Ottawa Hospital Research Institute
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Everything is complex, nothing is simple in healthcare - potential and limits of systematic reviews to inform health policy decisions

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Introduction

- Traditionally, systematic reviews have considered relatively simple interventions (for example, what are the benefits and harms of drug x)
- Increasingly systematic reviews are considering more complex interventions
  - biologics
  - complementary therapies
  - surgeon or therapist delivered interventions
  - team based care
  - quality improvement and organisation of care issues
  - health policy issues

Introduction

- Further the implementation of many simple interventions (eg influenza vaccination) often involves complexity:
  - who should deliver the intervention (family physicians, nurses, occupational health, public health, other)?
  - what knowledge and skills do they require?
  - where should the intervention be delivered (family practice, community clinic, workplace, other?
  - how do we ensure patient attendance (mass media campaigns, community campaigns, reminders, other)?
  - what information do patients need about aftercare

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Introduction

- In this presentation, I hope to:
  - explore the implications of complexity for the conduct and interpretation of systematic reviews
  - and to demonstrate some examples of knowledge tools try to promote the use of systematic reviews of complex interventions in health system and policy decisions

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Cochrane Effective Practice and Organisation of Care (EPOC) Group

EPOC aims to undertake systematic reviews of interventions to improve health care systems and health care delivery including:

- Professional interventions (e.g. continuing medical education, audit and feedback)
- Financial interventions (e.g. professional incentives)
- Organisational interventions (e.g. the expanded role of pharmacists)
- Regulatory interventions

Ballini, Bero, Eccles, Grimshaw, Gruen, Lewin, Mayhew, Munabi-Babigumira, Oxman, Pantoja, Paulsen, Shepperd, Tavender, Zwarenstein (2010). *Cochrane Library.*

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Cochrane Effective Practice and Organisation of Care (EPOC) Group

Progress to date - register and reviews

- Register of 7000+ primary studies
  - RCTs, CBAs, ITSs
- 68 reviews, 46 protocols
- Overviews of reviews (Bero 1998, Grimshaw 2001)
- Collaborating with over 600 researchers globally

Ballini, Bero, Eccles, Grimshaw, Gruen, Lewin, Mayhew, Munabi-Babigumira, Oxman, Pantoja, Paulsen, Shepperd, Tavender, Zwarenstein (2010). *Cochrane Library.*

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Outline

- Complexity in systematic reviews
- Issues relating to the conduct of the effectiveness of complex interventions
- Using systematic reviews to answer other types of questions for health system and policy decisions
- Use of systematic reviews in health system and policy decisions
- Practical tools to support the use of systematic reviews in health system and policy decisions

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Complexity in systematic reviews

Complexity may be due to:

- characteristics of the intervention
- contextual factors
- multiple outcomes
- methodological issues relating to the conduct of interventions.

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Complexity in systematic reviews

- These factors may result in greater variability or *heterogeneity* of estimates of effectiveness of such interventions: the real effect on an intervention may vary both in magnitude and direction depending on the modifying effect of such factors.
- Under such circumstances, reviewers need to consider in general whether primary research studies are sufficiently similar to be considered for inclusion within a single meaningful systematic review and in particular whether it is appropriate to undertake meta-analysis.

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Complexity in systematic reviews

- Complexity due to characteristics of intervention:
  - the intervention is intrinsically complex (multifaceted) e.g. all interventions delivered by a multi disciplinary team
  - the intervention is a heterogeneous mix of effective and ineffective components.

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Complexity in systematic reviews

- Complexity due to contextual factors:
  - The effectiveness of an intervention is modified by patient factors, provider and health care delivery factors.

    e.g. (1) the effectiveness of the intervention may be modified by the context in which it operates
    - mass media HIV awareness campaigns.

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Complexity in systematic reviews

- Complexity due to contextual factors
  - e.g. (2) the effectiveness of intervention is modified by diversity in patient population or in the interaction of the patient with the intervention
    - differential benefits of antiplatelet and cholesterol lowering therapies in high and low risk patient groups

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Complexity in systematic reviews

- Complexity may be due to:
  - characteristics of the intervention
  - contextual factors
  - multiple outcomes
  - methodological issues relating to the conduct of interventions.
- Often multiple sources of complexity exist.
- These issues form a spectrum.

