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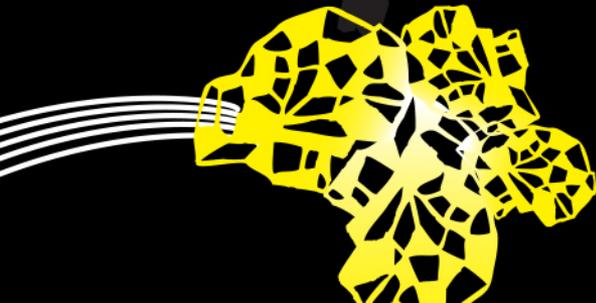
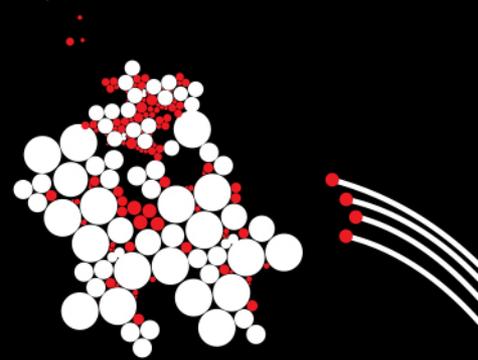
VALUE OF INFORMATION ANALYSIS A MINIMALIST APPROACH

H. (Erik) Koffijberg, PhD, MSc

Associate Professor - HTA

H.Koffijberg@utwente.nl

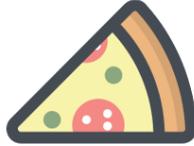
*Dept of Health Technology & Services Research
TechMed Centre, University of Twente, Netherlands*



Certainly (Un)certain
NVTAG Symposium
June 26, 2019



OVERVIEW

- Summary of the VOI perspective and VOI outcomes
- Why performing VOI is like eating pizza 
- VOI for research prioritization: a minimalist approach
- Simple case study
- Discussion and questions



INTRODUCTION TO VOI ANALYSIS

- The decisions we make in everyday life are based on information available to us
- This information is limited
- Limited information may cause us to make wrong decisions
- Making wrong decisions has negative consequences
- It might be valuable to extend the information available to us
 - This would reduce decision uncertainty
 - This would reduce the risk of making wrong decisions
 - This would avoid the corresponding negative consequences



