Global standards for decision-making: GRADE methods

Image attribution Peoples Daily: placing women at the decision table works

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The South African Medical Research Council

recognizes the catastrophic and persisting consequences of colonialism and

apartheid, including land dispossession and the intentional imposition of

educational and health inequities.

Acknowledging the SAMRC's historical role and silence during apartheid,

we commit our capacities and resources to the continued promotion of justice

and dignity in health research in South Africa.

Disclosures and Acknowledgements

Disclosures

- Director, Health Systems Research Unit
- Co-Director Cochrane Africa
- Co-director South African GRADE Network
- Member National Essential Medicines List Committee
- Member National Advisory Group for Immunisation
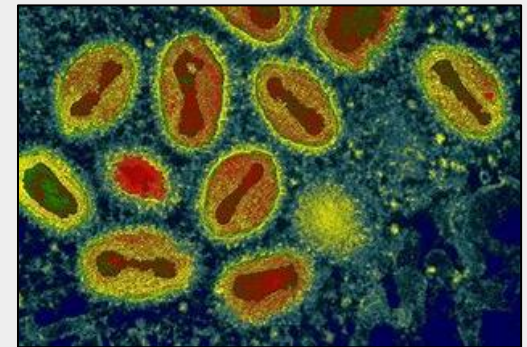- Board of Cochrane
- No commercial interests

Acknowledgements

- The GRADE Working Group - www.gradeworinggroup.org
- The South African GRADE Network
- Nandi Siegfried, methods expert
- Tasha Gloeck, senior researcher, SAMRC
- Holger Schunemann and Thomas Piggott

Mpox and treatment decisions

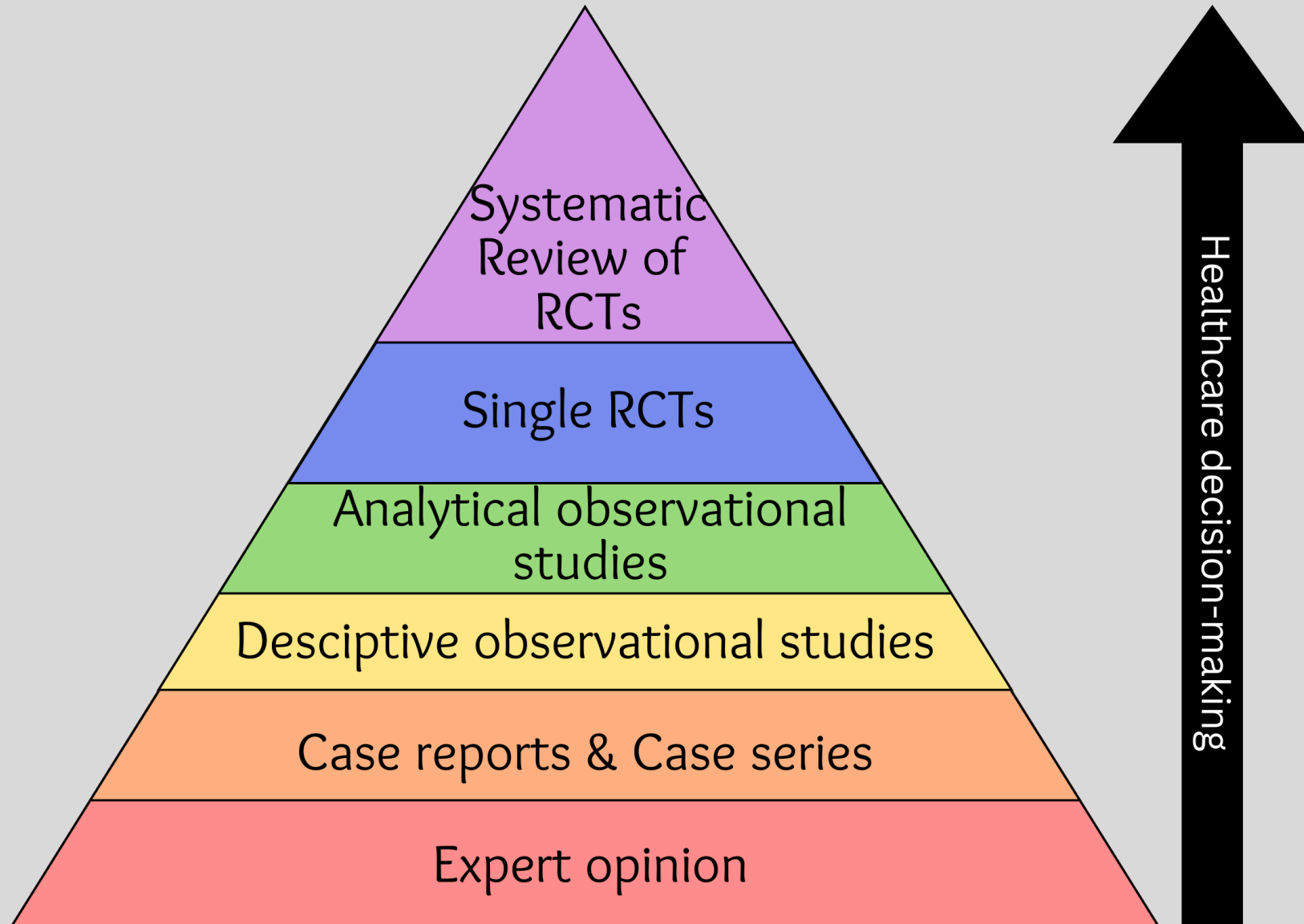There have been several cases of mpox in the Gauteng and KZN provinces of South Africa with two fatalities.