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Complexity in systematic reviews

- For any individual review, the reviewer has to decide whether issues relating to complexity are sufficiently important to need addressing in the review.
- This requires careful thought at the time of formulating the review question and writing the protocol.

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Conducting systematic reviews of the effectiveness of complex interventions

- **Chapter 5: Defining the review question and developing criteria for including studies**
- **Chapter 6: Searching for studies**
- Chapter 7: Selecting studies and collecting data
- Chapter 8: Assessing risk of bias in included studies
- **Chapter 9: Analysing data and undertaking meta-analyses**
- Chapter 10: Addressing reporting biases
- Chapter 11: Presenting results and 'Summary of findings' tables
- **Chapter 12: Interpreting results and drawing conclusions**

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Conducting systematic reviews of the effectiveness of complex interventions

Chapter 5: Defining the review question and developing criteria for including studies

- Defining the question
- Lumping versus splitting
- Definition of intervention
- Choice of study designs

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Conducting systematic reviews of the effectiveness of complex interventions

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Conducting systematic reviews of the effectiveness of complex interventions

Chapter 9: Analysing data and undertaking meta-analyses

- Analytical approach
- Handling common methodological errors

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Chapter 5: Defining the review question and developing criteria for including studies

Lumping and splitting

- Does CME work?
- In health care professionals, does CME lead to better prescribing practice?
- In family doctors, does a two day workshop improve appropriateness of antibiotic prescribing?

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Lumping and splitting

- The 'lumping' rationale
  - systematic reviews aim to identify the common generalisable features within similar interventions
  - minor differences in trial design are not important
- 'Lumped' reviews
  - allow generalisability and consistency of findings to be assessed across wide range of settings and populations
  - reduced risk of bias or chance results

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Lumping and splitting

- The 'lumping principle'
  - the results of two interventions should be combined unless there are good grounds to believe they will have *opposing* effects

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Lumping and splitting

- The 'splitting' rationale
  - it is only appropriate to combine trials which are very similar in design, patient selection, intervention characteristics and outcome recording
- Split reviews avoid combining 'apples and oranges'

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Lumping and splitting

- Reviews can be split by:
  - Participants
  - Interventions
  - Outcome
- Very narrowly focused reviews are *de facto* subgroup analyses

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Lumping and splitting: Practical considerations

- Lumped reviews
  - Challenging
    - Logistically (large number of included studies)
    - Analytically
  - Heterogeneity expected
  - Interpretation may be challenging
    - seeing the woods for the trees
- Split reviews
  - Easier, quicker, “cleaner”

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Lumped or split?

Lumped

- Audit and feedback: effects on professional practice and health care outcomes
- Educational games for health professionals
- Mass media interventions: effects on health services utilisation
- Tailored interventions to overcome identified barriers to change: effects on professional practice and health care outcomes

Split

- Capitation, salary, fee-for-service and mixed systems of payment: effects on the behaviour of primary care physicians
- Interventions for reducing medication errors in children in hospital
- Patient reminder and recall systems to improve immunization rates

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Chapter 5: Defining the review question and developing criteria for including studies

- Although the arguments for randomised trials are as compelling in studies of complex interventions, at times might be ethically, logistically and practically not possible to conduct individual patient randomised trial
- EPOC reviews include
  - Cluster randomised trials
  - Controlled before and after studies
  - Interrupted time series

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Chapter 5: Defining the review question and developing criteria for including studies

- Inclusion of additional designs raises methodological issues concerning:
  - How to identify studies
  - How to assess risk of bias
  - How to incorporate studies in analyses
  - How to handle common methodological problems (eg unit of analysis errors in cluster randomised trials)
  - How to interpret results especially relating to uncertainty due to use of 'weak' designs
- Inclusion of these designs has prob increased EPOC workload by 50-100% (not for the faint hearted)

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Chapter 9: Analysing data and undertaking meta-analyses

- Reviews of complex interventions likely to be extremely heterogeneous – frequently review authors conclude that it would be inappropriate to conduct formal meta-analysis of the included studies.
- Non meta-analytical methods poorly developed and problematic

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Chapter 9: Analysing data and undertaking meta-analyses

- Vote counting methods
  - Add up the number of positive and negative comparisons
    - Comparisons with a positive direction of effect (irrespective of statistical significance)
    - Number of comparisons with statistically significant effects
  - Conclude whether the interventions were effective on this basis

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Chapter 9: Analysing data and undertaking meta-analyses

