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DECIDE
GRADE
Developing and Evaluating Communication strategies to support Informed Decisions and practice based on Evidence

21 AUGUST 2014

Rating the confidence we can place in studies that evaluate the importance of the outcomes of interest

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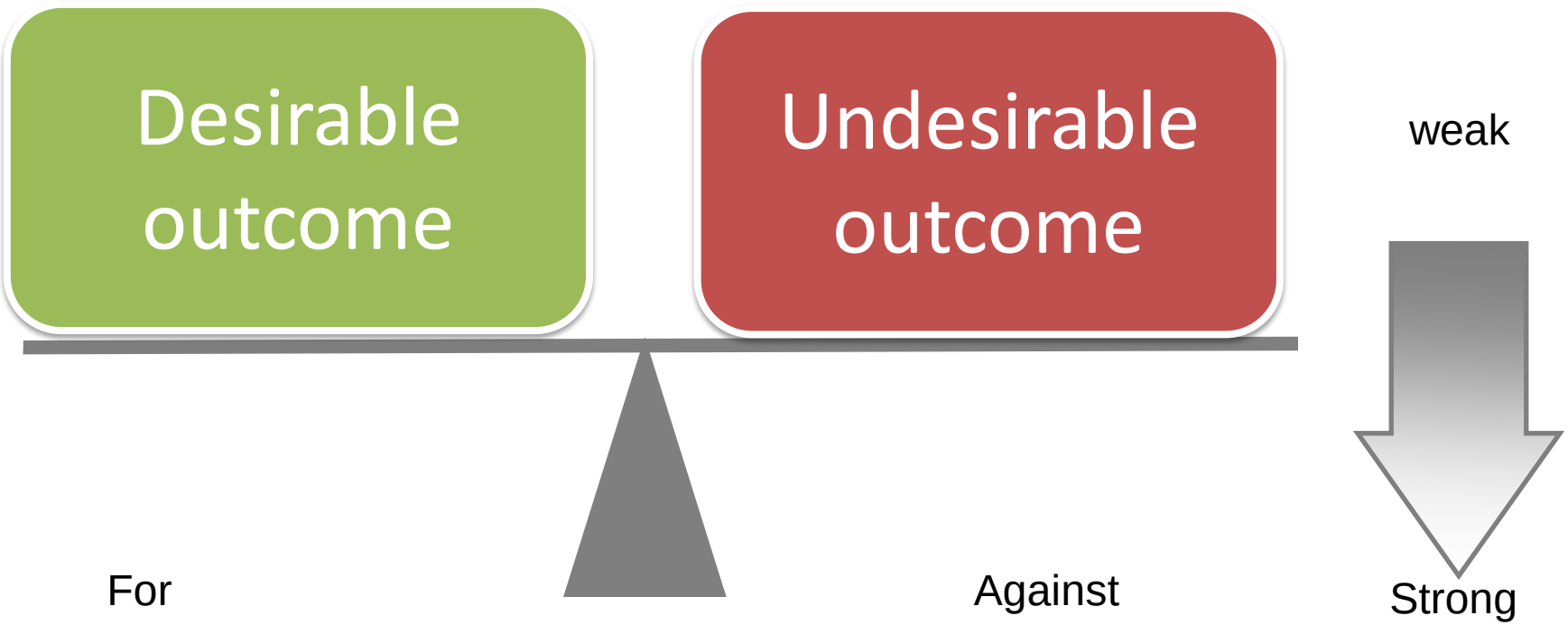
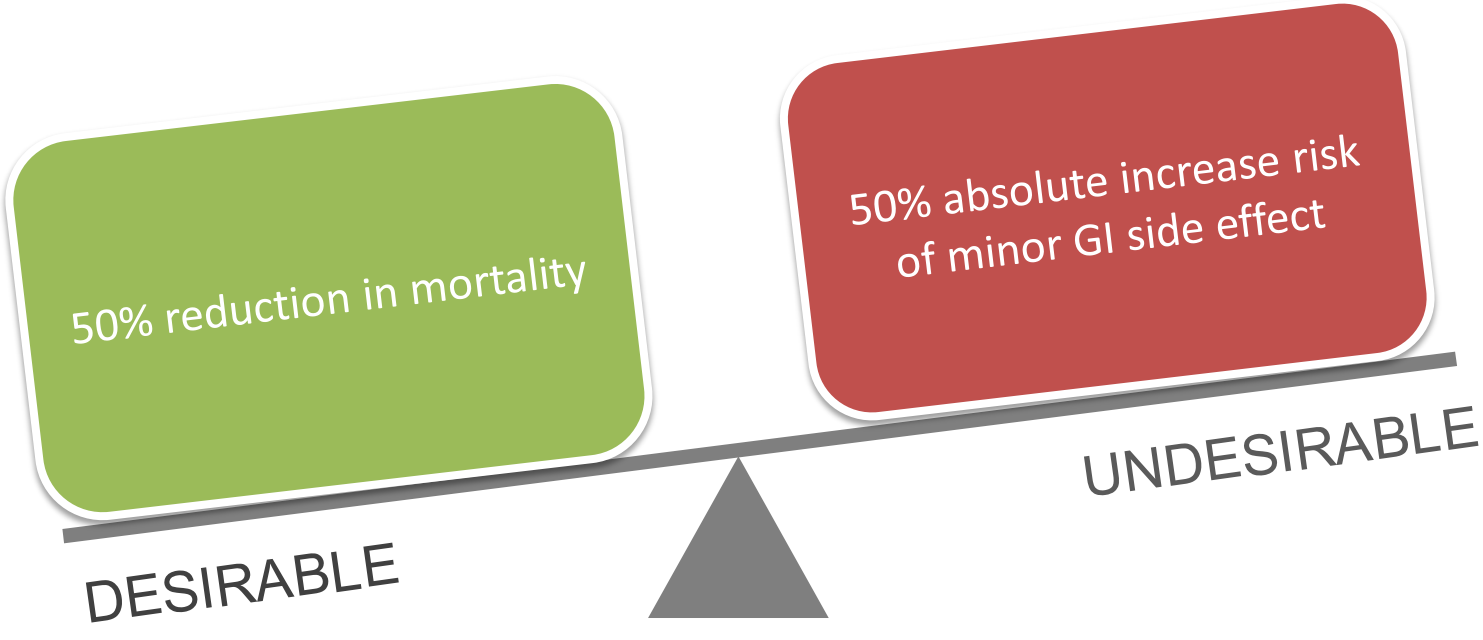
McMaster University
Inspiring Innovation and Discovery

