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Value of Information (VOI) Analysis: Principles, Applications and Good Practice Recommendations

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Outline

1. Introduction
2. VOI Principles, Methods & Applications
3. Selected Good Practice Recommendations

SECTION

1

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Introduction

Decision uncertainty

- Decisions to adopt healthcare interventions are based on the expected payoffs of alternative options
- In the absence of perfect information, these payoffs are uncertain, and thus, decisions made based on these payoffs are also uncertain
- Uncertainty may lead to suboptimal decisions
- Must read:

  Briggs et al. Model Parameter Estimation and Uncertainty: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force-6. *Value in Health* 2012; 15, 835-42 [5]

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Sources of Uncertainty

- **Stochastic uncertainty:**
  - ***Concept***: Random variability in outcomes between "identical" patients
  - ***Sometimes called***: variability, Monte Carlo error, First-order uncertainty,
  - ***Analogous term in regression analysis***: error term
- Example:
  - Cancer treatments – given all ***known*** factors equal, one patient dies before the other
- Decision consequences:
  - Cannot know which patient to prioritise for treatment (random)

Sources of Uncertainty

- **Parameter uncertainty:**
  - ***Concept***: The uncertainty in estimation of the parameter of interest
  - ***Sometimes called***: Second-order uncertainty
  - ***Analogous term in regression analysis***: Standard error of the estimate
- Example:
  - Clinical trial – 95% CI around the size of effect (OR, RR etc)
- Decision consequences:
  - Decision based on mean and probability of acceptability

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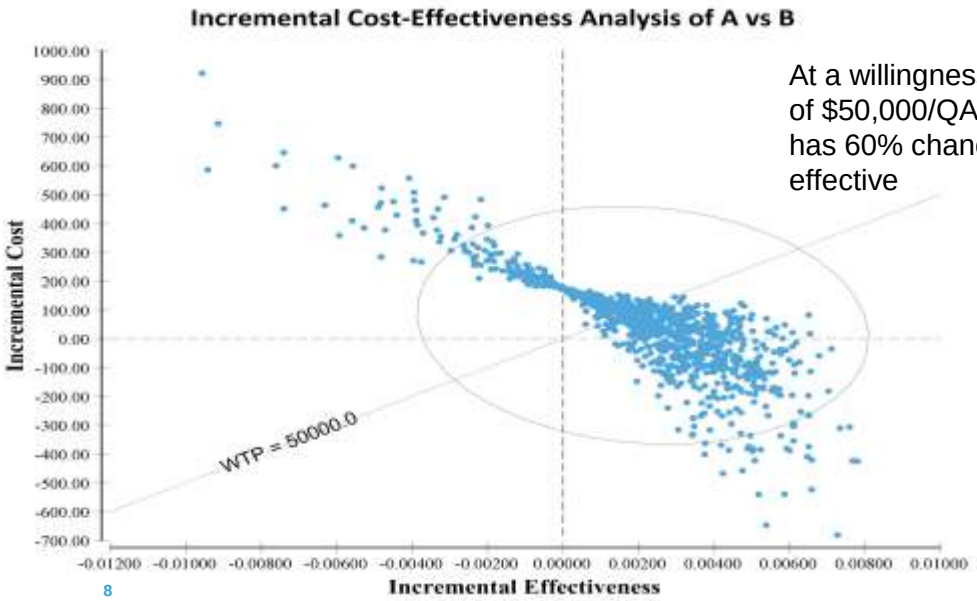

At a willingness-to-pay threshold of $50,000/QALY, Intervention A has 60% chance of being cost-effective

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Sources of Uncertainty

- **Heterogeneity:**
  - ***Concept***: The variability between patients that can be attributed to characteristics of those patients
  - ***Sometimes called***: Variability, observed or explained heterogeneity
  - ***Analogous term in regression analysis***: Beta coefficients (or the extent to which the dependent variable varies by patient characteristics)
- Example:
  - Identified sub-groups within a trial or real-world data (survival of females vs males)
- Decision consequences:
  - Need identified subgroups where value for money is acceptable