INTRODUCTION TO VOI ANALYSIS

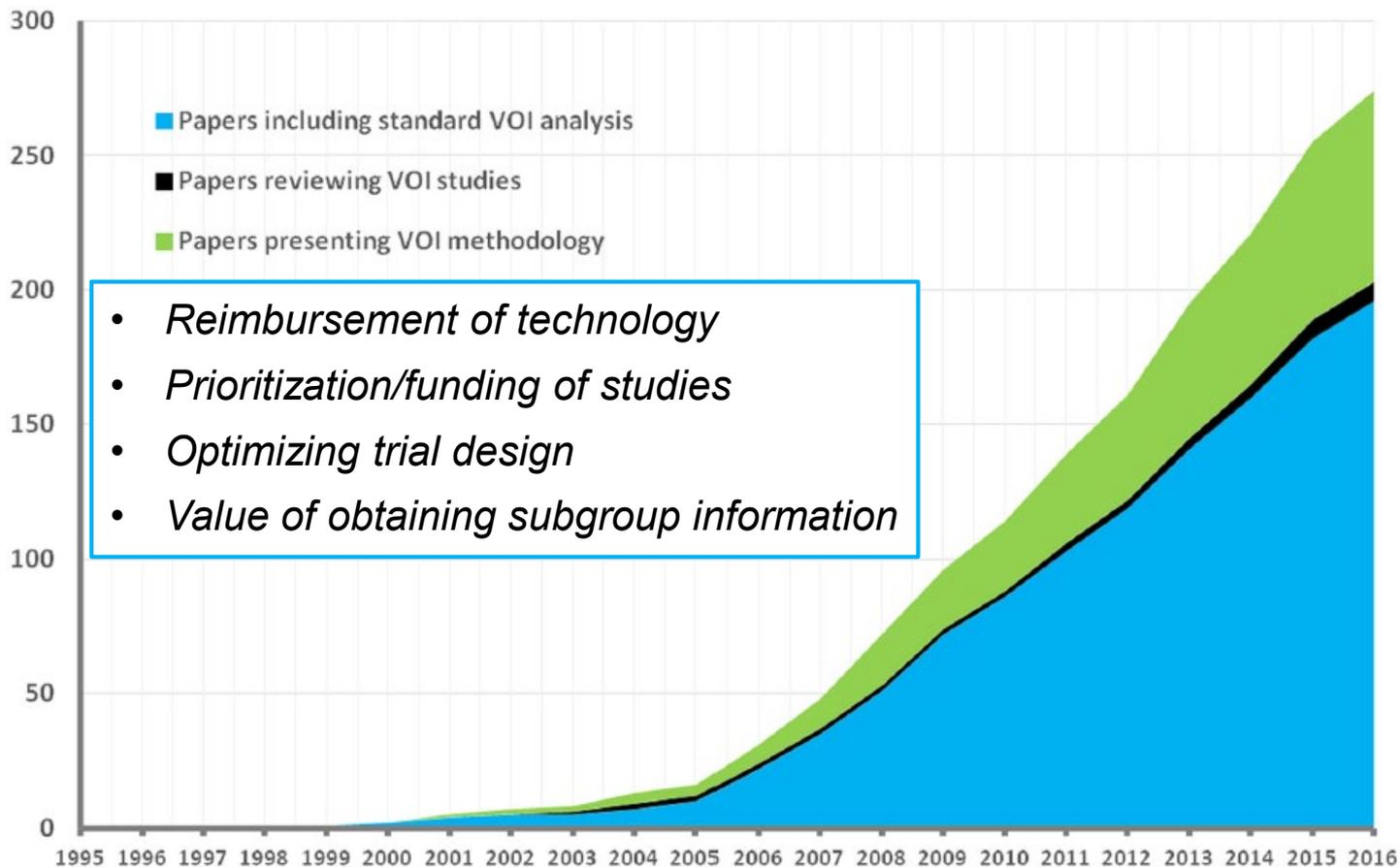
- Obtaining additional information may be valuable...
- But collection additional information is not costless
- Relevant questions are
 - What are the costs of collecting more information?
 - What are the benefits of having more information?
 - What is the balance between these costs and benefits?



VALUE OF INFORMATION ANALYSIS



INTRODUCTION TO VOI ANALYSIS



- *Reimbursement of technology*
- *Prioritization/funding of studies*
- *Optimizing trial design*
- *Value of obtaining subgroup information*



SUMMARY OF VOI ANALYSIS

STEPS IN APPLYING VOI

Application of VOI framework: 4 core steps

1. Define the decision problem
 - Target population, interventions, time horizon, relevant outcomes
2. Define a model adequately reflecting this decision problem
 - Health economic model (cohort, patient-level, structure,...)
3. Quantify uncertainty in this model
 - Probabilistic (sensitivity) analysis (standard)
4. Estimate VOI outcomes



SUMMARY OF VOI OUTCOMES

EVPI / EVPPI / EVSI / ENBS

Potential relevance of additional research

EVPI – Hypothetical value of perfect information

EVPPI – Hypothetical value of perfect parameter information

- *Necessary but not sufficient condition (hurdle)*

Efficient design of additional research

EVSI – Value of collecting evidence (design, sample size)

ENBS – Value of collecting evidence – cost of doing so

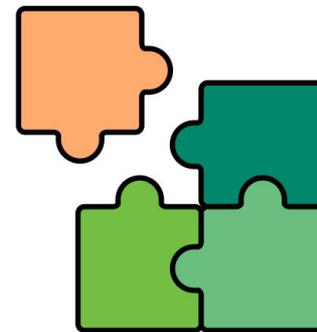
- *Useful alternative to statistical power calculations*



