E. faecalis</i> (18%) <i>S. aureus</i> (13%) <i>E. faecium</i> (9%) <i>E. aerogenes</i> (9%)	---
Ramos, R. <i>et al.</i>	---	CoNS (34.7%) <i>E. faecium</i> (14.7%) Gram-negative (13.3%) <i>Candida spp</i> (13.3%) <i>E. faecalis</i> (6.7%)	---
Hlinkova, S. <i>et al.</i>	---	<i>Acinetobacter spp</i> (21.6%) <i>K. pneumoniae</i> (21.6%) <i>Enterococcus spp</i> (16.2%) <i>P. aeruginosa</i> (13.5%) CoNS (10.8%)	---
Szabó, B. G. <i>et al.</i>	---	<i>E. faecalis</i> (22.1%) <i>A. baumannii</i> (15.6%) <i>P. aeruginosa</i> (11.5%) <i>S. aureus</i> (7.4%) <i>E. faecium</i> (6.6%)	---
Lepape, A. <i>et al.</i>	---	CoNS (18.1%) <i>P. aeruginosa</i> (15.8%) <i>E. faecalis</i> (11.8%) <i>S. aureus</i> (8.4%) <i>Klebsiella spp</i> (8.4%)	---
Bonazzetti, C. <i>et al.</i>	Charlson score (HR 1.16) SOFA score (HR 1.07)	<i>Enterococcus spp</i> (31.8%) <i>Enterobacterales</i> (14.4%) CoNS (14.1%) <i>S. aureus</i> (9.8%) <i>P. aeruginosa</i> (6.2%)	MDR <i>P. aeruginosa</i> (9.3%) CPE (6.2%) MRSA (5.2%) ESBL (3.3%) MDR <i>A. Baumannii</i> (3.3%)
Torrecillas, M. <i>et al.</i>	---	<i>Enterobacterales</i> (12.8%) CoNS (11.8%) Polymicrobial (6.4%) <i>S. aureus</i> (5.5%) <i>Candida spp</i> (5%)	---

Continued

Massart, N. <i>et al.</i>	Intubation (HR 5.18)	Enterobacterales (18%)	
	Male gender (HR 1.41)	<i>S. aureus</i> (8%)	
	Antiviral treatment (HR 1.41)	<i>Streptococcus spp</i> (7%)	MRSA (3%)
	ICU admission time (HR 1.03)	<i>P. aeruginosa</i> (6%)	
	SAPS II score (HR 1.01)	<i>Enterococcus spp</i> (5%)	
Cataldo, M. A. <i>et al.</i>	---	<i>Enterococcus spp</i> (39.3%)	P/T-R <i>P. aeruginosa</i> (14.3%)
		<i>Pseudomonas spp</i> (28.6%)	VRE (7.1%)
		<i>Candida spp</i> (17.9%)	ESBL (7.1%)

AMR: antimicrobial resistance; CoNS: coagulase-negative staphylococci; CPE: carbapenemase-producing Enterobacterales; ESBL: extended-spectrum beta-lactamase; ICU: intensive care unit; MDR: multidrug-resistant; MRSA: methicillin-resistant *Staphylococcus aureus*; P/T-R: piperacillin-tazobactam resistant; SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; VRE: vancomycin-resistant *Enterococcus*.

In seven of the ten studies that reported specific etiologic pathogens of BSI, gram-positive cocci were the most frequently identified bacterial class (**Table 2**). Noteworthy, *Enterococcus spp.* prevalence rates above 25% were described in five of the seven studies [6] [8] [11] [13] [17]. In contrast to the above, in the two largest studies gram-negative rods were identified the most although the difference was small (45.2% vs. 44.4% in the study by Lepape, A. *et al.* and 24% vs. 23% in the study by Massart, N *et al.*). Importantly, two studies reported a prevalence rate of *Acinetobacter spp.* above 15% [10] [11].

Concerning AMR, three studies described AMR patterns for the bacterial pathogens identified (**Table 2**). Vancomycin-resistant *Enterococcus* (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA) prevalence rates varied between 4.9% - 7.1% and 3.1% - 5.2%, respectively [6] [13] [17]. Extended-spectrum beta-lactamases (ESBL)-producing Enterobacterales were found in 3.3%, 4.7% and 7.1% in these studies. Finally, in one study carbapenemase-producing Enterobacterales (CPE) and multidrug-resistant *Pseudomonas aeruginosa* were more prevalent than ESBL [13].

