

Knowledge Synthesis for Knowledge Users



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Learning Objectives

1. Explain the importance of knowledge synthesis (KS) for decision-making by knowledge users (KUs)
2. Discuss different types of KS
3. Describe how to select a KS method for a particular research question



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What is knowledge synthesis?

Definition of knowledge synthesis

The contextualization and integration of research findings of individual research studies within the larger body of knowledge on the topic. A synthesis must be reproducible and transparent in its methods, using quantitative and/or qualitative methods.



Canadian Institutes of Health Research, <http://www.cihr-irsc.gc.ca/e/41382.html>



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**What is the role of
knowledge synthesis
in decision-making?**

Importance of knowledge synthesis

- Basing decisions on expert opinion can be biased
 - Experts (e.g., clinicians) 10 years behind on the latest research, did not mention effective therapies, recommended ineffective therapies
Antman et al., JAMA 1992
- Basing decisions on findings of an individual study might be misleading
 - 30% of highly cited clinical studies contradicted or had a reduced effect size in subsequent studies

Ioannidis et al., JAMA 2005



Importance of knowledge synthesis

- KS can be used to make sense out of the results of many different studies in a way that can be used by KUs who do not have the skills to summarize the evidence
- Difficult for KUs to keep up with the literature – 75 randomized controlled trials and 11 systematic reviews published per day! Bastian et al., PLoS Medicine 2010
- KUs may not have the skills or time to summarise evidence



Importance of knowledge synthesis

- KS can be used to statistically combine the results of multiple studies, increasing our confidence in the results (power and precision)
- KS can be used to sort through the results arising from conflicting studies

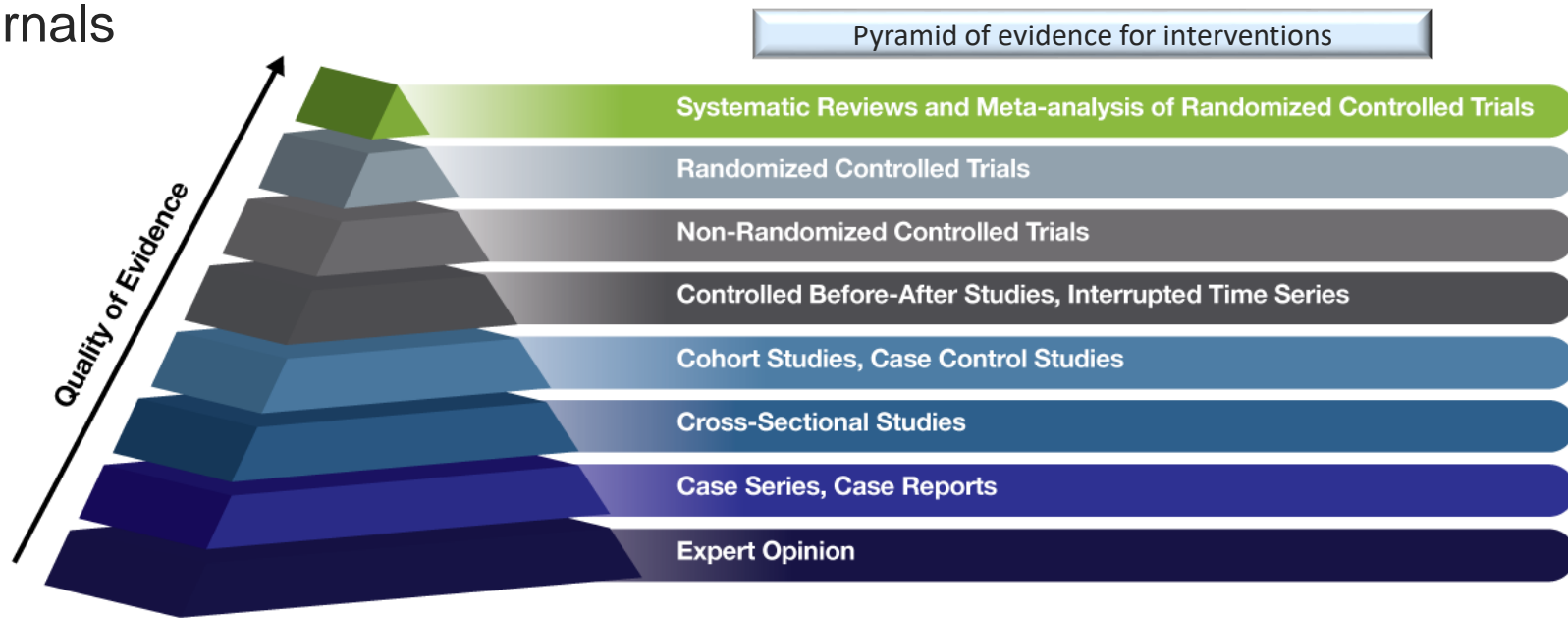
Cochrane Handbook, <http://handbook.cochrane.org/>



