

**Defining an Optimal Format  
for Presenting Research Needs**



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# *Methods Future Research Needs Report*

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## Number 3

### **Defining an Optimal Format for Presenting Research Needs**

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## Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To improve the scientific rigor of these evidence reports, AHRQ supports empiric research by the EPCs to help understand or improve complex methodologic issues in systematic reviews. These methods research projects are intended to contribute to the research base in and be used to improve the science of systematic reviews. They are not intended to be guidance to the EPC program, although may be considered by EPCs along with other scientific research when determining EPC program methods guidance.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality. The reports undergo peer review prior to their release as a final report.

We welcome comments on this Methods Research Project. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to [epc@ahrq.hhs.gov](mailto:epc@ahrq.hhs.gov).

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# **Methods Research on Future Research Needs: Defining an Optimal Format for Presenting Research Needs**

## **Abstract**

Systematic reviews and other secondary research reports that are based on data from multiple sources, such as decision or cost-effectiveness analyses, often conclude by noting gaps in the available evidence and make recommendations for future research. Potential users of these recommendations include policy makers and funders, as well as healthcare researchers. The purpose of this project is to determine an optimal format for presenting a new type of product of the Evidence-based Practice Center (EPC) Program, the Future Research Needs documents. In particular, we address the following questions: What level of specificity is needed by various funders or researchers for a research needs document to be useful? How can one categorize and present research needs? What are the specific barriers to making a research needs document useful to researchers and funders?

To answer these questions, we performed an empirical assessment of the literature to understand how future research needs have been presented in the published literature, and sought feedback from healthcare researchers, research funders, or payers in the form of open-ended interviews. Based on the results of the empirical assessment and the qualitative interviews we outline the preliminary recommendations. Future research needs documents for the EPC program should provide succinct yet adequate description of methods and results following guidelines for reporting for qualitative research and modeling, as applicable. It is important to justify the selection of the stakeholders who participate in identifying or prioritizing research needs, and to be clear on their degree of engagement. It may be useful to report results of future research needs assessments at two levels of detail: the more abstract level would mention general areas of future research without details on potential research designs or specific details on e.g., populations, interventions and outcomes, which could be elaborated in the second level. It may be preferable to avoid explicit prioritization of research needs when there are no clear differences in the perceived strength of alternative recommendations. Overall, future research needs recommendations are projections and therefore should not be prescriptive.

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# Background

Systematic reviews of medical research often conclude by noting gaps in the evidence and sometimes recommending specific research to fill them in order to improve the evidence base for medical decisions. To encourage this process, the Effective Healthcare Program of the Agency for Healthcare Research and Quality (AHRQ) has introduced a new type of report, Future Research Needs, to assess the needs for future research in a specific topic after the completion of a systematic review of the evidence. After the completion of a comparative effectiveness review, EPCs would prioritize the identified *evidence gaps* into *research needs*, and suggest potential research designs. The premise is that not all evidence gaps are of equal importance, and because resources are finite, future research should address the most important among the answerable evidence gaps using the most efficient research methods. These assessments are summarized in “future research needs documents,” which are intended to inform and support researchers and those who fund research to ultimately enhance the body of comparative effectiveness evidence and maximize its usefulness for decisionmakers.

There are many possible ways to present recommendations about future research needs; the optimal presentation depends in the underlying methodology. Overall, one can distinguish between approaches that are based exclusively on qualitative research methods to elicit and synthesize the opinions of a group of stakeholders, and approaches that are a mix of qualitative and quantitative methods (such as decision, economic, or value of information [VOI] modeling). Obviously, such diverse types of information should be reported in different ways.

The purpose of this project is to determine an optimal format for presenting future research needs. In particular, we attempt to address the following questions that were determined by AHRQ: What level of specificity is needed by various funders or researchers for a research needs document to be informative? How can one categorize and present research needs? Is quantitative ranking of research recommendations helpful or an obstacle? What are the specific barriers to making a research needs document useful to researchers and funders?

## Methods

We performed an empirical assessment of the reporting of recommendations for future research needs in secondary research publications (systematic reviews, cost-effectiveness analyses and VOI analyses).<sup>1</sup> Systematic reviews, cost-effectiveness analyses and VOI analyses are ideally poised to identify and present future research needs because they draw on multiple information sources, use explicit methods to identify, appraise and synthesize research results,<sup>2,3</sup> and are empirically known to have high impact on the conduct and interpretation of research.<sup>4</sup>

We also sought feedback from experts who are healthcare researchers, research funders, or payers in the form of open-ended interviews, to understand how familiar they are with evidence-based medicine and decision and economic analyses; how receptive they are to conclusions for future research needs that have been drawn from different methodologies (qualitative methods only, or combination of qualitative and quantitative methods); what reservations they have, if any; what information would the ideal future research needs document contain, and what minimum level of detail they would accept in terms of the recommendation itself (e.g., specificity by defining characteristics as per the PICO formalism) and the methodology it is based on (e.g., description of the process, model, assumptions). Based on the results of these explorations we provide preliminary guidance for presenting future research needs documents.

## Empirical Assessment of Evidence-based Documents

### Database Formation and Eligibility Criteria

We assembled a database of randomly selected systematic reviews that included quantitative evidence synthesis (meta-analysis) and cost-effectiveness (or cost-utility) analyses, published recently in selected medical journals, and of all published medical applications of VOI analyses we could identify. Appendix A provides details on our searches.

Specifically, we used computer-generated pseudorandom numbers to select 50 systematic reviews that included at least one meta-analysis of therapeutic interventions, published between 2005 and 2010 in the five general medical journals with the highest total annual citation count in 2009 according to Thompson ISI (*New England Journal of Medicine*, *Journal of the American Medical Association*, *Annals of Internal Medicine*, *The Lancet*, *British Medical Journal*). We considered eligible systematic reviews that had stated objectives, reported using a search strategy and predefined eligibility criteria for including studies, and included quantitative analyses (meta-analyses).

Cost-effectiveness or cost-utility analyses are most often published in specialty journals rather than in general medical journals. In addition to the aforementioned journals we considered cost-utility publications published in *Pharmacoeconomics*, *International Journal of Technology Assessment in Health Care*, and *Medical Decision Making*. Together with *Annals of Internal Medicine* and the *Journal of the American Medical Association*, these journals have published most cost-effectiveness analyses according to a recent bibliometric investigation.<sup>5</sup> We selected at random 50 recent publications (between 2005 and 2010). We considered eligible cost-effectiveness or cost-utility analyses that explored patient-level clinical decisions (by enumerating available management strategies and their potential outcomes) and used appropriate quantitative methods to assign probabilities of occurrence and utility values to patient outcomes.

We excluded analyses of resource allocation strategies, or of nonmedical public health interventions such as using mosquito nets for preventing malaria in underdeveloped countries.

Finally, we searched PubMed for English-language publications that applied VOI analyses in medical decision problems without any journal or date restrictions. We included methodology papers, provided that they also described applied analyses of the proposed methods in a probabilistic model that was parameterized using external data. As for cost-effectiveness and cost-utility analyses, we excluded VOI analyses of resource allocation strategies, or of nonmedical public health interventions. We also excluded VOI analyses that were based on data from a single clinical trial.

## Data Extraction

Four investigators extracted data in predefined forms. Forms were piloted in three papers to ensure that all investigators would extract data using the same operational criteria. From each eligible paper we recorded bibliographic information (first author name, title, year, journal, and country of publication). For systematic reviews with meta-analysis and for cost-effectiveness or cost-utility analyses we recorded if there was any discussion on the need for further research, and if yes, whether further research was recommended; whether suggestions for future research pertained to specific key questions of these studies; whether future research needs were discussed in a separate paragraph or section; whether methods for making research recommendations were clearly described, and if yes, what methods were used.

We extracted a different set of methodological and reporting characteristics from VOI papers, as they are tailored to address future research needs. Specifically, we extracted information on the decisional context including descriptions of populations, compared alternative strategies, perspective of analysis (societal, health care payer, other, or not stated), time horizon (yes/no, and months if the actual duration in months) and additional outcomes beyond monetary units (quality adjusted life expectancy, life expectancy, events of interest); type of intervention being studied (screening, other diagnostic, pharmaceutical, medical device, surgical, immunization, and other); whether the analysis pertained to prevention, and if yes what level (primary, secondary, tertiary); data sources used to parameterize models (nonsystematic review, systematic review, primary data, not stated); whether costs and effectiveness were discounted over time; and whether model predictions were calibrated or validated in independent datasets. We also recorded the type of sensitivity analyses used (one-way, two-way, multi-way, probabilistic), and the type of VOI calculations performed: expected value of perfect information (EVPI), expected value of partial perfect information (EVPPI), expected value of sample information (EVSI) or expected value of sample information for specific parameters (EVSI-P).<sup>a</sup>

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<sup>a</sup> A VOI analysis attempts to assign a value (usually a monetary amount) to the information that could be obtained by future research. The premise is that all decisions are made under uncertainty, which *could be reduced using information obtained by further research*. For example, a patient with coronary artery disease who needs revascularization can choose between percutaneous interventions and bypass surgery. However, the comparative effectiveness of the two interventions with respect to mortality, myocardial infarction, stroke, need for subsequent revascularizations, and the comparative safety of the interventions is not known with certainty. Either choice could be optimal or suboptimal for the particular patient, with different probabilities. The set of suboptimal choices represents the opportunity cost associated with the decision. The opportunity cost is high when there is a great deal of uncertainty around the decision, or low when the important decisional parameters are known with certainty. EVPI is an analysis that places *an upper bound* to this opportunity cost, or equivalently, an upper bound to the expected returns of future research. If EVPI is very low, then future research may not be necessary. EVPPI, refines the EVPI calculations by placing an upper bound to the value of research *on specific (groups of) parameters*. However, we will never be able to get perfect information; instead we can design studies that will reduce the uncertainty of current estimates. In order to examine specific

We also recorded whether modeling accounted for the stochastic dependence between parameter distributions (operationally defined as using Markov chain Monte Carlo analyses versus not); and what type of graphs were used to describe VOI analysis results.

## **Analysis**

We generated frequency tables for the extracted items per types of publication. Whenever statistical comparisons are reported, they are based on nonparametric tests (Fisher's exact test). Results are considered significant at the 0.05 level.<sup>b</sup>

## **Qualitative Interviews**

We performed semi-structured interviews to explore the experiences and opinions of four key informants (experts). Questions were open-ended, and were rephrased, as necessary, to elicit answers and themes.

## **Research Team and Reflexivity**

The interviews were conducted by the lead author, a researcher with experience in evidence-based medicine and decision science, and who also led a project on identifying future research needs pertinent to the comparison of percutaneous interventions and coronary artery bypass surgery in patients with coronary artery disease.

The interviewer had an established relationship with the interviewed experts prior to the commencement of the study, through their professional contact. In each interview both parties were familiar with each other's background and research interests. Although the interviewer did not discuss or express his personal opinions on the questions at hand, the interviewed experts might have been able to guess the interviewer's opinions based on their previous acquaintance. Given the established expertise of the individuals interviewed, we consider the possibility of "interviewer bias" to be minimal.

## **Study Design and Analysis**

The aim of the study was to understand what level of information on future research needs is most useful to potential users of future research needs documents, specifically health care researchers or decisionmaker scientists in a funding agency.

We used purposive sampling; that is, we invited experts because of their experience in health care, and because of their ability to provide complementary opinions and alternative viewpoints. We invited five experts to participate in the semi-structured interviews. Four participated, but the fifth did not respond to the invitation. Because very soon we reached saturation in terms of no longer identifying additional themes, we did not deem necessary to replace the fifth interviewer or to further expand the sample size. Experts still had profound disagreements on several of the initial issues, but did not bring up additional ones. Qualitative interviews are typically used to identify a range of themes, and not necessarily to reach a consensus (as is the goal of a Delphi process) or quantify frequencies of opinions (as is the goal with surveys).

