# Evidence as the start of the conversation at NICE: from systematic reviews to policy recommendations

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# Introduction to NICE guideline process

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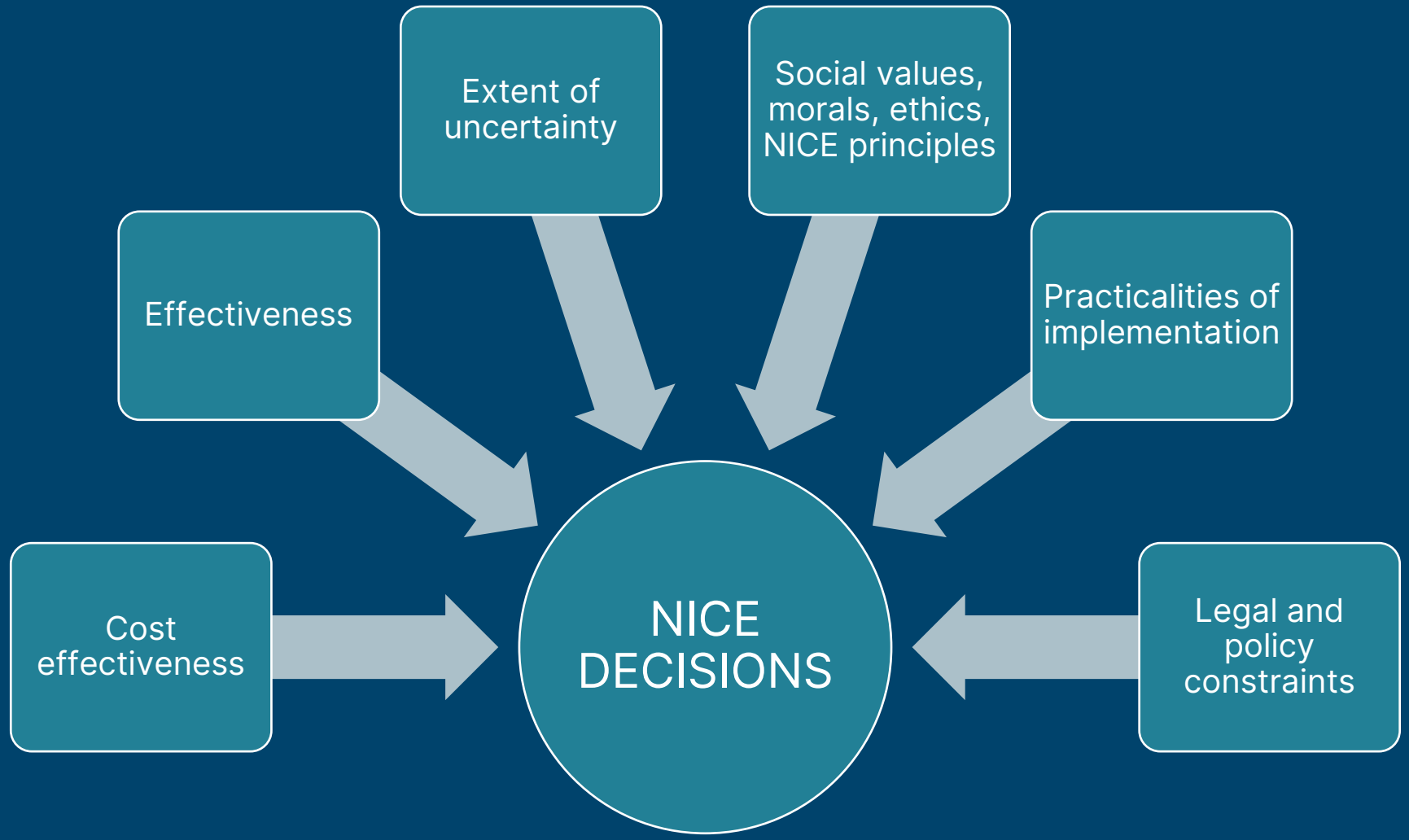
# NICE guidelines

•We produce evidence-based recommendations for health and social care developed by independent committees, including professionals and lay members, and consulted on by stakeholders.

•We develop recommendations on new topics referred by NHS England, the Department of Health and Social care and the Department for Education and update recommendations in existing topic areas.