Importance of knowledge synthesis

Can be used to justify why a new study (e.g., randomized trial, cohort study) is necessary

- Funding organizations
- Journals



Central to evidence-informed decision-making!



Types of knowledge syntheses

1. Systematic reviews
2. Network meta-analysis
3. Scoping reviews
4. Overview of reviews
5. Rapid reviews
6. Diagnostic reviews
7. Prognostic reviews
8. Economic reviews

Plus emerging methods



Discussion question

What kind of knowledge synthesis projects have you worked on in the past or are currently working on?





Systematic Review

Definition of systematic review

A systematic review uses systematic and explicit methods to identify, select, critically appraise, and extract and analyze data from relevant research



Cochrane Handbook, <http://handbook.cochrane.org/>

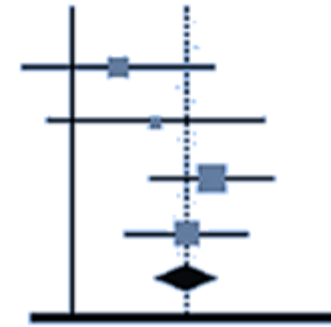


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Definition of meta-analysis

- A meta-analysis is a statistical technique used to pool the results from more than one study
- Data from many patients from multiple studies are being combined in the analysis so the results have more power and are more precise than the results from an individual study



Pairwise meta-analysis

Direct comparison

Cochrane Handbook, <http://handbook.cochrane.org/>



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Example

Efficacy and Safety of Cognitive Enhancers for Mild Cognitive Impairment: A Systematic Review and Meta-analysis

Highlights and Implications

- A systematic review and meta-analysis of 8 randomized controlled trials and 3 companion reports.
- No improvements in cognition, function or mortality were identified among patients who used cognitive enhancers.
- Numerous harms (nausea, diarrhea, vomiting, headaches) were associated with taking cognitive enhancers.
- Careful consideration needs to be made when determining whether to cover these agents for patients with MCI, given lack of evidence of effectiveness and risk

Reference: Tricco AC, Soobiah C, Berliner S, et al. Efficacy and safety of cognitive enhancers for patients with mild cognitive impairment: a systematic review and meta-analysis. *CMAJ*. 2013;185:1393-1401.

PMID: [24043661](https://pubmed.ncbi.nlm.nih.gov/24043661/)

For more information, please contact Dr. Andrea Tricco: triccoa@smh.ca

What is the current situation?

Mild cognitive impairment (MCI) is characterized by memory and cognitive deficits, and increases with age. Between 3% and 17% of MCI cases progress to dementia, a serious public health burden with over 4.6 million new cases a year. Cognitive enhancers, used to treat dementia, are a possible strategy to prevent the progression of MCI, but their efficacy in MCI patients is unclear.

What is the objective?

This study examines the efficacy and safety of cognitive enhancers for patients with MCI.

How was the review conducted?

- A systematic review and meta-analysis was conducted; two independent reviewers completed the screening, data abstraction and risk of bias appraisal.
- Selected studies examined MCI patients prescribed donepezil, rivastigmine, galantamine, and/or memantine compared to placebo, other cognitive enhancers and/or supportive care. Outcomes included cognition, function, mortality, and potential harms.

What did the review find?

- Of the 15, 556 titles and abstracts and 1,388 full-text articles, 8 RCTs (4 examining donepezil 5-10 mg, 2 examining galantamine 16-24 mg, 1 each examining memantine 10-20 mg and rivastigmine 3 -12 mg) and 3 companion reports were included.
- No statistically significant differences were found between cognitive enhancers and placebo across **cognition, function, and mortality** outcomes.
- Patients taking cognitive enhancers experienced significantly more **nausea, diarrhea, vomiting, and headaches** compared to those on placebo. There were no differences in **major adverse events** between those taking cognitive enhancers and placebo.



