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Hospital-related costs of sepsis around the world: A systematic review exploring the economic burden of sepsis

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ABSTRACT

Aim: The aim of this study was to examine the quality of manuscripts reporting sepsis health care costs and to provide an overview of hospital-related expenditures for sepsis in adult patients around the world.
Methods: We systematically searched the PubMed, EMBASE, Cochrane and Google Scholar to identify relevant studies between January 2010 and January 2022. We selected articles that provided costs and cost-effectiveness analyses, defined sepsis and described their cost calculation method. All costs were adjusted to 2020 US dollars. Medians and interquartile ranges (IQRs) for various costs of sepsis were calculated. The quality of economic studies was assessed using the Drummond 10-item checklist.
Results: Overall, 26 studies met our eligibility criteria. The mean total hospital costs per patient varied largely, between €1101 and €91,951. The median (IQR) of the total sepsis costs per country were €36,191 (€17,158 - €53,349), which equals €50 (€34 - €84) per capita annually. The relative amount of healthcare budget spent on sepsis was 2.65%, which equals 0.33% of the gross national product (GNP).
Conclusion: While general sepsis costs are high, there is considerable variability between countries regarding the costs of sepsis. Further studies examining the impact on sepsis costs, especially on the general ward, can help justify, design and monitor initiatives on prevention, diagnosis, and treatment of this time-critical and potentially preventable disease.

1. Introduction

Sepsis is a life-threatening syndrome of organ dysfunction caused by a dysregulated host-response to an infection [1]. Sepsis recognition and management is a major challenge for healthcare systems worldwide. Patients with sepsis need immediate treatment to combat the infection and to reverse life-threatening organ dysfunction. Sepsis is the leading cause of death in critically ill patients, with a mortality rate as high as 46.4% [1]. depending on its severity, which is determined by the presence and extent of acute organ dysfunction. The need for support of vital organs often necessitates admission to the intensive care unit (ICU) or medical wards and may necessitate prolonged use of these costly healthcare facilities; one in five patients with an infection deteriorates within 48 h after emergency department (ED) admission and may need admission to the ICU [1].

In 2017, the World Health Organization (WHO) presented a resolution in which sepsis was stated as a threat for global health [2]. This resolution emphasizes the importance of improved prevention, diagnosis, management and in particularly the healthcare budget of sepsis. However, recent incidence numbers and costs even underestimate the full burden of sepsis, as one should also take patients with covid-19 and multiple organ failure (i.e., more than lung failure) into account, as these cases should be defined as sepsis. The numbers of this complication of covid-19 are yet to come and will raise the global burden of sepsis even more.

Since the global burden of sepsis is large, sepsis has become an important point of attention for many healthcare institutions. Multiple studies have estimated the costs associated with sepsis, which seem to be large given the relatively high incidence and the advanced medical care needed for more severe cases. The relatively high healthcare expenditures for sepsis, may not only affect sepsis care, but can also be a threat to the total healthcare budget [1] and thereby also affect the

Abbreviations: ACCP, American College of Chest Physicians; ED, Emergency Department; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ICU, Intensive Care Unit; GNP, Gross National Product; OECD, Organization for Economic Co-operation and Development; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses; SCCM, Society of Critical Care Medicine; WHO, World Health Organization.

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rest of the health care system. Yet, precise healthcare related costs of sepsis are not available due to both controversy regarding the definition of sepsis as well as the nature of sepsis, which is typically accompanied by preexisting comorbidities and acute complications. Ageing of the population, leading to larger number of patients with comorbidities, led to growth in both sepsis incidence and in sepsis severity over the past years [1]. Consequently, efforts to increase life span that inadvertently leads to an aged population, will also augment the incidence of sepsis, severity of sepsis, and necessity of advanced care and ICU admission, thus putting even more pressure on health care budgets in the nearby future.

In order to keep health care affordable, it is critical to gain insight into the costs of sepsis and its determinants. Comprehensive knowledge of the global and national burden of sepsis is crucial to justify, design and monitor initiatives on prevention, diagnosis, and treatment of this time-critical and often preventable disease. Accurate national estimates regarding the epidemiology are important to appropriate allocate resources, clinical treatment initiatives and inform and monitor health policy interventions. Several complicating factors have to be taken into account when calculating and comparing health care expenditures between countries. First, national reported health care costs cannot be directly applied to other countries, because of different treatment guidelines and local prices. Second, previous studies used data from (before) the 2000s, which are no longer representative of current health care. Third, data on health care costs related to sepsis outside the ICU are scare, although the majority of sepsis patients are admitted to a general ward. Here, we aimed to investigate and provide an overview of hospital-related expenditures for sepsis in adult patients around the world. Therefore, we performed a systematic review of literature to examine the quality of manuscripts reporting sepsis health care costs and obtain comprehensive insight in global health care expenditures for sepsis in adult patients.