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designs, one can proceed to calculate EVSI, the expected value of information from a sample  $n$  (and compare it to the costs of performing actual studies).

<sup>b</sup>We did not perform extensive comparisons because many of the extracted items are subject to editorial requirements and space constraints.

One interview was conducted in person, and three over the telephone, with only the interviewer and the expert being present. The selected experts were all experienced in different aspects of health care research. The first expert is primarily a trialist who has designed and conducted several high impact trials in cardiovascular medicine, and who is also a practicing clinician. The second expert is a medical officer with the National Institute on Aging who also had long experience working in a major insurer. The third is a health care researcher with considerable experience in evidence-based medicine, health economics, and decision science, and is also a key member in a large professional organization (American College of Physicians). The fourth is key employee at the Center for Medicare and Medicaid Services. When applicable, in the description of the results we refer to experts as A, B, C and D. The correspondence of letters to experts is random and may or may not correspond to the order of presentation above.

The interviews followed a predefined series of questions, which had not been piloted in advance. Auxiliary material was available, including samples of statements describing future research needs in several topics, relevant tables with different layouts, and graphs. This material was referred to during the interviews on an as-needed basis, to facilitate descriptions or to elicit specific responses and reactions. The interviewer took notes but did not use any other type of recording (e.g., audio recording).

The interviewer identified themes after the end of each interview based on the discussions with the experts. No software was used to organize the derivation of themes. Both themes for which there was concordance and themes for which there was divergence of opinions between experts are described.

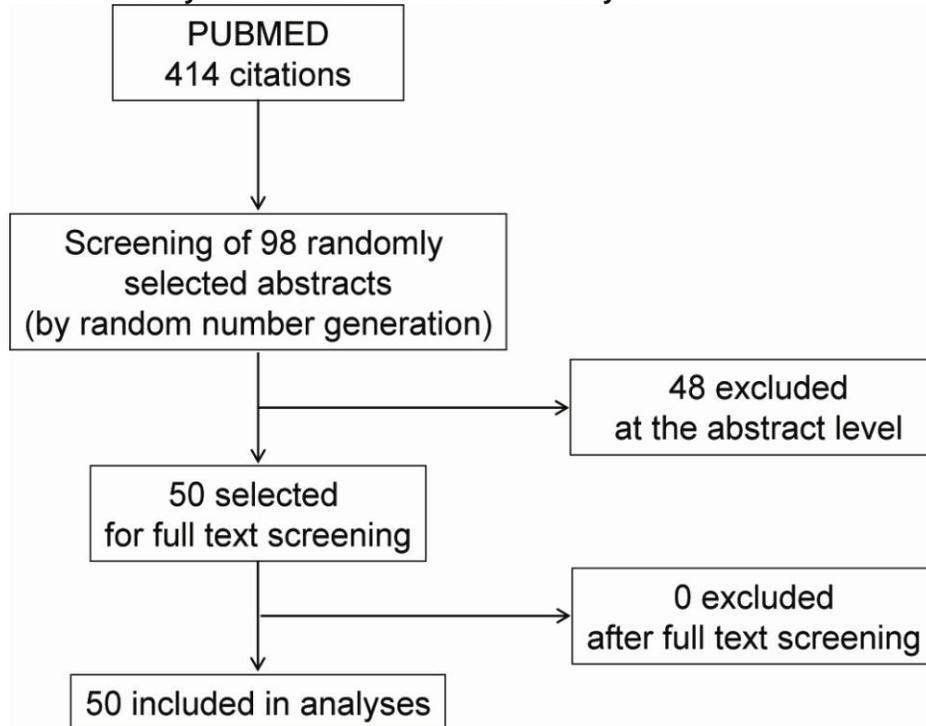
# Results

## Empirical Assessment of Evidence-based Documents

### Systematic Reviews With Meta-Analysis

Our literature search identified 414 systematic reviews with meta-analysis. Of the first 98 randomly selected abstracts, 48 were not considered eligible and were excluded. The remaining 50 studies were considered potentially eligible and were retrieved in full text. No studies were excluded after full text review (Figure 1).

Figure 1. Search flow for systematic reviews with meta-analysis



The majority of systematic reviews included some discussion of future research needs (n=40 out of 50, 80%). Most identified specific research questions that should be addressed by future studies (n=36, 72%). However, specific research designs were suggested in 23 out of 50 papers (46%). In 20 out of these 23 papers the recommendation was that more randomized controlled trials are necessary. Only 13 (26%) studies devoted a whole paragraph to discuss future research needs. None of the papers reported whether any specific methodology was used to identify or prioritize future research needs. Table 1 summarizes our findings from systematic reviews with meta-analysis.

**Table 1. Discussion of future research needs in 50 recent randomly selected systematic reviews with meta-analysis published in major journals**

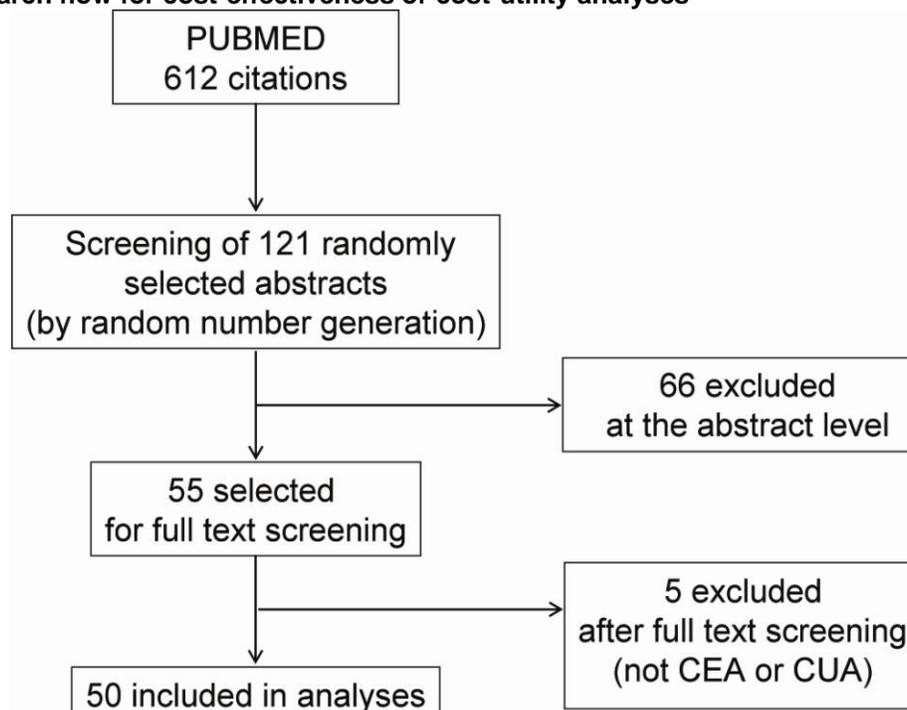
Characteristic	Number out of 50 papers, (%)
Any discussion of further research	40 (80)
"Further research is needed"	40 (80)
Research questions to be addressed	36 (72)
Specific designs proposed	23 (46)
Specific designs	
Any proposal for further RCTs	20 (87)
Any proposal for economic evaluations	5 (22)
Any proposal for observational studies	1 (4)
Meta-analysis (updating or IPD)	3 (13)
Paragraph on FRN	13 (26)
Separate section on FRN	7 (14)
Explicit methods for FRN	0

FRN = future research needs; IPD = individual participant data; RCT = randomized controlled trials

## Cost-Effectiveness and Cost-Utility Analyses

Our literature search for cost-effectiveness and cost-utility analyses identified 612 citations. Of the first 121 randomly selected abstracts, 66 were not considered eligible and were excluded. The remaining 55 studies were considered potentially eligible and were retrieved in full text. Of those, 5 studies were excluded resulting in 50 eligible studies (Figure 2).

**Figure 2. Search flow for cost-effectiveness or cost-utility analyses**



CEA = cost-effectiveness analyses; CUA = cost-utility analyses.

Cost-effectiveness and cost-utility analyses discussed future research needs less frequently (29 studies, 58%) compared to systematic reviews ( $p=0.030$  by Fisher's exact test). Twenty four (48%) reported specific key questions that merit further research and only 10 (20%) proposed specific designs to address these questions. Compared to systematic reviews, cost-effectiveness and cost-utility analyses were less likely to propose further randomized trials (4 out of 10), and

more likely to propose observational designs (3 of 10) for future research. Similar to systematic reviews, the text devoted to future research needs was limited, with only 5 (10%) devoting a whole paragraph. Four studies used formal methods to identify or prioritize research needs; three of those employed VOI methodologies and the fourth used a variance components analysis. Table 2 summarizes findings.

**Table 2. Discussion of future research needs in 50 recent randomly selected cost-effectiveness and cost-utility analyses published in major journals**

Characteristic	Number out of 50 papers (%)
Any discussion of further research	29 (58)
“Further research is needed”	28 (56) <sup>c</sup>
Research questions to be addressed	24 (48)
Specific designs proposed	10 (20)
Specific designs	Any proposal for RCTs 4 (40)
(% only among studies suggesting specific designs; several studies suggested more than one design.)	Any proposal for economic evaluations 5 (50)
	Any proposal for observational 3 (30)
	Meta-analysis (updating or IPD) 0
Paragraph on FRN	5 (10)
Separate section on FRN	4 (8)
Explicit methods for FRN	4 (8) <sup>d</sup>

FRN = future research needs; IPD = individual participant data; RCT = randomized controlled trials.

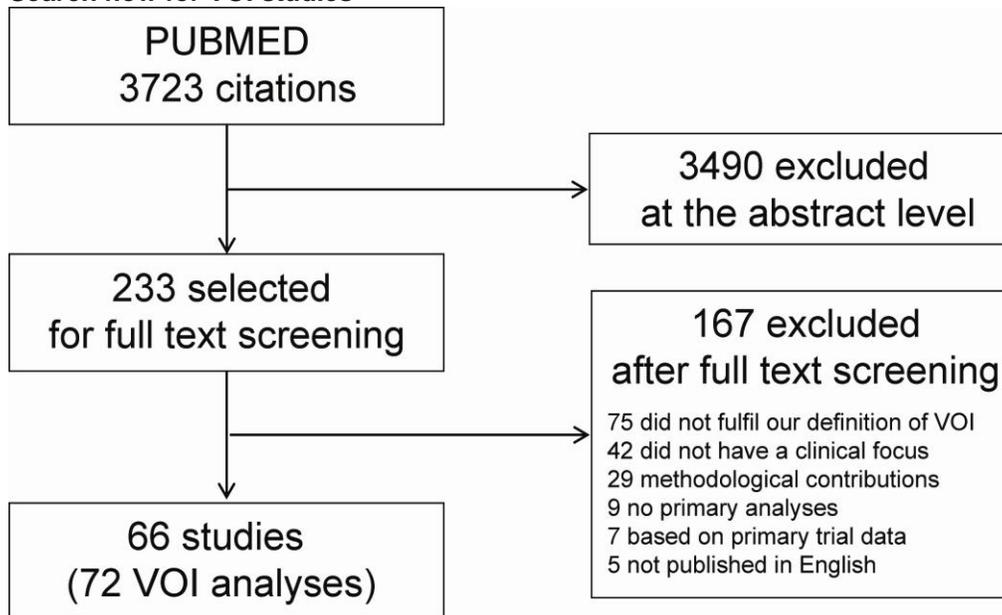
## VOI Analyses

Our MEDLINE search for VOI analyses identified 3,723 citations; 3,490 were excluded at the abstract level and 233 were considered potentially eligible and were retrieved in full text. Of those, 167 were excluded after full text screening and 66 studies, reporting on 72 independent VOI analyses, were included in this review. The search flow, including a list of reasons for exclusion, is presented in Figure 3. VOI analyses are specifically dedicated to appraising the value of future research on a given topic. They are frequently based on systematic reviews of the relevant literature and use cost-utility analysis methodologies. For these reasons we have extracted a more extensive set of methodological and reporting characteristics for the VOI studies that we considered.