# What is considered in guideline development?



# Role of the committee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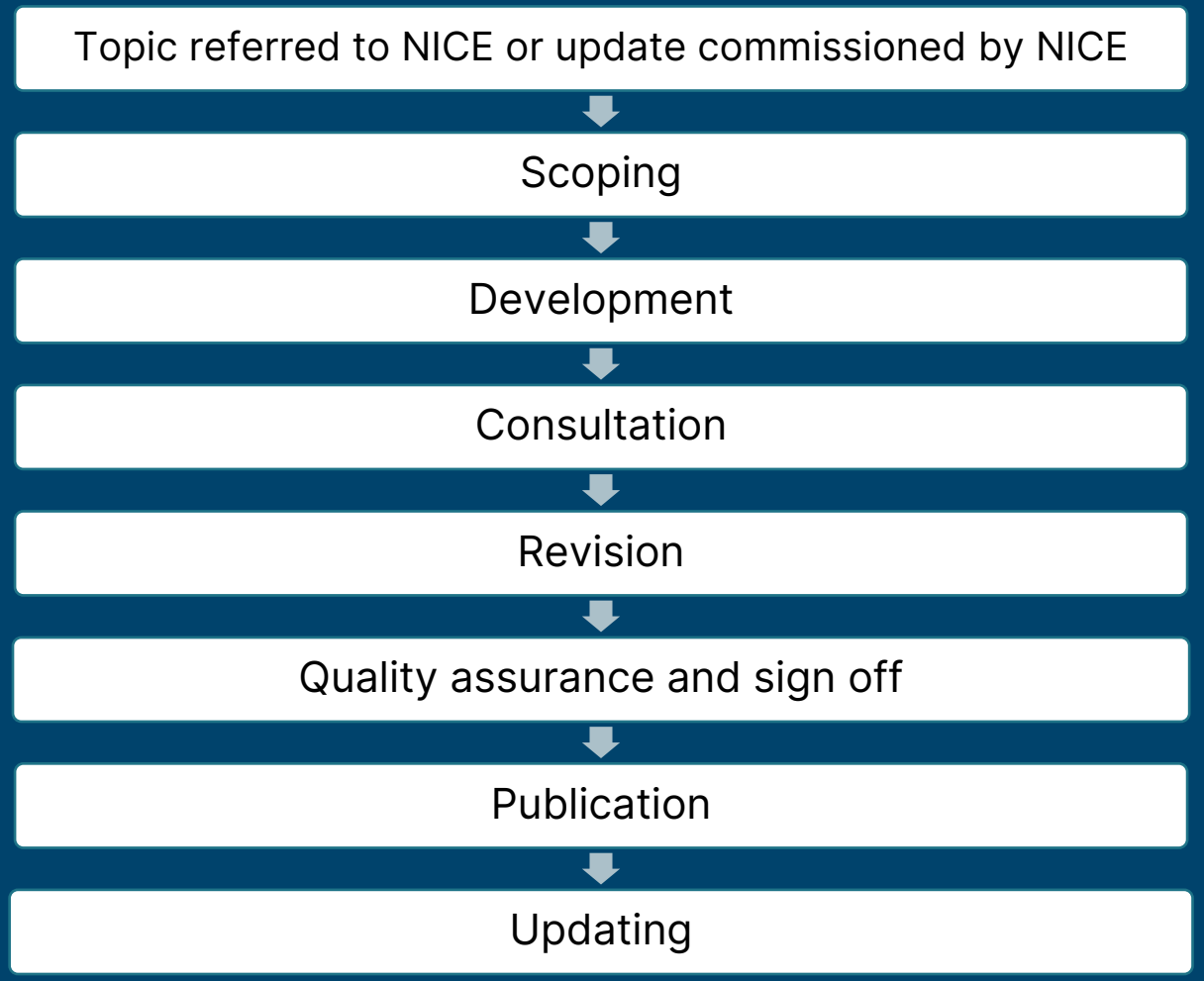
# Commissioning to publication



# Scoping


**The guideline scope sets boundaries to ensure work stays within the referral**

- defines the population(s) and setting(s) that will and will not be covered
- describes what the guideline will consider
- identifies the key issues & lists key questions
- describes the economic perspective(s) to be used