ONE CHALLENGE IN VOI ANALYSIS

Building a full health economic simulation model (step 2)

- Can be quite time consuming
- Requires modelling expertise
- Ideally makes use of comprehensive, accurate evidence



In a research prioritization context often time and evidence is quite limited (rank many proposals in short time)

- Need for research prioritization methods that are transparent and explicit, fast, provide easy interpretable results

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MAKING A GOOD PIZZA...

Step 10: Add Those Toppings



MAKING A GOOD PIZZA...

Genius Line Plus



ELECTRONIC
CONTROL

ENERGY
SAVING



The Physics of **Baking**
Pizza



WHAT IF YOU ARE HUNGRY RIGHT NOW?



Probably not as delicious...but an immediate, working solution, when making pizza is not feasible

MAKING A GOOD PIZZA...HIGH-TECH STYLE

Episode 2: Human-AI Collaborated Pizza



Human-AI collaborated pizzas we made with Tony at Crush Pizza

MINIMALIST VOI FOR RESEARCH PRIORITIZATION

Key questions in research prioritization

- Are the expected health benefits of additional evidence sufficient to regard a specific research proposal as potentially worthwhile?
- **If so**, should it be prioritized over other research proposals that could have been funded with the same resources? (opportunity costs)

Note*: The potential health benefits from encouraging the implementation of what existing evidence suggests may well exceed the potential health benefits from conducting further research!

* Fenwick E, et al. Med Decis Making. 2008 Jan-Feb;28(1):21-32.

* Hoomans T et al. Value Health. 2009 Mar-Apr;12(2):315-24.



MINIMALIST VOI FOR RESEARCH PRIORITIZATION

Key ingredients of VOI

The value of additional evidence depends on

1. How uncertain we are about the effectiveness of alternative strategies (interventions) given existing evidence
2. The consequences of this uncertainty
3. Whether findings of new research will actually be implemented in clinical practice



MINIMALIST VOI FOR RESEARCH PRIORITIZATION

Key ingredients of VOI from meta-analysis results

1. Start with effectiveness estimate from systematic review and meta-analysis (OR)
2. Integrate evidence on baseline risk and incidence
3. Use statistical distributions to represent uncertainty
4. Apply VOI methodology (EVPI) to assess consequences
5. Apply a minimum clinical difference



MINIMALIST VOI FOR RESEARCH PRIORITIZATION

KEY INGREDIENTS BASED ON META-ANALYSIS RESULTS

Working solution – VOI in Excel or R – based on

Annual impact
Total impact

1. Range for OR (from meta-analysis)
2. Range for baseline risk (from meta-analysis, control arms)
3. Incidence of the condition (from literature/registry)
4. Current utilisation of the new technology (from registry/claims data)
5. *Time over which information would be valuable*
6. Time to report if proposed research is commissioned
7. Discount rate
8. Costs of the proposed research





STREPTOKINASE IN ACUTE MI

CASE STUDY

Reinvestigation of the classic sequence of trials investigating early thrombolysis using streptokinase (SK) for the treatment of acute myocardial infarction (MI)

- Focus on the initial choice: SK vs no thrombolysis
- How did the estimated effectiveness of SK and the associated uncertainty change **the value of additional research and the value of implementation** with increasing evidence? **No hindsight!**



STREPTOKINASE IN ACUTE MI

CASE STUDY

Setup of analysis and assumptions

- Annual incidence (UK): 204,500 patients
- Baseline risk (no SK) derived from control arms (~12%)
- Implementation of SK in clinical practice will only start if improved effectiveness is statistically significant in the most recent trial and the cumulative meta-analysis of all evidence

