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Emerging Problems in Infectious Diseases

Mortality rates among adults with sepsis and septic shock in Indonesia: a systematic review and meta-analysis

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Abstract

Introduction: Sepsis and septic shock represent a critical global health challenge, accounting for a substantial proportion of patient fatalities worldwide. Despite this, Indonesia lacks a comprehensive, nationwide analysis of the mortality rates associated with these conditions. This study aimed to systematically evaluate the burden of sepsis and septic shock mortality across Indonesia, addressing a crucial gap in the existing healthcare data, which may aid clinical and policy considerations.

Methodology: We searched PubMed, Scopus, DOAJ, and citation lists for studies with sepsis and septic shock mortality rate , focusing on 28-day and in-hospital mortality. Study quality was assessed using the Newcastle-Ottawa Scale, and the protocol was registered with PROSPERO (CRD42025645312).

Results: Overall, 47 studies were included in this review , revealing a pooled 28-day mortality rate of 55.9% (95% CI, 48.7%–63.0%; I^2 = 79.5%) among patients with sepsis and septic shock, as determined by the Sepsis-3, Sepsis 2, and Not-Mentioned criteria. Additionally, the in-hospital mortality rates for the same cohort were higher at 67.4% (95% CI, 62.9%–72.0%; I^2 = 95.02%). Notably, among patients with septic shock specifically, in-hospital mortality reached 77.5% (95% CI, 67.3%–87.8%; I^2 = 91.18%).

Conclusions: Sepsis and septic shock mortality rates in Indonesian adults remain high. These findings underscore the need for enhanced sepsis management protocols, effective resource allocation, and targeted interventions for vulnerable patients.

Key words: sepsis; septic shock; meta-analysis; Indonesia.

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Introduction

Sepsis is a critical condition in which an infection triggers an uncontrolled immune response that leads to the failure of multiple organ systems [1]. Although international initiatives have aimed to lower sepsis-related deaths, the condition continues to be one of the primary causes of mortality among patients in critical care. It remains a major challenge for healthcare systems worldwide [2]. In 2017, approximately 48.9 million sepsis cases were documented globally, leading to nearly 11 million fatalities [3]. A recent meta-analyses indicates that sepsis mortality rates vary by region: North America 19.6%, Europe 23.6%, Australia 18.7%, China 29.0%, and South Korea 30%. Variations in sepsis mortality rates across countries are influenced by disease severity, time to treatment, standard of care, healthcare system, and geographic region. These factors are crucial in shaping patient outcomes and prognosis [4–6].

Understanding the mortality epidemiology of sepsis is crucial to inform healthcare planning, improve clinical decision-making, and develop targeted strategies to reduce preventable deaths in Indonesia. Several studies have explored sepsis mortality in Indonesia; however, a comprehensive, nationwide investigation remains lacking [7,8]. Hence, conducting a comprehensive review is imperative for accurately assessing mortality rates from sepsis and septic shock in Indonesia. To our knowledge, at the time of writing this manuscript, this review is the first to systematically synthesize available data on the subject. This study aims to determine the pooled mortality rates of adult patients with sepsis and septic shock in Indonesia by conducting a systematic review and meta-analysis of available literature. We chose to focus on adult sepsis to ensure clinical and methodological coherence, as adult patients are diagnosed using the Sepsis criteria, which differ from the frameworks used in pediatric or neonatal populations. Focusing on adult mortality rate allows us to directly inform the results of critical care policy, sepsis recognition protocols, and antimicrobial stewardship efforts in Indonesia.

Methodology

Reporting guidelines and protocol registration

This review follows PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [9]. The protocol was registered in advance with PROSPERO (Registration No. CRD42025645312).

Search strategy

We searched PubMed and Scopus databases to identify studies with sepsis and septic shock mortality data. Furthermore, we explored the Directory of Open Access Journals website and performed citation searches of relevant references for the articles included in this review, published from inception through December 2024. We designed our search method by combining Medical Subject Headings (MeSH) that pertain to "sepsis," "septic shock," and "Indonesia." A full breakdown of this approach is available in Table 1.

Eligibility criteria

We included original studies involving adult populations (17 years or older) diagnosed with sepsis and/or septic shock, conducted in Indonesia, and published from the earliest available records through December 2024. We selected December 2024 as the search cut-off to ensure the most comprehensive and up-to-date inclusion of studies published in the existing body of Indonesian sepsis literature. This time point reflects the latest complete calendar year of publications available during the making of this study period and allowed us to incorporate the most recent data in sepsis outcomes. We did not specify an intervention or comparison, as this study is a proportional single-arm meta-analysis. Eligible studies reported mortality outcomes such as in-hospital, 28-day, or 30-day mortality. We included observational study designs such as cohort, case-control, and cross-sectional studies to better reflect real-world clinical outcomes. Studies were excluded if they did not provide adequate data or belonged to categories such as reviews, clinical trials, editorials, case reports, letters, conference abstracts, meta-analyses, or animal studies.

Study selection

Title and abstract screening were performed independently by two reviewers (MRG and LRD). Both reviewers screened all records based on the predefined eligibility criteria. Duplication removal and record screening were performed using the Covidence reference manager [10]. Studies that passed title and abstract screening were retrieved in full text and reassessed for eligibility using the same criteria. The full-text screening was also conducted independently by both reviewers (MRG and LRD) to ensure consistency and minimize bias. Any reviewer discrepancies regarding study inclusion were resolved through discussion and consensus by a third reviewer (AA).

Data extraction

Two reviewers (AA and MRG) were responsible for extracting key information from the eligible studies. The data collected encompassed details such as the author and publication year, study design, number of centers involved, patient care settings (emergency department, general ward, or intensive care unit), Hospital location and provinces, total patient count, mortality statistics, the sepsis diagnostic criteria used, the outcome assessment timeframe (either in-hospital mortality or 28-day mortality), and the timeframe of the study. Any reviewer discrepancies regarding data extraction were resolved through discussion and consensus by a third reviewer (LRD).

Quality assessment

The rigor and methodological integrity of the studies in our inclusion set were systematically appraised by employing the Newcastle-Ottawa Scale, an assessment system in which scores are allocated to three domains: selection, comparability, and outcome. We applied a modified Newcastle-Ottawa scale for cross-sectional studies. Two reviewers (MRG and LRD) independently appraised each of the included studies, with disagreements resolved through discussion or consensus (AA) [11]. Cohort and case-control Studies were classified based on the Newcastle-Ottawa Scale into three quality levels: good quality if they had 3–4 stars in the selection domain, 1–2 in comparability, and 2–3 in outcome; fair quality if they had 2 stars in selection, 1–2 in comparability, and 2–3 in outcome; and poor quality if they had 0–1 stars in selection, or 0 stars in comparability, or 0–1 stars in outcome. For cross sectional studies, a study is

Table 1. Search Strategy of the included studies.

