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Value of Information (VOI) Analysis for Research Decisions: *Emerging Good Practices Task Force*

Final Recommendations

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Moderator:

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Presenters:

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Erik Koffijberg, PhD, Associate Professor, University of Twente, Enschede, The Netherlands

Task Force Members:

- **Claire Rothery, PhD**, **Co-Chair,** Senior Research Fellow, University of York, York, England, UK
- **Elisabeth Fenwick, PhD**, **Co-Chair,** Senior Director, Modelling & Meta Analysis, Pharmerit International, Oxford, UK
- **Anirban Basu, PhD**, Professor, Department of Pharmacy, University of Washington, Seattle, USA
- **Salah Ghabri, MD, PhD,** Health Economist, Department of Economic and Public Health Evaluation, Haute Autorité de Santé, Paris, France
- **Saskia Knies, PhD,** Senior Advisor Pharmacoeconomics at National Health Care Institute (Zorginstituut Nederland), Diemen, the Netherlands

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Task Force Members continued…

- **Erik Koffijberg, PhD,** Associate Professor, University of Twente, Enschede, The Netherlands
- **James F. Murray, PhD,** Research Fellow, Global Health Outcomes and Real World Evidence, Center of Expertise, Eli Lilly and Company, Indianapolis, USA
- **Gillian D. Sanders Schmidler, PhD**, Associate Professor of Medicine and of Biostatistics and Bioinformatics, Duke Clinical Research Institute, Duke University, Durham, NC, USA
- **Lotte M.G. Steuten, PhD,** Associate Member/Professor, Fred Hutch – HICOR / University of Washington – Department of Pharmacy, Seattle, USA
- **Mark Strong, PhD**, Section Director, Public Health, University of Sheffield, Sheffield, England, UK

And introducing our two youngest Task Force members…

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Recent examples of VOI

"an expected value of perfect information of $4,195 per patient at societal willingness to pay of $50,000/QALY. The estimated value of partial perfect information regarding the HR was $3,702 per patient."
Havrilesky, Chino, Myers, Gynecol Oncol, 2013

"The value of perfect information to reduce uncertainty was <euro>291.6M at its lowest."
Ramos, van Asselt, Kuiper, Severens, Maas, Dompeling, Knottnerus, van Schayck, Eur J Health Econ, 2013

"EVPI per patient would be €204 at a €20,000 threshold value of society's willingness to pay for one quality-adjusted life-year. Given a future population of 30,400 individuals, total EVPI would be €6.19 million."
Bartha, Davidson, Brodtkorn, Carlsson, Kalman, Trials, 2013

The expected value of perfect information is £43.1 million.
Wilson, Emery, Kinmouth, Prevost, Morris, Humphrys, Hall, Burrows, Bradshaw, Walls, Norris, Johnson, Walter, Value Health, 2013

The expected value of perfect information (EVPI) associated with this decision is substantial (6.9 million pounds for the 20/40 model and 14.5 million pounds for the 20/80 model), with a sizeable EVPI associated with the effect of PDT on quality of life.
Bojke, Claxton, Sculpher, Palmer, Med Decis Making, 2008

Task Force Objectives

Develop good practice guidance for VOI analysis methods to:

- Characterize uncertainty and perform VOI
- Aid in presentation and interpretation of VOI results
- Reduce barriers to VOI implementation
- Improve patient and health system performance outcomes

The task force will follow directly on from the ISPOR-SMDM Modelling Good Research Practices Task Force on Model Parameter Estimation and Uncertainty (Briggs et al., 2012) and the methods used to address recommendations in the ISPOR Good Practices for Performance-Based Risk-Sharing Arrangements Task Force Report (Garrison et al., 2013).

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Specific Aims

- Explain the importance of quantifying uncertainty and the value of further research for research prioritization decisions
- Develop recommendations to assess when additional evidence is required to reduce uncertainty in decision making
- Identify key steps and recommendations for good practices of performing, reporting, presenting and interpreting results of VOI analysis
- Provide clarity on how results of VOI analysis can be embedded into decision making processes
- Develop recommendations for use of VOI in jurisdictions that do not use cost-effectiveness information
- Identify areas where continued methodological development in VOI techniques is warranted

Report 1 – An Introduction

Audience:

- Decision makers / health care payers
- Stakeholder groups making research prioritization decisions

Content:

- Role of VOI analysis
- Definition of VOI concepts and terminology
- Overview of steps to conduct a VOI analysis
- Types of healthcare decisions supported by VOI analysis
- Implications for research and policy decisions with discussion of/references to examples

