Using a Conceptual Value of Information Approach to Decide When to and When not to Replicate Systematic Reviews

Kednapa Thavorn, PhD
On behalf of SR Replication Team

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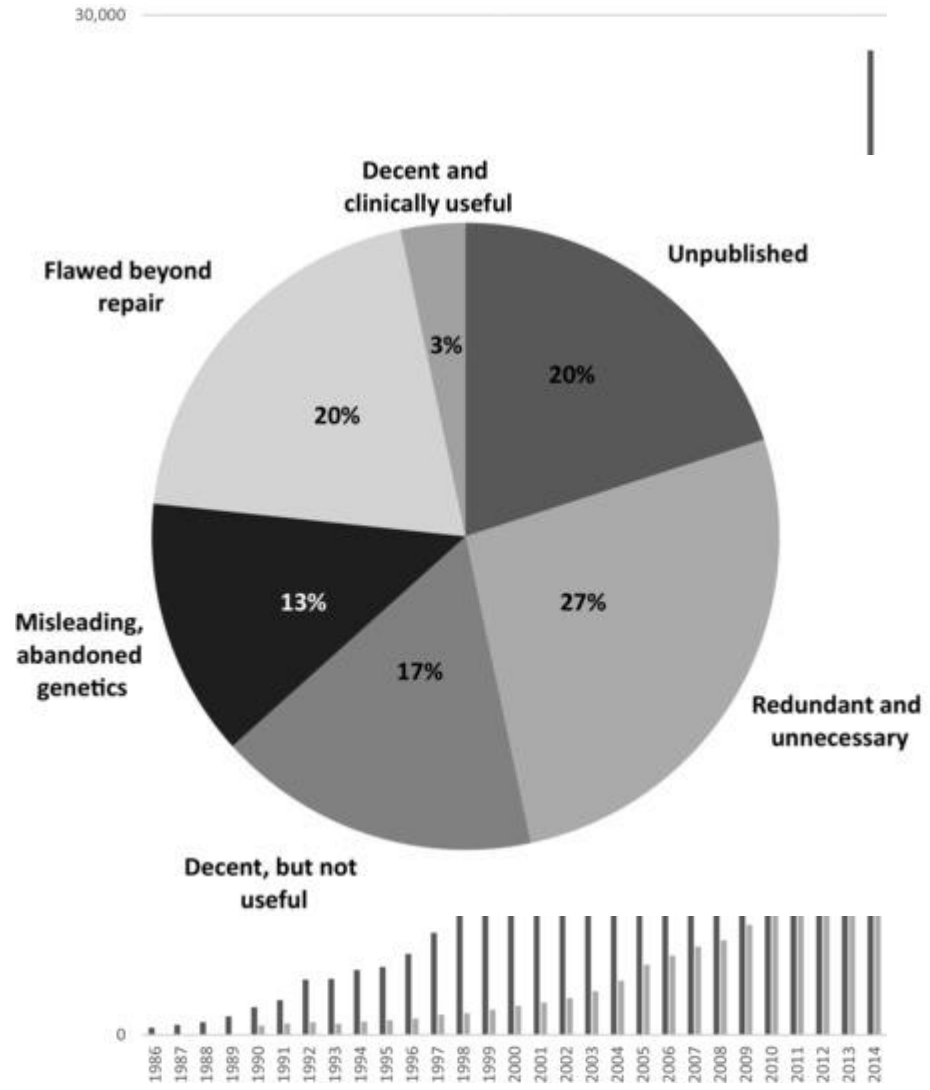
Outline

- Background
  - Definition of systematic review (SR) replication
  - Overarching aim of the project
- Objective of the presentation
- Value of information (VOI) analysis
  - Basic concept
  - Conceptual VOI
- Illustrative example of using a conceptual VOI to inform the replication of SRs
- Next steps

Background (1)

- Replication of a systematic review is conducted to test whether the results of the index review can be repeated or extended, and may or may not include new data, new methods or new analyses.



Ioannidis J. Milbank Q. 2016; 94(3): 485–514

Background (2)

- Overarching aim of the project

"To use an evidence-driven, transparent process and implement consensus approaches to develop value-added guidance on when to replicate and when not to replicate systematic reviews"

- Key activities
  - SR of guidelines and methods studies
  - Key informant interviews
  - Synthesize candidate criteria
  - Online survey to gather feedback on the candidate items
  - Consensus meeting (February 7-9, 2019)
  - Develop tools for knowledge users
  - End of grant KT

Objective of the Presentation

- To propose and illustrate the use of a conceptual VOI to help stakeholders identify when the replication of systematic reviews adds value.

VOI Framework (1)

- A set of analytic tools that can be used to assess the value of acquiring additional evidence to inform a clinical or policy decision.

- VOI quantifies the net benefit from the improvement of population health expected from additional research against the cost of conducting future research -> research prioritization.