<sup>c</sup>One study explicitly stated that further research on the topic it examined was not necessary.

<sup>d</sup>Three studies used VOI methods and one study used a variance components analysis (attributable variance) to determine parameters that required further research.

**Figure 3. Search flow for VOI studies**



VOI = value of information.

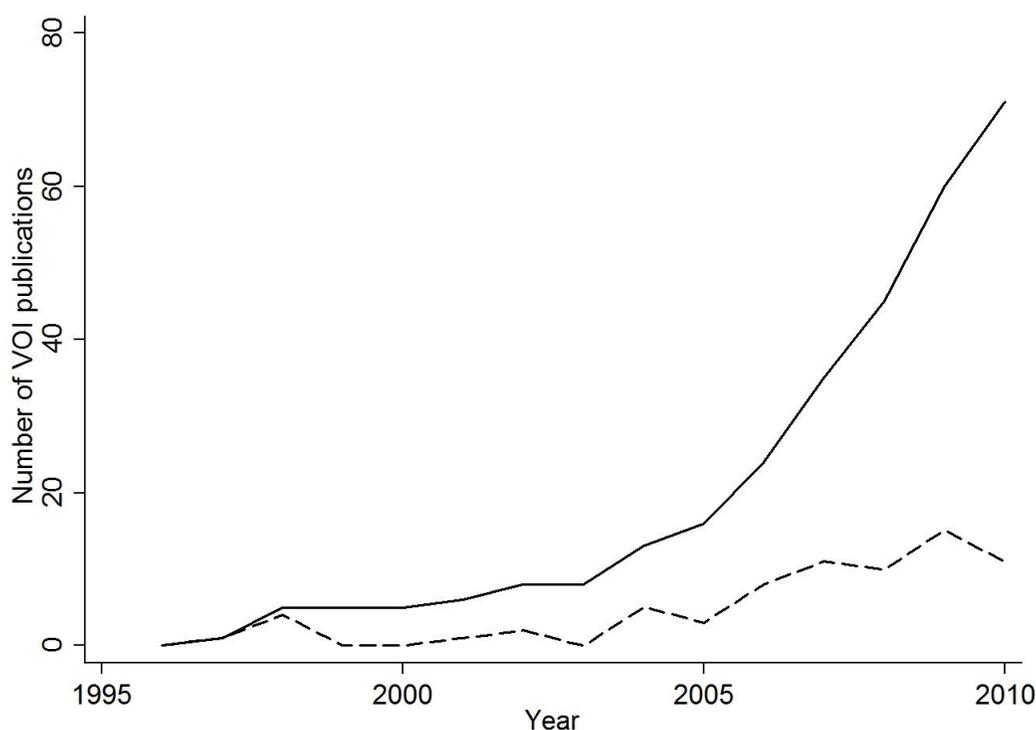
Figure 4 depicts the increase in published VOI applications since the mid-1990s. The majority of studies have originated from the United Kingdom (UK), and most have been conducted as part of Health Technology Assessments for the UK-based agencies, including the National Institute for Health and Clinical Excellence (NICE). Consequently, the majority of studies had received government funding.

Table 3 summarizes the methods employed and the reporting practices in the 72 different VOI analyses. Almost all studies calculated EVPI, the value of obtaining perfect information for all parameters (n=68, 94%) but fewer studies calculated EVPPI (n=42, 58%) and only a minority calculated EVSI (5 studies, 7%) or EVSI-P (1 study, 1%).

Figure 5 shows examples of typical graphs used in economic and VOI analyses, along with a brief explanation on their interpretation. In general, graphical presentations of results were underutilized, with most studies presenting “standard graphs” for cost-effectiveness analyses or cost-utility analyses, such as cost-effectiveness acceptability and frontier graphs. Thirty seven (51%) presented line graphs of EVPI over different willingness to pay thresholds but only a minority presented EVPPI bar charts (n=14, 19%) or EVPPI line graphs over willingness to pay (2 studies, 3%).

A minority of studies (n=25, 35%) proposed specific study designs for future research. Of those, the majority suggested that further RCTs are necessary (n=22, 88%); however, observational studies were also proposed (n=6, 24%).

**Figure 4. Growth of the VOI literature**



Number of published VOI applications per year (dashed line) and cumulative number (solid line) of VOI applications based on our PubMed searches. Note that data are not available for the last few months of 2010. A single study published in 1981 is not shown. VOI = value of information.

**Table 3. Methodological and reporting characteristics in publications of VOI applications<sup>e</sup>**

Characteristic	Number of studies (%)	
Country	USA	13 (18)
	Canada	4 (6)
	UK	41 (57)
	Europe (non-UK)	13 (18)
	Other/ multiple	1 (1)
Type of intervention	Screening	18 (25)
	Diagnosis	8 (11)
	Pharmaceutical treatment	33 (46)
	Surgical treatment	6 (8)
	Medical devices	8 (11)
	Immunization	3 (4)
Outcomes	Healthcare delivery, education, behavior	7 (10)
	QALYs	57 (79)
	Life years	6 (8)
	Discrete events	12 (17)

<sup>e</sup>Relative frequencies may not sum to 100% when studies compared more than one active intervention (for example a surgical and a medical treatment), reported on more than two outcomes (for example life years and quality-adjusted life years), were supported by multiple funding sources, performed multiple types of sensitivity analyses. Percentages have been rounded to the nearest integer.

**Table 3. Methodological and reporting characteristics in publications of VOI applications<sup>f</sup> (continued)**

<b>Characteristic</b>		<b>Number of studies (%)</b>
Funding	Government	50 (69)
	Industry	7 (10)
	Non-profits, foundations	6 (8)
	Professional membership organizations	1 (1)
	No funding	4 (6)
	Not reported	10 (14)
Data sources	Exclusively literature-based	57 (79)
	Primary and literature-based data	15 (21)
Time horizon stated	Yes	62 (86)
	No	10 (14)
Perspective	Societal	9 (13)
	Health payer	42 (58)
	Not stated	14 (19)
	Other	7 (8)
Discounting costs	Yes	47 (65)
	No/NR	25 (35)
Discounting of effectiveness	Yes	50 (69)
	No/NR	22 (31)
Calibration	Yes	15 (21)
	No/NR	57 (79)
Validation	Yes	5 (7)
	No/NR	67 (93)
Sensitivity analyses	One way	36 (50)
	Two-way	8 (11)
	Multivariate	3 (4)
	Probabilistic	57 (79)
	Other/unclear	3 (4)
	Not performed	4 (6)
Calculations for VOI	EVPI	68 (94)
	EVPPPI	42 (58)
	EVSI	5 (7)
	EVSI-P	1 (1)
Accounting for stochastic dependencies	Yes	7 (10)
	No/NR	65 (90)
Graphs	Tornado or other univariate	10 (14)
	CE plane	9 (13)
	CEAC	38 (53)
	CEAF	16 (22)
	EVPI over $\lambda$	37 (51)
	EVPPPI barchart	14 (19)
	EVPPPI over $\lambda$	2 (3)
Specific designs proposed	Yes	25 (35)
	No	47 (65) <sup>g</sup>

<sup>f</sup>Relative frequencies may not sum to 100% when studies compared more than one active intervention (for example a surgical and a medical treatment), reported on more than two outcomes (for example, life years and quality-adjusted life years), were supported by multiple funding sources, performed multiple types of sensitivity analyses. Percentages have been rounded to the nearest integer.

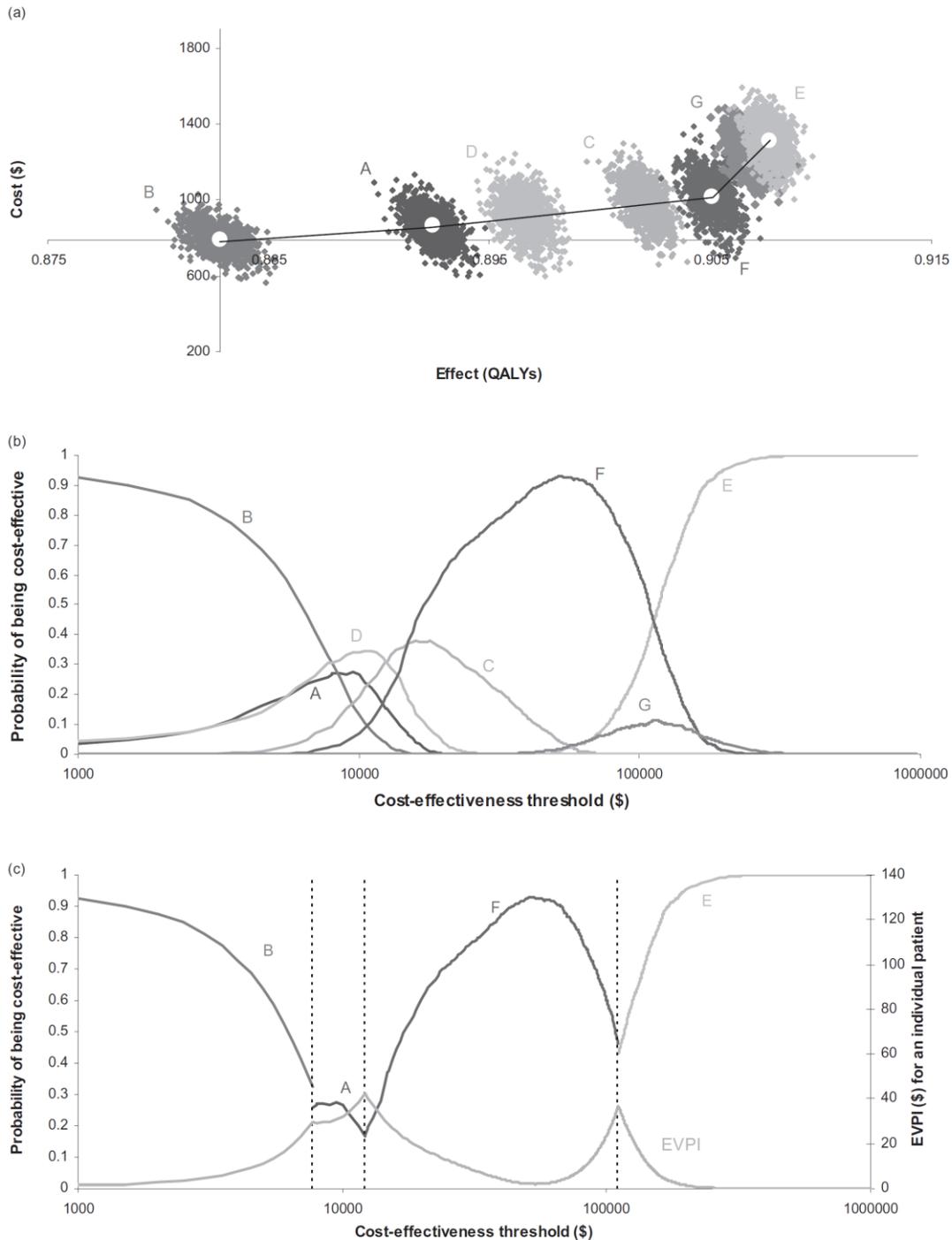
<sup>g</sup>In two cases a recommendation that no further research is necessary was based on low estimated EVPI values.