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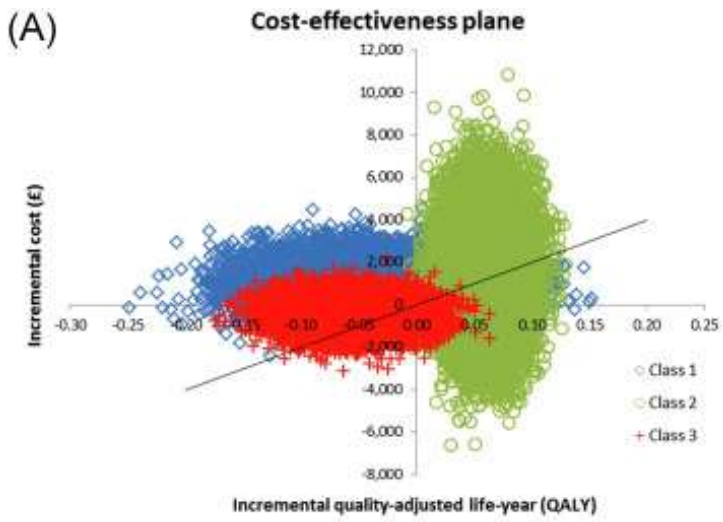

Patient-tailored care management for COPD patients

Sorenson et al. Examining the Heterogeneity and Cost Effectiveness of a Complex Intervention by Segmentation of Patients with Chronic Obstructive Pulmonary Disease. *Value in Health* 2018: 21(2), 239-47

Sources of Uncertainty

- **Structural uncertainty:**
  - ***Concept***: The assumptions inherent in the decision model
  - ***Sometimes called***: Model uncertainty
  - ***Analogous term in regression analysis***: The form of the regression model (e.g. linear, log-linear, etc)
- Example:
  - Clinical treatment algorithm for cancer drugs (cancer treatment model of 1st, 2nd, 3rd line chemotherapies, uncertainty in the algorithm around when radiotherapy is used)
- Decision consequences:
  - Model is inadequate to make informed decision?

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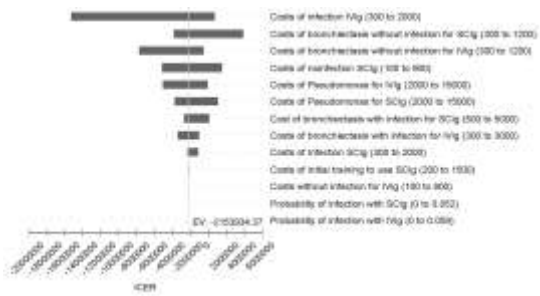
Dealing with uncertainty



- One-way sensitivity analysis?
  - Identify key drivers that affect the result which may change the decision
- Probabilistic sensitivity analysis?
  - Identify the probability of being acceptable value for money at various thresholds
  - Identify likelihood of cost-savings, making people worse off, potential for sub-group analysis
- Next level:
  - **Value of Information**

SECTION

2

VOI Principles, Methods and Applications

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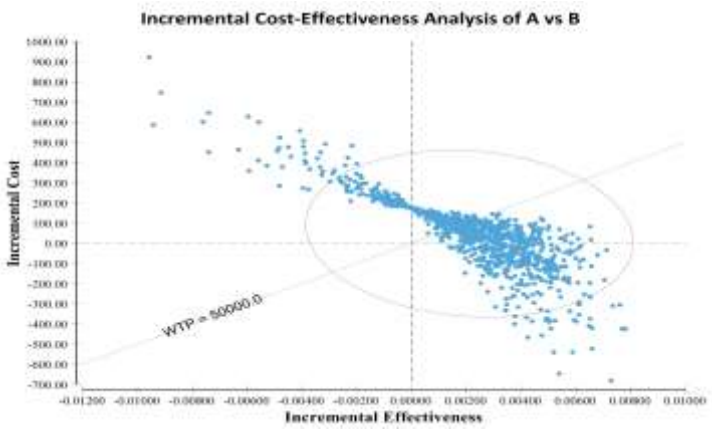

What will your decision be (by showing hands)?