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# Development


Review protocol

Evidence is systematically reviewed

Effectiveness | Cost effectiveness

Evidence review is drafted and sent to the committee

Evidence is presented to the committee

Effectiveness | Cost effectiveness

Guideline recommendations are drafted after consideration of the evidence

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# Timeframe for NICE guidelines

- *Reminder!* – NICE aims to provide recommendations in key areas of uncertainty so are required to be timely in producing guidance
- Timelines are dependent on what is commissioned:
  - Short updates to guidelines may include 1 or 2 review questions and may have a development time of a few months
  - Full guidelines can have as many as 15 review questions and will have a development time of less than 2 years
  - Rapid COVID-19 reviews – we had a week!
- A lot of work to complete in a short space of time so how do we manage this and maintain good quality?

# Pragmatic reviewing for decision-making

- Begins with the guideline scope
- Committee agree to pragmatic approaches made at the protocol stage
- Prioritized evidence presented to the committee

# Streamlining the guideline scope: our the road-map to recommendations

- Scope based on initial referral and drafted with topic-specific expertise and key stakeholders with the aim to address the key decision problem(s)
- Keeps the guideline focused on the areas where NICE can add value e.g. on areas of uncertainty,  or where there is new evidence

# Poll – How are NICE reviews different from Cochrane reviews?

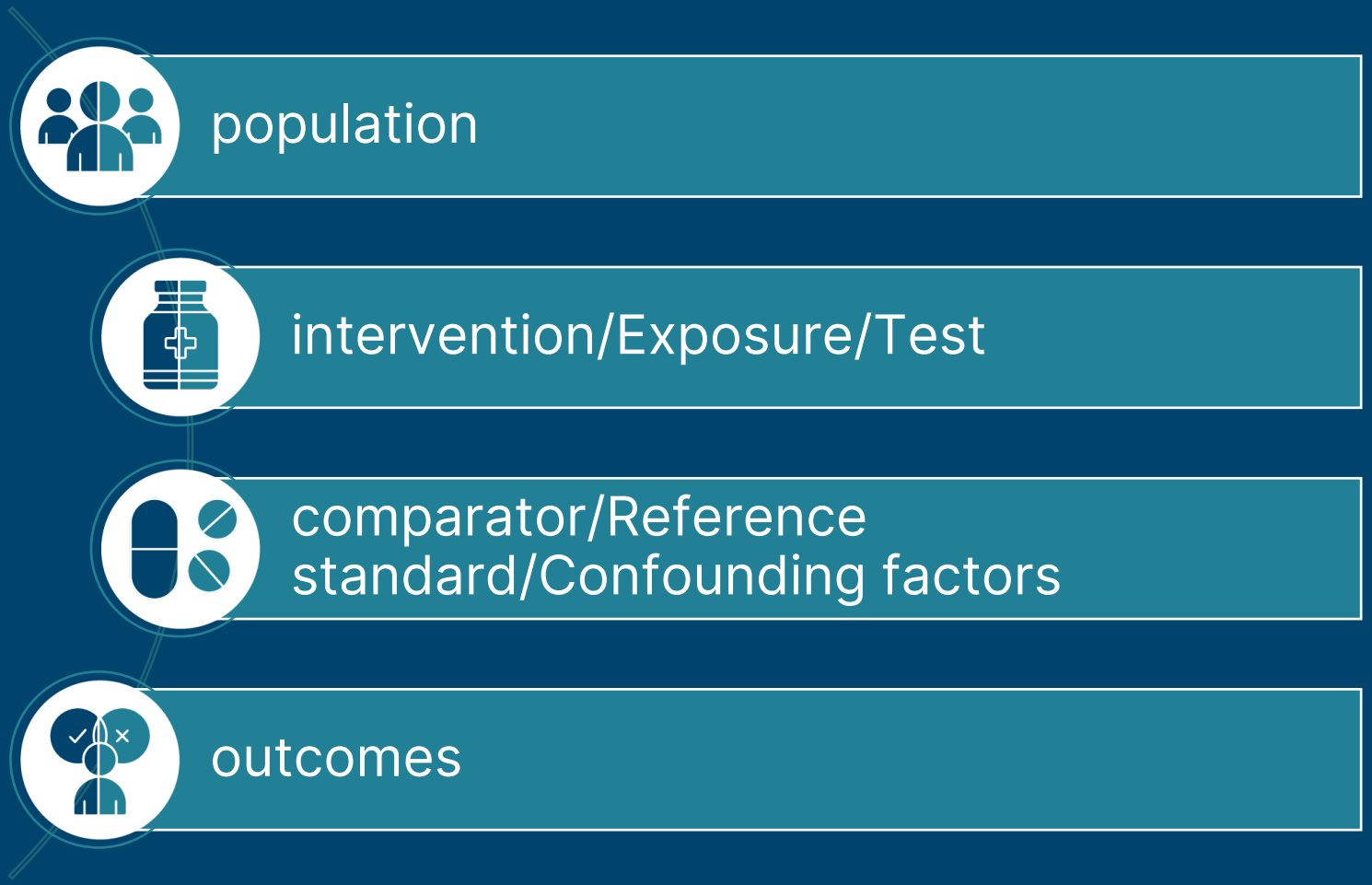
- Comprehensiveness?
- Expense?
- Focus?
- Methodology?
- Process?
- Timeliness?