VOI Framework (2)

- Person-level Expected Value of Information (EVI)

$$EVI = E_I \max_j E_{\theta|I} NB(j,\theta) - \max_j E_\theta NB(j,\theta)$$

- Population-level EVI

$$pEVI = \sum_t \beta^t \times Durability_t \times Uptake_t \times Incidence_t \times Population_t \times EVI$$

Where:
NB, net benefit, θ; a parameter vectors that determine NB of treatment option j;
I, outcomes and probabilities that could be obtained from a research activity;
β, discounting factor

Meltzer et al, 2011

VOI Approaches

- Full modelling

- Minimal modelling
  - VOI without constructing a decision model of the disease and treatment process to characterize the uncertainty in net benefit associated with an intervention
- Conceptual VOI
  - Bounding exercise using information on the conceptual elements of population-level VOI

Meltzer et al, 2011;Hoomans et al, 2012

Conceptual VOI (1)

$$\text{pEVI} = \sum_t \beta^t \times Durability_t \times Uptake_t \times Incidence_t \times Population_t \times EVI$$

- Expected value of information (EVI)
- Size of affected population: $Uptake_t \times Incidence_t \times Population_t$
- Durability of information: the rate at which new clinical evidence and/or better alternatives for patients will emerge

If any of the conceptual element of VOI has a value of "0" or small, the value of further research, including SR replication, is unlikely to be valuable.

Conceptual VOI (2)

Element of Conceptual VOI	Description	Potential Variables/ Sources of Evidence
Expected changes in benefits	• Expected changes in health outcomes, cost difference, net benefit, clinical and/or policy decision	Previous SRs, expert elicitation
Expected changes in uncertainty	• Ambiguity in evidence	Previous SRs (SD, 95% CI, methodological quality), expert elicitation
Size of affected population	• Disease burden (incidence) • Variability in diffusion of the interventions and variation in clinical practice (uptake)	National Statistics, MarketScan data, expert elicitation
Durability of information	• Potential for new evidence and/or new interventions to become available	Expert elicitation

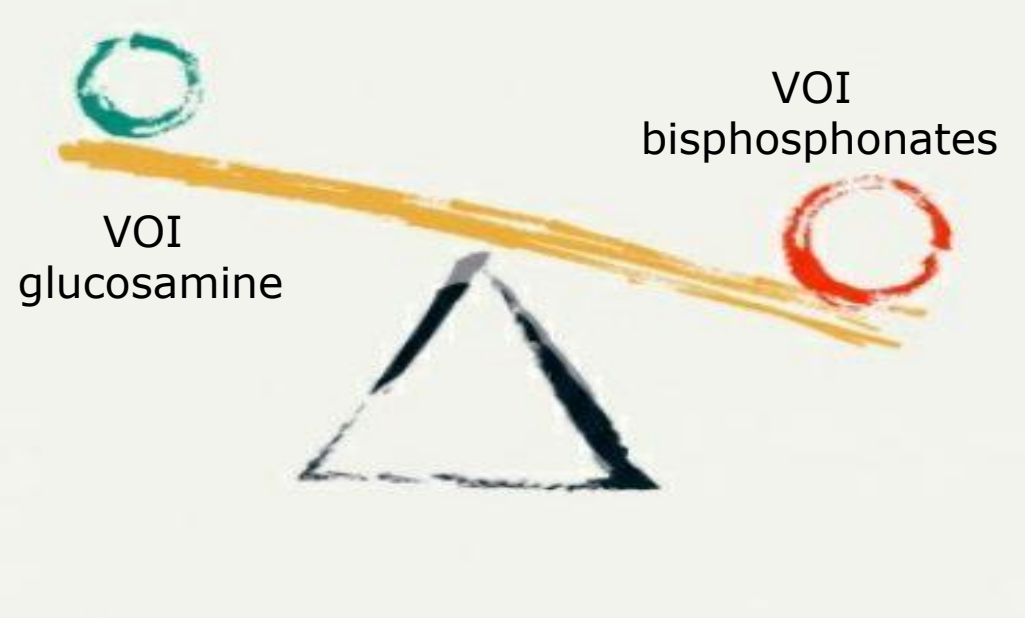
Illustrative Example (1)

- Assuming the role of an HTA agency, the team is interested in replicating SRs of glucosamine sulphate for osteoarthritis (OA) pain.
- The conceptual VOI is used to inform the decision.
  - The VOI of an SR replication for glucosamine vs. the VOI of the next best alternative use of resources – a replication of SRs of bisphosphonates for osteoporosis fracture prevention.

Illustrative Example (2)

Element	Glucosamine	Bisphosphonate Drugs
Expected changes in benefits	• Unlikely. Many large studies already published. New studies are unlikely to change conclusions.	• Likely. More studies in this area since it is an area of investigation.
Expected changes in uncertainty	Low. High degree of uncertainty and controversy about effects. Pre 2000 trials show benefit but post 2000- trials show no effect.	High. High degree of uncertainty about whether the more expensive drugs are better.
Durability of information	Low. It's possible that better alternatives for pain management will emerge in future.	Low. More new drugs (e.g. monoclonal antibodies) emerge.
Size of affect patient population	• Incidence: OA pain is 6th largest cause of disability in the world. • Uptake: Depends on the targeted knowledge users. Guidelines recommend against using glucosamine to treat patients with symptomatic OA.	• Incidence:1 in 3 women and 1 in 5 men over 50 • Uptake: High. Guidelines recommend bisphosphonates as the 1st line therapy.