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Conducted for the Canadian Institutes of Health Research
Drug Safety and Effectiveness Network

Impact

- Influenced the decision to continue delisting cognitive enhancers for mild cognitive impairment
- Informed the national guidelines on dementia
- Used in the Royal College of Physicians and Surgeons certification exam
- Featured in >125 mass media articles

Tricco et al., CMAJ 2013



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Network Meta-analysis

Definition of network meta-analysis

An extension of indirect comparisons that allows the combination of direct evidence from head-to-head studies with indirect comparisons, and also the simultaneous analysis of the comparative effects of many interventions

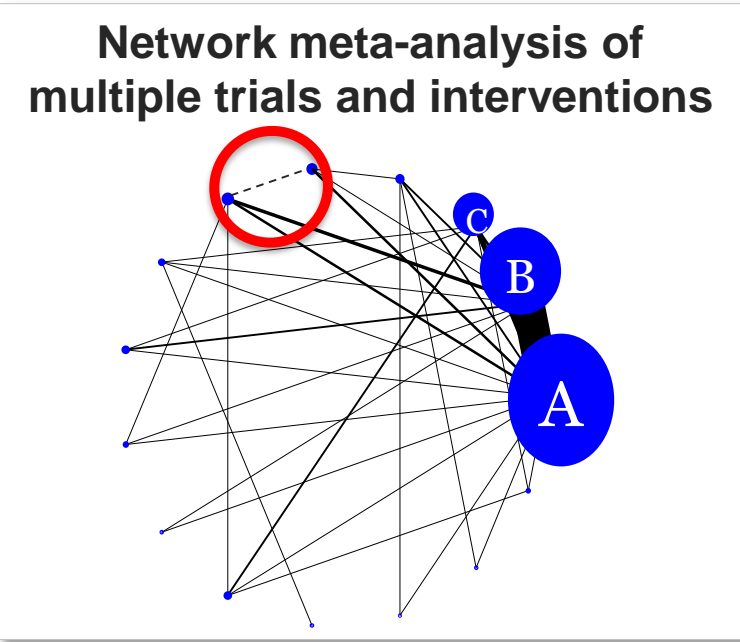
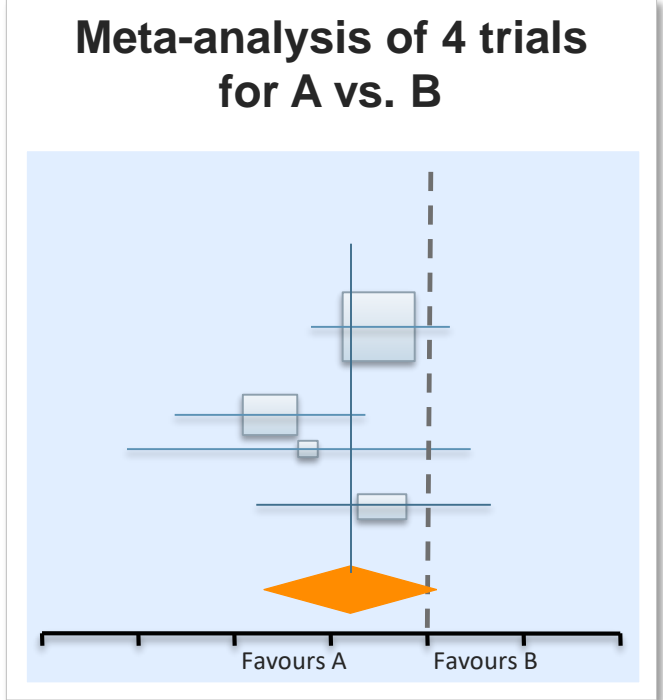
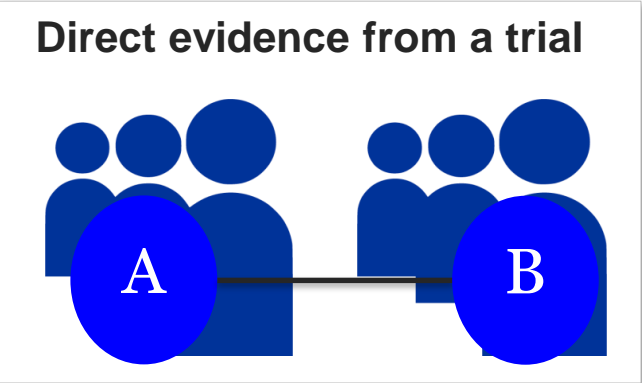