The Ministry of Health requires guidance on prevention and treatment and has approach the NEMLC for advice.

THE PROCESS OF DEVELOPING GUIDELINES

1
Identify the question

2
Find the research

3
Summarise evidence + assess its certainty

4
Discuss and recommend

5
Publish

6
Disseminate

Hierarchy of evidence for intervention questions

- Systematic Review of RCTs
- Single RCTs
- Analytical observational studies
- Desciptive observational studies
- Case reports & Case series
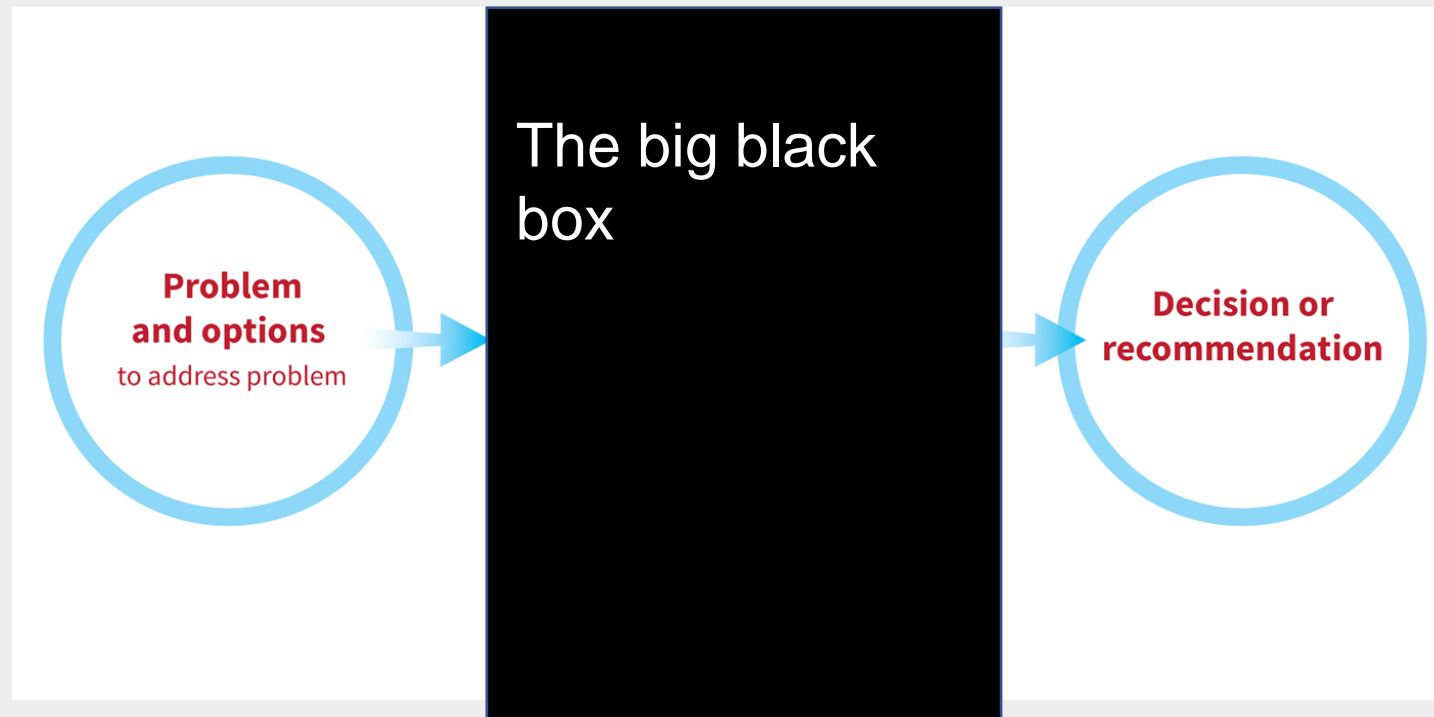- Expert opinion

Healthcare decision-making

Grading of Recommendations Assessment, Development and Evaluation (GRADE for short)