4. Discussion

To the best of our knowledge, this is the first literature review and meta-analysis of the incidence rate of BSI in patients with COVID-19 admitted to ICU. The incidence rate varied between 6.4 and 92 episodes per 1000 patient-days and a pooled incidence rate of 29.5 episodes per 1000 patient-days was estimated with substantial heterogeneity observed. Compared to the data from the European Centre for Disease Prevention and Control on BSI in ICU patients before the pandemic years (1.7 to 3.5/1000 patient-days), there is a significant increase in inci-

dence rates [18]-[21]. This difference remains evident although less pronounced when the observed incidence rates are compared to data from the selected studies on BSI in non-COVID-19 patients in ICU during the pandemic years (3.9 to 5.6/1000 patient-days). Mortality associated to BSI in COVID-19 patients admitted to ICU (25% to 54%) was also higher compared to non-COVID-19 patients described previously (15 to 20%) [22].

The substantial heterogeneity observed across studies limits the interpretability of a single summary measure and suggests that the incidence rate of BSI in COVID-19 patients admitted to ICU is highly context dependent. Four studies reported BSI incidence rates ranging from 37 to 92/1000 patient-days and contributed to the overall heterogeneity [6] [8] [13] [17]. Three important factors may explain such increased incidence rates compared to the remaining studies.

The first relevant aspect is the geographical and temporal context. All four studies were conducted in Italian centres during 2020 and 2021, corresponding to the early waves of the pandemic in one of the most affected countries worldwide. A second important factor is associated with infection prevention and control (IPC) practices. All four studies report disruption of IPC standard measures. For instance, shortages of basic equipment like sterile gloves and lack of IPC human resources were described [6] [13]. The third relevant aspect relates to the microbiological diagnostic approach. Several of these studies explicitly reported a lower clinical threshold for obtaining blood cultures [6] [8] [13]. This approach is associated with higher likelihood of identifying skin contaminants and may overestimate BSI incidence rate.

These findings suggest that the increased incidence rates may not be only attributable to disease-related factors, but rather reflect an interplay between pandemic context, IPC constraints, and diagnostic strategies. In addition, study-level characteristics such as methodological quality and sample size appear to play a relevant role in explaining this variability, as these studies were all classified as low-quality. This interpretation is supported by the lower incidence rates observed in the high-quality (6.4 to 12.1/1000 patient-days) and large-scale studies (6.4 to 10.3/1000 patient-days), which suggests the pooled estimate of 29.5/1000 patient-days may be overestimated.

Review studies have addressed BSI in COVID-19 patients admitted to ICU. In a systematic review and meta-analysis from 2021, Ippolito, M. *et al.* focused on BSI in hospitalized COVID-19 patients, including both ICU and non-ICU patients. An overall pooled occurrence rate of 7.3% (95% CI 4.7 - 11%; 1324/42,694 patients) and mortality rate of 41% (95% CI 30% - 52.8%; 189/482 patients) were calculated by the authors. [5] In the sensitivity analysis, concerning patients admitted to ICU, a pooled prevalence rate of 29.6% (95% CI 21.7% - 38.8%; 558/2487 patients) was calculated. However, no data on incidence, mortality or further context was presented. In a literature review published in 2023 by Ntziora, F. *et al.*, the BSI prevalence rate varied between 3.7 to 61% and the associated mortality rate between 22.8 and 100%, but no meta-analysis was conducted to summarize

data [2].

The increase in the incidence rates of BSI in COVID-19 compared to non-COVID-19 patients admitted to ICU may be related to disease-related factors, including the immunopathogenesis of the disease, the associated critical illness and the therapy itself. Regarding the immunopathogenesis, SARS-CoV-2 may trigger an acquired immunosuppression with concomitant lymphopenia but may also induce a coagulopathy affecting both the micro and macrocirculation, which leads to an increased risk of bacterial translocation [23] [24]. In terms of critical illness, several studies comparing ICU admitted patients with COVID-19 to non-COVID-19 during the pandemic reported that COVID-19 patients were admitted in ICU and used central venous catheter and mechanical ventilation for a longer period, increasing the risk of nosocomial infections [7] [10]. Finally, the current standard of care of severe COVID-19 includes immunomodulatory therapies and one study found an independent association between these and BSI [8]. In line with this fact, a systematic review and meta-analysis published in 2025 showed that corticosteroids alone or in combination with tocilizumab increase the risk of BSI in COVID-19 patients admitted to ICU [25].

