deprescribing.org

Reducing medications safely to meet life's changes

Moins de médicaments, sécuritairement – pour mieux répondre aux défis de la vie

GRADE, EBM and Deprescribing

Kevin Pottie MD CCFP, MClSc, FCFP

Associate Professor, Family Medicine, University of Ottawa

"Research is like turning on the light before you clean up the room: it doesn't clean it for you but does tell you where the problems are"

(Frank Davidoff, Annals of Internal Medicine)

GRADE Walkthrough

GRADE

- GRADE emerged from an informal meeting in Oslo, Norway in 2000.
- Led to a GRADE series in BMJ in 2008
- 26 GRADE methods series began in J Clin Epi 2012
- Leading WHO methods and Canadian Task Force, IOM Standards and over 100 guidelines organizations
- Over 400 international GRADE members, debate science evidence and guidelines and apply this across diverse fields

Examples of GRADE Recommendations

- PPI - Strong for deprescribing (low quality evidence) (Farrell CFP 2017)
- BZRA for insomnia- Weak for deprescribing (low quality evidence) Strong for elderly (low quality of evidence) (Pottie CFP in press)
- Antipsychotics in dementia: Taper and stop antipsychotics slowly in collaboration with the patient and caregivers (strong recommendation, moderate-quality evidence) (Bjerre 2018)

Strong and Weak Recommendations

- A strong recommendation implies that all patients in the given situation would want the recommended course of action, and only a small proportion would not.
- A weak recommendation implies that most patients would wish to follow the recommendation, but some patients would not. (more shared decision making)

Deprescribing can include stopping, stepping down, or reducing doses

- Stopping can be done either via abrupt discontinuation or a tapering regimen
- Stepping down involves abrupt discontinuation or tapering
- Reducing dose

Unique elements of GRADE: Patient Important Outcomes

Primary outcomes: GRADE lingo:critical outcomes

- Quality of life
- **Sleep quality**
- Effect on cognition
- Effect on anxiety
- Adverse drug withdrawal events
- **Cessation rate**
- **Harms**

Secondary outcome: GRADE lingo: Important outcomes

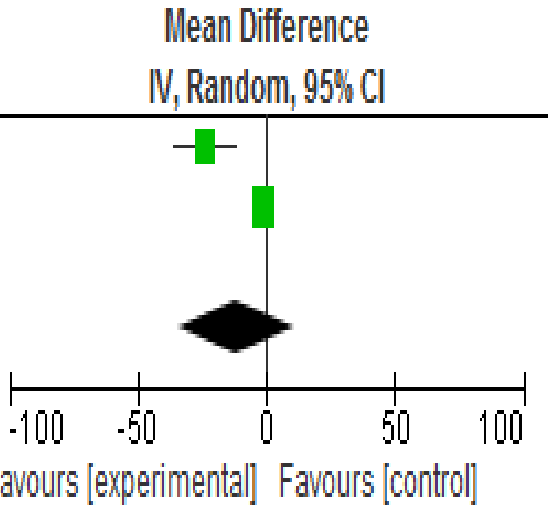
- **Patient satisfaction**
- **aBZRA pill burden**

Sleep Latency at 1 Year

Study or Subgroup	CBT+taper Mean	SD	Total	Taper Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Lichstein 2013	24.1	16.7	24	48	24.4	23	46.6%	-23.90 [-35.90, -11.90]
Morin 2004	23.82	4.77	27	24.78	5.07	24	53.4%	-0.96 [-3.67, 1.75]
Total (95% CI)			**51**			**47**	**100.0%**	**-11.65 [-34.08, 10.78]**

Heterogeneity: $Tau^2 = 243.41$; $Chi^2 = 13.35$, df = 1 (P = 0.0003); $I^2 = 93\%$

Test for overall effect: Z = 1.02 (P = 0.31)