2. Methods

2.1. Literature study

2.1.1. Study design

The systematic literature search and review was conducted according to accepted guidelines [3]. This review has been guided by the PRISMA (Preferred Reporting Items for Systematic Reviews and

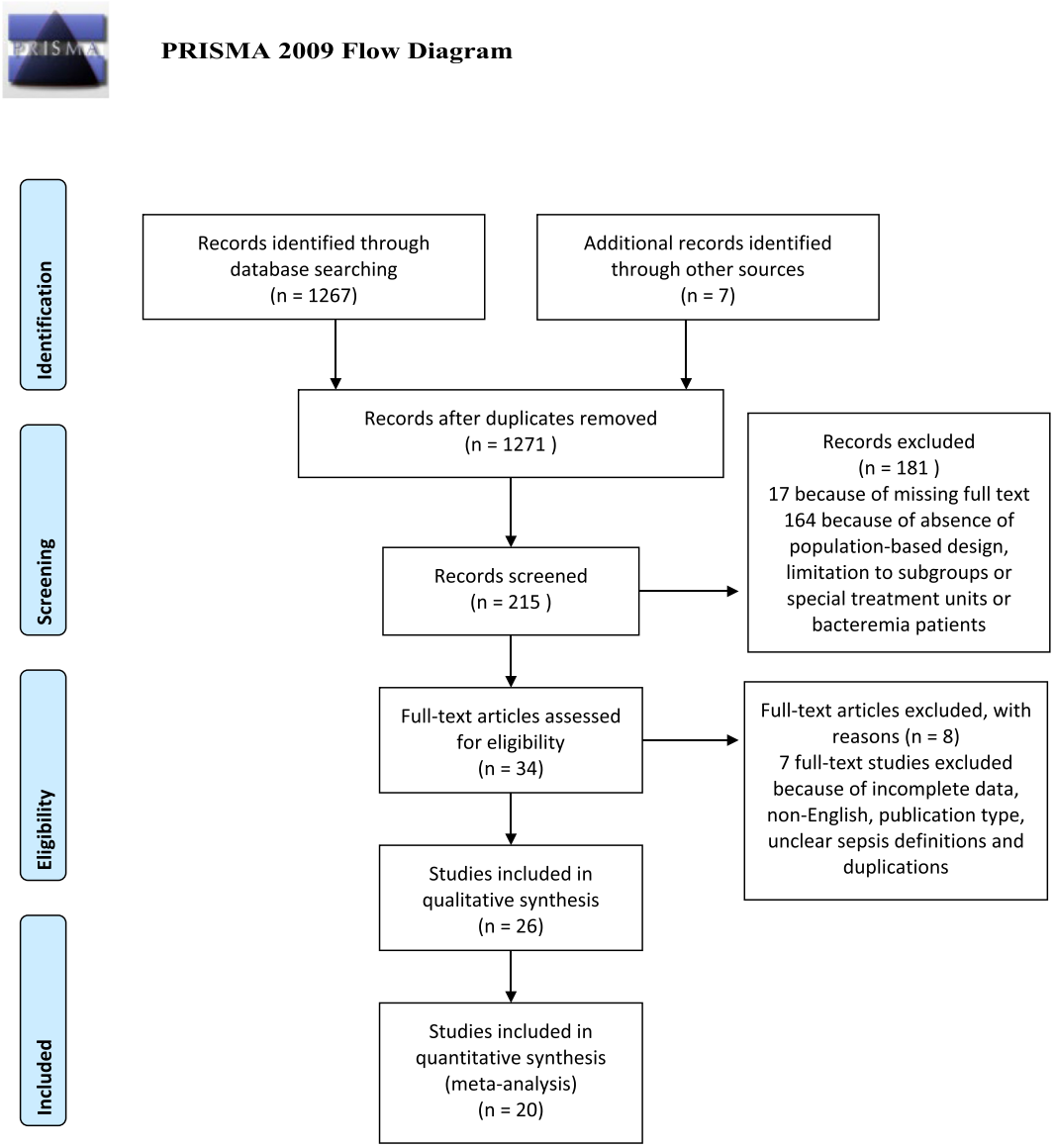

Fig. 1. PRISMA 2009 flow diagram.