# The review protocol: modifying our methods

## Cochrane systematic review methods vs guideline evidence review methods

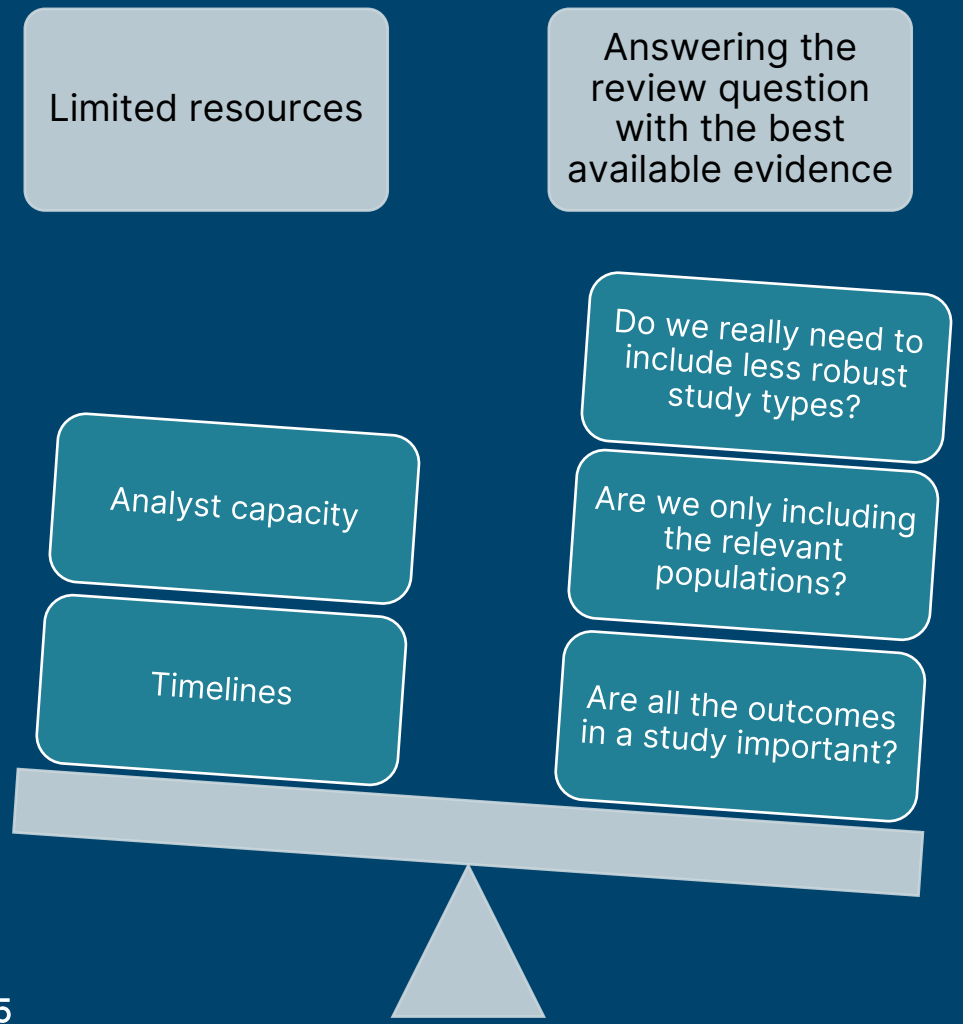
| Compared to Cochrane systematic reviews, NICE evidence reviews: | |
|---|---|
| Are not as comprehensive e.g.<br><br>• limit to published English language articles<br>• occasionally we may limit to OECD countries | Helps to manage the time needed to complete the review<br><br>Keeps the review focused and applicable to the guideline audience |
| Do not fully double screen titles and abstracts or double data extract with two independent reviewers but instead:<br>• we make use of priority screening<br>• our committees and stakeholders will identify missed studies | Helps manage resources needed<br><br>Means we rarely miss studies |