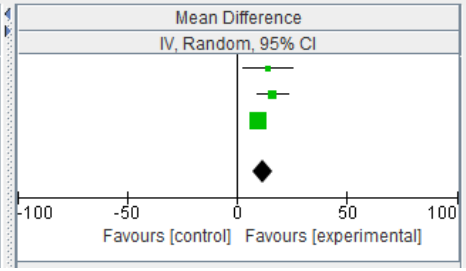


Sleep Efficiency

Post-treatment

Comparison: 1 Sleep Quality, Outcome: 1.5 Sleep Efficiency Post-treatment

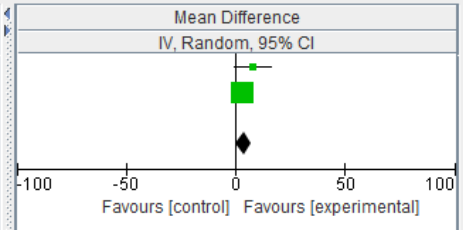
Study or Subgroup	CBT+taper Mean	CBT+taper SD	CBT+taper Total	Taper Mean	Taper SD	Taper Total	Weight	Mean Difference IV, Random, 95% CI
Belleville 2007	75.24	14.36	28	61.35	24.71	25	13.7%	13.89 [2.84, 24.94]
Lichstein 2013	85	7.5	24	69	15.5	23	25.9%	16.00 [8.99, 23.01]
Morin 2004	78.06	2.39	27	68.66	2.44	25	60.4%	9.40 [8.09, 10.71]
Total (95% CI)			79			73	100.0%	11.72 [7.09, 16.35]
Heterogeneity: Tau² = 8.79; Chi² = 3.85, df = 2 (P = 0.15); I² = 48%								