1. **Adopt intervention A**
2. **Adopt intervention B**
3. **Need more information, let's conduct a clinical trial**
4. **That depends**

At willingness-to-pay threshold of $50,000/QALY, Intervention A has 60% chance of being cost-effective

The Trade-off

Value of Information (VOI) analysis

- **VOI estimates the expected value of additional evidence to reduce decision uncertainty.**
- Function of:

1. Probability decision based on existing evidence will be wrong (chance of error)
2. Consequences of a wrong decision (e.g. benefits forgone)
3. Size of the population expected to benefit from the intervention
4. Life-time of the intervention

An example

Iteration	Intervention A	Intervention B	Preferred option	With perfect information
1	$10,000	$8,000	A	$10,000
2	$12,000	$9,500	A	$12,000
3	$8,000	$9,000	B	$9,000
4	$9,000	$8,000	A	$9,000
5	$11,000	$8,500	A	$11,000
6	$9,000	$9,500	B	$9,500
7	$10,500	$9,000	A	$10,500
8	$9,500	$10,000	B	$10,000
9	$8,500	$9,000	B	$9,000
10	$12,500	$9,500	A	$12,500
Average	**$10,000**	**$9,000**	**A**	**$10,250**

VOI = Expected benefit with perfect information – Expected benefit with current information

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VOI Measures

Expected Value of Perfect Information (EVPI):
Maximum value of collecting evidence on all parameters

→ Is additional evidence required?

Expected Value of Perfect Parameter Information (EVPPI):
Maximum value of additional research on certain parameters

→ What should we focus on?

Expected Value of Sample Information (EVSI):
The value of additional research for a specific sample size

→ How much uncertainty is expected to be reduced?

Expected Net Benefit of Sampling (ENBS):
The difference between population EVSI and research study cost

→ Is it worthwhile?

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VOI Applications

- Informing reimbursement decisions
- Early drug/technology development decisions
- Research prioritisation
- Optimising trial design

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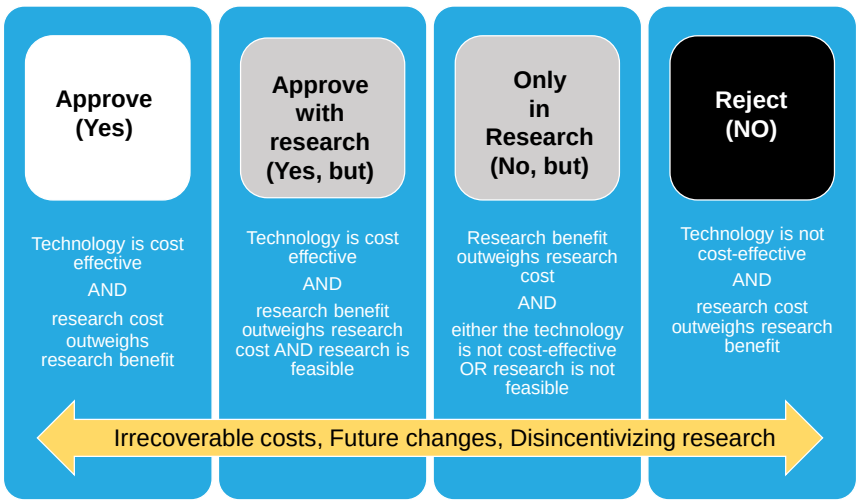
Informing reimbursement decisions



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Rothery et al 2017
Claxton et al 2016
Claxton et al 2012

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CADTH Evidence Driven.