Illustrative Example (3)

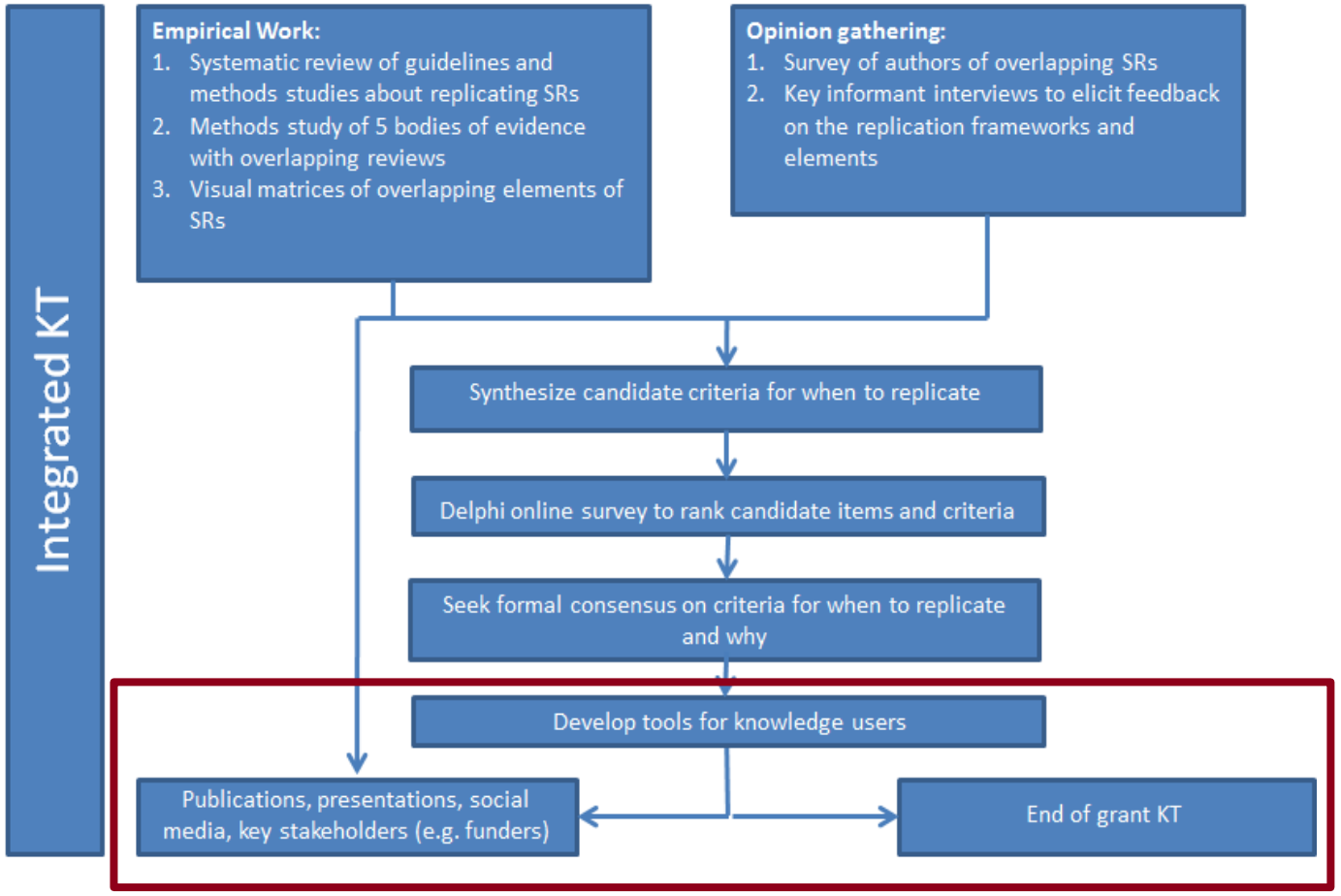


- not replicate SRs of glucosamine but allocate resources (funds, personnel, and time) to replicate SRs of bisphosphonates

Take Home Messages

- Conceptual VOI provides the informative bounds on the value of systematic review replications.
  - Informs the discussion without a complex modelling exercise.
- Comparison of the VOI of competing topics facilitate the efficient use of existing resources and avoid the exclusion of topics with small population size (e.g. rare diseases).
- Each VOI element requires further operationalization (sub-question or checklist) to ease the interpretation.

Next Steps


Integrated KT
Empirical Work:
1. Systematic review of guidelines and methods studies about replicating SRs
2. Methods study of 5 bodies of evidence with overlapping reviews
3. Visual matrices of overlapping elements of SRs
Opinion gathering:
1. Survey of authors of overlapping SRs
2. Key informant interviews to elicit feedback on the replication frameworks and elements
Synthesize candidate criteria for when to replicate
Delphi online survey to rank candidate items and criteria
Seek formal consensus on criteria for when to replicate and why
Develop tools for knowledge users
Publications, presentations, social media, key stakeholders (e.g. funders)
End of grant KT

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kthavorn@ohri.ca
@kednapat