Test for overall effect: Z = 4.96 (P < 0.00001)								



At 1 year follow-up

Comparison: 1 Sleep Quality, Outcome: 1.6 Sleep efficiency at 1 year

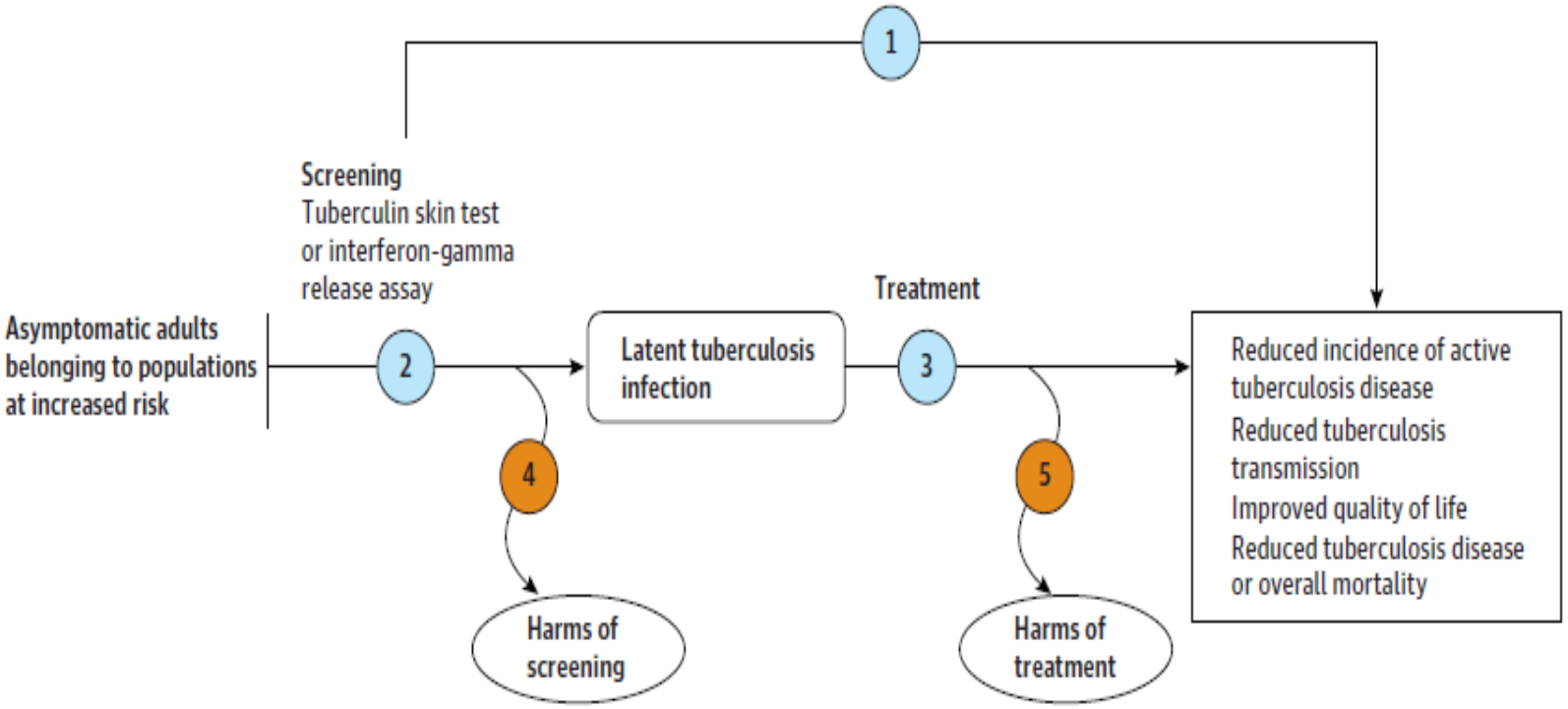
Study or Subgroup	CBT+taper Mean	CBT+taper SD	CBT+taper Total	Taper Mean	Taper SD	Taper Total	Weight	Mean Difference IV, Random, 95% CI
Lichstein 2013	85.4	8.3	24	77.4	18.7	23	15.7%	8.00 [-0.33, 16.33]
Morin 2004	78.71	2.49	27	75.77	2.66	25	84.3%	2.94 [1.54, 4.34]
Total (95% CI)			51			48	100.0%	3.73 [0.13, 7.34]
Heterogeneity: Tau² = 3.51; Chi² = 1.38, df = 1 (P = 0.24); I² = 27%								
Test for overall effect: Z = 2.03 (P = 0.04)								