**Table 3. Methodological and reporting characteristics in publications of VOI applications<sup>f</sup> (continued)**

<b>Characteristic</b>	<b>Number of studies (%)</b>	
Specific designs (% only among studies suggesting specific designs)	Any proposal for RCTs	22 (88)
	Any proposal for economic evaluations	2 (8)
	Any proposal for observational studies	6 (24)
	Meta-analysis (updating or IPD)	2 (8)

$\lambda$ = threshold for willingness to pay; CE plane | AC | AF = cost-effectiveness plane | acceptability curves | acceptability frontier; EVPI = expected value of perfect information; EVPPI = expected value of partial perfect information; EVSI = expected value of sample information; EVSI-P = expected value of partial sample information; IPD = individual participant data; NR = not reported; QALY = Quality adjusted life years; RCT = randomized controlled trial; UK = United Kingdom; USA = United States of America; VOI= value of information.

**Figure 5. Examples of graphs used in cost-effectiveness and VOI analyses: (a) Cost-effectiveness plane with probabilistic sensitivity analysis results; (b) Cost-effectiveness acceptability curves; (c) Cost-effectiveness acceptability frontier along with EVPI graph**



We briefly discuss the interpretation of each of these graphs: (a) the *cost effectiveness plane scatter plot* is a bivariate scatter plot of costs (measured in dollars in this example) over effectiveness (here quantified in QALYs). Interventions with higher cost are placed higher and those with increased effectiveness are placed to the right. In the example we have used, probabilistic sensitivity analysis was performed and the results of different simulations have been plotted together. The authors have assessed the cost-effectiveness of seven alternative management strategies (labeled A through G) for heartburn. The lines connecting the “clouds” of dots depict the cost-effectiveness frontier. (b) The *cost-effectiveness acceptability curves* represent the probability that each treatment is cost-effective (y-axis, ranging from 0 to 1) for given willingness-to-pay thresholds (x-axis). The probabilities of all

treatments at each willingness-to-pay threshold sum to 1. The strategy that is most likely to be cost-effective is the one plotted higher (for each threshold). Note that the relative probability of cost-effectiveness of treatments can change drastically as the willingness-to-pay threshold is modified. (c) The cost-effectiveness acceptability frontier can be derived from the cost-effectiveness acceptability curves, by selecting—for each willingness-to-pay value—the treatment with the highest probability of being cost-effective, and only plotting that value on the x-axis (i.e. by suppressing less cost-effective treatments). The *EVPI over willingness-to-pay* graph plots the expected value of a hypothetical study with infinite sample size that would inform all parameters in the decision model. Because the EVPI is often measured in monetary units (e.g., here it is measured in dollars per patient) it is plotted using a different y-axis, here shown on the right of panel (c). It is evident that the EVPI graph has local maxima when the cost-effectiveness acceptability curve has discontinuities or local minima. The figure is reprinted with permission from Barton GR, Value Health, 2008.<sup>6</sup> This paper presented several reanalyses of data from a cost-effectiveness and cost-utility analysis study by Goeree R, Value Health, 2001.<sup>7</sup> EVPI= expected value of perfect information; QALY= quality adjusted life years.

Overall, the frequency of recommending further randomized controlled trials was significantly different between meta-analyses, cost-effectiveness analyses, and VOI analyses ( $p=0.008$  by Fisher's exact test), with such a recommendation being more common among meta-analyses and VOI analyses and less common among cost-effectiveness analyses. There was also a suggestion that the frequency of proposing observational designs was different ( $p=0.059$  by Fisher's exact test) with such designs being more frequently proposed by cost-effectiveness analyses and less frequently by meta-analyses or VOI analyses.

## Qualitative Interviews

A number of themes emerged during the qualitative interviews. They are described below.

## Face Validity of the Stakeholder Group and of Stakeholder Participation

By their very nature, assessments of future research needs are subjective. This is true not only for future research needs that have been prioritized by stakeholders (such as clinicians, researchers, insurers, payers, or funders) using qualitative methods, but also for exercises that are informed by quantitative approaches such as decision, economic, or VOI modeling, since modeling depends on assumptions. Therefore the face validity of a future research needs document will depend not only on the appropriateness and soundness of the methods used, but also on the composition of the stakeholder group and the assumptions used in modeling. Most potential users of a future research needs document are likely to be aware of the challenges in identifying and prioritizing future research needs; however, optimal presentation methods can increase the usability of Future Research Needs documents.

All interviewed experts agreed that when presenting results of qualitative research with stakeholders, it is important to justify the appropriateness of the stakeholder group, to convincingly demonstrate their expertise, and to state that all stakeholders had opportunity to provide input. While all interviewed experts agreed that it is impossible to include all important leaders in a field, they differed in how strongly they would criticize an exercise that did not include a specific thinker whose opinion they value: Expert A stated that it is likely that the face validity of the whole process could suffer, while others did not feel as strongly. Therefore, a description of the credentials of the stakeholders and the perspective they bring is probably sufficient for the reader to judge the face validity of the composition of the group.

All interviewed experts concurred that it is important to clearly state whether all stakeholders participated in a meaningful way. For example, in large teleconferences (with more than 6 to 9 people) it is uncommon that all participants contribute. The latter situation would be an example

of questionable face validity. Thus, the future research needs documents should assess and report the degree to which stakeholders were engaged in the process.

## Description of Methods Other Than Stakeholder Selection

As in all scientific documents, methods should be described concisely and should follow standard reporting guidelines whenever these are available (expert B). Expert B did not suggest specific reporting guidelines, but we identified several both for reporting qualitative research<sup>8-11</sup> and for modeling.<sup>12-15</sup>

Based on input from the interviewees, the length of the methods section, the detail presented and the technical language used should be similar to what one would read in a general medical journal. For example, three to five pages of double-spaced text may be an appropriate length. To economize space, a future research needs document could refer to standard guidance or methods documents that could be developed by the Effective Healthcare Program, and report all detailed descriptions to an appendix, as needed.

## Description of Future Research Needs

The experts interviewed agreed that different potential users of a future research needs document have different interest or needs. Based on the interviews, we decided to distinguish between a more abstract presentation of the areas that merit future research (hereafter called “areas that merit future research”) and a more detailed presentation of a research design along with specification of populations, interventions or exposures, comparators (if applicable) and outcomes (hereafter called by the acronym PICO).

All experts agreed that a description of the “area” that merits future research is important. Examples of descriptions of areas meriting further research may be “effectiveness of drug eluting stents versus bypass surgery in a coronary artery disease” or “quantification of preferences or quality of life ratings for patients who experienced stroke or other health events.”

There was disagreement as to whether a more detailed specification of PICO elements is useful. An example of a detailed statement would be: “What is the effectiveness of *sirolimus* eluting stents versus *on-pump* bypass surgery with *respect to revascularization* in patients with coronary artery disease *who are older than 75 years of age and have diabetes.*”<sup>h</sup> Experts A and B cautioned that a more detailed description may be overinterpreted as being too prescriptive. One of the two experts was concerned that a too prescriptive document may “undermine [the current paradigm of] investigator-initiated research,” and that in an extreme case this “would drive the best researchers out of the field.” The other expert noted that inevitably, a PICO-level description could select, for example, one subpopulation over equally important subpopulations and that this could be a point of contention. However, both experts A and B agreed that their reservations were dependent on the framing of a future research needs document. Experts C and D did not share the reservations of experts A and B in any appreciable degree. They suggested that specifying the PICO elements can be useful in that it shows examples of what research is needed.

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<sup>h</sup>Emphasis added to highlight differences in the specificity of descriptions

## **Description of the Ranking of Future Research Needs**

All experts appreciated that explicit ranking of future research needs is subjective and challenging. They suggested that a *tiered presentation* of future research needs may be preferable, as it may attract less criticism. The interviewer suggested that such a tiered presentation could, for example, group research needs into thematic entities according to whether they address effectiveness of interventions, safety of interventions, role of testing, disease epidemiology, health care costs, patient preferences, or development of new resources (e.g., planning new registries). The experts apparently agreed but did not expand the discussion.

## **Description of How Proposed Research Designs Are Selected**

All experts agreed that it is useful to provide advantages and disadvantages of various research designs, and to describe the algorithms that were used to favor one design over another.

## **Description of Feasibility of Future Research and of Projected Future Research Cost**

Experts B and C commented that it is very difficult to assess the actual feasibility of a future study. For example, many planned trials were overly optimistic regarding their projected accrual rates, and were terminated early. It is even more difficult to project the cost of future research. When asked explicitly, experts A and D were also skeptical of any projections regarding the feasibility or cost of future research.

The interviewer proposed that operational definitions of feasibility and future research costs could be used. For example, if it is deemed that a randomized trial is important, one could do a power analysis under several scenarios and compare the calculated trial sample sizes with the largest trials in the field, as a yardstick for research feasibility or cost. The experts agreed that this can be useful, but cautioned that this will yield only an approximate estimate. Three experts commented that funders are unlikely to rely on projections of research feasibility or cost, but appreciated that such projections may serve as a sounding board for those who actually prioritize future research needs.

## **Appropriateness of Using Modeling To Inform Prioritization of Research Needs**

The experts interviewed had different familiarity with modeling and quantitative methods. Here, “modeling” is taken to mean quantitative analyses that enumerate choices (decisions) under hypothetical clinical scenarios and explore their potential outcomes by assigning probabilities of outcome occurrence and utility values; as such, modeling encompasses decision analyses, cost-effectiveness/utility analyses, and value of information analyses. All the experts were receptive to using modeling to inform prioritization of future research, but all agreed that modeling should not be the only method used to prioritize future research. The experts agreed that the assumptions required and insights afforded by modeling methods should be clearly stated. An example of a clear statement is “based on modeling, the comparative effectiveness of the treatments for frequency of revascularizations, rather than the prevalence of coronary artery disease, is a more important target for future research.” Three experts favored graphs over tables to present relevant insights from modeling (one expert was not asked).

## Discussion and Conclusions

Future research needs recommendations are valuable inputs for researchers, funders, and advocates making decisions about avenues for future scientific exploration. We performed an empirical evaluation of the published literature to appreciate the variability in the presentation of information on future research needs. We found that most systematic reviews, meta-analyses, or economic analyses do not focus on future research needs, and any referral to future research is most often cursory. Systematic reviews and meta-analyses often call for additional randomized trials, while economic analyses are more diverse in their suggestions.

In qualitative discussions with experts, we identified a number of general themes. The discussions were quickly saturated, and while additional one-to-one interviews could have generated more themes, it is unclear whether these would have been of major importance for defining the optimal format for presenting future research needs. An unanticipated theme from the qualitative interviews was that specificity in the recommendations for future research is not universally and unconditionally viewed as a desirable attribute. The rationale is that specific descriptions could be perceived as too prescriptive or restrictive, and in the extreme they may have unintended consequences, such as opposing the paradigm of investigator-initiated research. Experts disagreed on the importance of this point. Nevertheless it is probably prudent to take this point into account when reporting assessments of future research needs, and all experts agreed that proper framing of the future research needs documents could address this concern. A survey of a large and representative sample of potential users of future research needs assessments would clarify whether such reactions are prevalent. If yes, it would be also interesting to understand why some users are prone to seeing even moderately specific recommendations with skepticism. Ideology, cultural norms, or professional self-interests may be explanations.

Several limitations need to be considered when interpreting our results. First, we only recruited four experts for our qualitative interviews; hence, our results should be considered hypothesis forming and not representative of all stakeholders. However, the purpose of the qualitative interviews was to identify general themes with respect to the way different stakeholders would approach a document presenting and discussing future research needs, and not necessarily to get a representative quantification of different opinions. The optimal research design to quantify the frequency of different opinions is a survey using a representative sampling scheme, rather than qualitative interviews or even focus groups.