Databases	Search terms
Pubmed	("sepsis" OR "septic shock" OR "bacteremia") AND "indonesia"
scopus	("sepsis" OR "septic shock" OR "bacteremia") AND "indonesia"
DOAJ	"sepsis" AND "indonesia"

considered good quality if it receives 4 - 5 stars in the selection domain, and 1 - 2 stars in the comparability domain, and 2 - 3 stars in the outcome domain; fair quality if it has 2 - 3 stars in the selection domain, and 1 - 2 stars in the comparability domain, and 2 - 3 stars in the outcome domain; and poor quality if it has 0 - 1 star in the selection domain or 0 stars in the comparability domain or 0 - 1 star in the outcome domain. No threshold value was found for the adapted version of the Newcastle–Ottawa scale for cross-sectional studies. Therefore, we evaluated study quality by establishing criteria similar to the Agency for Healthcare Research and Quality (AHRQ) standard for cross-sectional studies.

Statistical analysis

Extensive pooled statistical analyses were carried out to quantify mortality rates in sepsis and septic shock cases, with an emphasis on projecting both in-hospital and 28-day mortality outcomes. To accommodate heterogeneity across studies and ensure robust estimations, a random-effects modelling approach was utilized for mortality rate assessment. However, we used a fixed-effects model in subgroup analysis, where there are only two studies. Distinct analyses were carried out for subgroups: those diagnosed under the Sepsis-3 and Non-Mentioned (NM) Criteria, those categorized by study design into retrospective, prospective, cross-sectional studies, and by the quality of the included studies. We assessed heterogeneity by quantifying it with the I^2 statistic. A Begg funnel plot and Egger's Z test were implemented as analytical tools to assess potential publication bias. All statistical computations were performed using Jamovi version 2.3.28, with a predefined significance criterion of a p below 0.05 to ensure the robustness of the findings [12-14].

Results

Study selection

The search initially identified 754 records. After eliminating 152 duplicates, 551 records were discarded following an abstract and title screening. Following a full article review, an additional 37 records were excluded for reasons including Wrong Population (n = 10), Wrong Outcome (n = 22), and both Wrong Population and Outcome (n = 5). Further searches were conducted through the Websites Directory of Open Access Journals (DOAJ), and citation searching contributed 43 records. Of these, 10 were excluded for reasons such as Wrong Population (n = 7), Wrong Population and Outcome (n = 2), and Wrong Study Design (n = 1). Consequently, this review includes 47 studies that examine mortality associated with sepsis and septic shock. Figure 1 illustrates the process used for selecting studies, which depicts the flowchart of this review.

Figure 1. Studies selection.

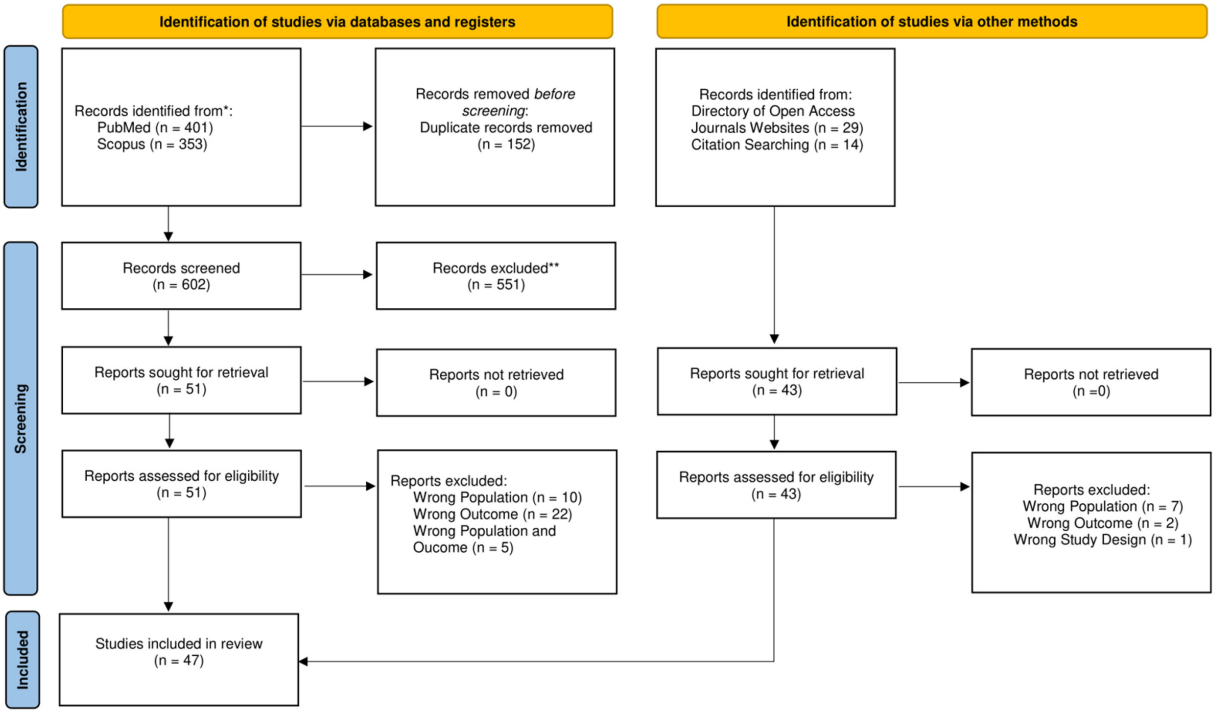


Table 2. Summary of the included studies.