Role of logic models

- Logic models demonstrate a chain of logic between inputs and outcomes and to capture possible alternative explanations
- Logic models can be used at different stages of a systematic review, for example,
  - scoping the review,
  - refining and conducting the review,
  - and making the review relevant to policy and practice

Figure 1. Analytic Framework and Key Questions



Key questions

1. Is there direct evidence that targeted screening for latent tuberculosis infection (LTBI) in primary care settings in asymptomatic adults at increased risk for developing active tuberculosis disease (eg, individuals in populations with a high prevalence of active TB disease or with documented increased risk for progression from LTBI to active TB disease) improves quality of life, or reduces active TB disease incidence, or reduces transmission of TB, or reduces disease-specific or overall mortality?

2. a. What is the accuracy and reliability of the TST or the interferon-gamma release assay (IGRA) for screening asymptomatic adults who are at increased risk for developing active TB disease?

   b. What is the accuracy and reliability of sequential screening strategies that include both TST and IGRA testing in asymptomatic adults who are at increased risk for developing active TB disease?

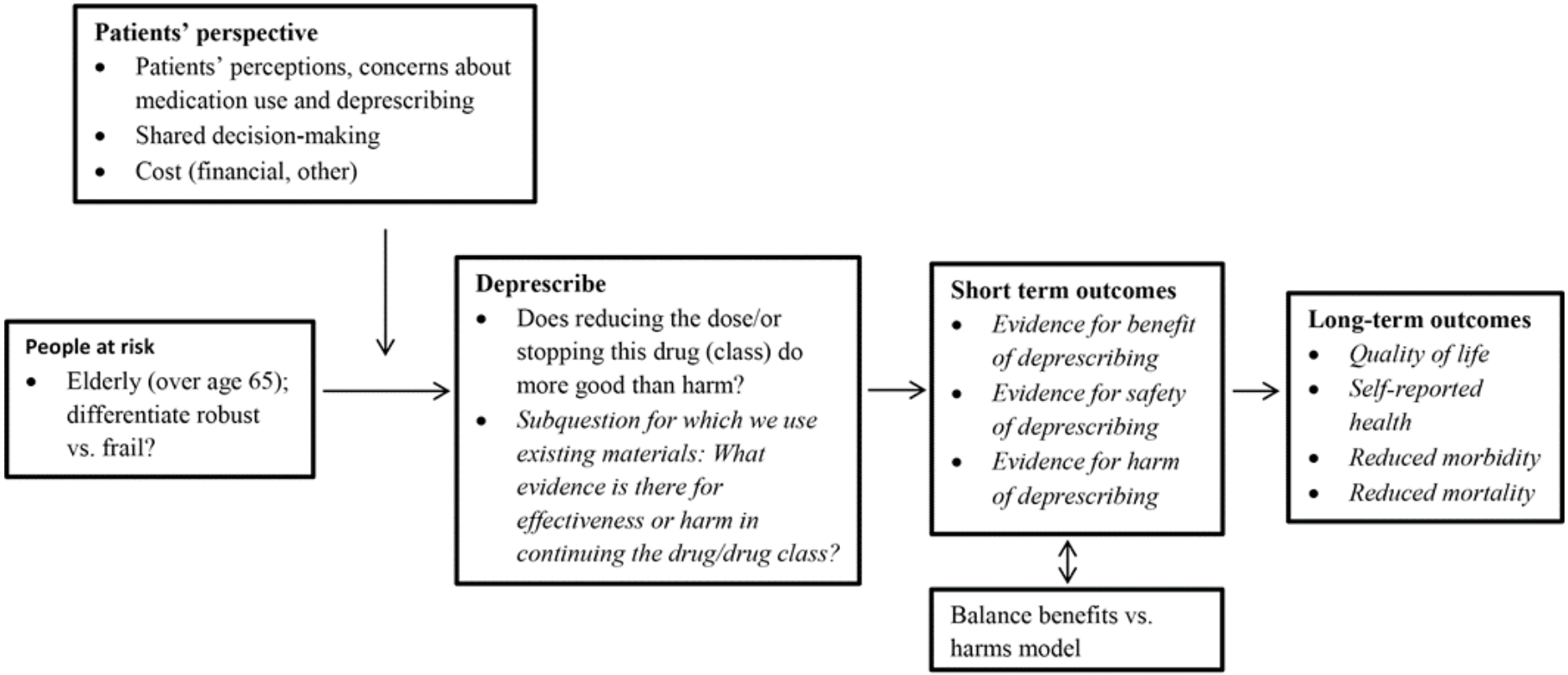
3. Does treatment of LTBI with CDC-recommended pharmacotherapy regimens improve quality of life or reduce progression to active TB disease, or reduce transmission of TB, or reduce disease-specific or overall mortality?

4. Are there harms associated with screening for LTBI?

   a. Do these harms differ by screening method or strategy?

   b. Do these harms differ by population?

5. Are there harms associated with treatment for LTBI with CDC-recommended pharmacotherapy regimens?



Patient important outcomes (examples provided; content and relevance to be determined):
Critical: Fractures related to falls, mortality, admission to Long-term care
Important: Emergency room visits, falls
Possibly important: Creatinine, blood pressure, orthostatic hypotension, blood sugar, general practitioner visits, number of medications taken, symptom control, reduced risk of drug interactions, increased chance of adherence, decreased cost, caregiver stress, dizziness, confusion