Regarding our empirical assessment of secondary research manuscripts, we focused on high impact general journals (for systematic reviews) or highly specialized technical journals (for cost-effectiveness/utility analyses). Thus our empirical assessment of future research presentation is not generalizable to all journals. If anything, because even in these “top-tier” journals the presentation of implications for future research was fairly cursory and informal, the situation is unlikely to be better in other research outlets. Further, determining future research needs is not the primary focus of systematic reviews and cost-effectiveness/utility analyses. Therefore it is doubtful that including a broader set of journals would change the essence of our conclusions.

The concept of a stand-alone document on future research needs is probably new to most of the individuals approached, and additional discussion is likely needed regarding potential uses prior to making very specific recommendations on the optimal presentation of future research needs documents. We outline the following preliminary recommendations for presenting future

research needs documents, based on the results of the empirical assessment and the qualitative interviews:

1. Provide succinct yet adequate description of methods and results, following guidelines for reporting of health care research (for example, reporting guidelines for qualitative research<sup>8-11</sup> and modeling<sup>12-15</sup>). Aim for a level of detail similar to that found in papers addressed to a general medical audience.
2. Be cognizant of the importance of the face validity of the process. Justify the selection of the stakeholders who participated in the identification or prioritization of research needs, and be clear about their degree of engagement.
3. Consider reporting the results of the future research needs assessment at two levels of detail. A suggestion would be to first present general areas that merit future research without specifying research designs or specific details on, for example, PICO elements. A second set of results could elaborate further on potential research designs, details on PICO elements, or other details as applicable.
4. Frame the more specific set of results as “examples” rather than strict recommendations.
5. Avoid explicit prioritization of research needs when there are no clear differences in the perceived strength of alternative recommendations. A general prioritization of future research recommendations as of “high,” “medium,” or “low” importance may be more appropriate than an explicit numerical ranking. Consider a grouped presentation of future research needs by thematic entities.
6. Clearly define how the feasibility of future research was assessed. It may be instructive to perform power analyses for specific research designs for a range of assumptions, and to compare the results with the size and type of existing studies in the field. For example, trials are typically more resource-intensive than secondary analyses of existing data.

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## Abbreviations

AHRQ	Agency for Healthcare Research and Quality
CE	Cost-effectiveness
CEAC	Cost-effectiveness acceptability curves
CEAF	Cost-effectiveness acceptability frontier
EPC	Evidence-based Practice Center
EVPI	Expected value of perfect information
EVPII	Expected value of partial perfect information
EVSII	Expected value of sample information
EVSII-P	Expected value of sample information for parameters
ICER	Incremental cost-effectiveness ratio
MIPD	Meta-analysis of individual patient data
NA	Not applicable
PCI	Percutaneous coronary intervention
QALY	Quality adjusted life year
RCT	Randomized controlled trial
VOI	Value of information

## Appendix A. Search Strategies

All searches were performed in MEDLINE (through the PubMed interface). The searches for systematic reviews with meta-analysis and cost-effectiveness analyses were performed on November 9, 2010; the search for value of information analyses was performed on July 16, 2010.

### *Searches for systematic reviews with meta-analysis*

((("meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms]) AND (new england journal of medicine[journal] OR lancet[journal] OR british medical journal[journal] OR annals of internal medicine[journal] OR journal of the american medical association[journal]) AND ("2005/11/11"[PDat] : "2010/11/08"[PDat])) NOT ("letter"[Publication Type] OR "editorial"[Publication Type] OR "comment"[Publication Type]))

### *Searches for cost-benefit analyses*

("cost-benefit analysis"[MeSH Terms]) AND (new england journal of medicine[journal] OR lancet[journal] OR british medical journal[journal] OR annals of internal medicine[journal] OR journal of the american medical association[journal] OR medical decision making[journal] OR Pharmacoeconomics[journal] OR International Journal of Technology Assessment in Health Care[journal]) AND ("2005/11/11"[PDat] : "2010/11/08"[PDat])) NOT ("letter"[Publication Type] OR "editorial"[Publication Type] OR "comment"[Publication Type]))

### *Searches for value of information analyses*

(value) AND ((perfect OR imperfect OR partial OR sample) AND information\*) OR "EVPI" OR "EVSI" OR "EVPII" OR "perfect information" OR "value of clairvoyance" OR "value of information" OR "value-of-information"

# Appendix B. Included and Excluded Studies for the Empirical Assessment of Systematic Reviews

## Included Studies

PMID	Title	Year	Journal
17622601	Efficacy and safety of incretin therapy in type 2 diabetes: systematic review and meta-analysis	2007	JAMA
19509383	Corticosteroids in the treatment of severe sepsis and septic shock in adults: a systematic review	2009	JAMA
17662881	Recurrence rates of video-assisted thoracoscopic versus open surgery in the prevention of recurrent pneumothoraces: a systematic review of randomised and non-randomised trials	2007	Lancet
19436018	Aspirin for the prevention of cardiovascular events in patients with peripheral artery disease: a meta-analysis of randomized trials	2009	JAMA
16418466	Aspirin for the primary prevention of cardiovascular events in women and men: a sex-specific meta-analysis of randomized controlled trials	2006	JAMA
18313501	Complex interventions to improve physical function and maintain independent living in elderly people: a systematic review and meta-analysis	2008	Lancet
20671013	Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis	2010	BMJ
16705109	Anti-TNF antibody therapy in rheumatoid arthritis and the risk of serious infections and malignancies: systematic review and meta-analysis of rare harmful effects in randomized controlled trials	2006	JAMA
20197533	Higher vs lower positive end-expiratory pressure in patients with acute lung injury and acute respiratory distress syndrome: systematic review and meta-analysis	2010	JAMA
19567909	The benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors: meta-analysis of randomised controlled trials	2009	BMJ
19460803	Use of non-invasive ventilation to wean critically ill adults off invasive ventilation: meta-analysis and systematic review	2009	BMJ
18495631	Hormone replacement therapy and risk of venous thromboembolism in postmenopausal women: systematic review and meta-analysis	2008	BMJ
17923720	Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis	2007	BMJ
19200918	Imaging strategies for low-back pain: systematic review and meta-analysis	2009	Lancet
18177773	Adjuvant chemotherapy in oestrogen-receptor-poor breast cancer: patient-level meta-analysis of randomised trials	2008	Lancet
19724046	Combined corticosteroid and antiviral treatment for Bell palsy: a systematic review and meta-analysis	2009	JAMA
16818928	Meta-analysis: Cysticidal drugs for neurocysticercosis: albendazole and praziquantel	2006	Ann Intern Med
17310052	Meta-analysis: anticoagulant prophylaxis to prevent symptomatic venous thromboembolism in hospitalized medical patients	2007	Ann Intern Med
19033591	Inhaled corticosteroids in patients with stable chronic obstructive pulmonary disease: a systematic review and meta-analysis	2008	JAMA
19017592	Comparative benefits and harms of second-generation antidepressants: background paper for the American College of Physicians	2008	Ann Intern Med
17237299	Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis	2007	BMJ
17426275	Corticosteroids for the prevention of atrial fibrillation after cardiac surgery: a randomized controlled trial	2007	JAMA

PMID	Title	Year	Journal
19141768	Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis	2009	JAMA
19661138	Corticosteroids for pain relief in sore throat: systematic review and meta-analysis	2009	BMJ
16458764	Self-monitoring of oral anticoagulation: a systematic review and meta-analysis	2006	Lancet
19303634	Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials	2009	Lancet
19995812	Neuraminidase inhibitors for preventing and treating influenza in healthy adults: systematic review and meta-analysis	2009	BMJ
18283206	Meta-analysis: effectiveness of drugs for preventing contrast-induced nephropathy	2008	Ann Intern Med
19620144	Systematic review: glucose control and cardiovascular disease in type 2 diabetes	2009	Ann Intern Med
19050195	Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis	2008	JAMA
18632672	Interventions before consultations to help patients address their information needs by encouraging question asking: systematic review	2008	BMJ
16473126	Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis	2006	Lancet
16443611	Effect of hepatitis B immunisation in newborn infants of mothers positive for hepatitis B surface antigen: systematic review and meta-analysis	2006	BMJ
20472172	Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials	2010	Lancet
17577006	Meta-analysis: acupuncture for osteoarthritis of the knee	2007	Ann Intern Med
16380593	Noninvasive ventilation in acute cardiogenic pulmonary edema: systematic review and meta-analysis	2005	JAMA
18390914	Healing by primary closure versus open healing after surgery for pilonidal sinus: systematic review and meta-analysis	2008	BMJ
16679330	Systematic review and meta-analysis of ethnic differences in risks of adverse reactions to drugs used in cardiovascular medicine	2006	BMJ
16389253	Meta-analysis: protein and energy supplementation in older people	2006	Ann Intern Med
17517853	Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes	2007	N Engl J Med
18594042	Early invasive vs conservative treatment strategies in women and men with unstable angina and non-ST-segment elevation myocardial infarction: a meta-analysis	2008	JAMA
19376798	Four layer bandage compared with short stretch bandage for venous leg ulcers: systematic review and meta-analysis of randomised controlled trials with data from individual patients	2009	BMJ
16616558	Effect of non-invasive positive pressure ventilation (NIPPV) on mortality in patients with acute cardiogenic pulmonary oedema: a meta-analysis	2006	Lancet
17438317	Meta-analysis: chondroitin for osteoarthritis of the knee or hip	2007	Ann Intern Med
19666987	Neuraminidase inhibitors for treatment and prophylaxis of influenza in children: systematic review and meta-analysis of randomised controlled trials	2009	BMJ
17606956	Beta-blockers and progression of coronary atherosclerosis: pooled analysis of 4 intravascular ultrasonography trials	2007	Ann Intern Med
18321957	Treatment of human brucellosis: systematic review and meta-analysis of randomised controlled trials	2008	BMJ
18299289	Effects of statins in patients with chronic kidney disease: meta-analysis and meta-regression of randomised controlled trials	2008	BMJ
19493939	A comparison of fluoroquinolones versus other antibiotics for treating enteric fever: meta-analysis	2009	BMJ

<b>PMID</b>	<b>Title</b>	<b>Year</b>	<b>Journal</b>
18480116	Effects of different regimens to lower blood pressure on major cardiovascular events in older and younger adults: meta-analysis of randomised trials	2008	BMJ

## **Excluded Studies**

No studies were excluded.

