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Review

The need for cost-effectiveness analyses of antimicrobial stewardship programmes: A structured review

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ABSTRACT

The cost effectiveness of antimicrobial stewardship (AMS) programmes was reviewed in hospital settings of Organisation for Economic Co-operation and Development (OECD) countries, and limited to adult patient populations. In each of the 36 studies, the type of AMS strategy and the clinical and cost outcomes were evaluated. The main AMS strategy implemented was prospective audit with intervention and feedback (PAIF), followed by the use of rapid technology, including rapid polymerase chain reaction (PCR)-based methods and matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) technology, for the treatment of bloodstream infections. All but one of the 36 studies reported that AMS resulted in a reduction in pharmacy expenditure. Among 27 studies measuring changes to health outcomes, either no change was reported post-AMS, or the additional benefits achieved from these outcomes were not quantified. Only two studies performed a full economic evaluation: one on a PAIF-based AMS intervention; and the other on use of rapid technology for the selection of appropriate treatment for serious *Staphylococcus aureus* infections. Both studies found the interventions to be cost effective. AMS programmes achieved a reduction in pharmacy expenditure, but there was a lack of consistency in the reported cost outcomes making it difficult to compare between interventions. A failure to capture complete costs in terms of resource use makes it difficult to determine the true cost of these interventions. There is an urgent need for full economic evaluations that compare relative changes both in clinical and cost outcomes to enable identification of the most cost-effective AMS strategies in hospitals.

1. Introduction

Use of antimicrobial agents to both treat and prevent infections is an essential component of medical care. Indeed, many advances in critical care medicine, surgery and transplantation would not be possible without the use of effective antimicrobials. Whilst antimicrobials benefit the individual patient, the emergence of resistance has consequences to all of society. In 2014, the World Health Organization (WHO) urged all countries to work together to improve surveillance and to address the issue of antimicrobial resistance (http://www.who.int/drugresistance/documents/surveillancereport/en).

An effective approach to improving antimicrobial use in hospitals may be achieved by an organised antimicrobial management programme known as antimicrobial stewardship (AMS). The overarching goals of an AMS programme are to optimise clinical outcomes while minimising unintended consequences of antimicrobial use, including toxicity, the selection of opportunistic pathogens (such as *Clostridium difficile*) and the emergence of antimicrobial resistance [1]. AMS interventions have been reported to reduce antimicrobial consumption by 22–36% and lead to a cost reduction of US$200 000–900 000 per annum in some hospitals in the USA [2]. Despite this, it has been reported that it is difficult to attract adequate support for these activities as AMS is competing for resources against many other healthcare initiatives.

Whilst there are many combinations of strategies available for the development of an AMS programme, it is unclear which are optimal. In evaluating the cost effectiveness of AMS interventions, all relevant changes to costs as well as health benefits achieved must be quantified and compared in order to understand whether the intervention offers value for money. Whilst there have been some studies that have reported AMS results in cost savings in

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terms of reducing drug acquisition costs, these do not include costs of AMS staff and other implementation activities, thus they may underestimate the cost of the intervention [3–10]. It is not clear whether the cost effectiveness of these programmes has been assessed fully. Such information is essential for making credible arguments to decision-makers about the value of funding these programmes.

The aim of this structured review was to synthesise the existing literature on the cost effectiveness of AMS programmes. We report the costs and health outcomes assessed, the economic evaluation methods used and the overall findings of this body of research, including important knowledge gaps in this area.

2. Methods

2.1. Literature search

A search for economic evaluations of AMS interventions was undertaken in the databases Embase, PubMed, Scopus, Web of Science, ProQuest, CINAHL and EconLit up to June 2014. Search terms used included the Mesh term 'Anti Infective' in conjunction with Stewardship, and search terms 'Antimicrobial Stewardship' AND 'cost*'; 'Antimicrobial Stewardship' AND 'cost effectiveness'; and 'Antimicrobial Stewardship' AND 'economic*'.

2.2. Inclusion and exclusion criteria

The inclusion criteria for critical assessment of studies on AMS cost effectiveness were: AMS intervention; cost-effectiveness analyses (CEAs) and cost analyses; based on adult inpatient population; AMS strategy clearly defined; and language restricted to English (Fig. 1). The exclusion criteria were: reviews; editorials; letters; commentaries; conference reports; and an AMS programme performed in a country that did not belong to the Organisation for Economic Co-operation and Development (OECD).

Duplicates, reviews, editorials, conference reports, commentaries and studies from non-OECD countries were removed (Fig. 1). This was done so that only countries with similar economic capacities would be compared. The following information was extracted from the remaining studies: a clear definition of AMS strategies; costs; outcomes; and the perspective of the economic analysis. Only studies that included cost data relating to AMS initiatives were reviewed in further detail. For studies that reported a full CEA or a cost-utility analysis, a specifically designed data extraction tool was used based on the Drummond [11] checklist for CEAs. Studies were evaluated by one author (SC) under the guidance of KH.