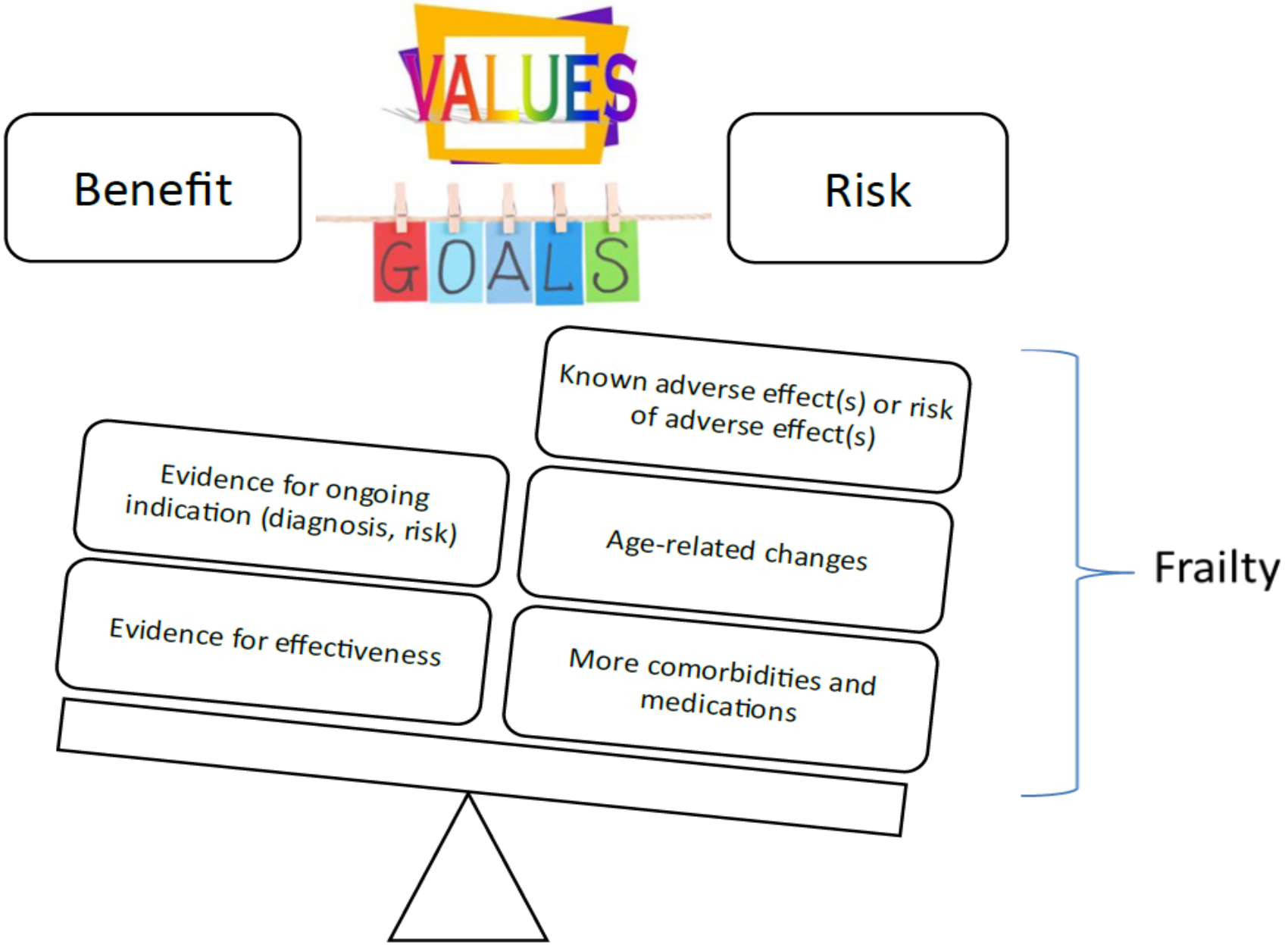
Logic models

- Scoping the review
  - Refining review question
  - Deciding on lumping or splitting a review topic
  - Identifying intervention components
- Defining and conducting the review
  - Identifying relevant study inclusion/exclusion criteria
  - Guiding the literature search strategy
  - Explaining the rationale behind surrogate outcomes used in the review
  - Justifying need for subgroup analyses (e.g., age, sex/gender, socioeconomic status)
- Making the review relevant to policy and practice
  - Structuring reporting of results
  - Illustrating how harms and feasibility are connected with interventions
  - Interpreting results based on intervention theory and systems thinking

Evidence to Decision Framework

- GRADE approach used to select, appraise, and synthesize best available evidence
- SOF tables show pooled estimates of effect and rate certainty of recommendations
- Transparently weigh effectiveness, harms, cost requirements, and values and preferences to determine recommendations

- GRADE: Grading of Recommendations Assessment, Development and Evaluation
- GRADE Evidence to Decision Frameworks, BMJ 2016.


Benefit
VALUES
GOALS
Risk
Known adverse effect(s) or risk of adverse effect(s)
Evidence for ongoing indication (diagnosis, risk)
Age-related changes
Evidence for effectiveness
More comorbidities and medications
Frailty

Methods Discussions (workshop)

A. Deprescribing Methods and Guidelines – "inside or outside GRADE Working Group"

B. Deprescribing Methods – "inside or outside general therapeutic guidelines"

- Guide research and methods
- Debates and inform strong versus weak and certainty of evidence
- Use methods that engage stakeholders across countries; ie GRADE recommendation and KT tools/ algorithms