Report 2 - Analytical Methods

Audience:

- Methodologists or analysts undertaking VOI analysis to inform decision making

Content:

- Characterizing sources of uncertainty for VOI
- Key concepts, definitions and notation of VOI
- Methods for computing EVP(P)I and EVSI
- Reporting of VOI results
- Other considerations
  - minimal modelling describe how to monetize the value of further research
  - relevance of VOI in different contexts
- Resources, skills and software

Forum Presentation

1. Overview of VOI
2. A selection of the Good Practice Recommendations

3. Discussion:
- VOI in practice
- Barriers and potential solutions
- Implications

Perspectives:
- Funders of research
- Industry
- Academic/Analyst

SECTION

1

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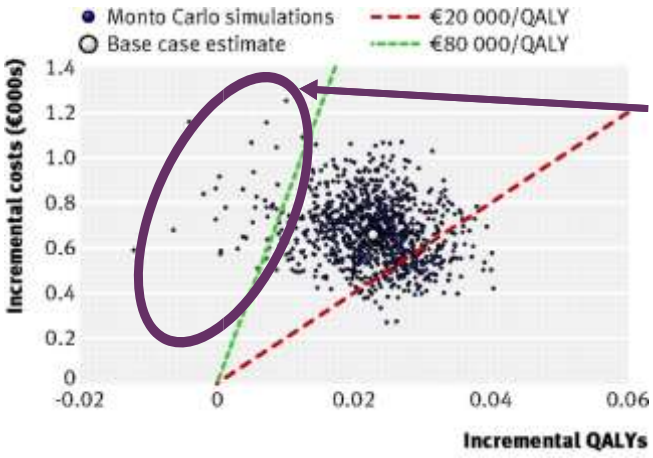
What is VOI?

Saskia Knies, PhD
Senior advisor pharmacoeconomics
National Health Care Institute
Diemen, The Netherlands

What is VOI?



By a show of hands:

Is it worth to conduct another trial?

A: Yes
B: No
C: That depends
D: Only if I am the 1st author

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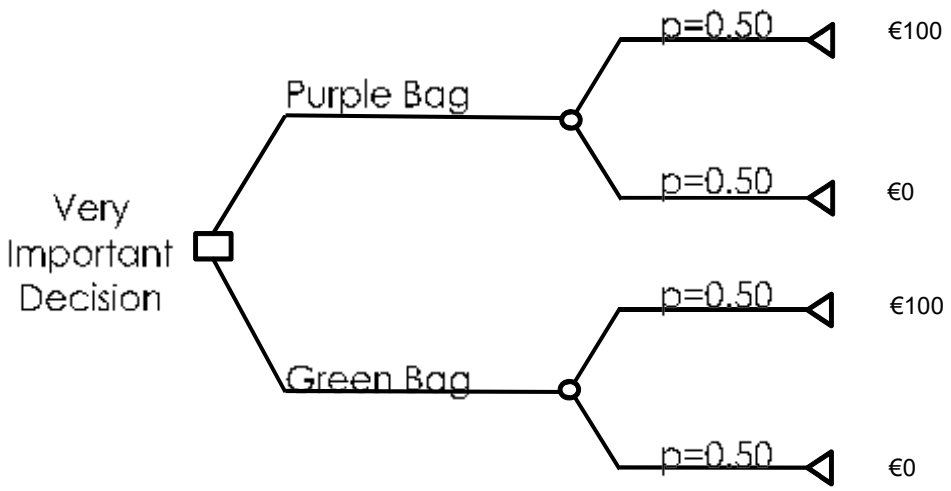
VOI: An intuitive example

One bag contains €100, while the other contains €0.
You must choose one (and only one!) bag

How much would you pay to look inside one bag before making your decision?

Decision tree



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Without looking inside you have a 50:50 chance of winning €100.

- Expected value = €50 (50% of €100)

After looking inside (i.e. with PERFECT information) there is a 100% chance of winning €100.

- Expected value = €100

Expected value of perfect information (EVPI)=€100-€50 =€50

What happens to VOI when there is more uncertainty?

- Expected value without peeking is now only €20.
  20% of €100

Value of PERFECT information is still €100.

- Expected value of perfect information (EVPI*) =
  €100 - €20 = $80

Value of information is higher when there is more uncertainty.

*peeking in 4 bags

One bag now contains €1000!