Author, year	Sepsis and Septic Shock Mortality	Total Sepsis and Septic Shock	Septic Shock Mortality	Total Septic Shock	Study Design	Number of Centers, Hospitals, Provinces	Patient Locations	Sepsis Diagnostic Criteria	The time of the outcome measurement	NOS score	Study period
Noviyani *et al*. [19] 2024	57	84	NM	NM	Retrospective cohort	1, Tabanan Hospital, Bali	NM	NM	In-Hospital	8	2020-2022
Rinaldi *et al*. [18] 2022	171	248	NM	NM	Retrospective cohort	1, Cipto Mangunkusumo Hospital, Jakarta	NM	Sepsis-3	In-Hospital	7	January 2016 - October 2022
Farhanah *et al*. [24] 2023	40	59	27	36	Prospective Cohort	1, Dr. Kariadi Hospital, Central Java	ED	Sepsis-3	In-Hospital	7	June-August 2019
Rahasto *et al*. [21] 2019	64	111	64	111	Prospective Cohort	1, Tangerang District General Hospital, Banten	NM	Sepsis-3	In-Hospital	7	December 2013-February 2016
Asdie *et al*. [22] 2023	65	88	NM	NM	Prospective Cohort	1, Dr. Sardjito Hospital, Special Region of Yogyakarta	ICU and Ward	Sepsis-3	28-Day Mortality	8	December 2018 - October 2019
Lestari *et al*. [57] 2021	27	41	NM	NM	Prospective Cohort	1, Dr. Mohammad Hoesin Central Hospital, South Sumatra	ICU	Sepsis-3	28-Day Mortality	7	February - June 2019
Nainggolan *et al*. [23] 2024	287	350	NM	NM	Retrospective cohort	1, Cipto Mangunkusomo Hospital, Jakarta	ICU and Ward	Sepsis-3	In-Hospital	7	January 2020 - December 2022
Farhanah *et al*. [20] 2023	95	211	NM	NM	Prospective Cohort	1, Dr. Kariadi Hospital, Central Java	ICU and Ward	Sepsis-3	28-Day Mortality	9	August 2021 - July 2022
Pradipta *et al*. [25] 2013	41	76	NM	NM	Retrospective cohort	1, Hasan Sadikin Hospital, West Java	NM	NM	In-Hospital	4	January - December 2011
Effendi *et al*. [26] 2022	66	128	NM	NM	Retrospective cohort	1, Cipto Mangunkusumo Hospital, Jakarta	ICU, Ward, and ED	Sepsis-3	28-Day Mortality	6	March 2017 - October 2020
Purba *et al*. [27] 2020	8200	14067	NM	NM	Retrospective cohort	4, Dr. Soetomo Hospital, Universitas Airlangga Hospital, Prof. Dr. Sulianti Saroso Center for Infectious Diseases Hospital, Dr. M. Djamil Hospital, East Java, Jakarta, West Sumatra	ICU and non-ICU	Sepsis-3	In-Hospital	6	1 January 2013 - 31 December 2016
Destiani *et al*. [28] 2017	66	90	NM	NM	Retrospective cohort	1, Public Hospital, West Java	NM	NM	In-Hospital	6	2010 - 2012
Octora *et al*. [29] 2021	253	355	NM	NM	Retrospective cohort	1, Dr. Soetomo Hospital, East Java	ICU	NM	In-Hospital	7	2017-2020
Dewi *et al*. [30] 2018	41	60	26	29	Cross-sectional	1, Dharmais Cancer Hospital, Jakarta	ICU	Sepsis-3	In-Hospital	6	February - May 2017
Hadi and Triyono. [58] 2010	27	50	NM	NM	Retrospective cohort	1, Dr. Soetomo Hospital, East Java	Ward	NM	In-Hospital	4	January - April 2007
Rachman *et al*. [8] 2024	82	107	NM	NM	Retrospective cohort	1, Dr. Hasan Sadikin Hospital, West Java	ICU	NM	In-Hospital	5	1 January 2021 - 31 December 2022
Marzuki *et al*. [31] 2022	45	80	NM	NM	Retrospective cohort	1, Dr. Saiful Anwar General Hospital, East Java	ED	NM	In-Hospital	7	January - June 2019
Hasanah *et al*. [32] 2023	43	63	NM	NM	Retrospective cohort	1, Dr. Wahidin SudiroHusodo General Hospital, South Sulawesi	ICU	Sepsis-3	In-Hospital	5	January 2018 - December 2020
Adani *et al*. [33] 2017	39	48	11	13	Retrospective cohort	1, Dr. Hasan Sadikin General Hospital, West Java	ICU	NM	In-Hospital	5	August - October 2014
Ansari *et al*. [34] 2024	42	47	42	47	Retrospective cohort	1, H. Adam Malik General Hospital, North Sumatra	ICU	NM	In-Hospital	4	January - December 2022
Utami *et al*. [35] 2020	55	100	NM	NM	Retrospective cohort	1, Dr. Mohammad Hoesin Central Hospital, South Sumatra	ICU	NM	28-Day Mortality	7	1 January - 31 December 2018
Lubis *et al*. [36] 2024	34	38	NM	NM	Prospective Cohort	1, H. Adam Malik Hospital, General Hospital, North Sumatra	ICU	NM	In-Hospital	6	April - June 2023
Zharfan *et al*. [37] 2019	22	50	NM	NM	Case-Control	1, Dr. Soetomo Hospital, East Java	NM	NM	28-Day Mortality	5	2014-2015
Suranadi *et al*. [38] 2022	131	228	NM	NM	Retrospective cohort	1, Sanglah General Hospital, Bali	ICU	Sepsis-3	28-Day Mortality	8	1 January 2018 - 31 December 2022
Wiraatmaja *et al*. [39] 2014	19	50	NM	NM	Prospective Cohort	1, Dr. Hasan Sadikin Hospital, West Java	ICU	Sepsis-2	28-Day Mortality	9	Agustus 2013 - January 2014
Maghfirah *et al*. [40] 2021	159	207	NM	NM	Cross-sectional	1, Dr. Wahidin Sudirohusodo Hospital, South Sulawesi	NM	NM	In-Hospital	5	1 January 2018 - 31 December 2020
Sulaiman *et al*. [59] 2020	40	59	NM	NM	Retrospective Cohort	1, Dr. Mohammad Hoesin Central Hospital, South Sumatra	ICU	NM	28-Day Mortality	7	February - Agustus 2019
Hanif *et al*. [41] 2024	53	71	NM	NM	Cross-sectional	1, H. Adam Malik General Hospital, North Sumatra	ICU	Sepsis-3	In-Hospital	6	2021-2022
Marzuki *et al*. [42] 2019	40	75	NM	NM	Prospective Cohort	1, Dr. Saiful Anwar General Hospital, East Java	HCU	Sepsis-3	In-Hospital	9	1 September 2018 - 31 Agustus 2019
Masyrifah *et al*. [43] 2022	79	110	NM	NM	Cross-sectional	1, Fatmawati Central General Hospital, Jakarta	NM	NM	In-Hospital	6	January - December 2020
Rahajeng *et al*. [60] 2020	88	93	34	34	Cross-sectional	1, Dr. Wahidin sudiroHusudo, South Sulawesi	ICU	NM	In-Hospital	5	January 2017 - April 2019
Jannah *et al*. [44] 2021	113	221	NM	NM	Cross-sectional	1, Dr. Soetomo General Hospital, East Java	Ward	NM	In-Hospital	5	January - December 2017
Katu *et al*. [45] 2015	63	126	57	75	Retrospective cohort	1, Cipto Mangunkusomo Hospital, Jakarta	ICU and Ward	NM	In-Hospital	7	January 2011 - July 2012
Lardo *et al*. [46] 2020	134	210	NM	NM	Retrospective Cohort	1, Army Central Gatot Soebroto Hospital, Jakarta	ICU and Ward	Sepsis-3	In-Hospital	6	2017 - 2019