Within critically ill patients with COVID-19, other risk factors for BSI have been identified from the selected studies, including well-established risk factors for nosocomial infections in other critically ill patients, such as comorbidities scores (Charlson), severity scores (SOFA and SAPS II), tracheal intubation and ICU admission time [8] [14] [16]. Other risk factors identified for BSI in COVID-19 patients admitted to ICU include male gender, diabetes, central venous catheter, extracorporeal membrane oxygenation and prolonged ICU stay [25].

In the two largest studies, the majority of BSI were caused by gram-negative rods [12] [16]. *Enterococcus spp.* prevalence rate was above 25% in five studies and *Acinetobacter spp.* above 15% in two studies [6] [8] [10] [11] [13] [17]. These three epidemiological findings deserve further analysis. The predominance of gram-negative rods in BSI in ICU patients has also been described in non-COVID-19 patients in recent years [26] [27]. The EUROACT-2 study analysed 2600 patients from 33 ICU from 52 countries from 2019 to 2021 [26]. In a subsequent analysis, COVID-19 and non-COVID-19 patients were compared, and gram-negative rods were more frequently observed in both groups (59.9 and 61.4%, respectively) [28]. In contrast, the high prevalence of *Enterococcus spp.* and *Acinetobacter spp.* in BSI in ICU patients has been specifically described in COVID-19 patients [29] [30]. In the same multicentric study, COVID-19 patients had prevalence rates of *Enterococcus spp.* and *Acinetobacter spp.* of 20.5% and 18.8%, respectively, which were significantly higher than non-COVID-19 patients [28].

Regarding antimicrobial resistance data, gram-positive resistant bacteria prevalence rates, such as VRE and MRSA, varied between 4.9% - 7.1% and 3% - 5.2%, respectively, and gram-negative resistant bacteria, such as ESBL, CPE and multi-drug-resistant *P. aeruginosa*, varied between 3.3% - 7.1%, 2.9% - 6.2% and 2.9% -

9.3%, respectively [6] [13] [16] [17]. Data from the study by Lepape, A. *et al.* showed that COVID-19 patients were at higher risk of BSI and VAP caused by multidrug-resistant bacteria than non-COVID-19 patients. [12] In the analysis from the EUROBACT-2 study, the authors reported that COVID-19 patients had higher incidence of BSI caused by difficult-to-treat gram-negative bacteria (19.4% vs. 13%) [28]. Piantoni, A. *et al.* assessed the incidence of BSI related to multidrug-resistant bacteria in ICU patients. Again, COVID-19 were at higher risk of BSI caused by multidrug-resistant bacteria than non-COVID-19 patients [31].

This literature review and meta-analysis has several limitations that must be considered. First, it was based on studies from 1st of January 2020 to 31st December 2023, which may have excluded relevant studies and introduced bias in the results and conclusions of this review. Second, studies addressing the topic of BSI in COVID-19 patients admitted to ICU using prevalence rate, or in non-European countries, or in non-English language were excluded. Although there was a rationale for this criterion to be implemented, the scope of this study remains limited because of it. Third, search records were screened and eligibility assessed by one reviewer which may have led to a source of potential selection error. Fourth, there was important variation in the data retrieved according to each objective. For the second objective, there was considerably less data reported in the selected studies compared to the first objective, in particular for risk factors and AMR rates. Last, as mentioned above, the substantial heterogeneity limits the validity of a single summary measure and suggests incidence rates must be contextualized.

5. Conclusions

In this literature review and meta-analysis, the incidence rate of BSI in COVID-19 patients admitted to ICU varied between 6.4 and 92 episodes per 1000 patient-days and associated mortality was found to be 25 to 54%. The estimated pooled incidence rate of 29.5 episodes per 1000 patient-days should be interpreted with caution due to substantial heterogeneity driven by differences in pandemic context, IPC practices and microbiological diagnostic approach. Future studies conducted in equivalent settings and using standardized definitions are needed to provide more robust estimates.