Beginning in 2000, GRADE developed a **single, transparent system for grading the certainty of evidence and making decisions**

- Over 100 organisations use GRADE - WHO, NICE, CADTH, CDC, AHRQ, professional societies, academic institutions

- Evidence synthesis (systematic reviews, HTA) and guidelines

CMAJ 2003, BMJ 2004, BMC 2004, BMC 2005, AJRCCM 2006, Chest 2006, BMJ 2008, JCE 2011-2018, EHI 2017 -

GRADE EVIDENCE-TO-DECISION FRAMEWORKS
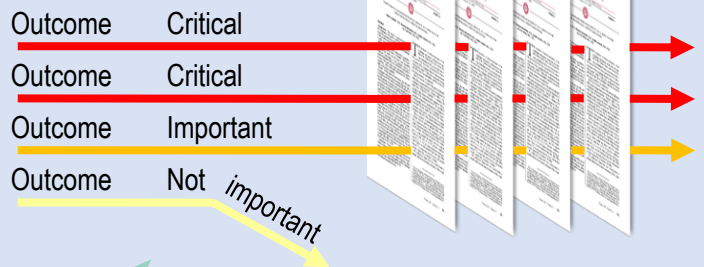
A move away from this type of decision making……
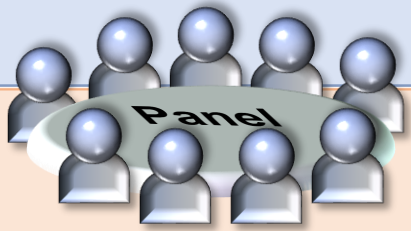
GRADEpro GDT

Formulate question

Assess single studies

Synthesize and Create evidence profile & Evidence to Decision Table with GRADEpro

Rate certainty of evidence for each outcome and other criteria

PICO

Outcome — Critical
Outcome — Critical
Outcome — Important
Outcome — Not important

Evidence synthesis (systematic review/HTA)

Recommendation/Decision

Panel

Guideline

Standard Treatment Guidelines and Essential Medicines List for South Africa

Primary Healthcare Level
2020 Edition

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

Grade recommendations (Evidence to Recommendation)
• For or against (direction)
• Strong or conditional/weak (strength)

Evidence to decision or recommendation framework

Criteria	Research evidence	Additional considerations	Panel's judgments
Benefits & harms of the options			
Values & balance of effects			
Resources required			
Cost effectiveness			
Equity			
Acceptability			
Feasibility			

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KEY EVIDENCE NEEDED FOR DECISION-MAKING

1. Balance of benefits and harms
2. Values and preferences
3. Costs/resources and cost-effectiveness
4. Acceptability
5. Equity issues
6. Feasibility

STEPS OF THE GRADE PROCESS FOR REVIEWS THAT INFORM DECISIONS

5 STEPS FOR GRADE-ING EVIDENCE

1. Formulate the question
2. Select outcomes important for decision making
3. Rate the outcomes for importance
4. Extract outcomes
5. Review the evidence – synthesis and overall interpretation

STEP 1. FORMULATE PICO QUESTIONS

- **P**opulation, **I**ntervention, **C**omparator, **O**utcome

- Precise PICO questions = central to GRADE

- *a priori* PICO questions limit the risk of selection bias

EXAMPLE OF A 'PICO' QUESTION

Question: In people with severe MPX, how effective and safe is tecovirimat for reducing illness and death?

Population	Intervention & comparison	Outcomes
People diagnosed with MPOX Subgroups - Age groups - Underlying immunosupression	Tecovirimat Orally or intravenous dosing Compared to **No treatment**	1. All-cause mortality, 2. Morbidity 3. Adverse effects 4. Serious adverse effects