Cochrane Handbook, <http://handbook.cochrane.org/>



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Network meta-analysis



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Example

Safety, effectiveness, and cost-effectiveness of long-acting versus intermediate-acting insulin for patients with type 1 diabetes: a systematic review and network meta-analysis

Summary

The objective of this review was to examine the safety, effectiveness, and cost-effectiveness of long-acting insulin compared to intermediate-acting insulin in patients with type 1 diabetes. A total of 38 studies including 27 RCTs were included in the review. Overall, the findings suggest that long-acting insulin analogs are slightly superior to intermediate-acting analogs for glycemic control and harms (weight gain and severe hypoglycemia).

Implications

Although long-acting insulin is superior to intermediate-acting insulin, it is likely more expensive. As such, patients and their physicians should tailor their choice of insulin according to their preference, cost, and accessibility.

Reference: Tricco AC, Ashoor HM, Antony J, et al. Safety, effectiveness, and cost effectiveness of long acting versus intermediate acting insulin for patients with type 1 diabetes: systematic review and network meta-analysis. *BMJ*. 2014 Oct 1;349:g5459.

PMID: [25274009](https://pubmed.ncbi.nlm.nih.gov/25274009/)

For more information, please contact Dr. Andrea Tricco: triccoa@smh.ca

What is the current situation?

- Hyperglycemia associated with type 1 diabetes has been commonly treated with intermediate-acting insulin such as isphane insulin (NPH) and zinc insulin (lente)
- Evidence suggests, however, that newer long-acting insulin analogs (i.e. glargine and detemir) may be safe and more effective than NPH and lente

What is the objective?

The objective of this systematic review was to examine the safety, effectiveness, and cost-effectiveness of long-acting insulin in patients with type 1 diabetes

How was the review conducted?

- The protocol (or plan) for the review was developed and revised with input from researchers, clinicians, and the British Columbia Ministry of Health
- 3 databases and unpublished literature were searched for randomized controlled trials (RCTs) or non-randomized studies of long- and intermediate-acting insulin in adults with type 1 diabetes
- The primary outcome of interest was glycosylated hemoglobin (A1C) and secondary outcomes included severe hypoglycemia, serious hyperglycemia, and weight gain
- Screening of literature search results, data abstraction, and risk-of-bias were conducted independently by two reviewers
- Random-effects pairwise meta-analysis (MA) and random-effects network meta-analysis (NMA) were conducted based on the availability of evidence

What did the review find?

- 38 relevant studies and 1 companion report were identified, including 27 RCTs representing 7,496 patients
- Glargine once daily, detemir once daily and detemir twice daily significantly reduced A1C compared to NPH once daily in an NMA (26 RCTs)
- In a subgroup analysis (12 RCTs), glargine once daily was significantly more effective compared to NPH once daily for patients with poorly controlled diabetes (A1C>8%)
- Patients receiving detemir once or twice daily experienced significantly fewer episodes of severe hypoglycemia compared to NPH once or twice daily (16 RCTs)
- NPH once daily and detemir once daily caused significantly more weight gain, however, detemir once or twice daily caused significantly less weight gain than NPH once or twice daily (13 RCTs)



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Conducted for the British Columbia Ministry of Health

Impact

- Influenced the decision to continue listing the insulin in the same manner for the province of BC
- Featured in >220 mass media articles
- Used to update the WHO List of Essential Medicines

Tricco et al., BMJ 2014



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Other types of knowledge synthesis

Scoping reviews

- **Definition:** Scoping reviews are exploratory projects that systematically map the literature available on a topic, identifying key concepts, theories, sources of evidence and gaps in the research
- **Example:** What care coordination quality improvement interventions provide support to primary healthcare providers of patients who are frequent users of the healthcare system?