3. Results

The final review included 36 studies [3–6,8–10,12–40] conducted in the USA (22), UK (2), Canada (2), France (2), Spain (2) Japan (2), Israel (1), Slovenia (1), Belgium (1) and Germany (1). The most common AMS strategy implemented was prospective audit with intervention and feedback (PAIF), followed by rapid technology such as rapid PCR-based methods, matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) technology, peptide nucleic acid probes for fluorescence in situ hybridisation (PNA FISH) and Etest strips, for the detection of minimum inhibitory concentrations of various antimicrobials for the treatment of bloodstream infections (BSIs). Specifically, the types of AMS strategies evaluated were: PAIF (18), rapid technology (6), antifungal stewardship (4), intravenous-to-oral (i.v.-to-p.o.) conversion (4), formulary restriction plus PAIF (2), rapid technology plus antifungal stewardship (1), and PAIF plus i.v.-to-p.o. conversion (1).

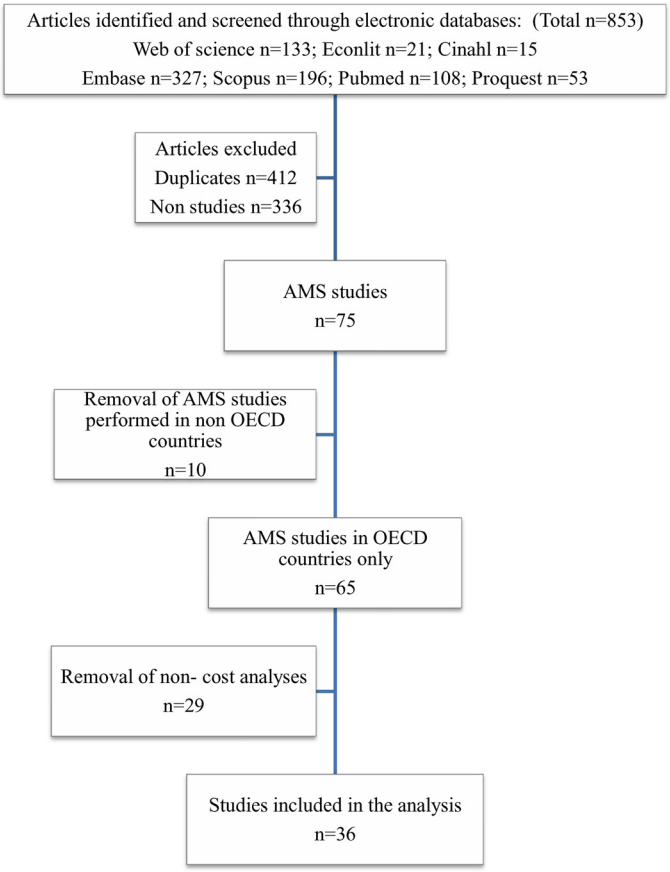

Fig. 1. Flowchart of selection of studies on cost-effectiveness of antimicrobial stewardship (AMS) based on the inclusion and exclusion criteria. OECD, Organisation for Economic Co-operation and Development.

Of the 36 included studies, 2 were full CEAs [13,14]; 27 studies reported changes to costs and health outcomes separately [3,5,8–10,12–14,22–40] and 9 reported only changes to costs [4,6,15–21]. Table 1 presents the methods and results for studies that measured only cost outcomes and Table 2 presents the methods and findings of those studies that measured both a clinical as well as a cost outcome.

3.1. Costing studies that did not measure clinical outcomes

Table 1 groups 9 of the 36 included studies that measured only the cost impact of AMS strategies [4,6,15–21]. PAIF was the most commonly evaluated strategy in this group (5/9; 56%) [4,6,15–17]; 2 studies focused on i.v.-to-p.o. conversion as a strategy [18,19] and 2 studies evaluated antifungal stewardship [20,21]. All nine studies reported a reduction in costs related to antimicrobial use as a result of implementing the AMS strategy.

Five of the nine studies assessed reduction in total antibiotic expenditure (TAE) as a measure of success of the AMS strategy [4,15,16,18,20]. One of the remaining four studies expressed the cost savings as TAE per patient-day (PD) [17], the second as TAE per 1000 PDs [6], the third as TAE per patient [21] and the final study as mean additional cost per patient [19].

3.2. Cost consequence studies that measured clinical outcomes

Table 2 groups the 27 studies that evaluated a change in cost as well as clinical outcome as a result of implementing an AMS strategy [3,5,8–10,12–14,22–40]. Thirteen (48.1%) of the studies measured cost savings as only TAE [3,5,8,10,22,23,25,26,28–32], 1