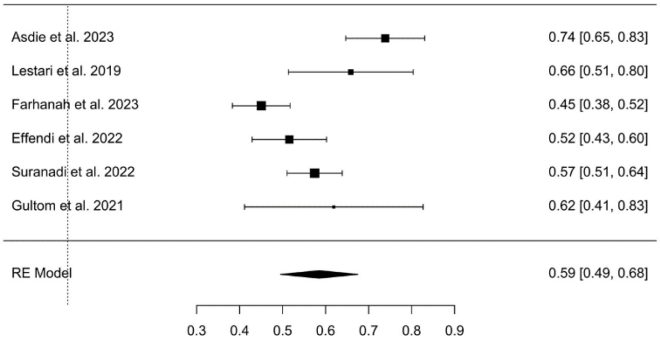
Table 2 (continued). Summary of the included studies.

Author, year	Sepsis and Septic Shock Mortality	Total Sepsis and Septic Shock	Septic Shock Mortality	Total Septic Shock	Study Design	Number of Centers, Hospitals, Provinces	Patient Locations	Sepsis Diagnostic Criteria	The time of the outcome measurement	NOS score	Study period
Gultom *et al*. [47] 2021	13	21	NM	NM	Prospective Cohort	1, Dr. Mohammad Hoesin Central Hospital, North Sumatra	ICU, ED and Ward	Sepsis-3	28-Day Mortality	6	December 2018 - February 2019
Raniputri *et al*. [48] 2022	43	55	NM	NM	Retrospective cohort	1, Dr. Moewardi General Hospital, Central Java	NM	NM	In-Hospital	6	July - December 2019
Dharmawan *et al*. [49] 2021	23	39	5	6	Retrospective cohort	1, Tarakan District Hospital, North Kalimantan	NM	NM	In-Hospital	4	January – December 2018
Isnaini and Harahap. [50] 2015	40	45	NM	NM	Cross-sectional	1, Dr. Kariadi Hospital, Central Java	ICU	NM	In-Hospital	5	1 January - 30 June 2013
Gusriadi *et al*. [51] 2022	22	56	NM	NM	Retrospective cohort	1, Dr. Wahidin sudiro Husudo Hospital, South Sulawesi	ICU	NM	In-Hospital	5	January - December 2021
Vivianni and Farhanah. [52] 2016	40	47	9	10	Case-Control	1, Dr. Kariadi Hospital, Central Java	ICU	NM	In-Hospital	6	April - May 2016
Dafitri *et al*. [61] 2020	18	43	NM	NM	Cross-sectional	1, Dr. M.Djamil Hospital, West Sumatra	Ward	NM	In-Hospital	4	September 2019 - February 2020
Pramono *et al*. [53] 2024	47	62	NM	NM	Cross-sectional	1, Yogyakarta City Hospital, Special Region of Yogyakarta	ICU	NM	In-Hospital	4	January - December 2023
Wicaksono *et al*. [7] 2022	54	110	28	41	Cross-sectional	1, Type B private Hospital, Banten	ICU	NM	In-Hospital	5	January - December 2020
Kahar *et al*. [54] 2023	42	80	NM	NM	Retrospective cohort	1, Dr. M Djamil Hospital, West Sumatra	ICU	Sepsis-3	In-Hospital	6	July - September 2022
Harsini *et al*. [55] 2024	365	615	78	171	Retrospective cohort	1, Dr. Moewardi Hospital, Central Java	ICU, HCU, and Ward	Sepsis-3	In-Hospital	8	1 January - 31 December 2022
Tameru *et al*. [56] 2022	84	106	NM	NM	Retrospective cohort	1, Dr. Moewardi Hospital, Central Java	ICU	NM	In-Hospital	7	1 July 2017 - 30 June 2018
Ayuni and Fadrian. [62] 2024	53	99	NM	NM	Cross-sectional	1, Dr. M. Djamil Padang Hospital, West Sumatra	Ward	NM	In-Hospital	4	August – December 2022

Study characteristics

In the collection of 47 studies analyzed, the breakdown of methodologies includes 9 prospective cohort studies, 25 retrospective cohort studies, 11 cross-sectional studies, two case-control studies, and this review only included one multicenter study. Most of these studies were situated within clinical settings, predominantly Intensive Care Units (ICU), general hospital wards, and Emergency Departments (ED). Regarding diagnostic criteria, 18 of the studies explicitly employed Sepsis-3 criteria, while 28 studies did not specify their criteria for diagnosing sepsis; one utilized the earlier Sepsis-2 criteria. Mortality assessments varied across the studies: 10 used a 28-day mortality assessment framework, whereas 37 studies either used an in-hospital mortality assessment or did not specify the parameters of the mortality assessment used. We found no study where both 28-day and in-hospital mortality were reported in a single study, no eligible study reported 30-day mortality. Most studies in Indonesia do not specify whether they used 28-day, 30-day, or in-hospital mortality. Therefore, we treat all mortality that does not specify this information as in-hospital mortality. In this review, most studies did not report mortality specifically for sepsis patients alone; instead, they provided combined data on mortality for both sepsis and septic shock patients, thereby necessitating the aggregation of their mortality data under the combined category of sepsis and septic shock mortality. However, some studies did provide distinct data concerning mortality in septic shock patients alone, allowing us to report separately on mortality specific to septic shock. The majority of the studies are conducted in tertiary public or university hospitals. Table 2 provides an overview of the key features of the included studies.

Figure 2. Twenty-eight-day sepsis and septic shock patient mortality using the sepsis-3 criteria.