# Appendix C. Included and Excluded Studies for the Empirical Assessment of Cost-Effectiveness Analyses

## Included Studies

PMID	Title	Year	Journal
19638648	Options for managing low grade cervical abnormalities detected at screening: cost effectiveness study	2009	BMJ
20059782	Cost-effectiveness of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers in newly diagnosed type 2 diabetes in Germany	2010	Int J Technol Assess Health Care
19354343	Cost-effectiveness evaluation of a quadrivalent human papillomavirus vaccine in Belgium	2009	Pharmacoeconomics
19372131	Surgical treatments for men with benign prostatic enlargement: cost effectiveness study	2009	BMJ
19690341	Lifestyle interventions for knee pain in overweight and obese adults aged > or = 45: economic evaluation of randomised controlled trial	2009	BMJ
17192116	Cost effectiveness of a pharmacy-based coaching programme to improve adherence to antidepressants	2007	Pharmacoeconomics
20550222	Impact of rapid methicillin-resistant Staphylococcus aureus polymerase chain reaction testing on mortality and cost effectiveness in hospitalized patients with bacteraemia: a decision model	2010	Pharmacoeconomics
17848402	Preventive strategies for group B streptococcal and other bacterial infections in early infancy: cost effectiveness and value of information analyses	2007	BMJ
17937835	Economic evaluation of laparoscopic surgery for colorectal cancer	2007	Int J Technol Assess Health Care
18310262	Helicobacter pylori test and treat versus proton pump inhibitor in initial management of dyspepsia in primary care: multicentre randomised controlled trial (MRC-CUBE trial)	2008	BMJ
16460137	The long-term cost effectiveness of treatments for benign prostatic hyperplasia	2006	Pharmacoeconomics
16571195	Early assessment of the likely cost-effectiveness of a new technology: A Markov model with probabilistic sensitivity analysis of computer-assisted total knee replacement	2006	Int J Technol Assess Health Care
18708248	Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea	2008	Lancet
17350965	Parenting programme for parents of children at risk of developing conduct disorder: cost effectiveness analysis	2007	BMJ
19331707	Microvolt T-wave alternans and the selective use of implantable cardioverter defibrillators for primary prevention: a cost-effectiveness study	2009	Int J Technol Assess Health Care
16920473	Cardiovascular disease prevention with a multidrug regimen in the developing world: a cost-effectiveness analysis	2006	Lancet
20584354	The cost-effectiveness of the SPHERE intervention for the secondary prevention of coronary heart disease	2010	Int J Technol Assess Health Care
16365467	Empirical anti-Candida therapy among selected patients in the intensive care unit: a cost-effectiveness analysis	2005	Ann Intern Med
19757866	Head lice treatments and school policies in the US in an era of emerging resistance: a cost-effectiveness analysis	2009	Pharmacoeconomics
18936502	Cost-effectiveness of nurse-led disease management for heart failure in an ethnically diverse urban community	2008	Ann Intern Med
18400123	Cost-effectiveness of a multidisciplinary fall prevention program in community-dwelling elderly people: a randomized controlled trial (ISRCTN 64716113)	2008	Int J Technol Assess Health Care

<b>PMID</b>	<b>Title</b>	<b>Year</b>	<b>Journal</b>
20133502	Economic evaluation of the DiAMOND randomized trial: cost and outcomes of 2 decision aids for mode of delivery among women with a previous cesarean section	2010	Med Decis Making
18782838	Paracetamol plus ibuprofen for the treatment of fever in children (PITCH): economic evaluation of a randomised controlled trial	2008	BMJ
16673687	Value of magnetic resonance cholangiopancreatography in the diagnosis of biliary abnormalities in postcholecystectomy patients: a probabilistic cost-effectiveness analysis of diagnostic strategies	2006	Int J Technol Assess Health Care
17909207	Cost-effectiveness of screening and vaccinating Asian and Pacific Islander adults for hepatitis B	2007	Ann Intern Med
16740528	Pressure relieving support surfaces (PRESSURE) trial: cost effectiveness analysis	2006	BMJ
16984065	Economic evaluation of empirical antisecretory therapy versus Helicobacter pylori test for management of dyspepsia: a randomized trial in primary care	2006	Int J Technol Assess Health Care
20406865	Cost effectiveness of home ultraviolet B phototherapy for psoriasis: economic evaluation of a randomised controlled trial (PLUTO study)	2010	BMJ
18063025	Prevention of cardiovascular disease in high-risk individuals in low-income and middle-income countries: health effects and costs	2007	Lancet
18199700	The impact of response to the results of diagnostic tests for malaria: cost-benefit analysis	2008	BMJ
17638858	Diagnostic accuracy and clinical utility of a simplified low cost method of counting CD4 cells with flow cytometry in Malawi: diagnostic accuracy study	2007	BMJ
20392321	Cost-effectiveness of enhanced external counterpulsation (EECP) for the treatment of stable angina in the United Kingdom	2010	Int J Technol Assess Health Care
20014877	A policy model to evaluate the benefits, risks and costs of warfarin pharmacogenomic testing	2010	Pharmacoeconomics
16525173	Cost-effectiveness of osteoporosis screening and treatment with hormone replacement therapy, raloxifene, or alendronate	2006	Med Decis Making
16984069	Cost-effectiveness analysis of strategies for HER2 testing of breast cancer patients in France	2006	Int J Technol Assess Health Care
19126247	Cost-effectiveness of magnetic resonance guided focused ultrasound for the treatment of uterine fibroids	2009	Int J Technol Assess Health Care
17960953	Strategies for the management of suspected heparin-induced thrombocytopenia: a cost-effectiveness analysis	2007	Pharmacoeconomics
20028779	Screening for postnatal depression in primary care: cost effectiveness analysis	2009	BMJ
16980315	A randomised controlled trial of acupuncture care for persistent low back pain: cost effectiveness analysis	2006	BMJ
18793033	Costs and effects of secondary prevention with perindopril in stable coronary heart disease in Poland: an analysis of the EUROPA study including 1251 Polish patients	2008	Pharmacoeconomics
19331713	Can calcium chemoprevention of adenoma recurrence substitute or serve as an adjunct for colonoscopic surveillance?	2009	Int J Technol Assess Health Care
18218176	Value of information of a clinical prediction rule: informing the efficient use of healthcare and health research resources	2008	Int J Technol Assess Health Care
17129076	Cost effectiveness of tumour necrosis factor-alpha inhibitors as first-line agents in rheumatoid arthritis	2006	Pharmacoeconomics
17488139	Economic evaluation of treatment administration strategies of ganciclovir for cytomegalovirus retinitis in HIV/AIDS patients in Thailand: a simulation study	2007	Pharmacoeconomics
19366497	Cost-effectiveness of human papillomavirus vaccination in Belgium: do not forget about cervical cancer screening	2009	Int J Technol Assess Health Care

<b>PMID</b>	<b>Title</b>	<b>Year</b>	<b>Journal</b>
19620143	When to start antiretroviral therapy in resource-limited settings	2009	Ann Intern Med
20194233	Cost-effectiveness of preparticipation screening for prevention of sudden cardiac death in young athletes	2010	Ann Intern Med
20446755	Cost effectiveness of leukotriene receptor antagonists versus long-acting beta-2 agonists as add-on therapy to inhaled corticosteroids for asthma: a pragmatic trial	2010	Pharmacoeconomics
20550224	Cost effectiveness of leukotriene receptor antagonists versus inhaled corticosteroids for initial asthma controller therapy: a pragmatic trial	2010	Pharmacoeconomics
17887807	Cost effectiveness of pegaptanib for the treatment of age-related macular degeneration in the UK	2007	Pharmacoeconomics

## **Excluded Studies**

<b>PMID</b>	<b>Title</b>	<b>Year</b>	<b>Journal</b>
20465313	Cetuximab for recurrent and/or metastatic squamous cell carcinoma of the head and neck: a NICE single technology appraisal.	2010	Pharmacoeconomics
18400122	Cost-effectiveness of primarily human papillomavirus-based cervical cancer screening in settings with currently established Pap screening: a systematic review commissioned by the German Federal Ministry of Health.	2008	IJTAHC
20059778	Prognostic value, clinical effectiveness, and cost-effectiveness of high-sensitivity C-reactive protein as a marker for major cardiac events in asymptomatic individuals: a health technology assessment report.	2010	IJTAHC
19640014	How to deal with cost differences at baseline.	2009	Pharmacoeconomics
16984676	Cost-effectiveness of self-management in asthma: a systematic review of peak flow monitoring interventions.	2006	IJTAHC

# Appendix D. Included and Excluded Studies for the Empirical Assessment of Value of Information Analyses

## Included Studies

PMID	Title	Year	Journal
6763124	Decision-analytic determination of study size. The case of electronic fetal monitoring	1981	Med Decis Making
9357611	Decision-analytic valuation of clinical information systems: application to an alerting system for coronary angiography	1997	Proc AMIA Annu Fall Symp
9456214	Sensitivity analysis and the expected value of perfect information	1998	Med Decis Making
9551284	The cost-benefit of a randomized trial to a health care organization	1998	Control Clin Trials
11329844	Bayesian value-of-information analysis. An application to a policy model of Alzheimer's disease	2001	Int J Technol Assess Health Care
12150601	Markov chain Monte Carlo estimation of a multiparameter decision model: consistency of evidence and the accurate assessment of uncertainty	2002	Med Decis Making
12098524	Planning the efficient allocation of research funds: an adapted application of a non-parametric Bayesian value of information analysis	2002	Health Policy
15248937	A pilot study on the use of decision theory and value of information analysis as part of the NHS Health Technology Assessment programme	2004	Health Technol Assess
15215017	Methods for expected value of information analysis in complex health economic models: developments on the health economics of interferon-beta and glatiramer acetate for multiple sclerosis	2004	Health Technol Assess
16076237	Using value of information analysis to inform publicly funded research priorities	2005	Appl Health Econ Health Policy
16097842	Economic evaluation of temozolomide in the treatment of recurrent glioblastoma multiforme	2005	Pharmacoeconomics
16022802	Cost-effectiveness of alternative strategies for the initial medical management of non-ST elevation acute coronary syndrome: systematic review and decision-analytical modelling	2005	Health Technol Assess
16948891	The cost-effectiveness of testing for hepatitis C in former injecting drug users	2006	Health Technol Assess
16997926	An iterative Bayesian approach to health technology assessment: application to a policy of preoperative optimization for patients undergoing major elective surgery	2006	Med Decis Making
16545207	Surveillance of Barrett's oesophagus: exploring the uncertainty through systematic review, expert workshop and economic modelling	2006	Health Technol Assess
16786498	Informing the efficient use of health care and health care research resources - the case of screening for abdominal aortic aneurysm in Sweden	2006	Health Econ
16706572	Comprehensive decision-analytic model and Bayesian value-of-information analysis: pentoxifylline in the treatment of chronic venous leg ulcers	2006	Pharmacoeconomics
16751321	Implications of cancer staging uncertainties in radiation therapy decisions	2006	Med Decis Making

<b>PMID</b>	<b>Title</b>	<b>Year</b>	<b>Journal</b>
16984067	Priority setting for research in health care: an application of value of information analysis to glycoprotein IIb/IIIa antagonists in non-ST elevation acute coronary syndrome	2006	Int J Technol Assess Health Care
16707071	The cost-effectiveness of screening for oral cancer in primary care	2006	Health Technol Assess
17887805	A comparison of the cost effectiveness of pharmacotherapy or surgery (laparoscopic fundoplication) in the treatment of GORD	2007	Pharmacoeconomics
17651659	Prenatal screening and treatment strategies to prevent group B streptococcal and other bacterial infections in early infancy: cost-effectiveness and expected value of information analyses	2007	Health Technol Assess
17848402	Preventive strategies for group B streptococcal and other bacterial infections in early infancy: cost effectiveness and value of information analyses	2007	BMJ
17181985	A systematic review and economic model of the clinical effectiveness and cost-effectiveness of docetaxel in combination with prednisone or prednisolone for the treatment of hormone-refractory metastatic prostate cancer	2007	Health Technol Assess
17579936	Value of information analysis for a new technology: computer-assisted total knee replacement	2007	Int J Technol Assess Health Care
17999842	The clinical effectiveness and cost-effectiveness of cardiac resynchronisation (biventricular pacing) for heart failure: systematic review and economic model	2007	Health Technol Assess
17493314	Modeling payback from research into the efficacy of left-ventricular assist devices as destination therapy	2007	Int J Technol Assess Health Care
17493305	Comparing the clinical and economic effects of clinical examination, pulse oximetry, and echocardiography in newborn screening for congenital heart defects: a probabilistic cost-effectiveness model and value of information analysis	2007	Int J Technol Assess Health Care
17720521	Should hemodialysis patients with atrial fibrillation undergo systemic anticoagulation? A cost-utility analysis	2007	Am J Kidney Dis
18077847	Cost-effectiveness of alternative outpatient pelvic inflammatory disease treatment strategies	2007	Sex Transm Dis
17261117	Economic evaluation of palliative management versus peritoneal dialysis and hemodialysis for end-stage renal disease: evidence for coverage decisions in Thailand	2007	Value Health
18263560	Identifying research priorities: the value of information associated with repeat screening for age-related macular degeneration	2008	Med Decis Making
18513466	The clinical effectiveness and cost-effectiveness of screening programmes for amblyopia and strabismus in children up to the age of 4-5 years: a systematic review and economic evaluation	2008	Health Technol Assess
18179675	Uncertainty in decision-making: value of additional information in the cost-effectiveness of lifestyle intervention in overweight and obese people	2008	Value Health. 2008 May-Jun;11(3):424-34. Epub 2007 Dec 17.
18796263	The effectiveness and cost-effectiveness of minimal access surgery amongst people with gastro-oesophageal reflux disease - a UK collaborative study. The REFLUX trial	2008	Health Technol Assess
18522663	Decision-Analytic Modeling to Assist Decision Making in Organizational Innovation: The Case of Shared Care in Hearing Aid Provision	2008	Health Serv Res
19036232	Curative catheter ablation in atrial fibrillation and typical atrial flutter: systematic review and economic evaluation	2008	Health Technol Assess