- Guidelines for the Economic Evaluation of Health Technologies: Canada — 4th Edition

> ***"To enable the development of additional research to inform future decisions, decision-makers increasingly consider reimbursement options that combine some degree of adoption of a technology into the health system.*** *There are a wide range of nomenclatures for such schemes, including* ***coverage with evidence development, risk-sharing, and access with evidence development.*** *An important differentiation in this area is between those* ***schemes that make the technology available to all patients (irrespective of engagement with the research process), and those that make the technology available only to patients contributing data to the research."***

> *"**The expected value of perfect parameter information** should be provided for all parameters identified as being critical to the decision in order to support the decision-maker's consideration of the contribution of each parameter or, where appropriate, groups of parameters (e.g., when parameters are correlated) to the total decision uncertainty."*
>
> ***"The population expected value of perfect parameter information** should also be provided, reflecting both the likely size of the population and the lifetime of the intervention "*
>
> ***"Value-of-sample information and net-benefit-of-sampling** analyses will support decision-makers' assessments of the return on investment of further research when specific parameters or groups of parameters are identified as being responsible for a substantial portion of the total decision uncertainty."*

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Early drug/technology development decisions

- VOI can be incorporated into the decision making process early in the development of new technologies
- Early assessment of a new technologies to inform stop/go decisions
- Manufacturers/funders can steer their R&D more effectively.

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Research prioritisation

- Research organisations have limited budgets
- Research projects competing for funding can be prioritised based on their expected net benefits

Study	Expected benefit	Total Cost	Expected net benefit	Rank
A	$10.0 million	$5.0 million	$7.5 million	2
B	$12.5 million	$2.5 million	$10.0 million	1
C	$5.0 million	$3.0 million	$2.0 million	4
D	$2.5 million	$5.0 million	-$2.5 million	5
E	$7.5 million	$2.5 million	$5.0 million	3

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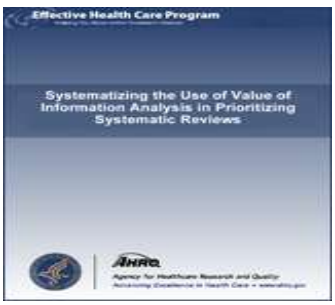
CONFERENCE PAPER

Using Value of Information Analysis to Prioritise Health Research

Some Lessons from Recent UK Experience




ORIGINAL RESEARCH

WILEY

Integrating value of research into NCI Clinical Trials Cooperative Group research review and prioritization: A pilot study

The Use of Value of Information Analysis for Research Prioritization

Year 1 activities

F.1	Appointment of a **Clinical Trial Prioritisation Working Group**	Appointment of Working Group
F.2	Development of best practice guidelines for determining value of information (to facilitate prioritisation of research questions by member networks)	Circulation for consultation of best practice guidelines for determining value of information

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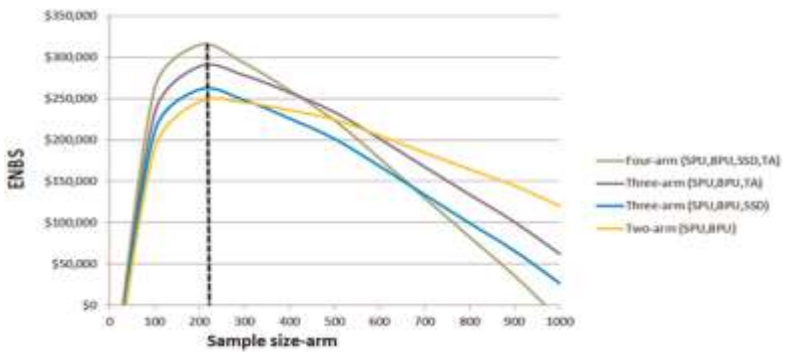
Optimising trial design

- VOI can be an alternative to the standard hypothesis testing approach, which is based on type I and type II errors
- In addition to sample size calculation, value of information analysis can optimize other aspects of research design such as possible comparator arms and follow-up times.