Meta-analyses) statement (Fig. 1) [4]. This review is registered in PROSPERO (Supplementary protocol 1) [5].

2.1.2. Data sources

An extensive search of the literature was conducted using PubMed, EMBASE, Cochrane and Google Scholar to identify relevant studies between January 2010 and January 2022. Various combinations of the terms "sepsis", "cost" and "epidemiology" have been used for a full MESH search in PubMed. One main search was conducted in PubMed, for the thorough breakdown of articles by scope.

2.1.3. Search strategy

The first sub-search focused on the epidemiology of sepsis, while the second sub-search focused on the direct costs of sepsis (Appendix A). The searches in Google Scholar and EMBASE used the terms "sepsis and epidemiology" and "sepsis and costs". Reference lists of retrieved articles were fully scanned. Finally, the Cochrane library was searched for publications describing the costs of sepsis. Reference lists of all retrieved reports and articles were scanned to identify additional publications that might have been missed in the search strategy. We also identified review articles and while they did not form part of the review, their reference lists were searched for further unidentified articles.

2.1.4. Inclusion and exclusion criteria

Limits applied to the search strategy included: published between January 2010 and January 2022; English or Dutch language; Human; Adults; Publication type included Conference, Doctoral Dissertation, Government Reports, Journal Article, Master's Thesis, Meta- Analysis, Proceedings, Review and Systematic Review. No restrictions were placed on the study population nationality, or statistical designs or methods.

2.1.5. Data extraction and classification of studies

Titles and abstracts were screened independently by two reviewers. Differences between reviewers' results were resolved by discussion and when necessary, in consultation with a third reviewer. Full paper copies were obtained for all reviews identified by the title/abstract screening. Full paper screening was conducted independently by two people. The extracted data included the title, authors, study type, country of origin, publication year, severity of sepsis (type of sepsis), calculated costs of sepsis, sepsis definition and number of participants. Severity of sepsis indicated the stated degree of severity of sepsis, i.e., sepsis or septic shock. If unclear despite reading by two researchers, we categorized the study as "sepsis". Additionally, we categorized the retrieved studies by the definition of sepsis used, being 1) the sepsis definition as proposed by the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) [6,7], 2) International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes and 3) other definitions. The calculation method of unit costs was examined and extracted. The different method of unit costs include: accounting, charges, CCR, mixed, micro-costing and other.

2.1.6. Quality assessment

The methodological quality of the retrieved articles was assessed using the Drummond checklist [8]. Any discrepancy between reviewers was resolved by discussion. The Drummond checklist was designed to guide the critique of economic evaluations and considers: 1) the research question; 2) the description of the study/intervention; 3) the study design; 4) the identification, 5) measurement, and 6) valuation of costs and consequences; 7) whether discounting was carried out; 8) incremental analysis; 9) presentation of results with uncertainty and sensitivity analyses; and 10) discussion of results in the context of policy relevance and existing literature.

2.1.7. Costs outcomes

To ensure comparability among studies conducted in different years and countries, we adjusted costs to the value of the Euro in the year 2022 [9]. Therefore, costs were converted to Euros from the provided currency and corrected to the value of the Euro in the year 2022 using inflation rates provided by the Organization for Economic Co-operation and Development (OECD) [10]. Rudd et al. [1] calculated the national incidence of sepsis worldwide, we used the same strategy. The OECD [10] provided the population per country, healthcare costs per capita and GNP per country, which we used for our calculations. To adjust the sepsis-related health care expenditure for the sepsis incidence per country, we used the estimated incidence of sepsis per country as calculated by Rudd et al. in the Global Burden of Disease Study [1] (Supplemental table 1).

3. Results

3.1. Calculated costs of sepsis

A total of 1271 potentially relevant publications were identified, 26 of which were publications that fulfilled the inclusion criteria (Fig. 1) [11-28].