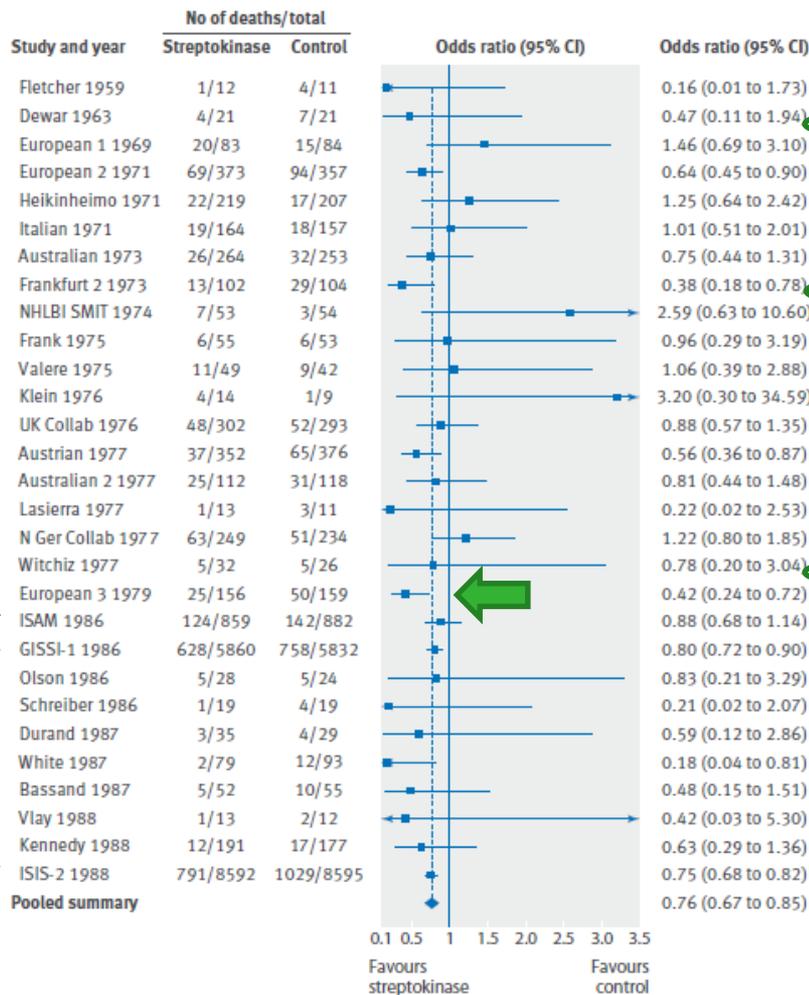


Fig 1 | Random effects meta-analysis of sequence of trials of early thrombolysis using streptokinase, with the endpoint of mortality