The increase in the incidence rates of BSI in COVID-19 compared to non-COVID-19 patients admitted to ICU may be related to the immunopathogenesis of the disease, the associated critical illness and the therapy of COVID-19. Other risk factors have been identified, including well-established risk factors for nosocomial infections in critically ill patients. The epidemiology of these BSI may be characterized by a predominance of gram-negative rods and a high prevalence of *Enterococcus spp.* and *Acinetobacter spp.* Clinical teams taking care of these patients should adapt BSI prevention protocols and antimicrobial treatments.

Author Contributions

Conceptualization, A.M. and D.R.; methodology, A.M.; formal analysis, A.M.;

writing—original draft preparation, A.M.; writing—review and editing, D.R.; All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

- [1] European Centre for Disease Prevention and Control (ECDC) (2024) Point Prevalence Survey of Healthcare-Associated Infections and Antimicrobial Use in European Acute Care Hospitals. <https://www.ecdc.europa.eu/sites/default/files/documents/antimicrobial-use-healthcare-associated-infections-point-prevalence-survey-version6-1.pdf>
- [2] Ntziora, F. and Giannitsioti, E. (2024) Bloodstream Infections in the Era of the COVID-19 Pandemic: Changing Epidemiology of Antimicrobial Resistance in the Intensive Care Unit. *Journal of Intensive Medicine*, **4**, 269-280. <https://doi.org/10.1016/j.jointm.2023.12.004>
- [3] Contou, D., Claudinon, A., Pajot, O., Micaëlo, M., Longuet Flandre, P., Dubert, M., *et al.* (2020) Bacterial and Viral Co-Infections in Patients with Severe SARS-CoV-2 Pneumonia Admitted to a French ICU. *Annals of Intensive Care*, **10**, 119. <https://doi.org/10.1186/s13613-020-00736-x>
- [4] Bonazzetti, C., Morena, V., Giacomelli, A., Oreni, L., Casalini, G., Galimberti, L.R., *et al.* (2020) Unexpectedly High Frequency of Enterococcal Bloodstream Infections in Coronavirus Disease 2019 Patients Admitted to an Italian ICU: An Observational Study. *Critical Care Medicine*, **49**, e31-e40. <https://doi.org/10.1097/ccm.0000000000004748>
- [5] Ippolito, M., Simone, B., Filisina, C., Catalanotto, F.R., Catalisano, G., Marino, C., *et al.* (2021) Bloodstream Infections in Hospitalized Patients with COVID-19: A Systematic Review and Meta-Analysis. *Microorganisms*, **9**, Article 2016. <https://doi.org/10.3390/microorganisms9102016>
- [6] Pozza, G., Casalini, G., Ciubotariu, C.L., Giacomelli, A., Galimberti, M., Zacheo, M., *et al.* (2023) Bloodstream Infections in Intensive Care Unit during Four Consecutive SARS-CoV-2 Pandemic Waves. *Antibiotics*, **12**, Article 1448. <https://doi.org/10.3390/antibiotics12091448>
- [7] Verberk, J.D.M., van der Kooi, T.I.I., Kampstra, N.A., Reimes, N., van Rooden, S.M., Hopmans, T.E.M., *et al.* (2023) Healthcare-Associated Infections in Dutch Hospitals during the COVID-19 Pandemic. *Antimicrobial Resistance & Infection Control*, **12**, Article No. 2. <https://doi.org/10.1186/s13756-022-01201-z>
- [8] Giacobbe, D.R., Battaglini, D., Ball, L., Brunetti, I., Bruzzzone, B., Codda, G., *et al.* (2020) Bloodstream Infections in Critically Ill Patients with COVID-19. *European Journal of Clinical Investigation*, **50**, e13319. <https://doi.org/10.1111/eci.13319>
- [9] Ramos, R., de la Villa, S., García-Ramos, S., Padilla, B., García-Olivares, P., Piñero, P., *et al.* (2023) COVID-19 Associated Infections in the ICU Setting: A Retrospective Analysis in a Tertiary-Care Hospital. *Enfermedades Infecciosas y Microbiología Clínica*, **41**, 278-283. <https://doi.org/10.1016/j.eimc.2021.10.014>
- [10] Hlinkova, S., Moraucikova, E., Lesnakova, A., Strzelecka, A. and Littva, V. (2023) Central Line Associated Bloodstream Infections in Critical Ill Patients during and before the COVID-19 Pandemic. *Healthcare*, **11**, Article 2415. <https://doi.org/10.3390/healthcare11172415>