3.1.1. Study overview and characteristics

The majority of studies were either performed in the United States of America (USA; $n = 6$, 37.5%) and in Europe (n = 6, 37.5%); other studies were performed in Asia, Australia and South-America. No studies were performed in Africa. Sepsis was assessed more frequently ($n = 15$, 93.75%) as compared to septic shock (n = 1, 6,25%). In total, 13 studies used the definitions of sepsis as provided by the ACCP/SCCM (59.1%), while 10 studies identified septic patients based on ICD-9/10-CM coding (40.9%). Four studies were relatively small and had fewer than 100 patients (30.8%), while seven studies included >5000 patients (53.8%). The included studies used different methods to calculate their unit costs: six studies based their calculations on accounting (35.3%), three studies used more than one cost approach to estimate the costs of sepsis (17.6%).

3.1.2. Health care costs of sepsis

We calculated the health care costs of sepsis for all patients (overall), survivors and non-survivors in the value of Euros for the year 2022 (Tables 1 and 2).

3.1.2.1. Total hospital costs per stay. In Table 1, the total hospital costs per stay are presented ($n = 18$ studies). As can be seen, the mean total hospital costs per patient varied largely, between €1101 [23] and €91,951 [13]. The median (interquartile range [IQR]) of the mean reported total hospital costs was €36,191 (€17,158 - €53,349). The median of the hospital-wide costs (IQR) of survivors was €8439 (€7633 - €16,072). These cited studies in Table 1 all provided total hospital costs of sepsis per case. Unfortunately, not all of these studies differentiated the hospital costs between patients who survived and those who did not survive sepsis. Seven of the cited studies provided the median hospital costs per patient with sepsis (i.e., both survivors and non-survivors), which varied between €7495 [12] and €35,292 [22]. This variation is presumably related to differences in the number of patients admitted to the ICU, as well as differences in the length of stay (i.e. at ICU and/or in hospital). Median (IQRs) hospital cost per patient was €12,235 (€11,451 - €23,686) for all sepsis patients (i.e., both survivors and non-survivors) and €17,828 (€8915 - €26,742) for sepsis survivors. Unfortunately, the hospital costs per stay for non-survivors were not calculated in these studies (Table 1).

3.1.2.2. Hospital costs per stay per disposition. Six studies differentiated costs for per disposition, being admission to the ICU and general ward of sepsis (Table 2). The mean ICU costs per stay (evaluated in

Table 1
Total annual hospital costs per stay in 2022 Euros.

Study ID	Country	Patients	Severity of sepsis*	Method	Parameter	Survivor cost (± SD or IQR) [€]	Non-survivor cost (± SD or IQR) [€]	Overall cost (± SD or IQR) [€]	Total Sepsis costs per country [x 10^6 €]	Sepsis costs per capita per country [€]	% healthcare budget spent on sepsis per country	% GNP spent on sepsis
Alvarez 2012 [11]	Spain	54	S + SSH	Accounting	Mean	n.d.	n.d.	44,164	3302	71	2.51%	0.27%
Baretto 2016 [12]	Brazil	95	S + SSH	Accounting	Median	n.d.	4139	7495	9219	44	4.07%	0.58%
Berto 2011 [13]	Italy	64	S + SSH	Mixed	Mean	n.d.	n.d.	91,951	8889	147	5.06%	0.50%
Bunchman 2020 [14]	USA	1,136,889	S	Charges	Median	n.d.	n.d.	16,727	12,860	39	0.44%	0.07%
Darbà 2019 [15]	Spain	311,674	S + SSH	Accounting	Median	n.d.	n.d.	9692	724	16	0.55%	0.06%
Giamarellos-Bourboulis 2014 [16]	Greece	298	S + SSH	Micro-costing	Median	3413	n.d.	n.d.	58	6	0.29%	0.03%
George Institute 2021 [17]	Australia	12,895	S + SSH	Charges	Mean	n.d.	n.d.	56,410	2272	87	1.17%	0.20%
Goodwin 2015 [18]	USA	84,575	S + SSH	Charges	Mean	35,656	n.d.	n.d.	27,414	84	0.93%	0.16%
Jones 2011 [19]	USA	79	SSH	Charges	Mean	n.d.	n.d.	13,465	10,352	32	0.35%	0.06%
Micek 2012 [20]	USA	754	S + SSH	Accounting	Median	20,291	n.d.	20,253	15,571	48	0.53%	0.09%
Mouncey 2015 [21]	UK	348	S	Mixed	Mean	n.d.	n.d.	18,131	2830	43	1.24%	0.12%
Noritomi 2014 [22]	Brazil	1882	S + SSH	Accounting	Mean	n.d.	n.d.	29,181	35,896	172	15.85%	2.27%
Page 2015 [23]	USA	34,829	S	Charges	Median	n.d.	n.d.	35,292	27,134	83	0.92%	0.16%
Purba 2020 [24]	Indonesia	2,566,689	S	Accounting	Mean	n.d.	n.d.	1101	5985	23	8.85%	0.68%
Sadique 2011 [25]	UK	1650	S	Mixed	Mean	n.d.	n.d.	24,037	3752	57	1.64%	0.16%
Suarez 2011 [26]	Spain	14,076	S + SSH	Charges	Mean	n.d.	n.d.	16,832	1258	27	0.96%	0.10%
Vaughan-Sarrazin 2011 [27]	USA	13,878	S + SSH	Other	Mean	n.d.	n.d.	67,206	51,671	158	1.76%	0.30%
Walkey 2014 [28]	USA	56,997	S	CCR	Median	n.d.	n.d.	24,830	19,090	58	0.65%	0.11%

