5. Summarize the evidence for all factors important to decision-making – complete the Evidence to Decision Framework

The Evidence-to-Decision (EtD) Framework shown in the latter half of Figure 2 includes the EtD Table and the Conclusions Table, both of which will be completed using GRADEpro Recommendations (see Appendix 9)

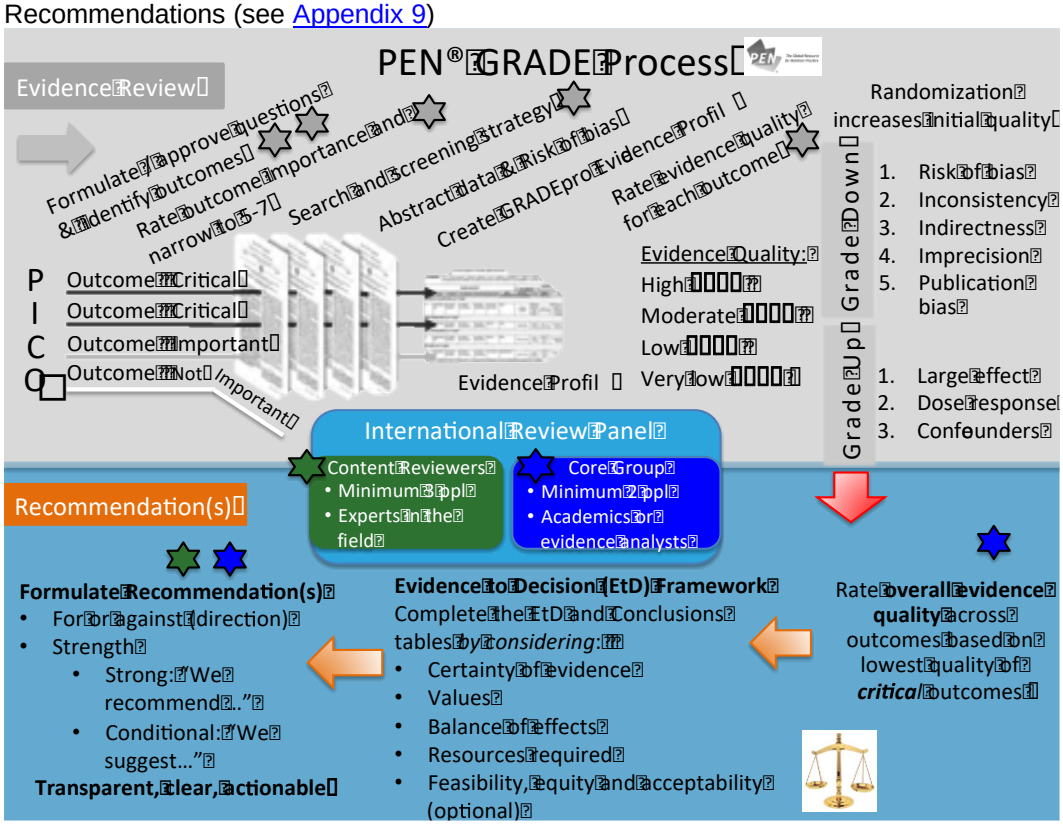

Figure 2: Overview of the PEN® GRADE approach with the processes related to Steps 5 & 6 shown in colour (Adapted from GRADE meeting, Edinburgh 2009).

The EtD Framework will be presented to the International Review Panel to facilitate decision-making on the recommendation.
For a quick tutorial on completing the EtD Framework visit:
https://www.youtube.com/watch?v=iGVEdNa1xFY

Completing the EtD Framework
The sections below outline key questions and considerations for each criterion in the two tables. For each criterion, a judgment must be made. In the judgment column, there will be four or five response options, from those that favour a recommendation against the intervention to those that favour a recommendation for the intervention (1). The EtD framework is filled out using the evidence identified in Sections 2, 3 and 4 and feedback from the Core Group. There may not be enough evidence to consider each criterion and in these situations the author or Core Group may decide to exclude it. Refer to the example completed EtD table in Appendix 9.

5.1 Certainty of Evidence

What is the overall certainty of this evidence of effects, across all of the outcomes that are critical to making a decision?