Problems with vote counting

- Fail to provide an estimate of the effect size of an intervention
  - Equal weight to comparisons that show a 1% change or a 50% change
- Ignores the precision of the estimate from the primary comparisons
  - Equal weight to comparisons with 100 or 1000 participants

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Chapter 9: Analysing data and undertaking meta-analyses

Problems with vote counting

- Problems handling studies where statistical significance is uncertain
  - Unit of analysis errors
- Problems handling small under powered studies
  - Potentially clinically significant but statistically insignificant effects would be counted as 'no effect comparisons'

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Chapter 9: Analysing data and undertaking meta-analyses

Alternative approaches

- Describe the range and distribution of effects across studies and explore probable explanations for the variation that is found
- In recent EPOC reviews, we have reported:
  - the median effect size across comparisons
  - interquartile range of observed effects
- In the primary analysis of 88 comparisons of audit and feedback compared to no intervention. The adjusted risk difference of compliance with desired practice varied from a 16 % absolute decrease in compliance to 70% increase in compliance (median = 5% absolute increase, inter-quartile range = +3% to +11%)

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Chapter 9: Analysing data and undertaking meta-analyses

- These approaches allow the reader to assess
  - Likely effect size
  - Consistency of effects across all included studies
  - Whether these effects differ between studies with and without unit of analysis errors
- and
  - Use information from all studies but do not have the same statistical uncertainty of the effects as we would using a vote counting approach

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Syntheses of other types of information about complex interventions

- In addition to understanding benefits and harms of complex interventions, decision makers often need additional information about:
  - Epidemiology of problem
  - Context in which complex interventions have been successfully used
  - Human resources and infrastructure needed to deliver complex interventions
  - Citizens' values and attitudes towards complex interventions
  - …..

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Syntheses of other types of information about complex interventions

- These factors are often poorly reported (if at all) in primary reports of the effects of complex interventions
- However information may be available from other research traditions (eg process evaluation data, qualitative studies of citizens' values etc)
- Syntheses of these bodies of research highly relevant and useful for health system and policy decisions

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Syntheses of other types of information about complex interventions

- Methods to conduct systematic reviews of qualitative studies have been developed and are being refined
- These methods tend to be interpretive and to go under a great many names:
  - Narrative summary
  - Thematic analysis
  - Grounded theory
  - Meta-ethnography
  - Meta-study
  - Realist synthesis
  - Cross-case techniques
  - Content analysis
  - Case survey
  - Qualitative comparative analysis
  - Bayesian meta-analysis

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Evidence informed decision making

Managers and policymakers can find themselves in three situations that require them to characterize policy options

1. An issue is already on the decision agenda and a policy option effectively selected to address the problem, in which case the best that managers and policymakers can often do is to identify how to maximize the benefits from the selected policy option, minimize its harms or risks, optimize the impacts achieved for the money spent, and (if there is substantial uncertainty about the policy option's likely costs and consequences) design a monitoring and evaluation plan

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Evidence informed decision making

Managers and policymakers can find themselves in three situations that require them to characterize policy options

2. Managers and policymakers are actively engaged in events in which policy options are being discussed or promoted, in which case they need to assess the policy options being presented to them as well as the problem and politics streams within the policymaking process that will determine whether the policy option comes up for serious consideration

Evidence informed decision making

Managers and policymakers can find themselves in three situations that require them to characterize policy options

3. Managers and policymakers face a tabula rasa (clean slate) in which they themselves have the opportunity to define a problem, identify and characterize policy options, and look for events within the political stream that might allow them to act

Lavis (2008)

Promoting use of systematic reviews in health systems and policy decision making

- Common criticisms of systematic reviews by policy makers
  - No relevant reviews
  - Reviews difficult to access
  - Reviews difficult to understand
- John Lavis and colleagues have created heatlhsystemsevidence.org to address these criticisms and facilitate use of reviews in health systems and policy decision making