* According: Sepsis-3 (qSOFA/SOFA); S = sepsis; SSH = septic shock.

six studies) ranged from €1555 to €74,245. The median (IQR) ICU cost per stay was €22,635 (€15,436 - €38,071). Presumably, this can be linked to the number of days in which admission was required. The median (IQR) costs associated with admission to the general ward was €48,993 (€25,064 - €74,057). Hence, costs for patients with sepsis admitted to a general ward (€48,993) are considerably higher than costs for patients admitted to the ICU (€22,635; Table 2). Despite the large difference in costs for sepsis treatment in the general ward and the ICU, it should be noted that length of stay and complexity of care are important determinants of treatment costs and the condition of the patient will affect the clinical decision to admit the patient.

3.1.3. Determinants of hospital costs for sepsis

To explore determinants of hospital costs for sepsis, we stratified the costs by study region, number of included patients, method to calculate costs and severity of sepsis. The median hospital costs of sepsis were lower in the USA (€29,629) than in Europe (€34,135). The median cost reported in studies with large numbers of patients (> 5000) was €31,200 (range €1107 - €67,206), compared to €18,132 in smaller studies with 101–500 patients. Studies that used 'other methods' than accounting to calculate costs reported higher costs (€67,206) as compared to accounting €18,294, as did studies that focused on sepsis and septic shock (€38,132) as compared to septic shock only (€13,466). Thus, the reported health care costs of sepsis are affected by study

Table 2
Total annual costs differentiated per disposition per case in 2022 Euros.

Study ID	Country	Patients	Severity of sepsis*	Method	Parameter	Total cost ward (range) [€]	Total cost ICU (range) [€]	Total Sepsis costs ward per country [x 10^6 €]	Total Sepsis costs ICU per country [x 10^6 €]
Fernando 2019 [29]	Canada	657	S	Micro-costing	Mean	98,553	26,213	5843	1554
Gümüş 2018 [30]	Turkey	291	SSH	Micro-costing	Mean	n.d.	74,245	n.d.	18,434
Jiang 2013 [31]	China	71	S + SSH	Micro-costing	Mean	n.d.	11,844	n.d.	51,118
Neira 2018 [32]	Brazil	724,258	S	Accounting	Mean	568	1554	698	1912
Paoli 2018 [33]	USA	2,566,689	S + SSH	Accounting	Mean	n.d.	40,265	n.d.	30,957
Sadique 2011 [25]	UK	1650	S	Mixed	Mean	n.d.	31,489	n.d.	4916

Study ID	Sepsis costs ward per capita per country [€]	Sepsis costs ICU per capita per country [€]	% healthcare budget spent on sepsis ward	% healthcare budget spent on sepsis ICU	% GNP spent on sepsis ward	% GNP spent on sepsis ICU
Fernando 2019	157	41	3.74%	0.99%	0.40%	0.11%
Gümüş 2018	n.d.	226	n.d.	21.78%	n.d.	2.82%
Jiang 2013	n.d.	36	n.d.	6.20%	n.d.	0.44%
Neira 2018	3	9	0.31%	0.84%	0.04%	0.12%
Paoli 2018	n.d.	94	n.d.	1.05%	n.d.	0.18%
Sadique 2011	n.d.	74	n.d.	2.15%	n.d.	0.20%

region, population size, sepsis severity studied and calculation method employed.