# Developing the review protocol



# Other factors to consider in the protocols

- **Study types to be included**
- **Sub-group analyses** – are there groups of the population for which we think the effect could be different?
- **Interventions/tests – are they accessible/feasible in the UK setting/NHS?**



# Prioritising outcomes for decision-making: “What matters most”

- We work with the committee to identify which outcomes are key to addressing the decision-problem and most likely to help us make recommendations that will add value to the healthcare system
- The committee includes lay-members to help us understand what matter most to patients
- Consider if the desired outcomes are likely to be found in the literature. Can we use proxy measures?
- But importantly, the committee need to understand the implications of decisions made at this stage

# How should the outcomes be measured?

- What would be the committee's preference?
  - E.g. Limit to validated scales used in practice? - Applicability
- What measures are more meaningful or intuitively easier to understand?
  - Dichotomous measures?
  - E.g. using eGFR thresholds corresponding to CKD stage instead of change in eGFR
- Timing of measures?
- Don't forget to ask the committee why!

# Our reviews aren't stand-alone

- Depending on the topic area, we may need to look at more than one type of question:
    - Clinical effectiveness
    - Cost effectiveness
    - Qualitative evidence

- These can be brought together in a committee meeting to inform decision-making discussions
- Common outcome measures can help bring these together

# Presenting evidence to a decision-making committee

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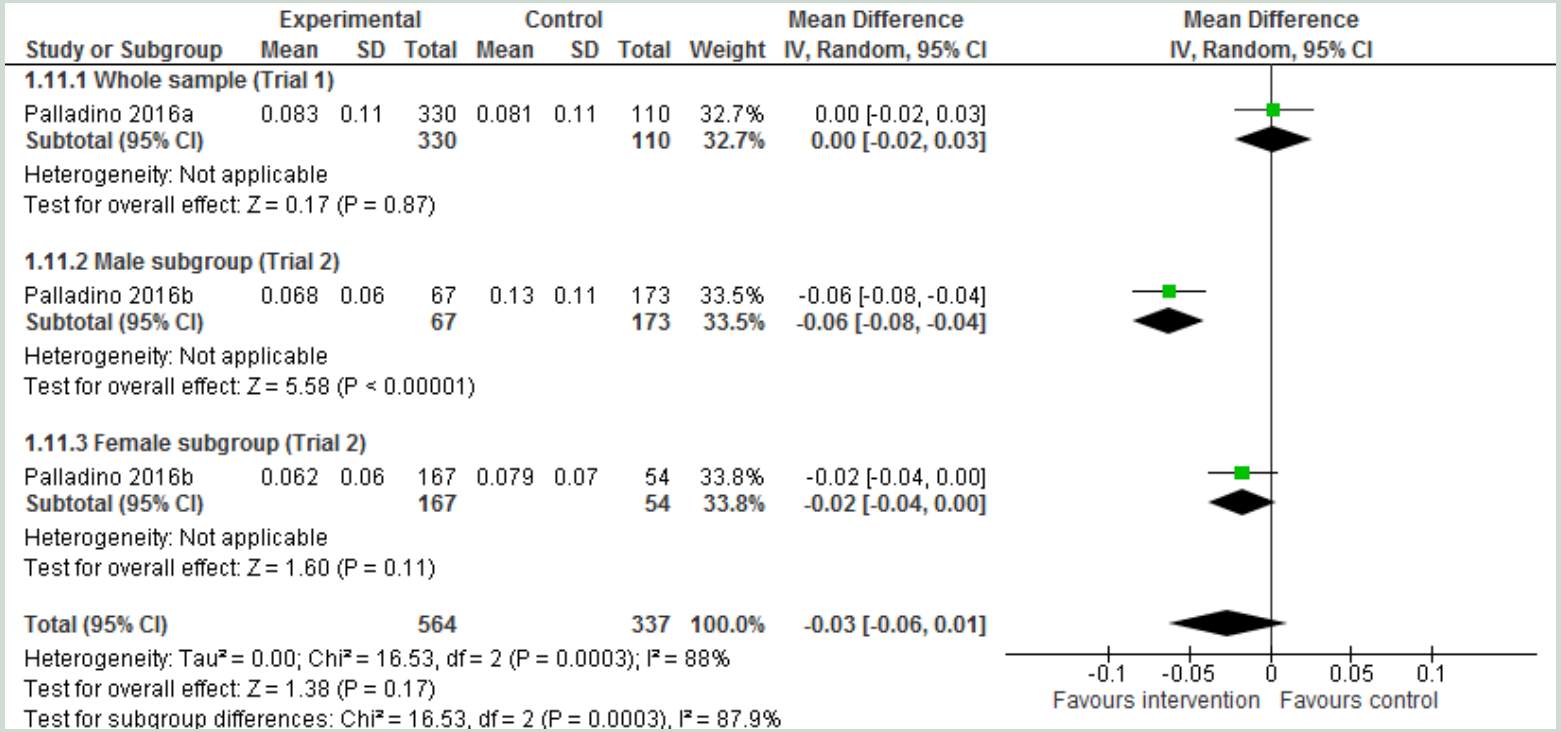
# Referring back to the decisions made in protocol