Overview of reviews

- **Definition:** Used to summarize multiple reviews addressing the effects of two or more potential interventions for a single condition or health problem
- **Example:** What are effective interventions for treat complex wounds?

Rapid reviews

- **Definition:** A knowledge synthesis in which components of the systematic review process are simplified or omitted to produce information in a timely manner
- **Example:** What are the comparative safety and effectiveness of inhaled corticosteroids and beta-agonists for chronic asthma?

Wilcox et al., JAMA 2014; Iles et al. , Occ Rehab 2009; Tricco et al., BMC Med 2015



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Other types of knowledge synthesis

Diagnostic reviews

- **Definition:** A type of knowledge synthesis that answers how well a diagnostic test works for a particular group of patients.
- **Example:** Does this patient have an exudative pleural effusion?

Prognostic reviews

- **Definition:** A type of knowledge synthesis that answers how to predict a disease outcome more accurately or efficiently.
- **Example:** Can recovery expectations predict outcomes in non-chronic non-specific low back pain?

Economic reviews

- **Definition:** Used to synthesize economic studies, such as cost-effectiveness analyses or costing studies.
- **Example:** What is the cost-effectiveness of interventions for complex wound care?

Wilcox et al., JAMA 2014; Iles et al. , Occ Rehab 2009; Tricco et al., BMC Med 2015



Example

Conducted for the Ontario Ministry of Health BRIDGES Initiative

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**Quality improvement strategies for frequent users of
the healthcare system: A scoping review**

Draft prepared by:

**Andrea C. Tricco,¹ Lianne Kark Ezer,¹ Paul A. Kahn,¹ Jesmin Antony,¹ Heather
MacDonald,¹ Marco Ghassemi,¹ Erik Blondal,¹ Huda Ashoor,¹ Charlene Soobiah,¹
Mariam Tashkandi,¹ Erin Lillie,¹ Sharon E. Straus.^{1,2}**



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Impact

- Influenced policy for alternate levels of care patients by the Ontario Ministry of Health and Long-term Care
- Used to establish the intervention for a clinical trial for the BRIDGES initiative
- Featured in >30 mass media articles

Tricco et al., 2014 CMAJ



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Emerging knowledge synthesis methods

Integrative review

- **Definition:** Used to describe synthesis methods for integrating qualitative and quantitative data.
- **Example:** What self-care management interventions led by nurse principal investigators exist for patients with cancer?

Meta-synthesis

- **Definition:** Used to combine separate elements to form a coherent whole using a process of logical deduction.
- **Example:** What are the lived experiences of individuals with tic disorders and Tourette's syndrome?

Mixed studies review

- **Definition:** Used to describe reviews combining or integrating (1) qualitative and quantitative studies, (2) only mixed methods studies, or (3) mixed methods studies and either qualitative or quantitative studies (or both).
- **Example:** What are the preferences of patients in the palliative phase of their illness?

Kastner et al., JCE 2016; Tricco et al, JCE 2016



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Emerging knowledge synthesis methods

Meta-interpretation

- **Definition:** Used to describe theoretical synthesis methods that provide a broader understanding of human behavior and experience and should lead to new insights that are not observed in the original studies.
- **Example:** How can public health agencies enhance the public's trust in the food safety regulatory system?

Concept synthesis

- **Definition:** Used to identify concepts, viewpoints, or ideas. Focuses on identifying the defining attributes of the concepts and can be used to develop a synthesis model.
- **Example:** What are the attributes of family-centered care and partnership in care?

Critical interpretive synthesis

- **Definition:** Uses an iterative approach to refine the research question, search and select articles from the literature, and define and apply codes and categories.
- **Example:** What is the risk in low vision rehabilitation for older adults with age-related vision loss?

Kastner et al., JCE 2016; Tricco et al, JCE 2016



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Emerging knowledge synthesis methods

Meta-ethnography

- **Definition:** Used to synthesize qualitative research or develop “translations of qualitative studies into one another” (i.e., reciprocal translation analysis).
- **Example:** How do smokers perceive their smoker identity, and what factors shape their beliefs, meanings, and attitudes attached to it?

Meta-narrative review

- **Definition:** Involves looking across different paradigms or research traditions to uncover their “unfolding storyline,” which results in maps of “meta-narratives” from which dimensions or themes can be revealed and distilled.
- **Example:** What are the thematic trends in the health equities knowledge base?