PMID	Title	Year	Journal
18380636	Gaussian process metamodeling in Bayesian value of information analysis: a case of the complex health economic model for breast cancer screening	2008	Value Health
18272361	Surveillance of Barrett's oesophagus: is it worthwhile?	2008	Eur J Cancer
18380629	Cost-effectiveness and value of information analyses of neuraminidase inhibitors for the treatment of influenza	2008	Value Health
19178122	Statin therapy in rheumatoid arthritis: a cost-effectiveness and value-of-information analysis	2009	Pharmacoeconomics
19903416	The clinical effectiveness of glucosamine and chondroitin supplements in slowing or arresting progression of osteoarthritis of the knee: a systematic review and economic evaluation	2009	Health Technol Assess
18647257	The potential clinical and economic outcomes of pharmacogenomic approaches to EGFR-tyrosine kinase inhibitor therapy in non-small-cell lung cancer	2009	Value Health
19553267	Analysis of cost effectiveness of screening Danish men aged 65 for abdominal aortic aneurysm	2009	BMJ
19789242	Value-of-information analysis to guide future research in colorectal cancer screening	2009	Radiology
19332851	Impact of whole-body CT screening on the cost-effectiveness of CT colonography	2009	Radiology
19624978	Methods to identify postnatal depression in primary care: an integrated evidence synthesis and value of information analysis	2009	Health Technol Assess
18657098	Value of information and value of implementation: application of an analytic framework to inform resource allocation decisions in metastatic hormone-refractory prostate cancer	2009	Value Health
19558190	Informing disinvestment through cost-effectiveness modelling: is lack of data a surmountable barrier?	2009	Appl Health Econ Health Policy
19409154	Enhanced external counterpulsation for the treatment of stable angina and heart failure: a systematic review and economic analysis	2009	Health Technol Assess
19908924	Cost effectiveness of herpes zoster vaccine in Canada	2009	Pharmacoeconomics
19207559	Economic analysis of esophageal stenting for management of malignant dysphagia	2009	Dis Esophagus
19573471	The effect of different treatment durations of clopidogrel in patients with non-ST-segment elevation acute coronary syndromes: a systematic review and value of information analysis	2009	Health Technol Assess
19509121	The cost-effectiveness of an RCT to establish whether 5 or 10 years of bisphosphonate treatment is the better duration for women with a prior fracture	2009	Med Decis Making
19539109	Results of a model analysis to estimate cost utility and value of information for intravenous immunoglobulin in Canadian adults with chronic immune thrombocytopenic purpura	2009	Clin Ther
20190188	Uncertainty and patient heterogeneity in medical decision models	2010	Med Decis Making
20303217	The cost-effectiveness of particle therapy in non-small cell lung cancer: Exploring decision uncertainty and areas for future research	2010	Cancer Treat Rev
20087087	Value-of-information analysis to guide future research in the management of the colorectal malignant polyp	2010	Dis Colon Rectum
19084367	The value of positron emission tomography in patients with non-small cell lung cancer	2010	Eur J Radiol
20492762	A systematic review and economic evaluation of the clinical effectiveness and cost-effectiveness of aldosterone antagonists for postmyocardial infarction heart failure	2010	Health Technol Assess

PMID	Title	Year	Journal
20093524	Minor head injury: CT-based strategies for management-- a cost-effectiveness analysis	2010	Radiology
20627875	Trabectedin in the treatment of metastatic soft tissue sarcoma: cost-effectiveness, cost-utility and value of information	2010	Ann Oncol
20375420	The Cost-Effectiveness of a Randomized Controlled Trial to Establish the Relative Efficacy of Vitamin K1 Compared with Alendronate	2010	Med Decis Making.
20384978	The Cost-Effectiveness of Group Cognitive Behavioral Therapy Compared with Routine Primary Care for Women with Postnatal Depression in the UK	2010	Value Health
20430289	Cost-effectiveness of breech version by acupuncture-type interventions on BL 67, including moxibustion, for women with a breech foetus at 33 weeks gestation: a modelling approach	2010	Complement Ther Med
20035545	Cost-utility and value-of-information analysis of early versus delayed laparoscopic cholecystectomy for acute cholecystitis	2010	Br J Surg

## Excluded Studies

PMID	Title	Year	Journal
16589926	MEASURES OF THE VALUE OF INFORMATION	1956	Proc Natl Acad Sci
5990730	[Value of information of kidney biopsy]	1966	Z Gesamte Inn Med
1197296	The price and value of information	1975	Proc R Soc Med
682303	Assessment of value of information for patients	1978	JAMA
12266151	An economic analysis of marital fertility: some notes	1981	Philipp Econ J
10267433	Information resources management: management focus on the value of information and information work	1984	J Inf Image Manage
10269803	Regulating uncertain health hazards when there is changing risk information	1984	J Health Econ
3831639	Maximum Shannon information content of diagnostic medical testing. Including application to multiple non-independent tests	1985	Med Decis Making
3882734	Treatment selection for cancer patients: application of statistical decision theory to the treatment of advanced ovarian cancer	1985	J Chronic Dis
3727069	[The value of information obtained from preoperative laboratory parameters in patients receiving elective surgery]	1986	Ugeskr Laeger
3597686	What's wrong with decision analysis? Can the left brain influence the right?	1987	J Chronic Dis
10301458	Capital expenditure planning: the value of information to hospitals	1987	Hosp Health Serv Adm
3185180	Focusing technology assessment using medical decision theory	1988	Med Decis Making
2646176	Full threshold versus quantification of defects for visual field testing in glaucoma	1989	Graefes Arch Clin Exp Ophthalmol
2792592	Statistical uncertainty in the no-observed-adverse-effect level	1989	Fundam Appl Toxicol
2112217	Targeting assessments of magnetic resonance imaging in suspected multiple sclerosis	1990	Med Decis Making
2115175	Value-of-information analysis of testing strategies: estimating the effect of uncertainty about the proportion of chemicals that are true human carcinogens	1990	Prog Clin Biol Res
2119006	Comparing the cost of spinal MR with conventional myelography and radiculography	1990	Neuroradiology

PMID	Title	Year	Journal
2196411	Judicial and legislative viewpoints on physician misestimation of patient dysutilities: a problem for decision analysts	1990	Med Decis Making
1487587	Decision analysis for periodontal therapy	1992	J Dent Educ
1538631	A pitfall in utility assessment--patients' undisclosed investment decisions	1992	Med Decis Making
1631608	To prescribe or not to prescribe: on the regulation of pharmaceuticals in less developed countries	1992	Soc Sci Med
8234948	The value of animal test information in environmental control decisions	1993	Risk Anal
10123827	Integrating capital budgeting techniques	1993	Health Care Strateg Manage
10129155	Creating a market: an economic analysis of the purchaser-provider model	1993	Health Policy
7942098	Differences in the value of clinical information: referring physicians versus consulting specialists	1994	J Am Board Fam Pract
7950082	Improving outpatient services--the value of information	1994	Proc Annu Symp Comput Appl Med Care
7964217	The value of risk-reducing information	1994	J Med Syst
7990173	Experimental design for parameter estimation through sensitivity analysis	1994	J Toxicol Environ Health
8187733	Statistical issues on the no-observed-adverse-effect level in categorical response	1994	Environ Health Perspect
7546223	Predictions of rodent carcinogenicity testing results: interpretation in light of the Lave-Omenn value-of-information model	1995	Mol Carcinog
7860318	Understanding the factors behind the decision to purchase varying coverage amounts of long-term care insurance	1995	Health Serv Res
8733196	A cost-benefit analysis of voluntary routine HIV-antibody testing for hospital patients	1996	Soc Sci Med
8783436	Regret graphs, diagnostic uncertainty and Youden's Index	1996	Stat Med
8868224	Risk-based environmental remediation: Bayesian Monte Carlo analysis and the expected value of sample information	1996	Risk Anal
8913550	Comparing and using assessments of the value of information to clinical decision-making	1996	Bull Med Libr Assoc
8934123	Outcomes research and cost-effectiveness analysis in radiology	1996	Eur Radiol
9003938	An economic approach to clinical trial design and research priority-setting	1996	Health Econ
9087883	Optimum investments in project evaluations: when are cost-effectiveness analyses cost-effective?	1996	J Med Syst
10162540	Evaluating methodologies for assessing the value of information: sifting the evidence	1996	Top Health Inf Manage
10172597	Applying the value-of-information paradigm to laboratory management	1996	Clin Lab Manage Rev
9333085	Cost-effectiveness analysis of treatment alternatives for beef bulls with preputial prolapse	1997	J Am Vet Med Assoc
9357709	A decision analytic method for scoring performance on computer-based patient simulations	1997	Proc AMIA Annu Fall Symp
10169100	Genetic information and investment in human capital	1997	J Health Econ
9520961	Assessing the value of a new pharmaceutical. A feasibility study of contingent valuation in managed care	1998	Med Care.
9554104	Quantitative information of specific diagnostic tests	1998	J Med Syst
9564416	The value of information and the cost of uncertainty: who pays the bill?	1998	Angle Orthod
9708589	The impact of risk information on patients' willingness to pay for autologous blood donation	1998	Med Care