- Present the evidence based on committee decisions in the protocol
    - E.g. prioritise outcomes considered to be the most important for decision-making
- Highlight anything that the committee might need to think about – “tell the story of the evidence”
    - E.g. context, generalisability or differences from UK practice
- Check that what you are presenting chimes with their experience.
- Differences between evidence and committee experiences need to be explored.
- Sometimes we need to remind the committee why they made certain decisions.

# Example 1: Bullying interventions in secondary education

| Behavioural outcomes | Certainty |
|---|---|
| Bullying perpetration – 2 NRCTs | VERY LOW |




↔ Bullying perpetration

↓ Bullying perpetration in male subgroup

# Example 2: Diagnostic accuracy

| No of studies (sample size) | Diagnostic accuracy | | | Quality | Interpretation of effect |
|---|---|---|---|---|---|
| | Sensitivity (95% CI) | Specificity (95% CI) | Likelihood ratios (95% CI) | | |
| **D-dimer with a threshold of 500ng/ml (no Wells score)** | | | | | |
| 9 (n=6245) | 96 (93 to 98)<br><br>Low FN rate<br>96% with PE correctly identified with a positive test | 14 (8 to 24)<br><br>High FP rate<br>14% without PE correctly excluded with a negative test | LR+ 1.13 (1.04 to 1.26) | Very low | Slight increase in probability of pulmonary embolism. |
| | | | LR- 0.28 (0.11 to 0.57) | Very low | Moderate decrease in probability of pulmonary embolism. |

# Summarising evidence

- Give the committee the headlines from the evidence, always relating back to their decisions at protocol stage.
- Describe the certainty in the evidence using GRADE.
- Keep it brief and to the point.
- This will provide the foundations for the committee to begin discussing the evidence and formulating recommendations.

# Example : Summary of evidence

| Group interventions by school staff | | | | |
|---|---|---|---|---|
| Certainty in evidence | Studies | Benefit | Outcome | Timepoint |
| VERY LOW | 1 NRCT | ↑ | Reduced behavioural difficulties | 8 weeks |
| VERY LOW | 1 NRCT | ↑ | Improved prosocial behaviour | 8 weeks |
| MODERATE to LOW | 4 NRCT | ↔ | In improving social and emotional skills | 7 weeks to 9 months |
| MODERATE | 2 NRCT | ↔ | In reducing behavioural difficulties | 7 weeks to 9 months |
| MODERATE | 1 NRCT | ↔ | In improving prosocial behaviour | 8 weeks |
| MODERATE | 1 NRCT | ↔ | In reducing mental health difficulties | 9 months |

Key:
Benefit ↑
No difference ↔
Harm ↓

# Example 2: Summary of diagnostic evidence

- Diagnostic accuracy of D-dimers with standard thresholds (500ng/mL) in people with COVID-19 and suspected PE showed **high sensitivity** (low false negative rate; fewer missed PE diagnoses) and a **moderate decrease** in probability of having PE with a **negative D-dimer test**.