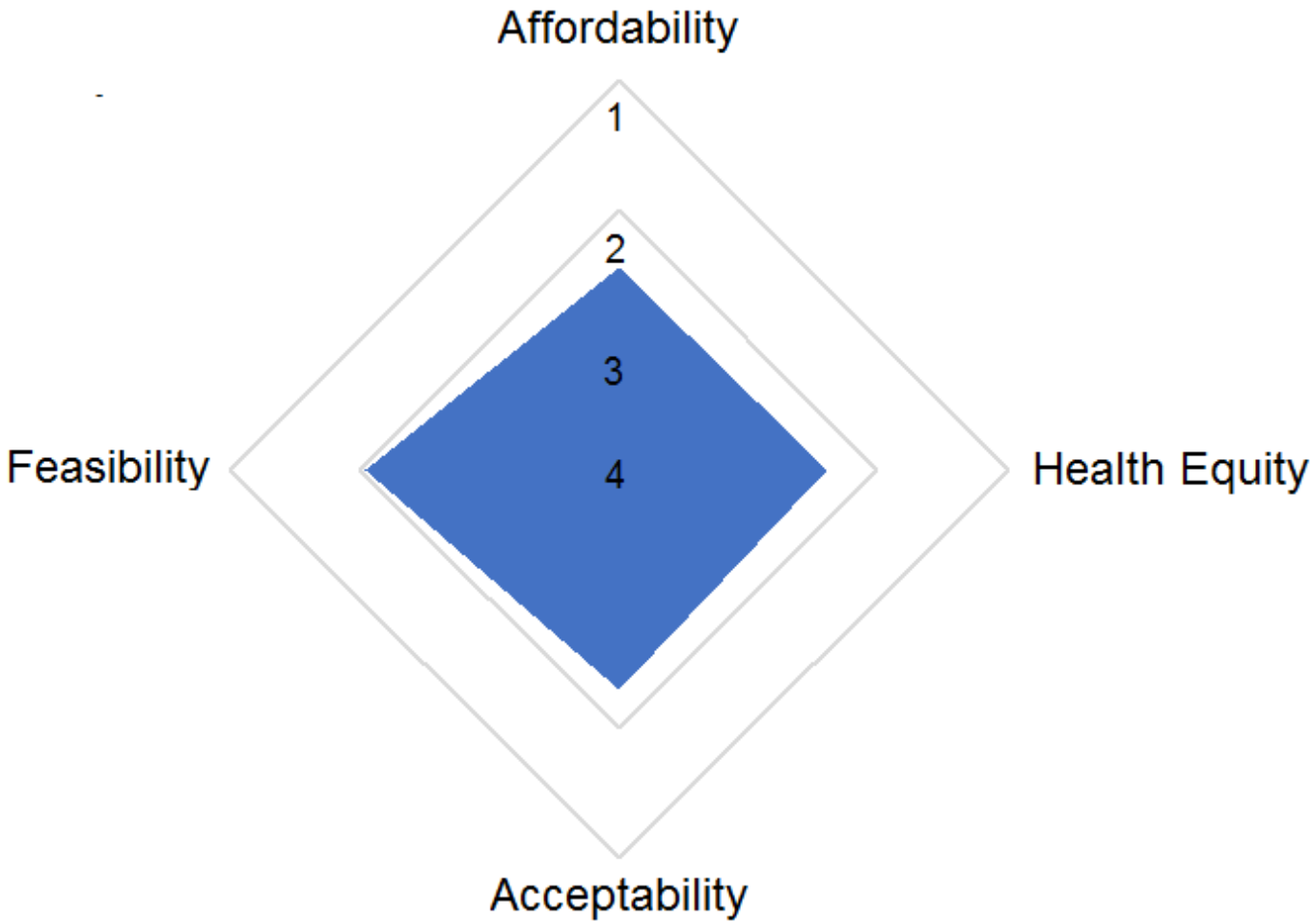
GRADE FACE Survey (GRADE Stakeholder Engagement special interest group)

- The GRADE Feasibility, Accessibility, Cost and Equity (FACE) Survey efficiently engages stakeholders to improve the quality and meaningfulness of implementation.