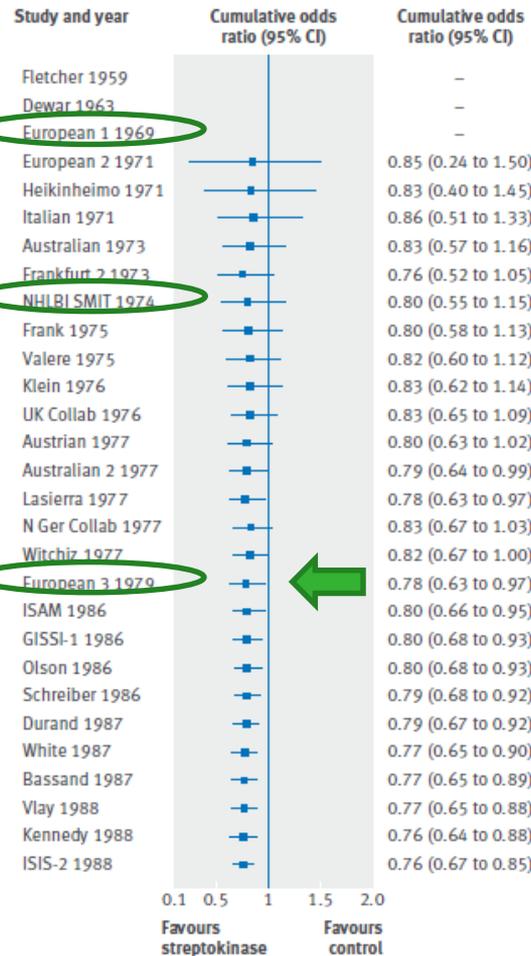
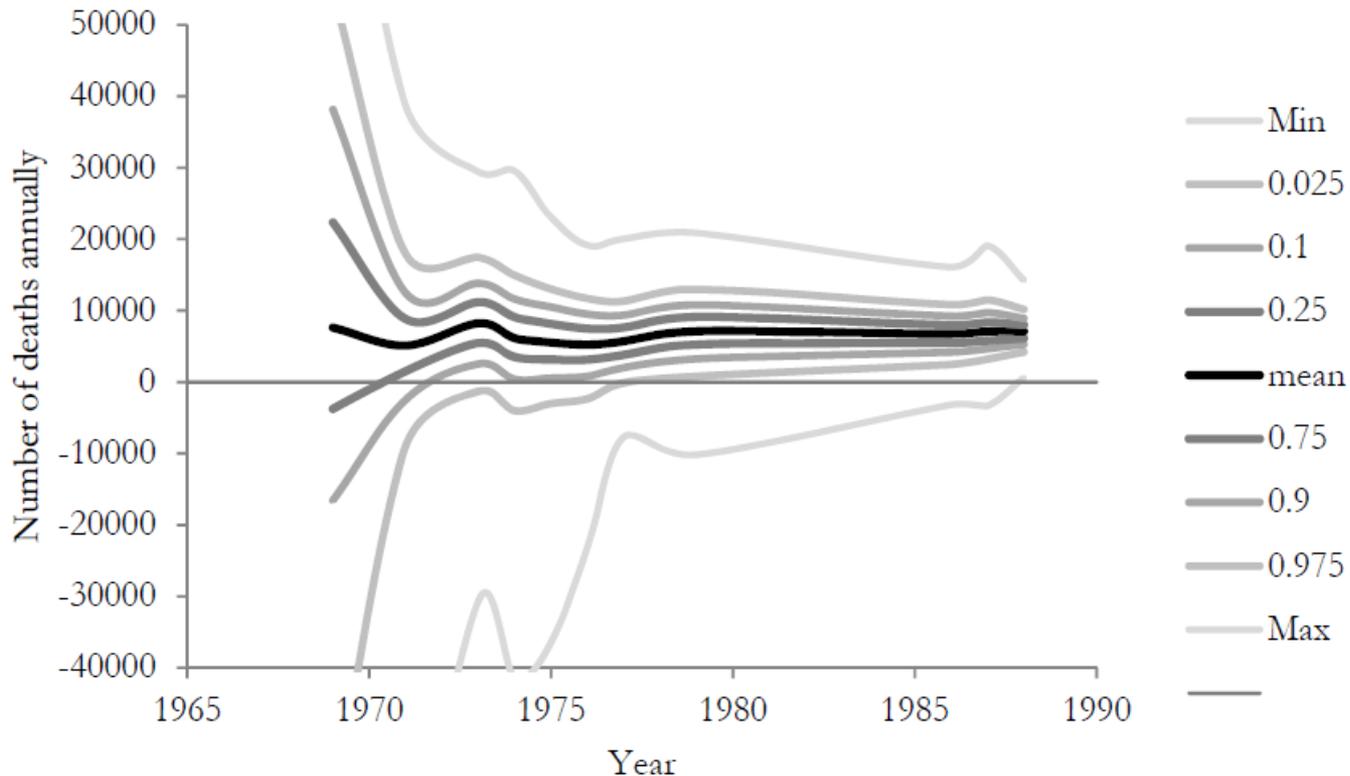