- Expected value with CURRENT info is now €500.
  50% of €1000

Value of PERFECT information is €1000.

- Expected value of perfect information =
  €1000- €500 = €500

Value of information is higher when consequences of a (wrong) decision are larger.

VOI metrics

- EVPI = expected cost of uncertainty
- EVPPI = expected cost of uncertainty about (groups of) individual parameters
- EVSI = expected reduction in uncertainty by a trial of a given sample size n
- ENBS = EVSI – minus costs of a study with sample size n

SECTION

2.1

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Selected Good Practice Recommendations

VOI Report 1 – An Introduction

Salah Ghabri, PhD
Scientific Project Coordinator/Health Economist
French National Authority for Health
Saint-Denis, France

Task Force 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.

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Selected Good Practice Recommendations – Report 1

- A probabilistic analysis (PA), which accounts for uncertainty in parameters simultaneously, is required for an appropriate quantitative assessment of uncertainty in outcomes
  - Detailed processes set out by ISPOR-SMDM Modeling Task Force Report - 6
- All uncertain parameters need to be assigned a probability distribution otherwise they will be excluded from the analysis of uncertainty and the assessment of VOI.

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. This should be adjusted for the number of patients to be enrolled in a future study if the reimbursement decision is delayed while more information is gathered, as they will generally not benefit from the information yielded.

- Justification for the effective time horizon should be stated explicitly, and the impact of alternative time horizons on the VOI results should be explored in scenario analyses.

Selected Good Practice Recommendations – Report 1

- Population EVPI should be compared against the costs of research to determine if further research is ***potentially*** worthwhile. Where expected costs of research ≥ EVPI then research is **not worthwhile** and the VOI process should stop.
- EVPPI should be undertaken for groups of parameters where it is likely that a new study (or studies) would be informative for the whole group, rather than for individual parameters.
- As with population EVPI, estimates of Population EVPPI should be compared to the expected costs of research on specific (groups of) parameters to determine whether research is potentially valuable.

Selected Good Practice Recommendations – Report 1

- 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.

- The most efficient study design should be identified as that with the greatest Expected Net Benefit of Sampling (ENBS).

SECTION

2.2

Selected Good Practice Recommendations

VOI Report 2 – Analytical Methods

Erik Koffijberg, PhD
Associate Professor – HTA
Dept. Health Technology & Services Research
University of Twente, The Netherlands

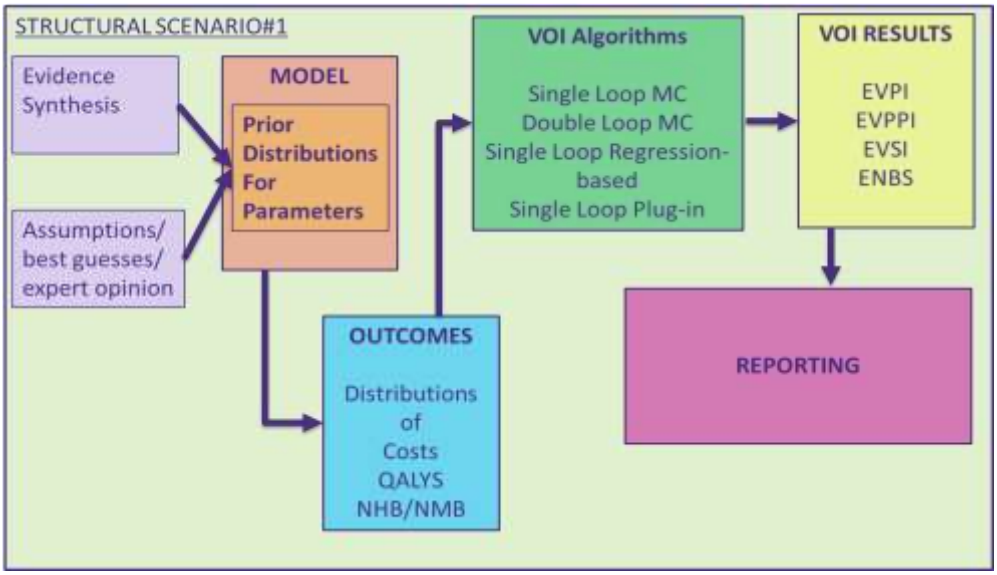
Task Force Objectives

- 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

Decision-making contexts where VOI 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