The "certainty of the evidence" is an assessment of the overall quality of evidence and the likelihood that the effect will not be substantially different from what the research found.

To make your judgement, examine the Evidence Profile table, only considering outcomes that were deemed *critical*. If there are no critical outcomes, the overall strength of the recommendation will be lower. When the quality of evidence across critical outcomes does not differ, that quality of evidence represents the overall certainty of the evidence. *For example, if the quality of evidence is 'very low' then our overall certainty in the effects is very low and this can be marked in the certainty of evidence judgement*. However, if the quality of evidence differs across critical outcomes **and**:

a) outcomes point in different directions (towards benefit and towards harm), **then** the lowest quality of evidence for any critical outcome determines the overall evidence quality.
b) all outcomes point in the same direction (towards either benefit or harm), **then** the highest quality of evidence for a critical outcome that by itself would suffice to recommend an intervention determines the overall evidence quality.
c) the benefits and harms/burdens is uncertain, **then** the lowest quality of evidence for any critical outcome determines the overall evidence quality.

In GRADEpro, insert the Evidence Profile table for critical outcomes into Research Evidence. In the Additional Considerations provide key reasons for down- or upgrading the evidence. Identify the critical outcomes for which there was no information. When there are many such outcomes, it will also affect the overall quality of the evidence.

5.2 Values

What is the certainty and/or variability about the values and preferences for the critical outcomes?

Patient values are difficult to weigh, as preference is personal and variable. The research evidence to support patient values and preferences is limited, and reviewers will often be uncertain about typical values and preferences. These situations typically lower the strength of the recommendation. It is okay to make judgments, but it is important to be explicit and transparent as to why the judgments were made.

To make your judgement, use the Evidence Profile table to consider:

- whether a high or low value was placed on outcomes.
- the perspective taken when making decisions (e.g. patient, policy, program).
- the source of value information (e.g. review panel assessment, observational studies, surveys, qualitative research).
- the variability in values amongst patients, policy makers or the review panel.

If there is no research evidence to support a judgement, in the Additional Considerations of GRADEpro, report that no research evidence was available or this was not searched for, and provide an explanation as to why the judgement was made (i.e. ranging from "important uncertainty or variability" to "no important uncertainty or variability" in patient values). The International Review Panel will have an opportunity to provide input into whether the method for determining values is satisfactory.

5.3 Balance of Effects

What is the balance between benefits and harms/burden?

Consider the magnitude of the desirable and undesirable effects (e.g. anticipated absolute effects). Authors are encouraged NOT to describe results as "not statistically significant", but to report the effect estimate and confidence interval (i.e. the range of values on either side of an effect estimate between which we can be 95% sure that the true value lies). *For example, a meta-analysis, which shows that the relative risk of headache at 24 hours with caffeine is 1.38 times the risk than with decaffeinated coffee (95% CI, 0.96 to 2.00) does not mean that there is no effect; it means there is an increased risk that could be as high as 2 times the risk, but there is*

also the possibility that the true effect could be a reduced risk (e.g. 0.96 lower confidence interval).

Consider the incremental harm/burden relative to the net benefit. Taking into account the values of those affected. When deciding the balance between desirable and undesirable outcomes (or "trade-offs"), two domains can be considered (1):

- Best estimates of effect size (e.g. Absolute effect or Risk difference) for both desirable and undesirable outcomes (summarized in the Evidence Profile Table); and
- The value or “weight” attached to each outcome by patients and by the review panel.

To make your judgement, insert the Evidence Profile table for all outcomes into the Research evidence of GRADEpro:

a) the larger the net benefit (or harm) between desirable and undesirable effects, the more likely it “favours the intervention” (or “favours the comparison”).
b) the smaller the net benefit (or harm) between desirable and undesirable effects, the more likely it “probably favours the intervention” (or “probably favours the comparison”).

5.4 Resources Required

Are the resources worth the expected net benefit from following the recommendation?

Depending on the practice question, authors may or may not choose to consider resource use in their judgments about the direction and strength of recommendations. Reasons for not considering resource use include a lack of reliable data, the intervention is not useful and the effort of calculating resource use can be spared, the desirable effects so greatly outweigh any undesirable effects that resource considerations would not alter the final judgment, or they have elected to leave resource considerations up to other decision makers. Under Additional Considerations in GRADEpro, authors should be explicit about the decision they made not to consider resource utilization and the reason for their decision (1).