STEP 2. SELECTING OUTCOMES

- Determine **perspective** of guideline panel: **public health**

- Outcomes should be **important for people** who are affected by the decision

STEP 3. SCORING THE OUTCOMES

RATING	IMPORTANCE
9	Critical
8	
7	
6	Important
5	
4	
3	Not important
2	
1	

Score each outcome from 1 - 9

1-3 not important

4-6 important

7-9 critical

Outcome with higher score influences the recommendation

STEP 4. REVIEW TEAMS EXTRACT OUTCOMES

Outcome #1

Outcome #2

Outcome #3

Question: antenatal steroids for accelerating fetal lung maturity for

Study or Subgroup	Corticosteroids Events	Corticosteroids Total	Placebo or no treatment Events	Placebo or no treatment Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Liggins 1972b	108	601	122	617	15.7%	0.91 [0.72 , 1.15]
Block 1977	11	101	6	54	1.0%	0.98 [0.38 , 2.50]
Schutte 1980	6	64	12	58	1.6%	0.45 [0.18 , 1.13]
Collaborative 1981	47	378	47	379	6.1%	1.00 [0.69 , 1.46]
Gamsu 1989	15	131	22	137	2.8%	0.71 [0.39 , 1.31]
Garite 1992	12	36	12	41	1.5%	1.14 [0.59 , 2.21]
Kari 1994	8	95	7	94	0.9%	1.13 [0.43 , 2.99]
Dexiprom 1999	4	105	10	103	1.3%	0.39 [0.13 , 1.21]
Amorim 1999	24	110	36	108	4.7%	0.65 [0.42 , 1.02]
Qublan 2001	21	72	41	67	5.5%	0.48 [0.32 , 0.72]
Porto 2011	1	144	3	131	0.4%	0.30 [0.03 , 2.88]
Gyamfi-Bannerman 2016	2	1427	0	1400	0.1%	4.91 [0.24 , 102.09]
Ontela 2018	1	155	0	155	0.1%	3.00 [0.12 , 73.08]
WHO 2020	393	1544	444	1526	58.2%	0.87 [0.78 , 0.98]
Total (95% CI)		**4963**		**4870**	**100.0%**	**0.85 [0.77 , 0.93]**
Total events:	653		762			

Heterogeneity: Chi² = 18.15, df = 13 (P = 0.15); I² = 28%
Test for overall effect: Z = 3.59 (P = 0.0003)
Test for subgroup differences: Not applicable

McGoldrick E, Cochrane Database of Systematic Reviews 2020, Issue 12. Art. No.: CD004454.

CERTAINTY OF EVIDENCE

- Are the research studies well done? Risk of bias

- Are the results consistent across studies ? Inconsistency

- How directly do the results relate to our question? Indirectness

- Is the effect size precise - due to random error? Imprecision

- Are these all of the studies that have been conducted? Publication bias

- Is there anything else that makes us particularly certain? Large effects, dose-response relationship

Levels of 'certainty'
(or confidence in the effect estimate)

High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	We are very uncertain about the estimate

GUIDELINE PROCESS

THE PROCESS OF DEVELOPING GUIDELINES
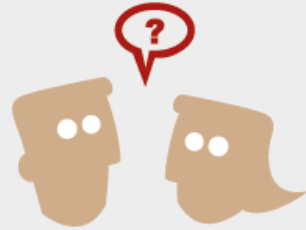
EVIDENCE IS ESSENTIAL TO INFORM DECISIONS, BUT NOT SUFFICIENT – JUDGEMENT IS REQUIRED

Evidence-to-decision tables:

- ✓ structured

- ✓ explicit

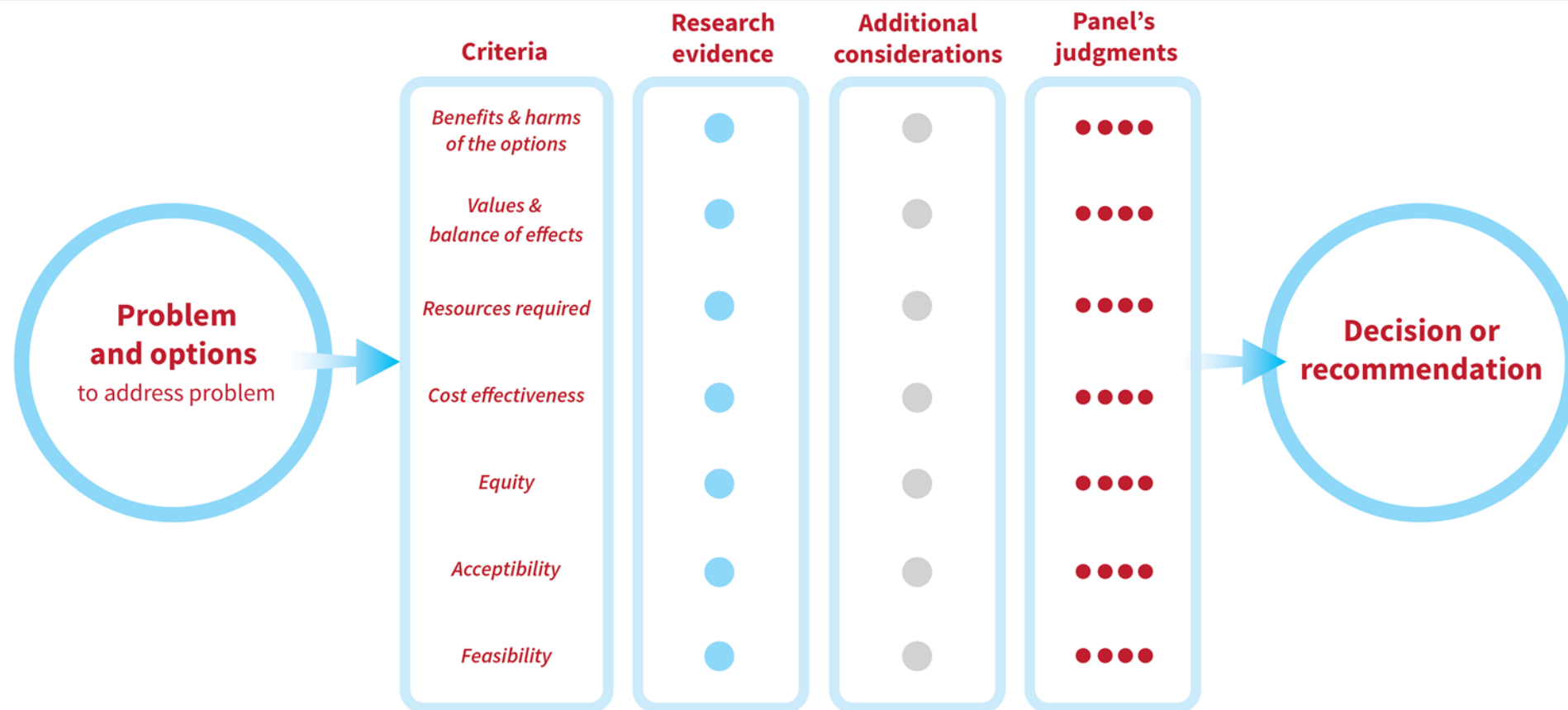- ✓ transparent way to develop clear and actionable recommendations