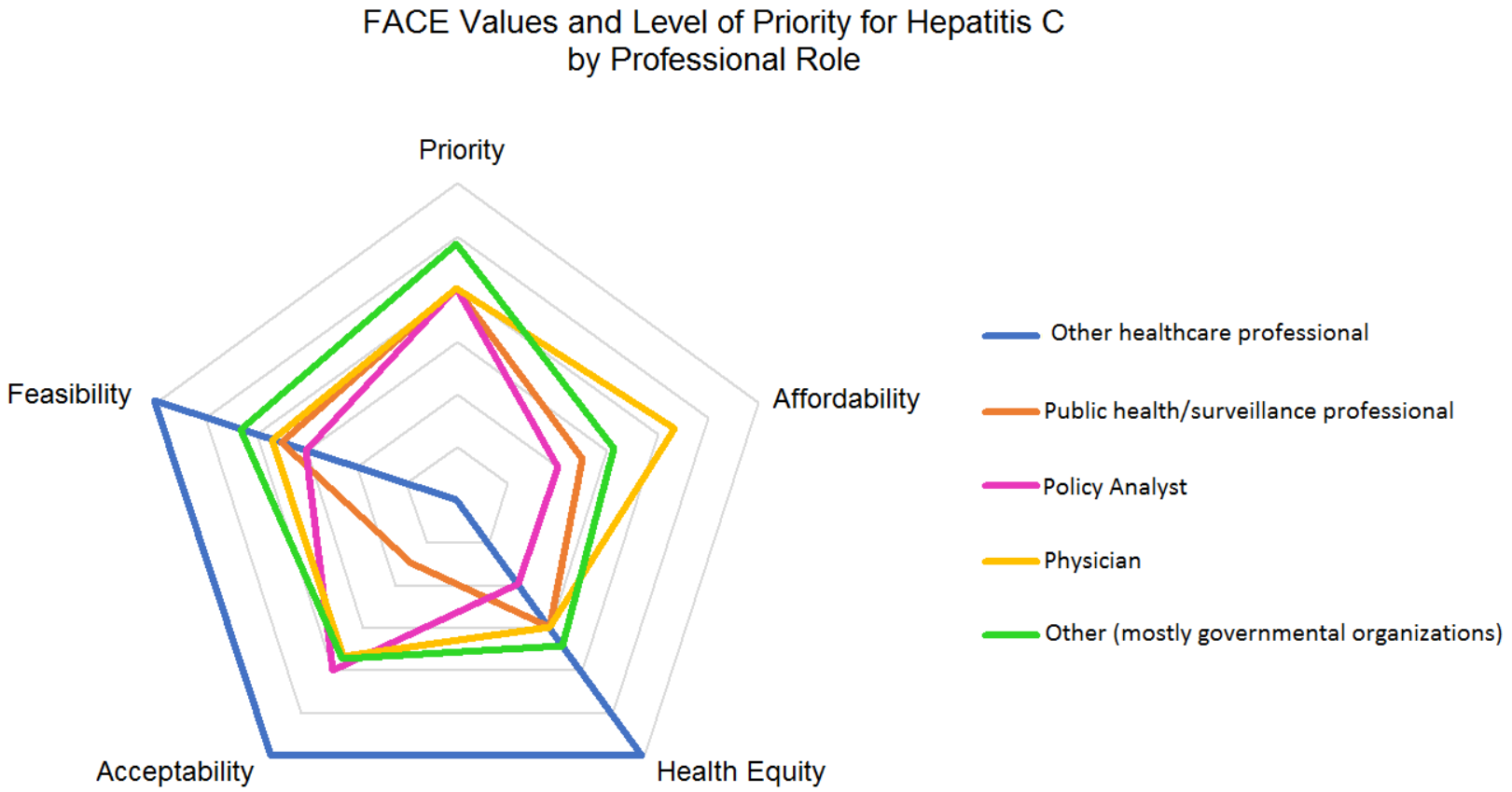
What are Recommendations?

- **For the purposes of FACE, we define:**
- **Recommendation** as a statement that includes the direction and strength based on: 1) the balance between desirable and undesirable outcomes; 2) certainty in the estimates of effect on the patient important outcomes; 3) variability in patient values and preferences; 3) variability in resource use.
- **Implementation considerations** are knowledge translation strategies to address any concerns about the feasibility, acceptability, cost and equity of the recommendation.

Canadian Task Force Hep C screening recommendations CMAJ (2017)



FACE Spider stakeholder graphs



Conclusions

- GRADE is a series of methods from panel formation to guideline implementation
- Highest quality methods will support international and national knowledge mobilization
- GRADE has track record transforming WHO guidelines, and we have an opportunity through GRADE to be part of ongoing Deprescribing methods

Acknowledgments

- *Deprescribing guideline developed with funding from the Government of Ontario the Ontario Pharmacy Research Collaboration and presentation developed with funding through the Bruyère Centre for Learning, Research and Innovation in Long Term Care.*
- *The views expressed in this presentation are the views of the author(s)/presenter(s) and do not necessarily reflect those of the Province.*