Disclosure

- Co-chair GRADE Working Group
- Board of Trustees – GIN
- No direct financial COI

Recommendations in a simple world




50% reduction in mortality
50% absolute increase risk of minor GI side effect
DESIRABLE
UNDESIRABLE

Preference sensitive vs insensitive situations

- Aspirin after MI
  - Reduction in myocardial infarction
  - Small harm/burden
  - Low cost

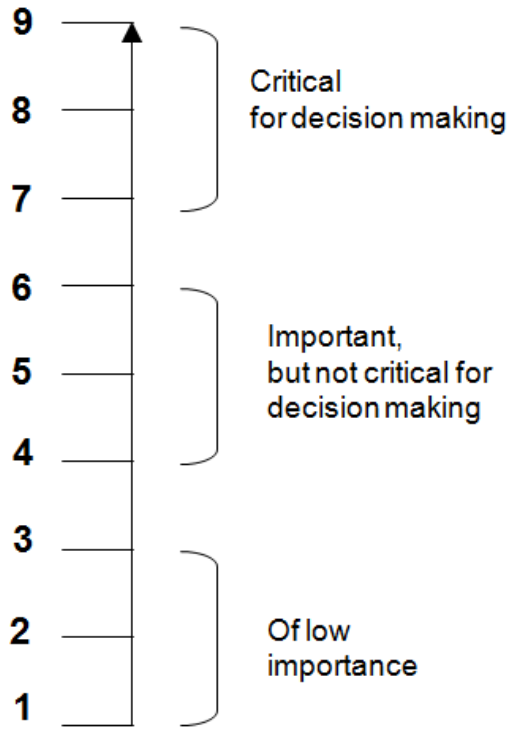
Strong recommendation

- 2nd line chemotherapy in non small cell lung carcinoma
  - Limited increase survival (< 3 months)
  - Similar quality of life
  - Toxicity and burden

Weak recommendation

Relative importance of outcomes

- Decision makers (and guideline authors) need to consider the relative importance of outcomes when balancing these outcomes to make a recommendation
- How to evaluate our confidence or certainty in this judgment?
- Whose judgments (i.e. whose values and preferences for these outcomes)?



How to determine how much patients value the main outcomes?

- Systematic review
- Use guideline panel members
  - act as proxies for their patients'
- Patients on panel
  - problematic
- De novo research with patients
  - Resource intensive

How is importance of outcomes information expressed?