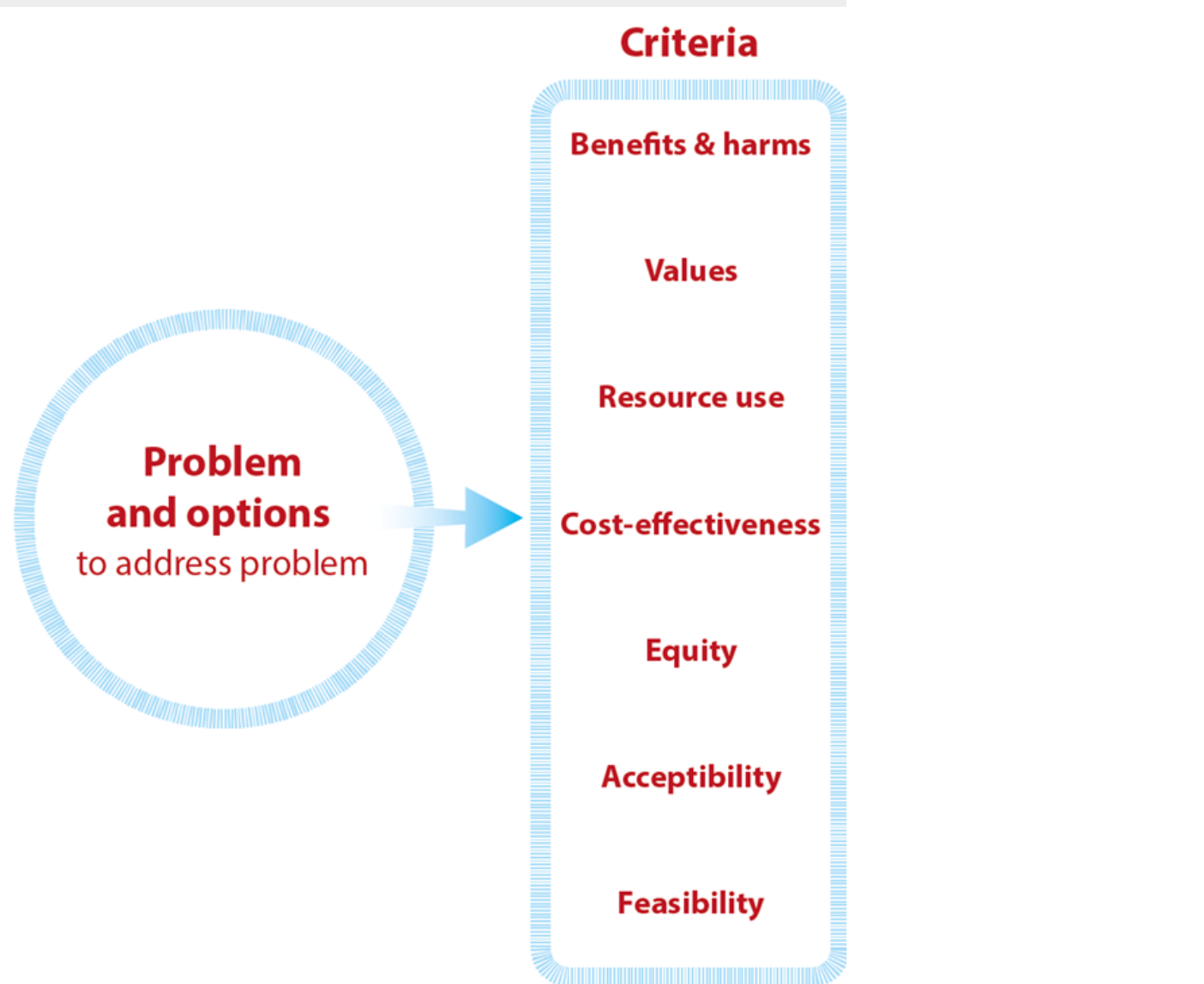
PRESENTING THE BEST AVAILABLE EVIDENCE
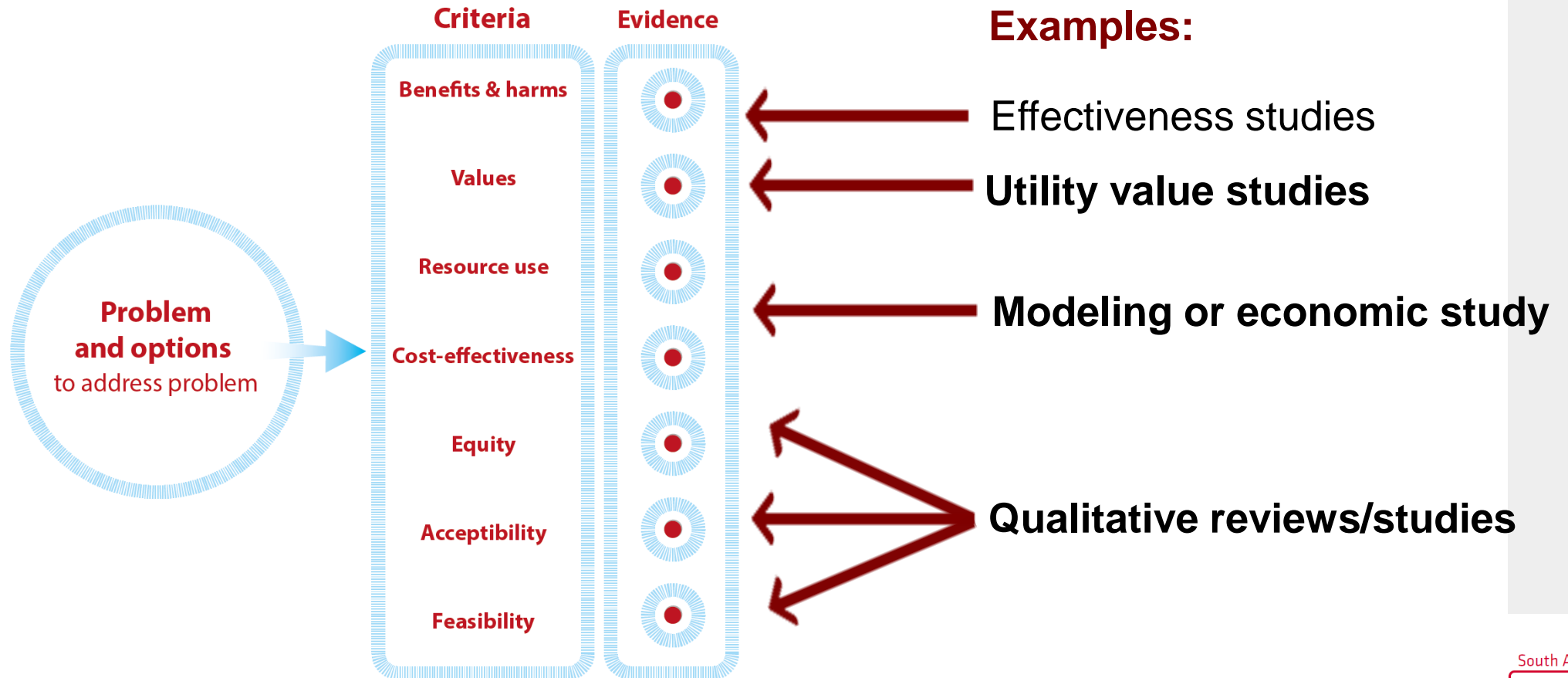