VOI Calculations & Reporting



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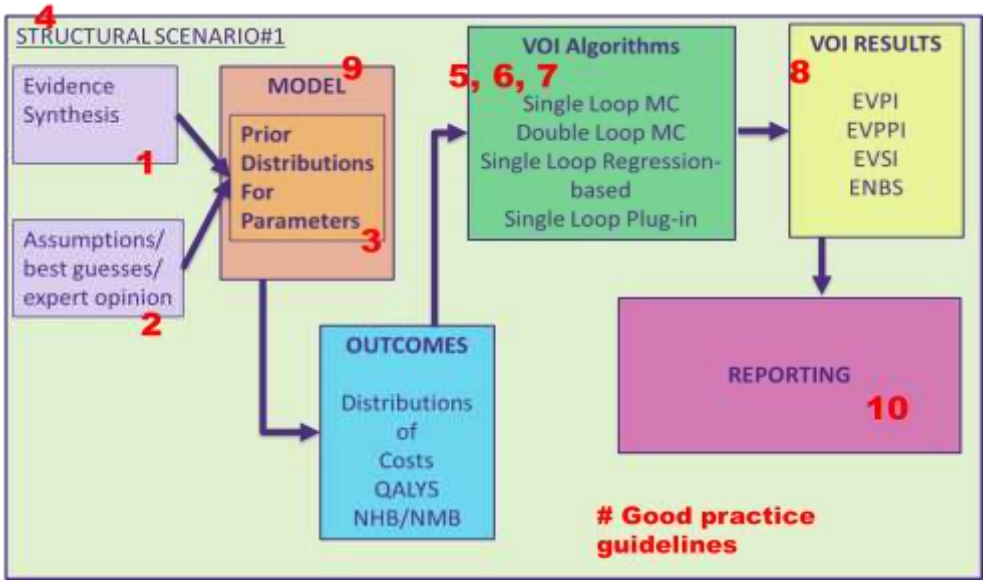
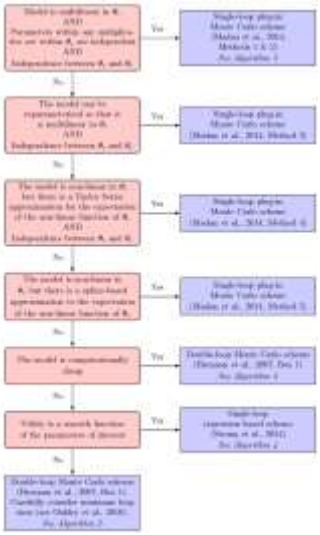
VOI Calculations & Reporting



Selected Good Practice Recommendations – Report 2

4. For the computation of EVPPI, the form of the utility function that allows a single-loop 'plug-in' scheme is preferred because it leads to an exact computation of the inner expectation
5. When using the single-loop methods proposed in Strong et al. (2014) and Madan et al. (2014) check that the underlying assumptions of methods hold.
6. When using the nested double-loop method choose inner and outer loop simulation sizes to ensure acceptable bias and precision (Oakley et al. 2010)



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Selected Good Practice Recommendations – Report 2

7. The likelihood chosen for the EVSI computation should reflect how the data would be analysed if the proposed study were to actually go ahead. The choice of likelihood should not be driven by a need to ensure conjugacy between the prior and likelihood.
8. Processes that are expected to 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.

SECTION

3

Panel Discussion

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Moderator:

Elisabeth Fenwick, PhD, Senior Director, Modelling & Meta Analysis, Pharmerit International, Oxford, UK

Panel:

Salah Ghabri, MD, PhD, Health Economist, Department of Economic and Public Health Evaluation, Haute Autorité de Santé, Paris, France

Saskia Knies, PhD, Senior Advisor Pharmacoeconomics at National Health Care Institute (Zorginstituut Nederland), Diemen, the Netherlands

Erik Koffijberg, PhD, Associate Professor, University of Twente, Enschede, The Netherlands

Lotte Steuten, PhD, MSc, Fred Hutchinson Cancer Research Center and The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, University of Washington

Potential Topics for Panel Discussion

1. How could/should VOI methods be utilized within current decision-making frameworks?
2. How could/should decision-making frameworks be altered to allow greater use of VOI?
3. What needs to be done to improve understanding of VOI methods?
4. What challenges exist for analysts when applying VOI methods?
5. How could/should industry use VOI in stop/go decisions
6. How best to compare the value of research to the cost of research?
7. What should we do when decision-making does not consider cost/QALY in their objective function?

The task force reports will be submitted to *Value in Health* in 2018. Expected publication is early 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.