Sepsis and Septic Shock Mortality Rate

The Sepsis-3 criteria identified a 28-day mortality

rate of 58.5% (95% CI 49.5% - 67.5%; I^2 = 81.7%) in patients with sepsis and septic shock, as detailed in Table 3 and Figure 2. The NM criteria found a 28-day mortality of 55.9% (95% CI 43% - 68.8%; I^2 = 72.28%) Additionally, when including data from studies employing Sepsis-3, Sepsis 2 and Not Mentioned (NM) criteria, we found the 28-day mortality rate to be at 55.9% (95% CI, 48.7%–63%; I^2 = 79.5%), as shown in Figure 3. Subgroup analysis revealed a 28-day mortality of 57% (95% CI, 51.9%–62.1%; I^2 = 25.59%) in retrospective cohort studies, whereas it was at 56.7% (95% CI, 42.9%–70.4%; I^2 = 85.99%) in prospective studies, we also found that Good Quality studies showed 28 day mortality rate of 57.5% (95% CI, 48.2%–66.8%; I^2 = 85.14%), whereas Fair Quality studies showed a 28 day mortality rate of 49.5% (95% CI, 38%–60.9%; I^2 = 49.6%) according to the data presented in Table 3.

The reviewed studies reported an in-hospital mortality rate of 64.7% (95% CI 59.6% – 69.9%; I^2 = 91.07%) for patients with sepsis and septic shock

Figure 3. Twenty-eight-day sepsis and septic shock mortality using the sepsis-3 and Not Mentioned Criteria. RE, Random Effect.

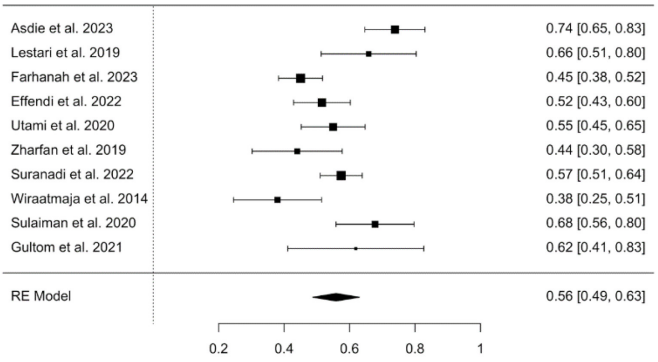


Table 3. Subgroup Analysis of the Included Studies.

Characteristic	No. of Studies	Proportion (95 % CI)	*p*	I^2 (%)
Sepsis and septic shock				
28-Day Mortality				
Criteria				
Sepsis-3, Sepsis 2 & NM	10	55.9 (48.7–63.0)	< 0.01	79.5
Sepsis-3	6	58.5 (49.5–67.5)	< 0.01	81.7
NM	3	55.9 (43 – 68.8)	< 0.01	72.28
Study Design				
Prospective	5	56.7 (42.9–70.4)	< 0.01	85.99
Retrospective	4	57.0 (51.9–62.1)	< 0.01	25.59
Quality				
Fair	2	49.5 (38.0-60.9)	< 0.01	49.6
Good	7	57.5 (48.2-66.8)	< 0.01	85.14
In-Hospital Mortality				
Criteria				
Sepsis-3 & NM	37	67.4 (62.9–72.0)	< 0.01	95.02
Sepsis-3	12	64.7 (59.6–69.9)	< 0.01	91.07
NM	25	68.7 (62.4 -75.0)	< 0.01	92.58
Study Design				
Prospective	4	67.1 (51.2–83.1)	< 0.01	89.27
Retrospective	21	66.2 (60.9–71.6)	< 0.01	94.46
Cross-Sectional	11	68.2 (58.2–78.3)	< 0.01	93.97
Quality				
Poor	21	67.4 (60.4-74.5)	< 0.01	92.37
Good	14	66.9 (60.9-72.9)	< 0.01	94.89
Fair	2	70.6 (63.8-77.5)	< 0.01	0
Septic Shock				
In-Hospital Mortality				
Criteria				
Sepsis-3 & NM	11	77.5 (67.3–87.8)	< 0.01	91.18
Sepsis-3	4	66.6 (47.4–85.7)	< 0.01	93.14
NM	7	85.1 (76.2-94.1)	< 0.01	76.56
Study Design				
Prospective	2	62.8 (55.1–70.5)	< 0.01	75.37
Retrospective	5	74.6 (57.5–91.7)	< 0.01	90.61
Cross-Sectional	3	86.5(69.3–103.7)	< 0.01	89.89
Quality				
Good	4	63.0 (48.5-77.6)	< 0.01	88.87
Poor	6	87.1 (77.4-96.9)	< 0.01	73.51

CI: Confidence interval; NM: Not Mentioned.

diagnosed according to the Sepsis-3 criteria as shown in Figure 4, we also found in-hospital mortality rate of 68.7% (95% CI 62.4% – 75.0%; I^2 = 92.58%) for the NM criteria as depicted in Table 3. Additionally, when data from studies using Sepsis-3 and NM criteria were combined, the in-hospital mortality rate increased to 67.4% (95% CI, 62.9%–72.0%; I^2 = 95.02%), as shown in Figure 5. Subgroup analysis further delineated in-hospital mortality rates: 66.2% (95% CI, 60.9%–71.6%; I^2 = 94.46%) in retrospective cohort studies, 67.1% (95% CI, 51.2%–83.1%; I^2 = 89.27%) in prospective studies, and 68.2% (95% CI, 58.2%-78.3%; I^2 = 93.97%) in cross-sectional studies, between Good and Poor Quality studies, we found Good quality studies to have in hospital mortality rate of 66.9% (95% CI, 60.9%–72.9%; I^2 = 94.89%), poor quality studies to have in hospital mortality rate of 67.4% (95% CI, 60. 4%–74.5%; I^2 = 92.37%), Fair quality studies to have in hospital mortality rate of 70.6% (95% CI, 63.8%–77.5%; I^2 = 0 %) all noted in Table 3.

Septic Shock Mortality Rate

The analysis was limited to in-hospital mortality outcomes for septic shock. Cases diagnosed based on the Sepsis-3 criteria showed a mortality rate of 66.6% (95% CI 47.4% - 85.7%; I^2 = 93.14%) as depicted in Figure 6, When incorporating only NM criteria we found in hospital mortality rate of 85.1% (95% CI 76.2% - 94.1%; I^2 = 76.56%) as detailed in Table 3. Furthermore, when considering data including both Sepsis-3 and NM criteria for septic shock, the in-hospital mortality rate increased to 77.5% (95% CI, 67.3%–87.8%; I^2 = 91.18%), highlighted in Figure 7. Subgroup analysis revealed varying mortality rates: 74.6% (95% CI, 57.5%–91.7%; I^2 = 90.61%) in retrospective cohort studies, 62.8% (95% CI, 55.1%–70.5%; I^2 = 75.37%) in prospective studies, and a notably higher 86.5% (95% CI, 69.3%-103.7%; I^2 = 89.89%) in cross-sectional studies, in the Good Quality studies we found in hospital mortality rate of 63.0% (95% CI, 48.5%-77.6%; I^2 = 88.87%) whereas in Poor Quality studies we found in hospital mortality rate of 87.1% (95% CI, 77.4%-96.9%; I^2 = 73.51%) documented in Table 3.