PROVIDING SPACE FOR OTHER IMPORTANT INFORMATION
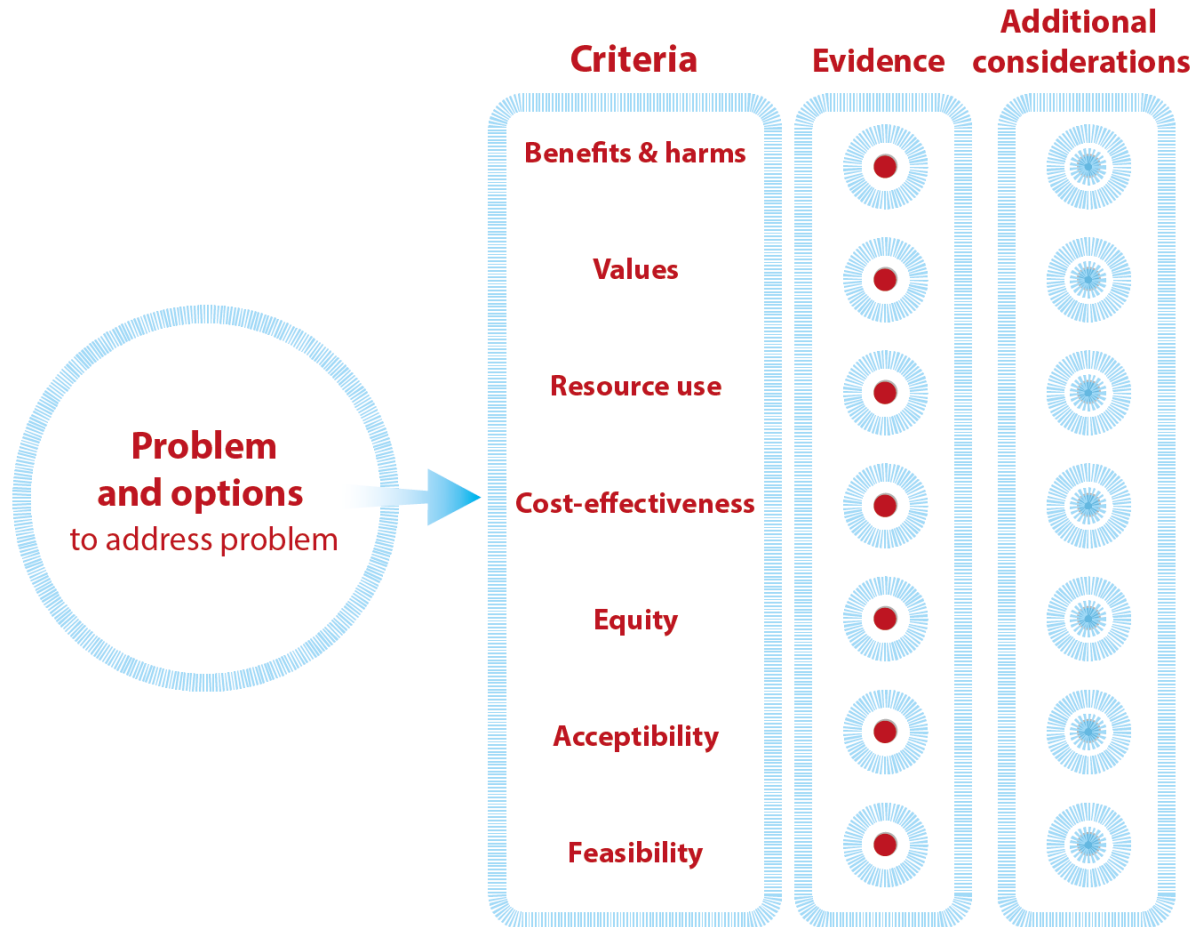
HOW RECOMMENDATIONS ARE MADE