Tuffaha HW, Reynolds H, Gordon LG et al. Value of information analysis optimizing future trial design from a pilot study on catheter securement devices. Clinical Trials. 2014, 11(6) 648–656

Sample size/arm	EVSI (AUD)	Research sites number	Trial duration (y)*	Total trial cost† (AUD)	ENBS‡ (AUD)	ROI, %
100	1,645,000	4	1.25	656,250	988,750	151
200	2,114,000	4	1.50	907,500	1,206,500	133
300	2,275,000	4	1.75	1,158,750	1,116,250	96
400	2,345,000	4	2.00	1,410,000	935,000	66
500	2,380,000	4	2.25	1,661,250	718,750	43
600	2,415,000	4	2.50	1,912,500	502,500	26
700	2,432,500	4	2.75	2,163,750	268,750	12
800	2,448,250	4	3.00	2,415,000	33,250	1
900	2,457,350	4	3.25	2,666,250	−208,900	−8
1000	2,460,500	4	3.50	2,917,500	−457,000	−16

ROI = return on investment.
*Based on recruitment rate of 200 patients per site per year and additional 1 y for data analysis.
†Total trial cost = fixed + variable costs + opportunity cost.
‡ENBS = the difference between EVSI and total trial cost.
§ROI = ENBS/total cost.

VOI

Hypothesis testing

Negative Pressure Wound Therapy in high-risk caesarean section wounds

Tuffaha HW, Gillespie BM, Chaboyer W, et al. Cost-utility analysis of negative pressure wound therapy in high-risk cesarean section wounds. J surg Res. 2015; 195(2)612-22.

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SECTION

3.1

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Selected Good Practice Recommendations

VOI Taskforce Report 1: An Introduction to VOI

Report I Objectives

1. Introduce VOI analysis
2. Explain why it should be important to decision-makers
3. Identify the types of healthcare decisions that can be supported by VOI analysis, as well as its limitations
4. Describe how the methods should be used and how the results should be interpreted
5. Explain how VOI analysis can support decision-making in different contexts.

The report does not provide detail on the costing or grading of evidence from specific studies.

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Decision-making contexts where VOI is helpful

1. guiding commissioning and research prioritization decisions among competing research priorities;
2. informing conditional coverage decisions within health technology assessment, where decisions about the reimbursement of technologies can be delayed until research that is needed is mandated;
3. supporting early development decisions of new pharmaceutical or other medical products; and
4. identifying research needs and priorities in areas where there is limited evidence and important uncertainties

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Selected Good Practice Recommendations – Report 1

- For a proper quantitative assessment of uncertainty, which accounts for uncertainty in all parameters simultaneously, a probabilistic analysis of the decision model is required.

- Model structure to be determined by decision problem; NOT simply by data availability.
  - All current evidence should be considered with the uncertainty appropriately characterized.
  - Parameters should not be excluded due to a lack of data as anything not captured in the model structure or parameters will not be captured in VOI.

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Selected Good Practice Recommendations – Report 1

- The size of the beneficiary population should be calculated based on the prevalent and/or incident cohorts as appropriate given the decision problem.
  - Beneficiary population should be reduced by the number of patients to be enrolled in a future study if the decision is delayed to gather more information, as they will generally not benefit from the information yielded.

- Justification for the effective time horizon should be stated explicitly
  - alternative durations should be explored in a scenario analysis.

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Selected Good Practice Recommendations – Report 1

- Population EVP(P)I should be calculated and compared against costs of research to determine if further research is potentially worthwhile.
- EVPPI should be undertaken for groups of parameters where it is likely that further research would be informative for the whole group, rather than for individual parameters.
- EVSI estimates for each proposed study design should be compared to the expected costs of the study to determine if the specific study is valuable.
  - Where the number of proposed study designs is large, optimization methods can be used to identify the study with the greatest Expected Net Benefit of Sampling (ENBS) (Conti and Claxton, 2009).

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Selected Good Practice Recommendations – Report 1

- Other factors with potential relevance to decisions that should be considered in VOI analysis include:
  1. likelihood that further research will be undertaken if an intervention is generally funded, compared with being funded only in the context of research
  2. the extent of irreversible costs being incurred in delivering a new intervention
  3. whether other information of relevance is likely to emerge over time.