- [11] Szabó, B.G., Czél, E., Nagy, I., Korózs, D., Petrik, B., Marosi, B., *et al.* (2023) Clinical and Microbiological Outcomes and Follow-Up of Secondary Bacterial and Fungal Infections among Critically Ill COVID-19 Adult Patients Treated with and without Immunomodulation: A Prospective Cohort Study. *Antibiotics*, **12**, Article 1196. <https://doi.org/10.3390/antibiotics12071196>
- [12] Lepape, A., Machut, A., Bretonnière, C., Friggeri, A., Vacheron, C. and Savey, A. (2023) Effect of SARS-CoV-2 Infection and Pandemic Period on Healthcare-Associated Infections Acquired in Intensive Care Units. *Clinical Microbiology and Infection*, **29**, 530-536. <https://doi.org/10.1016/j.cmi.2022.10.023>
- [13] Bonazzetti, C., Rinaldi, M., Giacomelli, A., Colombo, R., Ottolina, D., Rimoldi, S.G., *et al.* (2023) Risk Factors Associated with Bacteremia in COVID-19 Patients Admitted to Intensive Care Unit: A Retrospective Multicenter Cohort Study. *Infection*, **51**, 129-136. <https://doi.org/10.1007/s15010-022-01853-4>
- [14] Bloch, N., Rüfenacht, S., Ludwinek, M., Frick, W., Kleger, G., Schneider, F., *et al.* (2023) Healthcare-Associated Infections in Intensive Care Unit Patients with and without COVID-19: A Single Center Prospective Surveillance Study. *Antimicrobial Resistance & Infection Control*, **12**, Article No. 147. <https://doi.org/10.1186/s13756-023-01353-6>
- [15] Torrecillas, M., Gumucio, V.D., Padullés, A., Tubau, F., Marco, D., Shaw, E., *et al.* (2022) Antimicrobial Use and Aetiology of Bloodstream Infections in Critically Ill Patients during Early Stages of SARS-CoV-2 Pandemic. *Infection Prevention in Practice*, **4**, Article 100241. <https://doi.org/10.1016/j.infpip.2022.100241>
- [16] Massart, N., Maxime, V., Fillatre, P., Razazi, K., Ferré, A., Moine, P., *et al.* (2021) Characteristics and Prognosis of Bloodstream Infection in Patients with COVID-19 Admitted in the ICU: An Ancillary Study of the COVID-ICU Study. *Annals of Intensive Care*, **11**, Article No. 183. <https://doi.org/10.1186/s13613-021-00971-w>
- [17] Cataldo, M.A., Tetaj, N., Selleri, M., Marchioni, L., Capone, A., Caraffa, E., *et al.* (2020) Incidence of Bacterial and Fungal Bloodstream Infections in COVID-19 Patients in Intensive Care: An Alarming “Collateral Effect”. *Journal of Global Antimicrobial Resistance*, **23**, 290-291. <https://doi.org/10.1016/j.jgar.2020.10.004>
- [18] European Centre for Disease Prevention and Control (ECDC) (2023) Annual Epidemiological Report for 2019—Healthcare-Associated Infections Acquired in Intensive Care Units. ECDC. <https://ecdc.europa.eu/sites/default/files/documents/healthcare-associated-infections-intensive-care-units-annual-epidemiological-report-2019.pdf>
- [19] European Centre for Disease Prevention and Control (ECDC) (2024) Annual Epidemiological Report for 2016—Healthcare-Associated Infections Acquired in Intensive Care Units. ECDC. https://www.ecdc.europa.eu/sites/default/files/documents/AER_for_2016-HAI_0.pdf
- [20] European Centre for Disease Prevention and Control (ECDC) (2024) Annual Epidemiological Report for 2017—Healthcare-Associated Infections Acquired in Intensive Care Units. ECDC. https://www.ecdc.europa.eu/sites/default/files/documents/AER_for_2017-HAI.pdf
- [21] European Centre for Disease Prevention and Control (ECDC) (2024) Annual Epidemiological Report for 2018—Healthcare-Associated Infections Acquired in Intensive Care Units. ECDC. <https://ecdc.europa.eu/sites/default/files/documents/healthcare-associated-infections-intensive-care-units-annual-epidemiological-report-2018.pdf>