FORMULATING A RECOMMENDATION

MAKING THE RECOMMENDATION

CONCLUSIONS

Type of recommendation

| ☐	☐	☐	☒	☐
Strong recommendation against the option	Conditional recommendation against the option	Conditional recommendation for either the option or the comparison	Conditional recommendation for the option	Strong recommendation for the option

- For or against? Strong or conditional?

- Consensus descion-making

STRENGTH OF A RECOMMENDATION

- A strong recommendation - there is confidence that the desirable effects clearly outweigh the undesirable effects.

- A conditional recommendation - the Group concludes that the desirable effects probably outweigh the undesirable effects or are closely balanced, but the Group is not confident about these trade-offs in all situations. At implementation, monitoring and evaluation is needed to address these uncertainties.

Evidence ecosystem of health decision-making
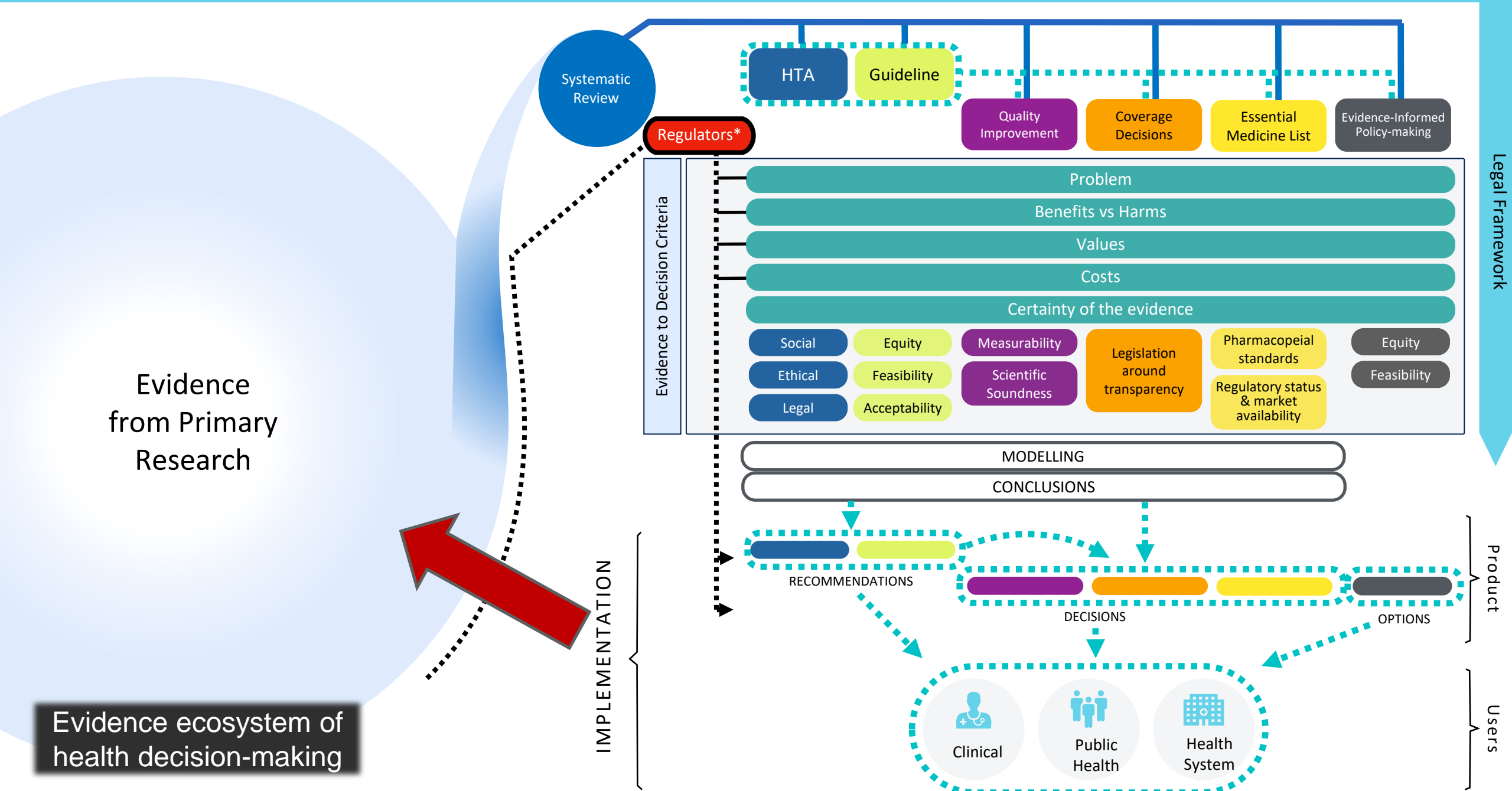
TAKE HOME MESSAGES

- Research evidence is central to health (and all) decision making
- Experts are best placed to inform decisions
    - Patients and public
    - Health care workers
    - Academics
    - Policymakers
    - Public health/ methodologists
- GRADE provides a framework for decision-making for transparency and with equity in focus
- In SA, NEMLC already used these methods and it would be ideal to build on the process to extend to all areas of health decision-making for UHC

THANKS

USEFUL RESOURCES AND KEY READINGS

- WHO Guideline Handbook: http://apps.who.int/medicinedocs/en/m/abstract/Js22083en/

- GRADE guidelines: A new series of articles in the Journal of Clinical Epidemiology. Guyatt, Gordon H. et al. Journal of Clinical Epidemiology, Volume 64, Issue 4, 380 – 382 https://www.jclinepi.com/article/S0895-4356(10)00329-X/fulltext

- Alonso-Coello P, Oxman AD, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. *GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines*. BMJ. 2016;353:i2089.

- Schünemann HJ, Mustafa RA, Brozek J, Santesso N, Bossuyt PM, Steingart KR, et al. GRADE guidelines: 22. The GRADE approach for tests and strategies—from test accuracy to patient-important outcomes and recommendations. Journal of Clinical Epidemiology. 2019;111:69-82. https://doi.org/10.1016/j.jclinepi.2019.02.003

- GRADE working group website: http://www.gradeworkinggroup.org/

- Grade software for systematic reviews and guidelines: https://gradepro.org/

- GRADE Hand book: https://gdt.gradepro.org/app/handbook/handbook.html