3.2. Comparison of the financial burden of sepsis between countries

3.2.1. Differences in incidence of sepsis between countries

Both the total sepsis-related health care expenditure and number of inhabitants demonstrate large differences between reported countries (Supplemental Table 1). The lowest number of sepsis cases are diagnosed in Greece (n = 171,610 per year) [16], while sepsis is most frequently diagnosed in Indonesia (n = 5,432,814 per year) [24] (Supplemental table 1).

3.2.2. Differences in sepsis-related health care expenditures between countries

Total sepsis-related health care expenditure was the lowest in Greece (€58,574,325) [16] and the highest in the USA (€51,671 × 10^6) [27] (Table 1). The median (IQR) of sepsis-related health care expenditure was €15,262,206,307 (€2,948,651,506 - €18,210,857,813; Table 1). By dividing the sepsis-related health care expenditures by the number of inhabitants per country, we obtained the sepsis costs per capita: these were the lowest in Greece (€6 per year) [16] and the highest in Brazil (€172 per year) [22]. The median (IQR) sepsis costs per capita was €50 (€34 - €84) (Fig. 2).

The relative amount of the health care budget that is spend on sepsis varied widely between the countries of the reported studies. For example, Greece spent the least money on sepsis-related health care (0.29% of health care budget) [16], while Brazil spent relatively the most money on sepsis-related health care (15.85% of health care budget) [22]. The median sepsis-related health care expenditure per country was 2.65% of the total health care budget (Table 1). In total seven studies described sepsis-related costs in the USA, showing roughly the same amount of healthcare expenditure spent on sepsis (0.35–1.76%) [14,17-19,22,26,27]. Finally, there was a wide range of gross domestic product (GDP) spent on sepsis between the different countries included in our systematic review, ranging from 0.03% (Greece) [16] to 2.27% (Brazil) [22] and a median (IQR) amount of GNP spent on sepsis-related health care of 0.33% (0.03% - 2.27%).

4. Discussion

Despite the high incidence and mortality of sepsis, data on its health care costs are limited. We have conducted a systematic review of studies reporting the cost of sepsis. Our review found 18 studies with overall sepsis costs per patient ranging from €1101 to € 91,951. Our literature review showed that the estimated cost of treating a septic patient varied considerably among these studies. Estimates of the hospital-related costs of sepsis, total sepsis costs per country, percentage of healthcare budget spent on sepsis and the percentage of GDP spent on sepsis varied considerably across the included studies. However, treatment of sepsis is consistently extremely expensive among the countries studied.

Various characteristics have been found in the existing literature to be associated with high treatment costs, including increased severity of disease, older age, surgical indication for hospitalization and a specific infection site (e.g., catheter-related infections) [34]. Sepsis is a severe disease, with a mortality as high as 46.4%, and its incidence is relatively high in the ageing population with multiple comorbidities [32].

However, since most risk factors for high expenditure of sepsis costs are related to fixed characteristics of the sepsis patient, our study does not provide a direct approach to reduce costs. Perhaps reducing inefficient diagnostics and therapeutic procedures would improve cost-effectiveness. In light of the ageing population and worldwide increasing problems such as obesity and comorbid disease, and the -almost unlimited – medical possibilities, scarcity in health care budgets is evident and costs cannot be ignored when taking decisions in medical processes.

Our analysis showed that the costs for patients with sepsis admitted to a general ward (€48,993) are higher than the costs for sepsis patients admitted to the ICU (€22,635). This is a remarkable result, considering that ICU treatment is more intensive and requires more supplies and personnel. However, this seeming contraction can be explained by the fact the majority of sepsis patients are admitted to a general ward. Besides that, the length of stay on a general ward is often longer than on the ICU. Our analysis also showed that more data is available on the costs of sepsis treatment on the ICU than sepsis treatment on the general ward. Since sepsis is both more prevalent as well as expensive on the general ward, more research should be conducted on the costs of sepsis on the general ward. Touching upon some ethical aspects is inevitable when describing research on healthcare costs. From a societal perspective there is a tendency to assign higher monetary value to a treatment is the individual would be worse off without receiving treatment.