- Diagnostic accuracy of D-dimers with standard thresholds (500ng/mL) in people with COVID-19 and suspected PE showed **low specificity** (high false positive rate; increased unnecessary imaging) and a **slight increase** in probability of having PE with a **positive D-dimer test**.

- Studies looking to increase specificity by increasing the D-dimer threshold generally found that as specificity increased, sensitivity decreased (increase in false negatives; decrease in false positives) with minimal change in probability of having PE either with a **positive or negative D-dimer test**.

- Less evidence was found for DVT but the trend is similar to PE.

# Linking evidence to recommendations

- Interpreting the evidence
- The outcomes that matter most
- The quality of the evidence
- Benefits and harms
- Other factors the committee took into account

- What outcome is the most important for you to make a decision? And why?

- How certain are you in the quality of the evidence?
- Is the evidence applicable to the people affected by this guideline?

- What benefits and harms might you expect to see after implementation of the intervention?
- Do the benefits of the interventions outweigh any unintended consequences?

- Are there any other factors that you need to take into account?
- E.g. legislation specific to the UK
- Health inequalities

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# Making recommendations

## Recommendations should be:

- Short, direct and unambiguous
- Active rather than passive
- Respect a person's choice and involvement in decision making

## Recommendations should reflect the strength of the evidence:

**Strong recommendations when there is clear evidence to support the rec**

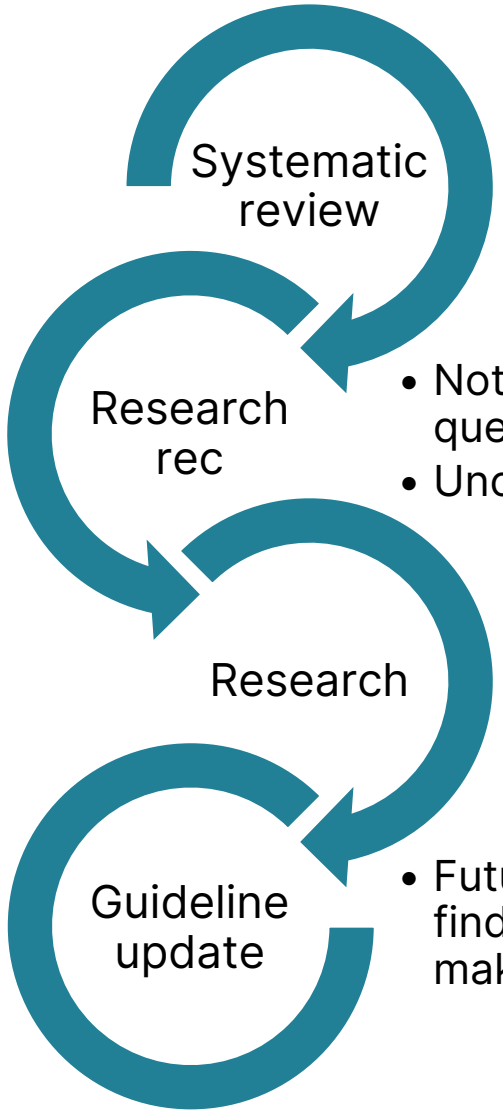
- **Offer** lifestyle advice to people with …
- **Use** dipstick testing for babies and children between 3 months and 3 years with…
- **Advise** a person with depression and their family or caregiver to be …
- **Refer** people with incurable melanoma to…
- **Do not offer** hyperbaric oxygen to treat …
- **Do not use** CT before endoscopic resection for