Fig 2 | Cumulative random effects meta-analysis of sequence of trials of early thrombolysis using streptokinase, with the endpoint of mortality

OR for mortality of SK vs control (RE)

STREPTOKINASE IN ACUTE MI

Forecast for reduction in deaths from implementing streptokinase over time

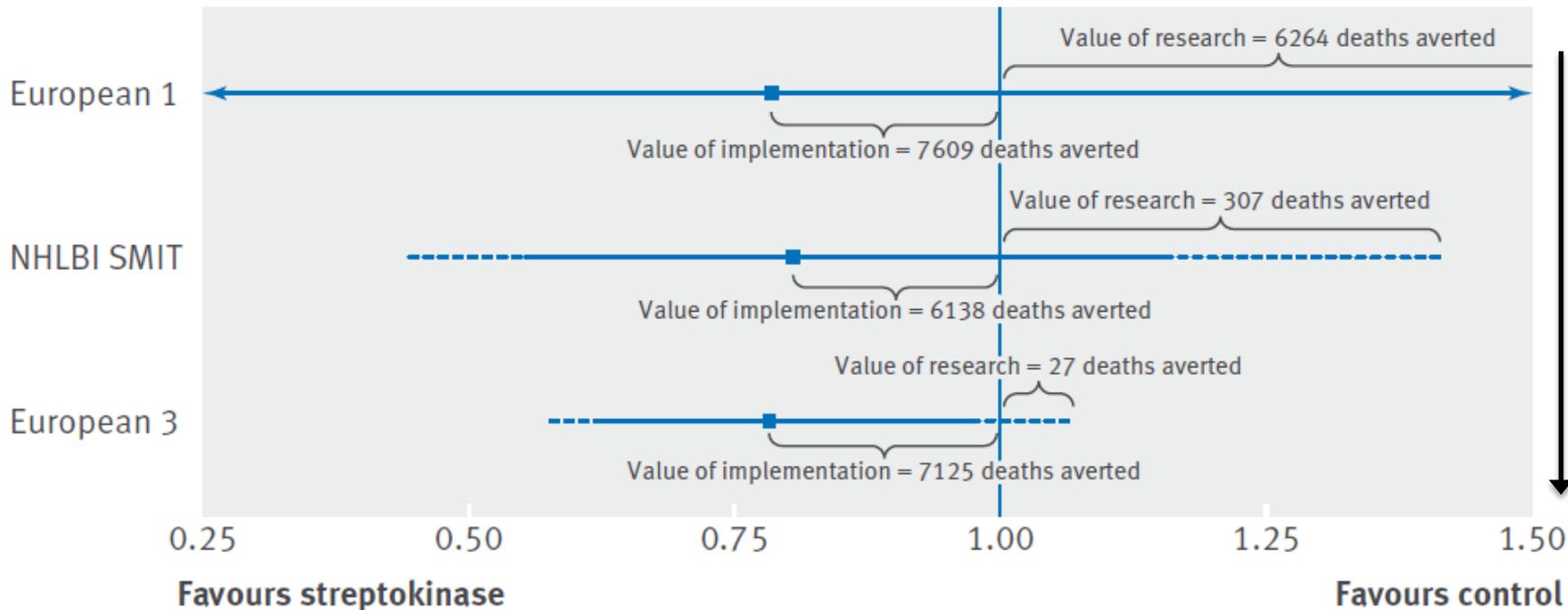


Impact of accumulating evidence on uncertainty in the treatment decision



STREPTOKINASE IN ACUTE MI

Odds ratio mortality (95% CI)



Expected benefits of implementation of SK following MI and potential benefits of further research, according to selected trials in the meta-analysis.