- [22] Kallel, H., Houcke, S., Resiere, D., Roy, M., Mayence, C., Mathien, C., *et al.* (2020) Epidemiology and Prognosis of Intensive Care Unit-Acquired Bloodstream Infection. *The American Journal of Tropical Medicine and Hygiene*, **103**, 508-514. <https://doi.org/10.4269/ajtmh.19-0877>
- [23] Giamarellos-Bourboulis, E.J., Netea, M.G., Rovina, N., Akinosoglou, K., Antoniadou, A., Antonakos, N., *et al.* (2020) Complex Immune Dysregulation in COVID-19 Patients with Severe Respiratory Failure. *Cell Host & Microbe*, **27**, 992-1000.e3. <https://doi.org/10.1016/j.chom.2020.04.009>
- [24] Cardinale, V., Capurso, G., Ianiro, G., Gasbarrini, A., Arcidiacono, P.G. and Alvaro, D. (2020) Intestinal Permeability Changes with Bacterial Translocation as Key Events Modulating Systemic Host Immune Response to SARS-CoV-2: A Working Hypothesis. *Digestive and Liver Disease*, **52**, 1383-1389. <https://doi.org/10.1016/j.dld.2020.09.009>
- [25] Wang, J. and Jiang, T. (2025) Risk Factors for Bloodstream Infection in COVID-19 Patients in Intensive Care Units: A Systematic Review and Meta-Analysis. *BMC Infectious Diseases*, **25**, Article No. 13. <https://doi.org/10.1186/s12879-024-10420-1>
- [26] Tabah, A., Buetti, N., Staiquly, Q., Ruckly, S., Akova, M., Aslan, A.T., *et al.* (2023) Epidemiology and Outcomes of Hospital-Acquired Bloodstream Infections in Intensive Care Unit Patients: The EURO-BACT-2 International Cohort Study. *Intensive Care Medicine*, **49**, 178-190. <https://doi.org/10.1007/s00134-022-06944-2>
- [27] Pérez-Crespo, P.M.M., Lanz-García, J.F., Bravo-Ferrer, J., Cantón-Bulnes, M.L., Sousa Domínguez, A., Goikoetxea Aguirre, J., *et al.* (2021) Revisiting the Epidemiology of Bloodstream Infections and Healthcare-Associated Episodes: Results from a Multicentre Prospective Cohort in Spain (PRO-BAC Study). *International Journal of Antimicrobial Agents*, **58**, Article 106352. <https://doi.org/10.1016/j.ijantimicag.2021.106352>
- [28] Buetti, N., Tabah, A., Loiodice, A., Ruckly, S., Aslan, A.T., Montrucchio, G., *et al.* (2022) Different Epidemiology of Bloodstream Infections in COVID-19 Compared to Non-COVID-19 Critically Ill Patients: A Descriptive Analysis of the Eurobact II Study. *Critical Care*, **26**, Article No. 319. <https://doi.org/10.1186/s13054-022-04166-y>
- [29] Toc, D.A., Mihaila, R.M., Botan, A., Bobohalma, C.N., Risteiu, G.A., Simut-Cacuci, B.N., *et al.* (2022) Enterococcus and COVID-19: The Emergence of a Perfect Storm? *International Journal of Translational Medicine*, **2**, 220-229. <https://doi.org/10.3390/ijtm2020020>
- [30] Rangel, K. and De-Simone, S.G. (2022) Acinetobacter Baumannii during COVID-19: What Is the Real Pandemic? *Pathogens*, **12**, Article 41. <https://doi.org/10.3390/pathogens12010041>
- [31] Piantoni, A., Houard, M., Piga, G., Zebian, G., Ruffier des Aimes, S., Holik, B., *et al.* (2023) Relationship between COVID-19 and ICU-Acquired Bloodstream Infections Related to Multidrug-Resistant Bacteria. *Antibiotics*, **12**, Article 1105. <https://doi.org/10.3390/antibiotics12071105>

Appendix

Table S1. PRISMA 2020 checklist.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	First page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6

Continued

Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 6
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 6

RESULTS

Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 23
Study characteristics	17	Cite each included study and present its characteristics.	Page 20
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Suppl 2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 20
	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 20
Results of syntheses	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 8
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 8
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 8

Continued

Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	---
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	---
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 10
	23b	Discuss any limitations of the evidence included in the review.	Page 13
	23c	Discuss any limitations of the review processes used.	Page 13
	23d	Discuss implications of the results for practice, policy, and future research.	Page 14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 6
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	---
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	First page
Competing interests	26	Declare any competing interests of review authors.	First page
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	---