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# A dynamic programming approach to the efficient design of clinical trials

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**Abstract**

If the prospective evaluation of all feasible strategies of patient management is not possible or efficient then this poses a number of questions: (i) which clinical decision problems will be worth evaluating through prospective clinical research; (ii) if a clinical decision problem is worth evaluating which of the many competing alternatives should be considered "relevant" and be compared in the evaluation; (iii) what is the optimal (technically efficient) scale of this prospective research; (iv) what is an optimal allocation of trial entrants between the competing alternatives; and (v) what is the value of this proposed research? The purpose of this paper is to present a Bayesian decision theoretic approach to the value of information which can provide answers to each of these questions. An analysis of the value of sample information was combined with dynamic programming and applied to numerical examples of sequential decision problems. The analysis demonstrates that this approach can be used to establish: optimal sample size; optimal sample allocation; and the societal payoff to proposed research. This approach provides a consistent way to identify which of the competing alternatives can be regarded as "relevant" and should be included in any evaluative study design. Bayesian decision theory can provide a general methodological framework that can ensure consistency in decision making between service provision, research and development, and the design, conduct and interpretation clinical research. 

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## 1. Introduction

In many circumstances, valid inferences cannot be made about the expected costs and benefits of alternative strategies of patient management simply by observing current clinical practice. Two key reasons for this failure emerge. First, many key parameters, particularly measures of efficacy, are vunerable to selection bias. Second, some feasible strategies of patient management are not part of current practice and consequently they have never been observed. Most clinical decision problems offer a choice between a potentially large number of possible patient management strategies. However, the prospective evaluation of all these strategies is unlikely to be regarded as ethical and certainly not efficient (or even possible) given limited resources for research and development, and a recognition of the opportunity costs (health benefits forgone) for those enrolled in the trial and for the population of patients awaiting the results of the research.

In practice many feasible strategies are ruled out as irrelevant during the design of prospective research. However, if the identification of "relevant alternatives" to be included in prospective research is either arbitrary, or uses an implicit decision rule inconsistent with those that will be applied when the study is complete, then there is a danger that research will revolve around an arbitrarily selected sub set of strategies, with the real possibility that the optimal strategy be ruled out of the analysis prematurely as an "irrelevant alternative". The evaluation of a particular clinical decision problem should, consider all feasible alternatives, at least initially, rather than focus only on those currently used or those identified as of interest in some arbitrary way. The "relevant alternatives" that should be compared in prospective research should be identified explicitly and consistently.

If alternatives cannot be ruled out a priori but the prospective evaluation of all feasible strategies is not possible or efficient then this poses a number of questions: (i) which clinical decision problems will be worth evaluating through prospective clinical research; (ii) if a clinical decision problem is worth evaluating which of the many competing alternatives should be considered "relevant" and be compared in the evaluation; (iii) what is the optimal (technically efficient) scale of this prospective research; (iv) what is an optimal allocation of trial entrants between the competing alternatives; and (v) what is the value of this proposed research? These are questions of how to establish technical efficiency in research design (including the selection of relevant alternatives as well as optimal scale) and how to achieve allocative efficiency in research and development.

The purpose of this paper is to present a Bayesian decision theoretic approach to the value of information that can provide answers to each of these questions. Our aim is to provide a general methodological framework that can ensure consistency in decision making between service provision, research and development and the design, conduct and interpretation clinical research. The general methodology for the selection of relevant alternatives is applicable to all clinical decision problems where more than two alternative strategies of patient management are possible (almost all clinical decision problems). The use of dynamic programming (which exploits the sequential nature of decision making) to reduce computational requirements can be applied to any clinical decision problem where a sequence of contingent decisions exists. This is clearly the case when any diagnostic process precedes treatment, but it is also the case when failure of one of a number of possible first