Solid line = 90% credible interval; dashed line = 95% credible interval

STREPTOKINASE IN ACUTE MI - SUMMARY

CASE STUDY

- Likelihood of implementation of results from additional research needs to be considered explicitly...
- Demanding a high level of statistical significance or large clinical difference influences costs/time to implementation and thereby potential benefits
- The value of implementation may well exceed the value of performing additional research
 - Additional research is unlikely to be the most effective dissemination method





MINIMALIST VOI FOR RESEARCH PRIORITIZATION

KEY MESSAGE

- Minimalist VOI based on systematic review and meta-analysis (commonly required) provides a practical and useful starting point for research prioritization and commissioning
- Not technically challenging or computationally burdensome, requires only evidence on **effectiveness, baseline risk, utilization, and incidence** (and prevalence for chronic diseases)
- Adds transparency and accountability **but does not capture all scientific and social value judgments**
- More challenging contexts may require evidence weighting (expert elicitation), and network meta-analysis

Inputs

Outcome measure

Is the outcome a benefit or harm?

Harm

What is the outcome?

deaths

Effectiveness parameters

	Mean value	Lower 95% CI	Upper 95% CI
Relative effect for new technology	0.800	0.550	1.150
(Relative effect favours new technology)			
Baseline probability of outcome event	0.100	0.066	0.131

Run analysis for changes in effectiveness parameters

Other parameters

	Value
Minimum clinical difference in outcomes required (% absolute difference)	0%
Incidence per annum	25,000
Utilisation of the new technology	0%
Time over which evidence would be valuable (years)	10
Time to report of suitable research (years)	3
Discount rate	1.5%
Costs of suitable research (£)	£2,000,000

Outputs

Current evidence

Current evidence suggests the use of
Probability new technology is effective

Value of implementing current evidence findings per annum
Expected consequences per annum

New technology

0.88

430 deaths averted

28 deaths

Histogram of consequences of uncertainty

Additional research

Value of implementing the findings of suitable research:

Per annum

458 deaths averted

Over the time horizon which evidence is valuable

4,290 deaths averted

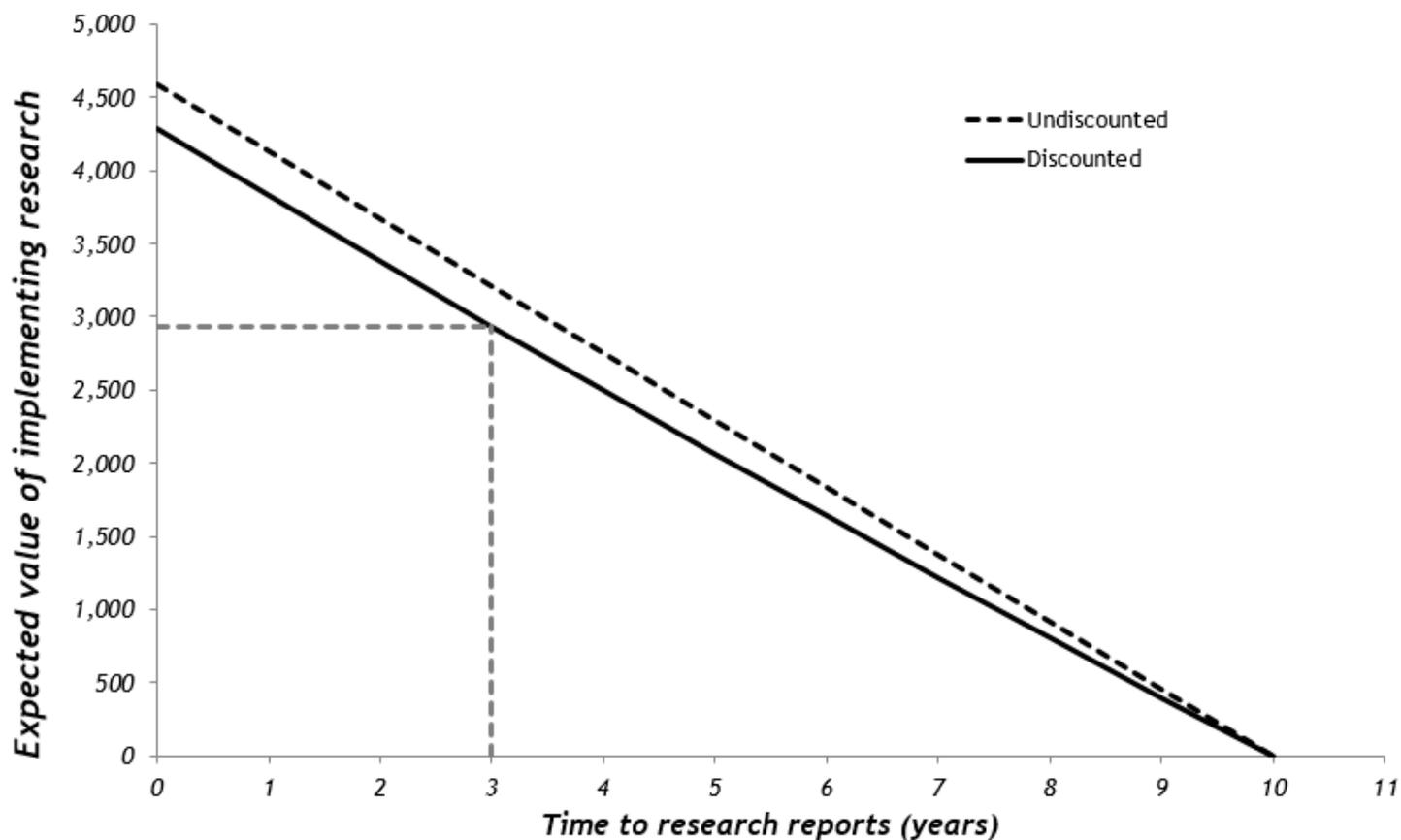
By the time for research to report

2,935 deaths averted

Cost-effectiveness of suitable research

£681 per deaths averted

Value of research by time to report



Time to report of suitable research **3 years**
Value of research by time to report **2,935** **deaths averted**



VOI APPLIED TO META-ANALYSIS RESULTS

MORE INFORMATION

For details on a minimalist approach to VOI see

- Claxton K, Griffin S, Koffijberg H, McKenna C. *How to estimate the health benefits of additional research and changing clinical practice*. BMJ. 2015 Nov 25;351:h5987.
- McKenna C, Griffin S, Koffijberg H, Claxton K. *Methods to place a value on additional evidence are illustrated using a case study of corticosteroids after traumatic brain injury*. J Clin Epidemiol. 2016 Feb;70:183-90.
- Claxton K, Griffin S, Koffijberg H, McKenna C. *Expected health benefits of additional evidence: Principles, methods and applications*. CHE Report 83. York. With Technical Appendix.

For VOI choices and handling constraints see

- Koffijberg H, Rothery C, Chalkidou K, Grutters J. *Value of Information Choices that Influence Estimates: A Systematic Review of Prevailing Considerations*. Med Decis Making. 2018 Oct;38(7):888-900.
- Koffijberg H, Knies S, Janssen MP. *The Impact of Decision Makers' Constraints on the Outcome of Value of Information Analysis*. Value Health. 2018 Feb;21(2):203-209

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Thank you! Are there any questions?



H. (Erik) Koffijberg, MSc PhD
Associate Professor

Health Technology & Services Research | Technical Medical Centre | University of Twente
Postal address: Technohal - Room 3104 | P.O. Box 217 | 7500 AE Enschede, the Netherlands
Appointments: +31(0)53 489 7475 (secretary Ingrid de Kaste-Krisman)
Contact & Info: +31(0)53 489 5384 | h.koffijberg@utwente.nl | [LinkedIn](#) | [Website](#)