Meta-study

- **Definition:** It is a multifaceted, interpretive approach to synthesis developed to study the experiences of patients living with chronic illness.
- **Example:** What is the meaning of spirituality at the end of life?

Kastner et al., JCE 2016; Tricco et al, JCE 2016



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Emerging knowledge synthesis methods

Meta-summary

- **Definition:** A quantitatively oriented summary of qualitative findings developed to accommodate the distinctive features of qualitative surveys. That is used to combine descriptive quantitative and qualitative studies.
- **Example:** What are the experiences (such as emotions, perceptions, and attitudes) of adult heart transplant recipients?

Narrative synthesis

- **Definition:** Synthesis method that includes a formal analytical process to generate new insights or knowledge by seeking to be systematic and transparent.
- **Example:** What are patient and public attitudes of clinical practice guidelines?

Realist review

- **Definition:** A method rooted in realist philosophy that is used to investigate “what works for whom, under what circumstances, and why.”
- **Example:** What change agency interventions and strategies are effective, for whom in what circumstances, and why to enable evidence-informed healthcare?

Kastner et al., JCE 2016; Tricco et al, JCE 2016



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Example

Review

Cancer
Epidemiology,
Biomarkers
& Prevention

Systematic Review and Meta-study Synthesis of Qualitative Studies Evaluating Facilitators and Barriers to Participation in Colorectal Cancer Screening

Gladys N. Honein-AbouHaidar¹, Monika Kastner^{2,3}, Vincent Vuong¹, Laure Perrier², Corinne Daly¹, Linda Rabeneck⁴, Sharon Straus^{2,5}, and Nancy N. Baxter^{1,5}

Abstract

Screening reduces the incidence, morbidity, and mortality of colorectal cancer, yet participation tends to be low. We undertook a systematic review and meta-study synthesis of qualitative studies to identify facilitators and barriers to colorectal cancer screening participation. We searched major bibliographic databases for records published in all languages from inception to February 2015. Included primary studies that elicited views and perceptions towards colorectal cancer screening were appraised for relevance and quality. We used a two-stage synthesis to create an interpretation of colorectal cancer screening decisions grounded in primary studies; a thematic analysis to group themes and systematically compare studies and a meta-synthesis to generate an expanded theory of colorectal cancer screening participation.

Ninety-four studies were included. The decision to participate in colorectal cancer screening depended on an individual's awareness of colorectal cancer screening. Awareness affected views of cancer, attitudes towards colorectal cancer screening modalities, and motivation for screening. Factors mediating awareness included public education to address misconceptions, primary care physician efforts to recommend screening, and the influence of friends and family. Specific barriers to participation in populations with lower participation rates included language barriers, logistical challenges to attending screening tests, and cultural beliefs. This study identifies key barriers, facilitators, and mediators to colorectal cancer screening participation. *Cancer Epidemiol Biomarkers Prev*; 25(6): 907-17. ©2016 AACR.



Impact

- Influenced cancer screening policies at Cancer Care Ontario

Honein-AbouHaidar et al., Cancer Epidemiol Biomarkers Prev. 2016



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Activity

Activity: What kind of review would you do?

1 Read the scenario.

2 Identify the type of review you would do based on the question.



Activity: What kind of review would you do?

What type of review would you do if you wanted to know:

- 1 What is known from the existing literature about mental health issues among immigrant and refugee youth in Canada?

Realist Review

Diagnostic Review

Scoping Review

Systematic Review

Meta-Summary



Activity: What kind of review would you do?

What type of review would you do if you wanted to know:

2 What are the effects of participating in creative activities on the health and well-being of children's self-confidence, self-esteem, levels of knowledge and physical activity?

Realist Review

Diagnostic Review

Scoping Review

Systematic Review

Meta-Summary



Summary

- 20 different types of KS were presented today, each has a unique purpose
- Can use this information to match a KS question posed by a KU to a specific KS method



Learning Objectives

1. Explain the importance of knowledge synthesis (KS) for decision-making by knowledge users (KUs)
2. Discuss different types of KS
3. Describe how to select a KS method for a particular research question



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Questions

Do you have any questions about today's presentation?



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Canadian Agency for Drugs and Technologies in Health

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Canada Research Chair in KS



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Thank you for your attention!

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