Figure 4. In-hospital sepsis and septic shock mortality using sepsis-3 criteria.

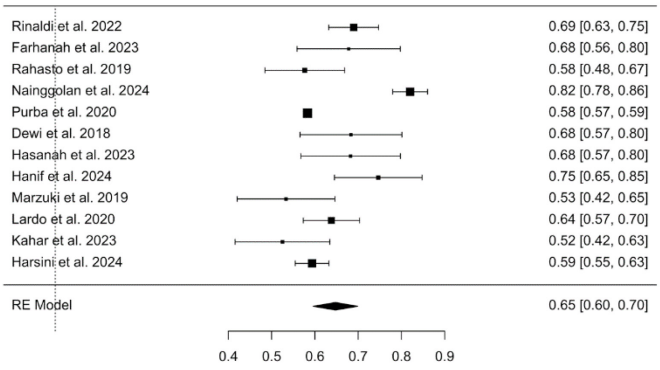


Figure 5. In-hospital mortality from sepsis and septic shock using the sepsis-3 and Not Mentioned criteria. RE, Random Effect.

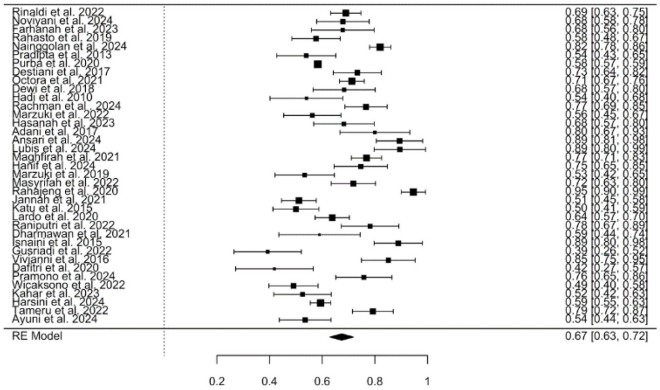


Figure 6. In-hospital septic shock mortality by including sepsis-3 criteria.

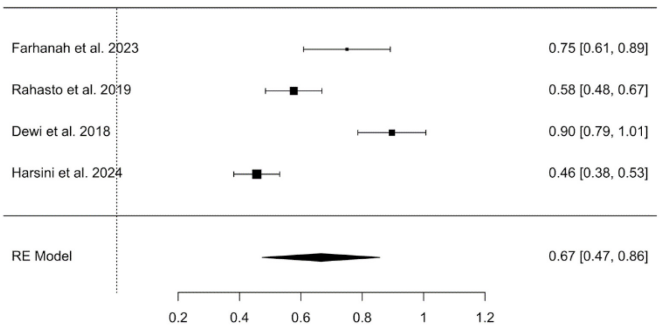


Figure 7. In-hospital mortality from septic shock using the sepsis-3 and Not Mentioned criteria. RE, Random Effect.

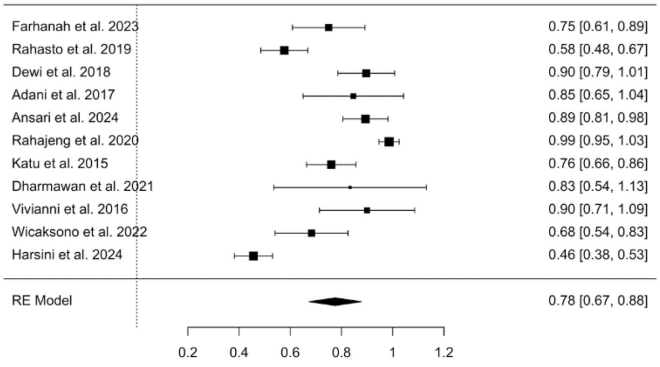


Table 4. Newcastle Ottawa scale score for cross-sectional studies.

Author	Selection				Comparability	Outcome		Total	
	Representatives of the sample	Sample size justified	Non responded	Ascertainment of exposure	Confounding controlled	Outcome assessment	Statistics		
Dewi *et al*. 2018	★		★	★	★	★	★	6	Fair
Maghfirah *et al*. 2021	★		★	★		★	★	5	Poor
Hanif *et al*. 2024	★	★	★	★		★	★	6	Poor
Masyrifah *et al*. 2022	★		★	★	★	★	★	6	Fair
Rahajeng *et al*. 2020	★		★	★		★	★	5	Poor
Jannah *et al*. 2021	★		★	★		★	★	5	Poor
Isnaini *et al*. 2015	★		★	★		★	★	5	Poor
Dafitri *et al*. 2020			★	★		★	★	4	Poor
Pramono *et al*. 2024			★	★		★	★	4	Poor
Wicaksono *et al*. 2022	★		★	★		★	★	5	Poor
Ayuni *et al*. 2024	★			★		★	★	4	Poor

Table 5. Newcastle Ottawa scale score for Case-Control.

Author	Selection				Comparability	Exposure			Total	
	Case definition	Representativeness	Control selection	Control definition	Control for important factor or additional factor	Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-response rate		
Zharfan *et al*. 2019	★	★			★	★		★	5	Fair
Vivianni *et al*. 2016	★		★	★		★	★	★	6	Poor

Figure 8. Twenty-eight-day mortality for sepsis and septic shock patients using Sepsis-3 and Not Mentioned Criteria.

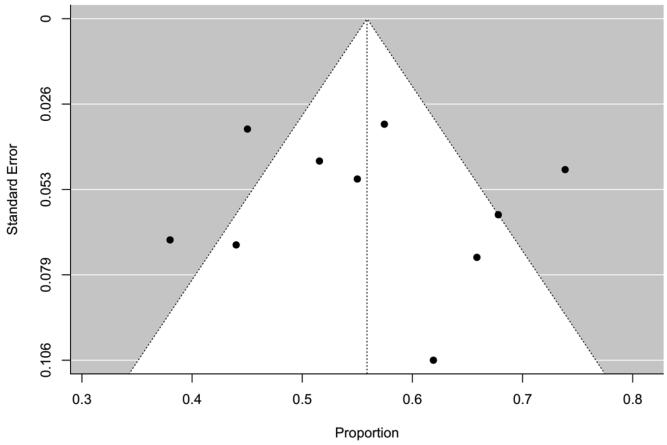


Figure 9. In-Hospital mortality for sepsis and septic shock patients using Sepsis-3 and Not Mentioned Criteria.