Strengths of this study relate to the use of data collection as part of a literature study and a data study. This allows us to provide detailed information about cost components and to compare costs between countries. However, a limitation of this study is investigating sepsis-associated health-care costs by the use of administrative data to identify sepsis and estimate expenditure, which inhibits the calculation of health

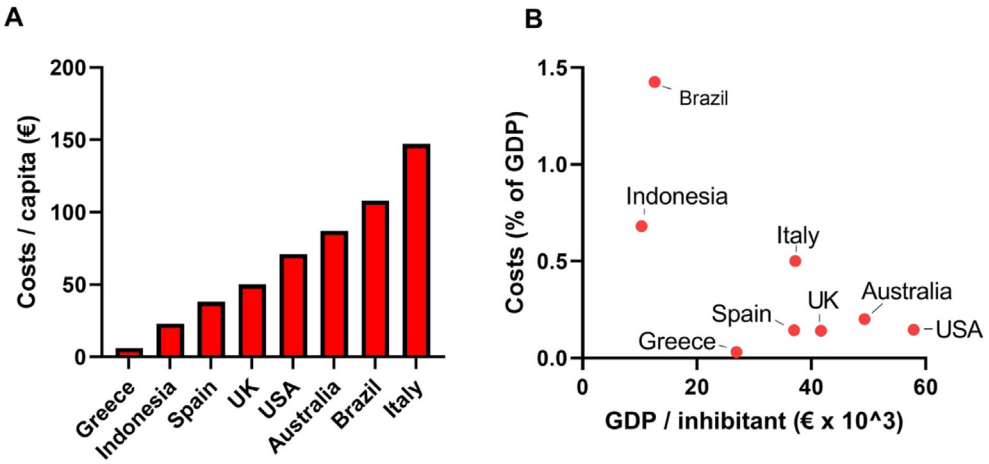

Fig. 2. Hospital costs related to sepsis. Total annual hospital costs for sepsis per capita in euro (A), total annual hospital costs for sepsis expressed relative to gross domestic product (GDP; B).

care costs on a patient level. As a result, the intensity of care of individual patients was not reflected in the health care expenditure. Secondly, several studies on costs of sepsis may have been overlooked, since studies on costs of sepsis may have been published in non-scientific journals (i.e., policy reports, books) or in languages other than English. Such publications are not included in our review, but the expectations are a similar or more pronounced variability.

To provide more reliable and comparable costs, we standardize the estimation of sepsis-related costs; utilize consensus sepsis definitions to reduce the heterogeneity of sepsis diagnoses, with the "Third International Consensus Definitions for Sepsis and Septic Shock" representing an important step in the correct direction; standardize economic methods; and use the Drummond checklist to guide the critique of economic evaluations. Appraising study quality proved to be rather difficult. A stated method for calculating unit costs appears to be a major quality indicator for cost studies, as precise calculation methods promise more reliable results. In our appraisal of cost calculation methods, we followed the order proposed by Drummond et al.in which microcosting is the most precise cost measurement method.

In light of the ageing population and worldwide increasing problems such as obesity and comorbid disease, and the -almost unlimited – medical possibilities, scarcity in health care budgets is evident and costs cannot be ignored when taking decisions in medical processes. The majority of costs of an ICU admission for sepsis are due to expenditures on personnel, residence, and general disposables per day in the ICU. Diagnostic procedures and therapeutic interventions only comprise a quarter of all costs. Therefore, only strategies that could effectively reduce ICU length of stay could lead to decrease in costs.

5. Conclusion

In conclusion, there is a large variability between different countries regarding the costs of sepsis. The costs are highest for sepsis patients on the general ward. Further studies examining the impact on sepsis costs, especially on the general ward, can help justify, design and monitor initiatives on prevention, diagnosis, and treatment of this time-critical and often preventable disease. In the field of sepsis, much has already been discovered, but much more remains to be discovered. The fact remains that limited attention has so far been given to the economic aspect of this syndrome. Hopefully, this study provides a first step towards incorporating potential cost saving strategies.

Declaration of Competing Interest

None.

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Appendix A

The current search strategy has been used: ((“Sepsis”[Mesh] OR Sepsis[tiab] OR Septicemia*[tiab] OR “Blood Poisoning*”[tiab]) AND (“Costs and Cost Analysis”[Mesh] OR Pricing[Tiab] OR Cost*[Tiab] OR economic*[tiab] OR financ*[tiab] OR “economics” [Subheading] OR calculat*[tiab]) AND OR ((“Sepsis”[Mesh] OR Sepsis[tiab] OR Septicemia*[tiab] OR “Blood Poisoning*”[tiab]) AND (“Incidence”[Mesh] OR “Epidemiology”[Mesh] OR Incidence*[tiab] OR Epidemiol*[tiab]).

Appendix B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2022.154096.

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