PMID	Title	Year	Journal
9753380	Risk adjustment and the trade-off between efficiency and risk selection: an application of the theory of fair compensation	1998	Health Econ
10186453	Cost-of-illness studies. Useful for health policy?	1998	Pharmacoeconomics
10348422	Bayesian approaches to the value of information: implications for the regulation of new pharmaceuticals	1999	Health Econ
10538846	Benefits foregone: too much of the wrong and too little of the right. Based on a presentation by Bernard S. Bloom, PhD	1999	Am J Manag Care
10548220	Discriminant power and information content of Ranson's prognostic signs in acute pancreatitis: a meta-analytic study	1999	Crit Care Med
10566413	Scoring performance on computer-based patient simulations: beyond value of information	1999	Proc AMIA Symp
10765446	Adaptive spatial sampling of contaminated soil	1999	Risk Anal
11844400	Menu Analysis for Improved Customer Demand and Profitability in Hospital Cafeterias	1999	Can J Diet Pract Res
10795342	Risk estimation and value-of-information analysis for three proposed genetic screening programs for chronic beryllium disease prevention	2000	Risk Anal
11148867	Addressing uncertainty in medical cost-effectiveness analysis implications of expected utility maximization for methods to perform sensitivity analysis and the use of cost-effectiveness analysis to set priorities for medical research	2001	J Health Econ
11332553	Estimation of error and bias in Bayesian Monte Carlo decision analysis using the bootstrap	2001	Risk Anal
11558649	A dynamic programming approach to the efficient design of clinical trials	2001	J Health Econ. 2001
11695561	Assessment of human cancer risk: challenges for alternative approaches	2001	Toxicol Pathol
11916800	How to schedule elective surgical cases into specific operating rooms to maximize the efficiency of use of operating room time	2002	Anesth Analg
11918821	The bias against new innovations in health care: value uncertainty and willingness to pay	2002	Value Health
12002189	Quantification of variability and uncertainty in lawn and garden equipment NOx and total hydrocarbon emission factors	2002	J Air Waste Manag Assoc
19807328	Decision analysis and drug development portfolio management: uncovering the real options value of your projects	2002	Expert Rev Pharmacoecon Outcomes Res
12568827	Using decision analytic methods to assess the utility of family history tools	2003	Am J Prev Med
14499052	The role of modelling in prioritising and planning clinical trials	2003	Health Technol Assess
14554141	Simulation modeling to derive the value-of-information for risky animal disease-import decisions	2003	Prev Vet Med
14601158	Estimating the marginal value of 'better' research output: 'designed' versus 'routine' data in randomised controlled trials	2003	Health Econ
14984281	The use of decision models in mental health economic evaluation: challenges and opportunities	2003	Appl Health Econ Health Policy
19807372	Bayesian approach in pharmacoeconomics: relevance to decision-makers	2003	Expert Rev Pharmacoecon Outcomes Res
15090106	Expected value of sample information calculations in medical decision modeling	2004	Med Decis Making
15112789	Learning as an objective within a structured risk management decision process	2004	Environ Sci Technol

PMID	Title	Year	Journal
15155018	Value of information literature analysis: a review of applications in health risk management	2004	Med Decis Making
15209935	Value of information analysis in environmental health risk management decisions: past, present, and future	2004	Risk Anal
15356229	Forecasting the number of soil samples required to reduce remediation cost uncertainty	2004	J Environ Qual
15484602	Setting priorities for research	2004	Health Policy
15633986	A probabilistic and interactive decision-analysis system for unruptured intracranial aneurysms	2004	Neurosurg Focus
15660617	Tiered chemical testing: a value of information approach	2004	Risk Anal
15688986	Precautionary principles: a jurisdiction-free framework for decision-making under risk	2004	Hum Exp Toxicol
15386668	The role of consumer knowledge of insurance benefits in the demand for preventive health care among the elderly	2005	Health Econ
15647219	When is evidence sufficient?	2005	Health Aff (Millwood)
15693724	Role of pharmacoeconomic analysis in R&D decision making: when, where, how?	2005	Pharmacoeconomics
15700300	Information and sorting in the market for obstetrical services	2005	Health Econ
15787767	Research strategies for magnetic fields and cancer	2005	Risk Anal
15806619	The value of information and optimal clinical trial design	2005	Stat Med
15876209	Additivity of information value in two-act linear loss decisions with normal priors	2005	Risk Anal
16046019	The value of genetic information in selecting dairy replacements	2005	Prev Vet Med
16091019	Establishing the cost-effectiveness of new pharmaceuticals under conditions of uncertainty--when is there sufficient evidence?	2005	Value Health
16268932	Optimal tracking and testing of U.S. and Canadian herds for BSE: a value-of-information (VOI) approach	2005	Risk Anal
16433092	Integrating seasonal climate prediction and agricultural models for insights into agricultural practice	2005	Philos Trans R Soc Lond B Biol Sci
16639994	The application of special technologies in diagnostic anatomic pathology: is it consistent with the principles of evidence-based medicine?	2005	Semin Diagn Pathol
16389669	Identifying key parameters in cost-effectiveness analysis using value of information: a comparison of methods	2006	Health Econ
16389671	A Bayesian approach to analysing the cost-effectiveness of two primary care interventions aimed at improving attendance for breast screening	2006	Health Econ
16539993	[Probabilistic cost-effectiveness analysis of the treatment of sleep apnea]	2006	Gac Sanit
16652389	The economics of diagnosis	2006	Health Econ
16753098	[The value of information and information as a value]	2006	Gac Sanit
17059697	Estimating the value of information in strategies for identifying patients at high risk of cardiovascular disease	2006	Inform Prim Care
17067191	Using value of information analysis to prioritise health research: some lessons from recent UK experience	2006	Pharmacoeconomics
17067194	Analysis sans frontieres: can we ever make economic evaluations generalisable across jurisdictions?	2006	Pharmacoeconomics
17184397	Global surveillance and the value of information: the case of the global polio laboratory network	2006	Risk Anal
16945438	Efficient computation of partial expected value of sample information using Bayesian approximation	2007	J Health Econ
16981193	Expected value of information and decision making in HTA	2007	Health Econ
17327242	Sample-size calculations for trials that inform individual treatment decisions: a 'true-choice' approach	2007	Clin Trials

PMID	Title	Year	Journal
17328046	Expected value of sample information for Weibull survival data	2007	Health Econ
17328053	Setting priorities for research: a practical application of 'payback' and expected value of information	2007	Health Econ
17367372	Rapid humanitarian assessments and rationality: a value-of-information study from Iraq, 2003-04	2007	Disasters
17409361	Limitations of acceptability curves for presenting uncertainty in cost-effectiveness analysis	2007	Med Decis Making
17409362	Value of information on preference heterogeneity and individualized care	2007	Med Decis Making
17676057	Learning the value of information in an uncertain world	2007	Nat Neurosci
17715257	Clinical decision making and the expected value of information	2007	Clin Trials
17761960	Calculating partial expected value of perfect information via Monte Carlo sampling algorithms	2007	Med Decis Making
17901602	The value of information for decision-making in the healthcare environment	2007	Stud Health Technol Inform
17985703	Value of information analysis in remedial investigations	2007	Ambio
18229486	The role of experience in decisions from description	2007	Psychon Bull Rev
17638032	Estimating the expected value of partial perfect information: a review of methods	2008	Eur J Health Econ
17764096	Cost-effectiveness analysis of a multinational RCT with a binary measure of effectiveness and an interacting covariate	2008	Health Econ
17767994	Learning-by-catching: uncertain invasive-species populations and the value of information	2008	J Environ Manage
17854433	Assessing the impact of censoring of costs and effects on health-care decision-making: an example using the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study	2008	Value Health
18179665	Time and expected value of sample information wait for no patient	2008	Value Health
18218176	Value of information of a clinical prediction rule: informing the efficient use of healthcare and health research resources	2008	Int J Technol Assess Health Care
18227539	Value of information analysis used to determine the necessity of additional research: MR imaging in acute knee trauma as an example	2008	Radiology
18263559	The value of implementation and the value of information: combined and uneven development	2008	Med Decis Making
18356312	Health technology assessment in the cost-disutility plane	2008	Med Decis Making
18368045	Choice, uncertainty and value in prefrontal and cingulate cortex	2008	Nat Neurosci
18438203	A forensic evaluation of the National Emphysema Treatment Trial using the expected value of information approach	2008	Med Care
18448701	The half-life of truth: what are appropriate time horizons for research decisions?	2008	Med Decis Making
18480035	The option value of delay in health technology assessment	2008	Med Decis Making
18489513	Optimal cost-effectiveness decisions: the role of the cost-effectiveness acceptability curve (CEAC), the cost-effectiveness acceptability frontier (CEAF), and the expected value of perfection information (EVPI)	2008	Value Health
18539311	Assessment of the value of reducing uncertainty by sampling in a groundwater remediation system	2008	Sci Total Environ
18697843	Determining optimal sample sizes for multi-stage randomized clinical trials using value of information methods	2008	Clin Trials

PMID	Title	Year	Journal
18806189	Decision analysis for resource allocation in health care	2008	J Health Serv Res Policy
18998811	Value of information in virtual patient performance evaluations	2008	AMIA Annu Symp Proc
18998813	Value of information in virtual patients portraying pharyngitis	2008	AMIA Annu Symp Proc
19025425	Prioritizing future research on off-label prescribing: results of a quantitative evaluation	2008	Pharmacotherapy
19029207	Optimal sample size determinations from an industry perspective based on the expected value of information	2008	Clin Trials
19602213	Expected value of perfect information: an empirical example of reducing decision uncertainty by conducting additional research	2008	Value Health
18435429	Globally optimal trial design for local decision making	2009	Health Econ
18524652	Costs of back pain in Germany	2009	Eur J Pain
18804324	Assessing the value of information for water quality management in the North Sea	2009	J Environ Manage
19150015	[Cost-effectiveness analysis of a genetic screening program in the close relatives of Spanish patients with familial hypercholesterolemia]	2009	Rev Esp Cardiol
19394574	Health technology assessment and primary data collection for reducing uncertainty in decision making	2009	J Am Coll Radiol
19432841	Enhancing value of information analyses	2009	Value Health
19509337	Multidimensional evaluation of managed relocation	2009	Proc Natl Acad Sci
19657882	The use and value of information systems as evaluated by dairy and specialty crop farm managers	2009	J Agromedicine
19694535	Quantifying the adaptive value of learning in foraging behavior	2009	Am Nat
19712008	A decision-theoretic framework for the application of cost-effectiveness analysis in regulatory processes	2009	Pharmacoeconomics
19762100	Risk-based sample size calculation for consecutive surveys to document freedom from animal diseases	2009	Prev Vet Med
19816524	Propaganda, Public Information, and Prospecting: Explaining the Irrational Exuberance of Central Place Foragers During a Late Nineteenth Century Colorado Silver Rush	2009	Hum Ecol Interdiscip J
19816857	Investment in antiviral drugs: a real options approach	2009	Health Econ
19399753	Optimal clinical trial design using value of information methods with imperfect implementation	2010	Health Econ
19688780	Cost-effectiveness acceptability curves--caveats quantified	2010	Health Econ
19818058	Value of information analyses of economic randomized controlled trials: the treatment of intermittent claudication	2010	Value Health
19903571	Economic valuation of environmental benefits from wastewater treatment processes: an empirical approach for Spain	2010	Sci Total Environ
20022648	Modelling collective effectiveness of voluntary vaccination with and without incentives	2010	Prev Vet Med
20035544	Commentary on Cost- utility and value-of-information analysis of early versus delayed laparoscopic cholecystectomy for acute cholecystitis (Br J Surg 2010; 97: 210- 219)	2010	Br J Surg.
20040743	Exploring the research decision space: the expected value of information for sequential research designs	2010	Med Decis Making
20085386	Can't get no satisfaction? Will pay for performance help?: toward an economic framework for understanding performance-based risk-sharing agreements for innovative medical products	2010	Pharmacoeconomics
20107161	Researchers consider value-of-information theory for selecting trials	2010	J Natl Cancer Inst

<b>PMID</b>	<b>Title</b>	<b>Year</b>	<b>Journal</b>
20307281	Current sample size conventions: flaws, harms, and alternatives	2010	BMC Med
20366697	Time walkers and spatial dynamics of aging information	2010	Phys Rev Lett
20378190	Simulation sample sizes for Monte Carlo partial EVPI calculations	2010	J Health Econ
20392316	Study of progesterone for the prevention of preterm birth in twins (STOPPIT): findings from a trial-based cost-effectiveness analysis	2010	Int J Technol Assess Health Care
20455926	Controlling established invaders: integrating economics and spread dynamics to determine optimal management	2010	Ecol Lett
20525915	Experience matters: information acquisition optimizes probability gain	2010	Psychol Sci
20629473	The Value of Value of Information: Best Informing Research Design and Prioritization Using Current Methods	2010	Pharmacoeconomics
20632291	Cost-utility and value-of-information analysis of early versus delayed laparoscopic cholecystectomy for acute cholecystitis (Br J Surg 2010; 97: 210-219)	2010	Br J Surg