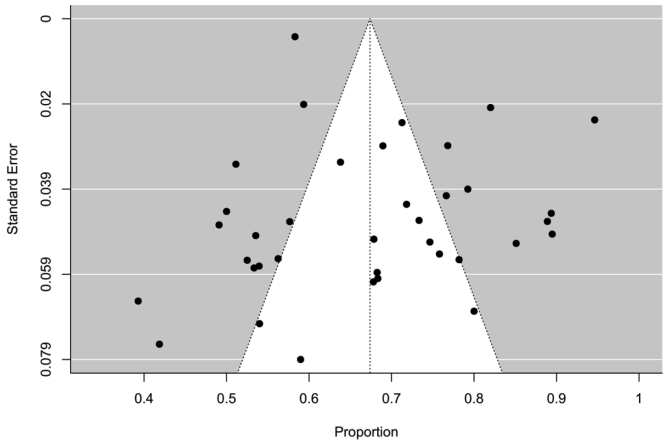
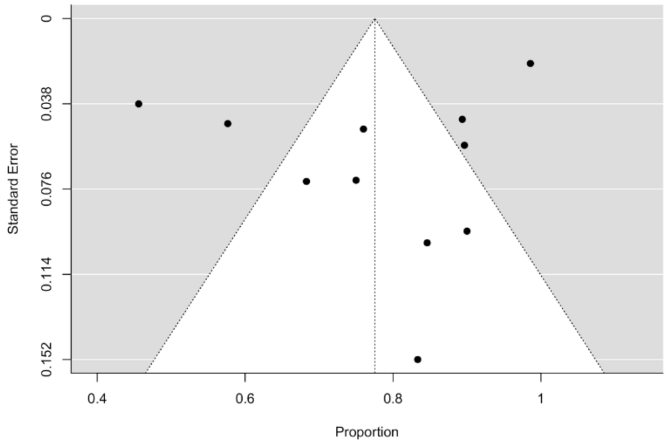


Figure 10. In-Hospital mortality septic shock patients using Sepsis-3 and Not Mentioned Criteria.



Quality assessment

The Newcastle-Ottawa Scale assessment showed that cross-sectional studies had scores ranging from 4 to 6, with most scoring 5. The case-control studies received scores of 5 and 6. Cohort studies had a wider range of scores, from 4 to 9, with several studies reaching the maximum score. Overall, cohort studies tended to have higher scores compared to cross-sectional and case-control studies, as detailed in Tables 4-6. 21 of the 34 cohort studies included in this review were rated as good quality, with the rest being rated as poor quality. In contrast, nine cross-sectional and one case-control study were rated poor quality, with the rest of the cross-sectional and case-control studies rated fair quality, largely due to weaknesses in sample justification, exposure ascertainment, and lack of adjustment for confounders. As a result, findings derived from these designs were to be interpreted cautiously.

Publication bias

The funnel plot illustrating 28-day mortality in sepsis and septic shock patients appears symmetrical. Additionally, the Egger test showed no statistical significance ($Z = 0.226$, $p = 0.821$), indicating a low probability of publication bias. The funnel plots for in-hospital mortality in both sepsis and septic shock patients, as well as those specifically with septic shock, demonstrate noticeable asymmetry. However, the Egger Test for in-hospital mortality for sepsis and septic shock patients ($Z = -1.704$, $p = 0.088$) and septic shock specifically ($Z = 0.368$, $p = 0.713$) showed no statistical significance in publication bias. Funnel plots are provided in Figures 8-10.

Discussion

This study represents the first comprehensive review investigating mortality rates among individuals affected by sepsis and septic shock in Indonesia. Our

Table 6. Newcastle Ottawa scale score for Cohort.

Author	Selection			Comparability		Outcome			Total	
	Representativeness of the exposed cohort	Selection of the unexposed cohort	Ascertainment of exposure	Outcome of interest not present at start of study	Control for important factor or additional factor	Outcome assessment	Follow-up long enough for outcome to occur	Adequacy of follow-up of cohorts		
Rinaldi *et al*. 2022	★		★	★	★★	★		★	7	Good
Noviyanti *et al*. 2024	★	★	★	★	★	★	★	★	8	Good
Farhanah *et al*. 2023	★	★	★	★	★	★		★	7	Good
Rahasto *et al*. 2019	★		★	★	★	★	★	★	7	Good
Asdie *et al*. 2023	★	★	★	★	★	★	★	★	8	Good
Lestari *et al*. 2019	★		★	★	★	★	★	★	7	Good
Nainggolan *et al*. 2024	★		★	★	★★	★		★	7	Good
Farhanah *et al*. 2023	★	★	★	★	★★	★	★	★	9	Good
Pradipta *et al*. 2013	★		★			★		★	4	Poor
Effendi *et al*. 2023	★	★	★			★	★	★	6	Poor
Purba *et al*. 2020	★	★	★		★	★		★	6	Good
Destiani *et al*. 2017	★	★	★		★	★		★	6	Good
Octora *et al*. 2021	★	★	★		★★	★		★	7	Good
Hadi *et al*. 2010	★		★			★		★	4	Poor
Rachman *et al*. 2024	★	★	★			★		★	5	Poor
Marzuki *et al*. 2022	★	★	★		★★	★		★	7	Good
Hasanah *et al*. 2023	★	★	★			★		★	5	Poor
Adani *et al*. 2017	★		★	★		★		★		Poor
Ansari *et al*. 2024	★		★			★		★	4	Poor
Utami *et al*. 2020	★	★	★		★★	★		★	7	Good
Lubis *et al*. 2024	★		★	★	★	★		★	6	Good
Suranadi *et al*. 2022	★	★	★		★★	★	★	★	8	Good
Wiraatmaja *et al*. 2014	★	★	★	★	★★	★	★	★	9	Good
Sulaiman *et al*. 2020	★	★	★		★	★	★	★	7	Good
Marzuki *et al*. 2019	★	★	★	★	★★	★	★	★	9	Good
Katu *et al*. 2019	★	★	★		★	★	★	★	7	Good
Lardo *et al*. 2020	★	★	★			★	★	★	6	Poor
Gultom *et al*. 2021			★	★	★	★	★	★	6	Fair
Raniputri *et al*. 2022	★	★	★			★	★	★	6	Poor
Dharmawan *et al*. 2021			★			★	★	★	4	Poor
Gusriadi *et al*. 2022		★	★			★	★	★	5	Poor
Kahar *et al*. 2023		★	★	★		★	★	★	6	Poor
Harsini *et al*. 2024	★	★	★		★★	★	★	★	8	Good
Tameru *et al*. 2024	★	★	★		★	★	★	★	7	Good