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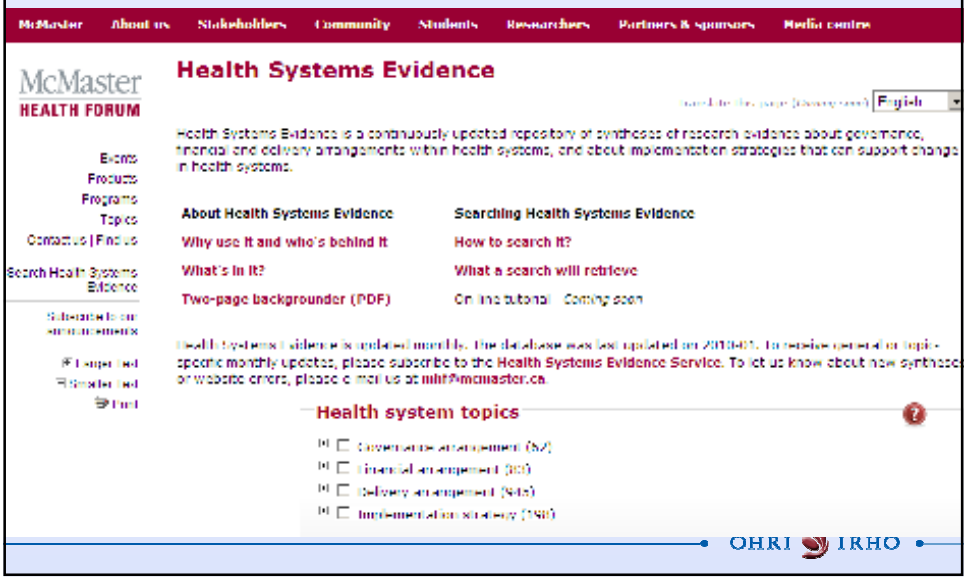
Healthsystemsevidence.org



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- Over 1300 citations
  - policy briefs
  - overviews of systematic reviews
  - systematic reviews
    - Cochrane reviews and protocols

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- Scenario:
  - What is the evidence about the effect of role substitution in primary care on patient outcomes and resource utilization?

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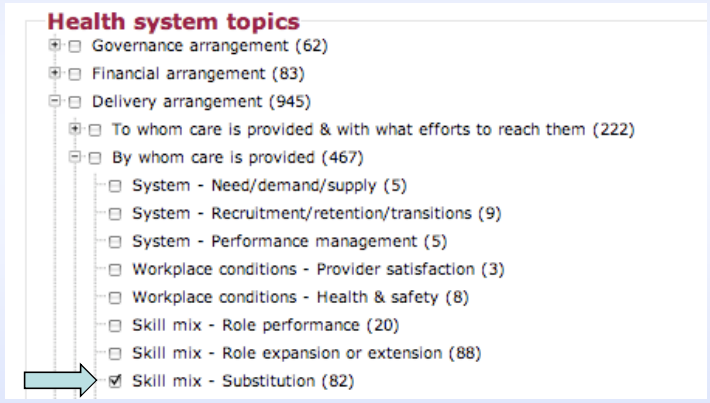

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Links to any freely available user-friendly summaries, scientific abstracts, and full-text reports.

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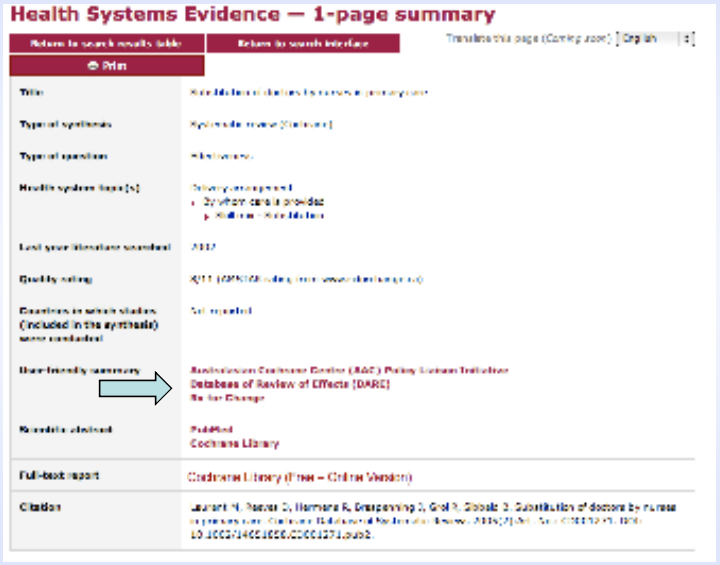
Health Systems Evidence — 1-page summary



