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REVIEW

Hospital-related cost of sepsis: A systematic review

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Summary *Objectives:* This article systematically reviews research on the costs of sepsis and, as a secondary aim, evaluates the quality of economic evaluations reported in peer-reviewed journals.
Methods: We systematically searched the MEDLINE, National Health Service (Abstracts of Reviews of Effects, Economic Evaluation and Health Technology Assessment), Cost-effectiveness Analysis Registry and Web of Knowledge databases for studies published between January 2005 and June 2015. We selected original articles that provided cost and cost-effectiveness analyses, defined sepsis and described their cost calculation method. Only studies that considered index admissions and re-admissions in the first 30 days were published in peer-reviewed journals and used standard treatments were considered. All costs were adjusted to 2014 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.

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Results: Overall, 37 studies met our eligibility criteria. The median of the mean hospital-wide cost of sepsis per patient was $32,421 (IQR $20,745—$40,835), and the median of the mean ICU cost of sepsis per patient was $27,461 (IQR $16,007—$31,251). Overall, the quality of economic studies was low.
Conclusions: Estimates of the hospital-related costs of sepsis varied considerably across the included studies depending on the method used for cost calculation, the type of sepsis and the population that was examined. A standard model for conducting cost improve the quality of studies on the costs of sepsis.
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Introduction

Sepsis, regardless of its precise definition, is a severe syndrome with a high mortality rate that affects over one million people in the US each year.[1] Worldwide, there are 35 million sepsis cases and 19.4 million severe sepsis cases annually.[2] Treatment of sepsis is listed as the most expensive condition in US hospitals, costing more than $20 billion annually.[3] However, precise costs are not available due to both controversy regarding the definition of sepsis[4] and the nature of sepsis, which is typically accompanied by comorbidities, such as diabetes or pneumonia. Each disease entails individual treatment costs, which increases the difficulty of calculating the costs attributable to specific treatments. Because there is no widely accepted approach available to circumvent this challenge, it can be assumed that to an extent, this issue negatively impacts many studies on sepsis costs.

In the present study, we conducted a systematic review that examined previous publications on the costs of sepsis. The primary aim of this systematic review was to provide an overview of hospital-related costs of sepsis reported in previous publications. The secondary aim was to examine the quality of each study's estimated costs of sepsis because determining the quality of published economic studies is essential for appropriately interpreting the results of these studies and allocating resources rationally.[5]

Methods

Data sources and search strategy

We conducted our review according to accepted guidelines[6] and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement while preparing our manuscript.[7] We searched MEDLINE, three National Health Service databases (Database of Abstracts of Reviews of Effects, Economic Evaluation Database and Health Technology Assessment Database), the Cost-effectiveness Analysis (CEA) registry and Web of Knowledge (WOK) for articles from January 2005 to June 2015 with the aim of comparing the costs of sepsis over this long period. Only studies published in English were included. The search strategy for eligible publications in MEDLINE is shown in Appendix 1. To identify other possibly relevant studies, we searched the references of publications obtained from the search.

Selection criteria

Two independent reviewers applied the inclusion and exclusion criteria and extracted the data from eligible studies by screening titles, abstracts and full-text articles. Inclusion in the analysis required the publication to 1) describe the definition of sepsis applied, 2) describe the method used to calculate the stated costs and 3) calculate the costs for either index admissions or re-admissions within the first 30 days.

A publication was excluded if 1) it was not a peer-reviewed article in a journal listed in the Journal Citation Reports,[8] 2) it was an abstract, editorial, letter or review or 3) the study only provided costs for non-standard therapies (e.g., recombinant human activated protein C (rhAPC)). There were no age or gender restrictions in our systematic review.

Data extraction

The extracted data included the title, authors, study type, country of origin, publication year, severity of sepsis (type of sepsis), cost method, cost perspective, calculated costs of sepsis, sepsis definition, number of participants, age group and source of funding. Any disagreements between the reviewers were resolved by discussion.

Definition

The ***study type*** was categorized into *cost-effectiveness* or *cost-analysis* studies and into *retrospective*, *prospective* or *mixed model* studies. ***Severity of sepsis*** indicated the stated degree of severity of sepsis, i.e., *sepsis*, *severe sepsis*, *septic shock* or *septicemia*. If in doubt, the category used was sepsis. The ***sepsis definition*** categorized studies according to how they identified septic patients. The possible categories were 1) *ACCP/SCCM*, the sepsis definition proposed by the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM)[9]; 2) *ICD-9*, if patients were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes[10]; and 3) *other*, if other definitions were used.

Statement of discounting identified whether a study considered discounting. This categorization could be accomplished by naming a currency year to which costs were discounted or by discounting health measurements (QALYs) or future long-term costs. The ***stated cost perspective*** was

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