Quantitative vs Qualitative

Values and preferences studies

- Utilities
  - Direct methods (SG, TTO, VAS, etc.)
  - Indirect
    - Multiattribute instruments
    - Back transformation from QoL instruments
- Relative importance of outcomes
  - Forced choices/Discrete choice
- Non utility measures
  - Frequency
  - Quality of life
- Qualitative studies

Studies that elicit utilities

- Utility: a measure of the preferences of an individual for different health states compared to death of perfect health .
  - Its value reflects the opinion or attitude of a participant in relation to a health state or outcome

Confidence in the importance of outcomes

- Not addressed in detail so far
  - Brings additional complexity
  - No specific approach available
    - No GRADE guidance
  - Most groups ignore this

Definition of confidence in the importance of outcomes

- *Systematic review:*
  - The extent of our confidence that the estimates of the relative importance the outcomes (and variability) are correct.
- *Clinical guideline:*
  - The extent of our confidence that the estimate of the relative importance the outcomes (and variability) are adequate to support a particular recommendation?

Confidence in the importance of outcomes (quantitative)

- *Similar approach as for other issues:*
  - *Risk of bias*
  - *Inconsistency*
  - *Indirectness*
  - *Imprecision*
  - *Publication bias*

GRADE

Author(s): Ray Yuan Zhang, Holger Schunemann, Pablo Alonso Coello

Date: 2014-05-28

Question: What are patients with atrial fibrillation views about the relative value/importance of outcomes of interest in decision making for oral anticoagulant therapy compared to aspirin?

Bibliography: MacLean S. Chest 2012; 141:e1S-e23S.

Measure	Quality assessment: Design / Measurement instrument	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	No of Studies	No. of patients	Value (95%CI or other measure of variability)	Quality	Importance
Non fatal severe stroke											
Utility	Cross-sectional[1,2] SG, TTO	Serious risk of bias [2]	Serious Inconsistency [3]	No serious indirectness	Serious imprecision [4]	none	5	376	0.1-0.51 (range) 0.27, 95% CI: 0.04-0.50 (result from Protheroe 2000 not included)	⊕OOO VERY LOW	CRITICAL
Direct Choice: Relative disutility of severe stroke to major bleeding	Cross-sectional [1] and RCT of two preference elicitation methods [5]	No serious risk of bias	Serious Inconsistency [6]	Serious indirectness [7]	Serious imprecision [4]	none	5 (3 cross-sectional studies, and 2 RCTs)	360	1.3 ~3 :1 on average The results were also influenced by the elicitation methods used, in Man-Song-Hing 1996, the results were 1.5:1 for known efficacy method, and 3:1 for PTOT, respectively.	⊕OOO VERY LOW	CRITICAL
Non-Utility Measurement of Health States	Cross-sectional interview with decision analysis [8]	No serious risk of bias	No Serious inconsistency	Serious [9]	No serious imprecision	none	1	97	Guideline authors placed a higher disutility on stroke and a lower disutility on bleeding and burden with warfarin than did the patients.	⊕⊕⊕O MODERATE	IMPORTANT
Major Bleeding											
Utility	Cross-sectional [10] SG	Serious risk of bias [10]	No Serious inconsistency	No serious indirectness	Serious imprecision [4]	none	2	212	0.44-0.84 0.68, 95% CI: 0.44-0.93	⊕⊕OO LOW	CRITICAL

Risk of bias – explanations (footnotes)

- 5 cross-sectional studies reported the utilities of severe stroke. The representativeness of the studies were impacted by low response rate in some of the studies: Protheroe 2000, 57 of the 180 invited patients completed the interview; Thomson 2000, 97 of 260 invited patients responded. Participants in Gage 1995 might have problem of understanding, 57 of 69 who finished the interview understood the time trade off technique.

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Risk of bias

- Representativeness
  - Appropriate sampling or sample frame
    - Facing the decision of interest
  - Representative sample from the frame
    - Random sample from your sample frame vs. convenient/consecutive
  - Response rate
- Accuracy of measurement
  - Reliability and validity of the instrument used
    - Authors mention the instrument/s measurement properties / validated in the setting of interest.
    - Demonstrate them within the course of the study
  - Context validity
    - Instrument used inappropriately (poor description of health states, checking understanding, etc.)

Consistency

- Is inconsistency explained? (PICO)
  - Population
  - Intervention and comparison:
    - Bleeding outcome different
    - Different alternatives
  - Outcomes
    - Different description
  - Methods
    - Approach used (e.g. inconsistent results from utility based research and qualitative results)
    - Tools used (e.g. different utilities depending on the instrument used)

Imprecision

- Sample size
  - 400 participants
  - Optimal information size for each outcome

Indirectness

- Use PICO framework (how similar?)
  - Population
  - Intervention
  - Comparison
  - Outcome
  - Follow-up

Indirectness

- Use PICO framework
  - Population:
    - The optimal is facing the decision of interest
    - Populations at risk of facing the decision of interest
    - Surrogates (panel members)

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Uncertain

- How will this judgment affect our overall quality or certainty of the evidence (GRADE)

Key messages

- Important to assess relative importance of outcomes in most situations
- Different approaches to doing this
- GRADE criteria can be used to assess confidence in the relative importance