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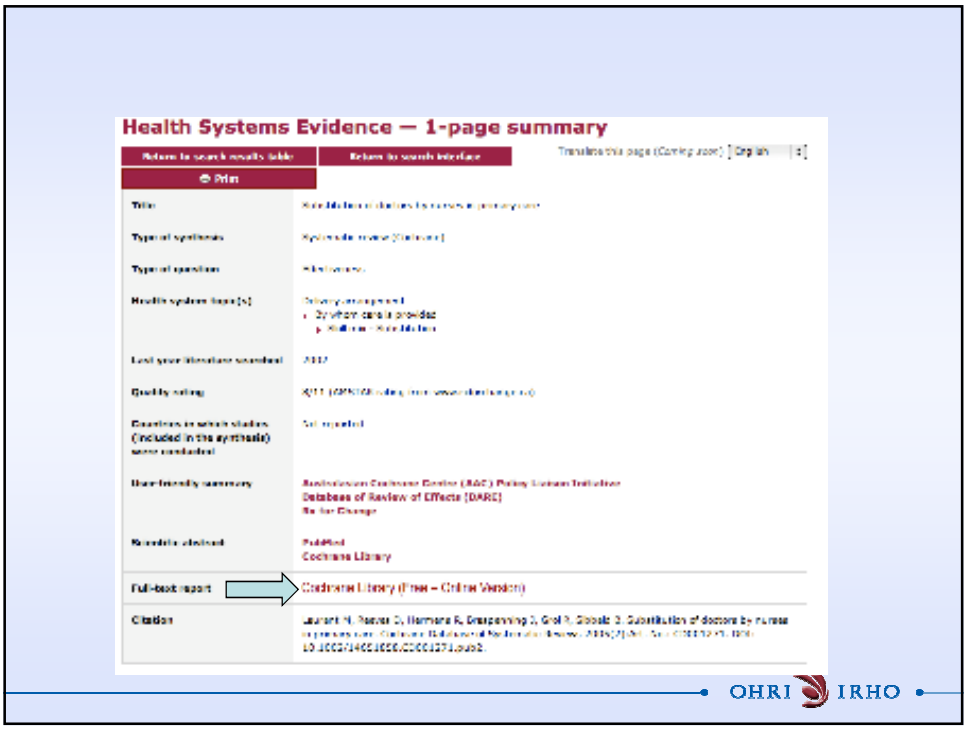

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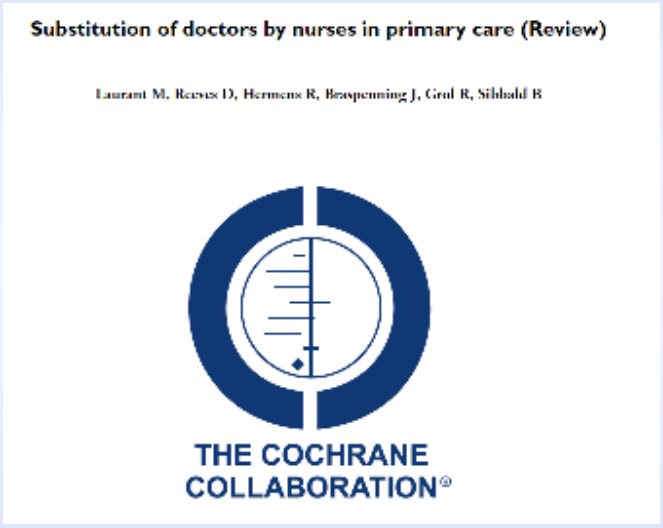

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Promoting use of systematic reviews in health systems and policy decision making

Other resources

- SUPPORT tool is a series of 18 papers about how policy makers can better use research evidence to support their decision making
- Available through Health Research Policy and Systems http://www.health-policy-systems.com/supplements/7/S1

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Summary

- There is increasing awareness of value of systematic reviews of complex interventions to inform health system and policy decisions
- The conduct of systematic reviews of complex interventions are particularly challenging due to issues relating to:
  - lumping and splitting
  - intervention definition
  - inclusion of broad range of study designs
  - identification of sources of heterogeneity
  - analytical challenges

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Summary

- Further syntheses of other types of knowledge also frequently needed to supplement evidence on benefits and harms of complex interventions
- Substantial methodological innovation in this area currently
- Policy makers often unaware of the availability of relevant reviews and find them difficult to access and understand
- Healthsystemsevidence.org and SUPPORT tool are practical tools to support policy makers to make better use of reviews in decision making

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