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SECTION

3.2

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Selected Good Practice Recommendations

VOI Taskforce Report 2: Analytical Methods

Report 2 Objectives

- Detailed guidance and emerging good practices on the principal methods required for assessing the value of research to inform a range of decisions
- Primary audience for this report are methodologists or analysts who are responsible for undertaking and implementing VOI to support research decisions

Selected Good Practice Recommendations – Report 2

- Process to identify the evidence, and any uncertainty arising from it, should be made explicit.
- When 'best' technique or approach for data handling/synthesis is unclear or inadequate, and choices or assumptions are required, these should be parameterized and uncertainty about these choices should be included in the analysis.
  - Alternatively, separate scenarios should be defined and VOI should be calculated for each
- Structural uncertainties, and how these are handled, should first be made explicit; then parameterized, or handled in separate scenarios.

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Selected Good Practice Recommendations – Report 2

- For computation of the EVPPI, the single loop "plug-in" methods of Strong (2014) is recommended as it allows for computing EVPPI directly from the probabilistic analysis sample.
  - Check whether the underlying assumptions for this method hold.
- When using the nested double-loop method, choose inner and outer loop simulation sizes large enough to ensure acceptable bias and precision (Oakley et al. 2010)
- SAVI and BCEAweb are easy-to-use, open access, web-based VOI calculators that implement computationally cheap single loop schemes for EVPPI.

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Selected Good Practice Recommendations – Report 2

- The EVSI computation should reflect how the data would be analysed if the proposed study were to actually go ahead.
- Research processes that are expected result in censoring, missing data and measurement bias should be modeled in the EVSI data generation step so that this mimics the true data generating process.
- Although it is rarely important to estimate EVPI, EVPPI or EVSI with high precision, it is important to know and report, to an order of magnitude, the size of any Monte Carlo sampling error so that gross imprecision is avoided.

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Survey Time!

Survey Question #1

What is your general assessment about the importance of VOI in applied decision-making? (e.g., in HTA, research prioritization / funding)

1.1 In the current situation, the importance is:

A. High
B. Medium
C. Low
D. Not Sure

1.2 In an ideal world, the importance should be:

A. High
B. Medium
C. Low
D. Not Sure

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Survey Question #2

What do you see as the main *Practical Barriers* to conducting a VOI analysis? (max 3 answers)

A. Access to tools to conduct a VOI
B. Complexity of methods
C. Lack of expertise on VOI
D. Lack of necessary data
E. Time required to conduct a VOI analysis
F. VOI does not incorporate all uncertainties
G. No accepted WTP threshold for endpoint of interest
H. Other practical barriers

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Survey Question #3

What do you see as the main barriers for *Acceptance* of VOI? (max 3 answers)

A. Lack of uniform VOI Guidelines/Roadmaps
B. Unsolved methodological issues in VOI
C. No clear criteria for when a VOI should be performed
D. Decision makers do not think it is useful
E. Optimal research designs indicated by VOI may not be feasible
F. Unclear who would/should pay for additional research
G. Decision makers do not understand VOI
H. The need to define a WTP threshold for the endpoint of interest
I. Other

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Survey Question #4

What would you need the most to be able to conduct a VOI analysis?
(maximum 1 answer)

A. Training on VOI Basic Concepts w/case studies
B. Training on VOI Advanced Concepts w/case studies
C. VOI Consultation
D. VOI Analytical Software
E. Other

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Questions??

Task force reports to be submitted to *Value in Health* in Fall 2018. Expected publication is end 2018/start 2019

VALUE OF INFORMATION ANALYSIS FOR RESEARCH DECISIONS: EMERGING GOOD PRACTICES

Value of Information Analysis for Research Decisions Emerging Good Practices:

- Report 1: Value of Information Analysis for Research Decisions Emerging Good Practices – An Introduction
- Report 2: Value of Information Analysis for Research Decisions Emerging Good Practices – Analytical Methods

Thank you to those who reviewed these reports. Your insight and expertise contribute to the high quality, multi-perspective and consensus nature of ISPOR Good Practices for Outcomes Research Task Force Reports.

VOI Task Force Activities at Upcoming ISPOR Conferences

- **VOI Short Course** at ISPOR Europe 2018: Barcelona
- **Forum** at ISPOR Europe 2018: Barcelona

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