analysis reveals a pooled 28-day mortality rate of 55.9% and an in-hospital mortality rate of 67.4% for these patients. Notably, for septic shock specifically, the available data only reported in-hospital mortality, which was found to be 77.5%. These findings describe the clinical prognosis of sepsis and septic shock patients in Indonesia; furthermore, to our knowledge at the time of writing this manuscript, no national cohort studies are available for direct comparison, indicating a gap in epidemiological data.

Our study demonstrated that sepsis mortality rates in Indonesia were higher than those documented in previous meta-analyses from other regions, such as Australia (18.7%), the United States (19.6%), China (29.1%), Europe (23.6%), and South Korea (24.8%) [4–6]. When compared to global estimates in 2017, our study reported a higher reported mortality rate; the Global Burden of Disease Study reported an overall sepsis-related mortality rate of 19.7% [3]. Similarly, the mortality rate among septic shock patients in our study is high compared to other meta-analyses figures. For instance, regions such as North America (33.7%), Australia (26.4%), China (35.9%), South Korea (25.1%), and Europe (32.5%) report lower rates [4–6]. Also, a key finding from our study is that in-hospital mortality in patients with sepsis and septic shock was greater than the 28-day mortality rate. The higher in-hospital mortality rate compared to 28-day mortality rate likely reflects differences in the data capture time rather than a true survival paradox. In-hospital mortality in this meta-analysis, data were reported from tertiary or ICU settings that most likely treat the most critically ill patients, resulting in a higher early death rate. In contrast, 28-day mortality may miss deaths that occur after early discharge, especially where post-discharge follow-up is limited. These factors suggest that these results need to be interpreted cautiously. However, this trend is consistent with findings from prior meta-analyses, further reinforcing the pattern observed in global sepsis mortality research [5,6,15]. Additionally, the comparisons with high-income country settings should be interpreted cautiously, given structural differences in health-system capacity, GDP per capita, ICU bed density, referral and discharge practices, case-mix, and antimicrobial resistance patterns, all of which plausibly influence observed mortality independent of bedside care quality. One potential explanation for these high mortality rates in our analysis is that the studies included in our analysis encompassed cases of sepsis and septic shock, potentially contributing to increased heterogeneity and an artificially inflated mortality rate. Additionally, as our analysis spans studies conducted from inception through the end of 2024, it incorporates data based on multiple sepsis diagnostic criteria, further introducing variability and heterogeneity across the included studies. To our knowledge, at the time of this writing this manuscript, there are no meta-analyses regarding sepsis mortality rates from other Southeast Asian countries for comparison to our study.

Several determinants contribute to Indonesia's high sepsis-related mortality rates, with delayed recognition and suboptimal management being critical issues. These issues are attributed mainly to constrained healthcare resources and insufficient training among medical personnel. A qualitative investigation identified multiple barriers, including the incomplete execution of the hour-1 sepsis bundle, deficiencies in clinical knowledge, financial constraints, inadequate healthcare infrastructure, and fragmented coordination among healthcare providers [16]. Furthermore, specific high-risk patients, particularly those with comorbidities, exhibit markedly increased mortality rates [17]. These findings underscore the critical necessity for improved sepsis management protocols, efficient resource allocation, and targeted interventions targeting vulnerable patient populations to mitigate the burden of sepsis-related mortality in Indonesia.

Our findings highlight that sepsis and septic shock mortality rates in Indonesia are high. This not only contributes new epidemiological data to the global sepsis literature, particularly from low- and middle-income and developing countries, but also underscores systemic issues in sepsis management across Indonesian healthcare facilities. For clinical practice, our results call for urgent implementation of standardized early recognition protocols, wider training among healthcare workers, and investments in diagnostic and critical care infrastructure.

This study has several limitations. First, the included analyses with high heterogeneity need to be considered, with an I^2 score surpassing 75% in all but five subgroup analyses. A major contributor to this variability is the diversity in study designs, disease characteristics, and severity. Furthermore, discrepancies in the definition of sepsis compound this issue, as the Sepsis-3 criteria were only established in 2016. The lack of uniform diagnostic standards likely influenced the wide range of reported mortality rates, necessitating a stratified analysis with studies that applied the Sepsis-3 criteria explicitly. Second, the potential for data duplication remains a concern, as single-center investigations utilize overlapping datasets. Third, this meta-analysis did not account for

individual patient characteristics, such as medical history and variations in clinical care, both of which are significant determinants of sepsis-related mortality. Fourth, most included studies in this analysis were conducted in tertiary hospitals or high-performing institutions, while data from lower-resource facilities were not included. This selective representation may have resulted in an inaccurate overall sepsis mortality count. Fifth, although we made every effort to conduct a comprehensive search, we acknowledge that some studies may have been inadvertently omitted due to methodological limitations.

Future research should aim to conduct large-scale, multicenter prospective studies that reflect the diversity of healthcare settings in Indonesia, including underrepresented rural and primary care hospitals. Moreover, studies exploring patient-level predictors of mortality, such as comorbidities, delay in diagnosis, antimicrobial resistance patterns, and adherence to treatment protocols, are urgently needed. Implementation science research is also recommended to evaluate the real-world effectiveness of sepsis bundles, early warning scores, and task-shifting strategies in improving sepsis outcomes, particularly in resource-limited settings.

Conclusions

To conclude, this study is the first systematic review and meta-analysis to evaluate the sepsis mortality rate in Indonesia in-depth. The analysis identified a pooled 28-day mortality rate of 55.9%, alongside an in-hospital mortality rate of 67.4% among individuals diagnosed with sepsis and septic shock, underscoring the critical burden of the condition in this region. Specifically, in cases of septic shock, in-hospital mortality rose to 77.5%. These results emphasize a higher burden of sepsis-related mortality in Indonesia compared to reported rates in North America, Europe, China, and South Korea, highlighting the critical need for enhanced sepsis management strategies.

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Conflict of interest

No conflict of interest is declared.

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