**Weak recommendations when the balance between harms and benefits is less clear**

- **Consider** supervised therapeutic exercise sessions for people with …

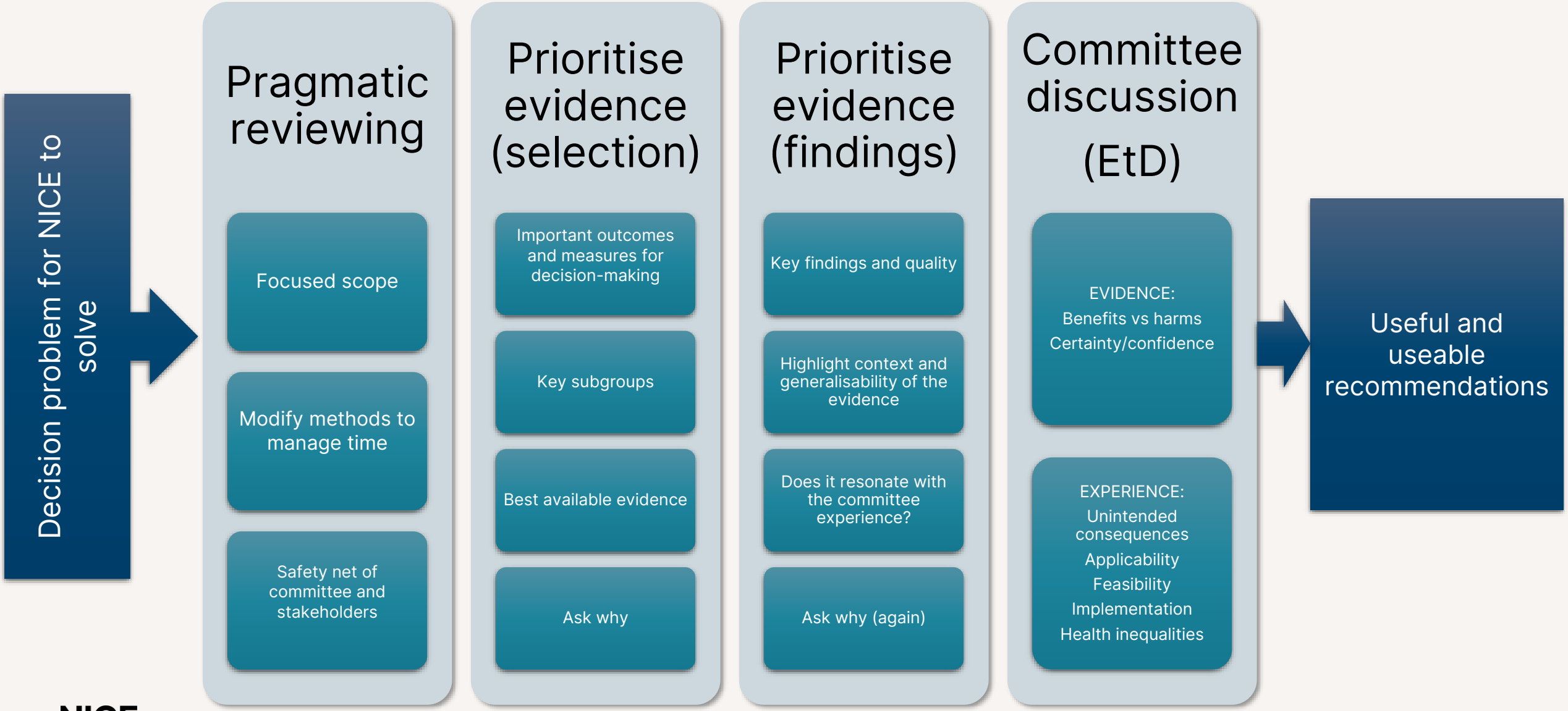
# Research recommendations

E.g. For people in long-term care, is a multicomponent non-pharmacological intervention more clinically and cost effective than usual care in preventing the development of delirium?




- Guideline development - systematic review conducted to answer review question
- Not enough evidence to answer the question
- Uncertainties – only ‘weak’ rec made
- External research to improve the quantity and quality of evidence
- Funding for prioritised research recs provided by NIHR
- Future guideline updates can use findings to strengthen existing recs or make new recs

# In summary

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# Thank you

We invite you to share your questions, challenges or ambitions - however big or small...

We'll work together to understand your needs and create a tailored plan to support you.

Visit our website nice.org.uk/niceinternational to learn more about our work or contact us.

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