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ORIGINAL ARTICLE

Methods to place a value on additional evidence are illustrated using a case study of corticosteroids after traumatic brain injury

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Abstract

Objectives: To establish whether evidence about the effectiveness of a health care intervention is sufficient to justify the use of the intervention in practice and show how value of information (VOI) analysis can be used to place a value on the need for additional evidence and inform research prioritization decisions.

Study Design and Setting: Meta-analysis provides an estimate of the effect of an intervention with uncertainty. VOI analysis determines the adverse health consequences of not resolving this uncertainty. A case study examining the evidence before the high profile trial of Corticosteroid Randomisation After Significant Head injury (CRASH) shows the consequences on patient outcomes if this trial had not been successfully funded.

Results: The consequences of uncertainty before CRASH were high at 40 deaths and 1,067 years of full health per annum. VOI analysis indicates that CRASH was worthwhile and the UK National Health Service would have had to spend an additional £205 million elsewhere to generate health benefits similar to CRASH.

Conclusions: VOI analysis can be integrated with the results of meta-analysis to help inform whether a particular research proposal is potentially worthwhile and whether it should be prioritized over other research topics that could be commissioned with the same resources.

Keywords: Research prioritization; Uncertainty; Value of information analysis; Meta-analysis; Corticosteroids; Head injury

1. Introduction

The evidence about the effectiveness of a health care intervention might suggest that it achieves better health outcomes than the available alternative interventions. However, the estimate of treatment effect may still be uncertain, which creates uncertainty in any decision about whether to use the intervention in clinical practice. If the expected health benefits of the intervention are not realized in practice, there may be a detrimental effect to patient health outcomes. In addition, the resources committed by the use of the intervention may be wasted. Similarly, if an intervention is not expected to perform better than the available alternatives, rejecting its use in clinical practice may risk failing to provide access to a valuable intervention if the health benefits are actually greater than expected. These uncertainties can never be entirely eliminated, but they can be reduced by collecting further evidence, which in turn facilitates better decisions for patient outcomes and better use of finite resources.

Value of information (VOI) analysis provides a very useful tool for establishing: (1) whether the evidence currently available is sufficient to support the use of the intervention in practice; (2) whether additional evidence is required to resolve the uncertainties; (3) the type of evidence that is required; and (4) the circumstances under which an intervention should be withheld until additional evidence becomes available [1−8]. There are now many applications of VOI analysis in the context of decision models used to estimate the cost effectiveness of alternative interventions. In this article, we show that the same type of analysis can

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What is new?

Key findings

- A simple extension of standard meta-analysis with methods of value of information (VOI) analysis provides an estimate of the health benefits of further research, which can be used to inform research prioritization and commissioning decisions.

What this adds to what was known?

- Until now, methods of VOI analysis have been applied to situations where probabilistic decision analytic models or estimates of cost effectiveness are available, but we show that the same principles and methods are relevant to a range of different types of health care systems and decision-making contexts, even those where there is no explicit assessment of cost effectiveness.

What is the implication and what should change now?

- Research proposals that are likely to be worthwhile can be identified in a systematic way. The health benefits expected from different proposals, competing for the same resources, can be compared to each other to establish which topic offers the greatest value. This adds transparency and accountability to research prioritization decisions.

also be applied to standard results of meta-analysis, without the necessity to undertake a cost-effectiveness analysis. Furthermore, the methods provide a framework to assess the relative importance of alternative research topics and proposals, which is invaluable for research prioritization decisions.

Meta-analysis provides an estimate of the magnitude of treatment effect and the level of uncertainty in this estimate, for example, the confidence interval (CI) around the mean estimate of effect is used to represent the range of values in which the unknown ''true'' effect lies [9]. When this uncertainty is combined with information about baseline risk and incidence, the absolute effect of the uncertainty on health outcomes can be assessed [10]. VOI analysis determines an estimate of the health benefits that could be gained if the uncertainty about treatment choice was resolved completely. These health benefits can then be compared with the costs of undertaking the research to establish whether it represents an efficient use of resources. Furthermore, the health benefits of different research topics (or proposals for funding) can be compared to establish which topic should be prioritized from those competing for the same resources.

This article shows how the methods of VOI analysis can be integrated with the results of meta-analysis to directly inform the questions posed in research prioritization and commissioning decisions. We take as a starting point that research proposals will include a systematic review of existing evidence and, where appropriate, a meta-analysis because funding additional research without knowledge of existing evidence would seem inappropriate and potentially unethical. We use the case of corticosteroids after traumatic brain injury (TBI) to offer a demonstration of the ease with which the methods can be applied.

2. Corticosteroids after TBI

Despite 19 randomized controlled trials before the CRASH trial (Corticosteroid Randomisation After Significant Head injury) [11,12], the effect of corticosteroids on death and disability after TBI remained unclear. The CRASH trial was stopped early after enrolling 10,008 adults with TBI. It reported a higher risk of death or severe disability associated with the use of corticosteroids compared with not using them [12]. As a consequence of this definitive, and to some extent, unexpected result clinical practice changed dramatically, resulting in many thousands of deaths averted around the world (before CRASH, corticosteroids was used in 64% of patients with TBI in the United States [13] and 12% in the United Kingdom [14]). The global value of the CRASH trial appears, with hindsight, self-evident. However, the prevention of thousands of unnecessary iatrogenic deaths hinges on the fact that the funding application for CRASH was successful. In this article, we conduct a retrospective analysis of the evidence available before CRASH to show how methods of VOI analysis would have been useful for quantifying the value of obtaining further evidence and the expected health consequences of not obtaining the evidence.

2.1. Evidence available before CRASH

The evidence from the trials comparing the use of corticosteroids to placebo or no treatment in acute TBI before CRASH is illustrated in Fig. 1 for the primary end point of mortality. These trials dating from 1972 to 1995 were of varying study quality, length of follow-up, steroids administered, doses, and time to administration [15−30]. Standard meta-analysis suggests substantial uncertainty about the effectiveness of corticosteroids in TBI [31,32]. For example, a random-effects meta-analysis suggests that the use of steroids after TBI reduces the risk of death with an expected odds ratio (OR) of 0.93. However, the 95% CI crosses the line of no difference indicating that the change in the risk of death could be as much as 12.5% lower to 9.9% higher (using the average pooled death rate in the control arms of 35.3%).