Possible considerations for resources:

- monetary – the financial cost of the intervention as compared to the comparison;
  - NHS Economic Evaluation Database: http://community.cochrane.org/editorial-and-publishing-policy-resource/overview-cochrane-library-and-related-content/databases-included-cochrane-library/nhs-economic-evaluation-database
  - Public Health Intervention Cost Effectiveness Database (may require special access): https://www.herc.ox.ac.uk/downloads/health_datasets/browse-data-sets/public-health-interventions-cost-effectiveness-database-phiced
- human – the human resources required to fully implement the intervention;
- environmental – design of the health care system, the physical space required, necessary equipment and/or tools, etc.;
- social – community resources, social and professional networks, integration with other allied health, etc.;
- opportunity costs – are the effects of this intervention worth withdrawing resources from or not allocating resources to other interventions; and
- costs with respect to each partner country.

5.5 Equity, Acceptability, Feasibility (optional)

What would be the impact on health inequities? Is the option acceptable to key stakeholders (patients, clients, healthcare providers, policymakers, etc.)? Can the option be accomplished or implemented?

There is not often a lot of evidence on equity, acceptability or feasibility, and if there is it usually appears under Additional Considerations. It is optional whether this section is included in the EtD

table in GRADEpro. If authors wish to include any of these criterion, they should be explicit if a criterion was included but no evidence was found.

Possible considerations for equity (derived from the PROGRESS Framework: Applying an Equity Lens to Interventions) (3):

- Place of residence
- Race/ethnicity/culture/language
- Occupation
- Gender/sex,
- Religion,
- Education,
- Socioeconomic status (SES),
- Social capital

Possible considerations for acceptability (1):

- Who benefits (or is harmed)?
- Who pays (or saves)?
- When are the benefits, adverse effects and/or costs are expected to occur?
- Are there ethical considerations?

Possible considerations for feasibility (4):

- Intervention characteristics (e.g. complexity, trialability, attractiveness, compatibility, adaptability, etc.);
- Characteristics of the health care professionals (e.g. knowledge, motivation, belief, self-efficacy, etc.);
- Patient characteristics (e.g. beliefs, knowledge, skills, adherence, motivation, etc.);
- Professional interactions (e.g. referral processes, opinions and influence of peers, culture of collaboration and communication, etc.);
- Incentives and resources (e.g. health care payment schemes, funding availability, etc.);
- Capacity for organizational change (e.g. workload, capacity for new knowledge, support across leadership chain, bureaucracy, organizational structure, etc.); and
- Political, legal, and social factors (e.g. political stability, current policies and regulations, ideology, etc.).

5.6 Summary of Judgment Table

The Summary of Judgment Table is automatically completed in GRADEpro based on the aforementioned judgements (i.e. certainty of evidence, values, balance of effects and resources required – see Appendix 9). This table will be shared with the International Review Panel but will not be posted on PEN®.

5.7 Conclusions Table

The Conclusions Table is completed in GRADEpro using information from the Evidence-to-Decision and Summary of Judgments Tables (see Appendix 9). In the table below, each criterion is described using directive questions and an explanation (1). This table will form the basis of the Recommendations and Remarks sections, which are fully described in Step 6.

Should <Intervention> vs. <Comparison> be used in <Population> with <Condition>?

	Strong recommendation against the intervention ○	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
Conclusions					
Type of recommendation	Directive Question: *Based on the balance of the consequences in relation to all of the criteria in framework, what is your recommendation?* Explanation: Decide whether the recommendation is 'for' or 'against' the intervention. When it is clear that the balance of consequences tips in one direction, then a 'strong recommendation' is more likely. When it is less clear, or less probable, the recommendation is likely to be 'conditional'. **See Step 6 for more information on recommendation strength.**				
Recommendation	Directive Question: *What is the recommendation in plain language?* Explanation: A concise, clear and actionable statement. **See Step 6 for more information on forming a recommendation.**				
Justification	Directive Question: *What criteria in the framework drove the recommendations?* Explanation: A concise summary of the reasoning underlying the recommendation i.e. quality of evidence for benefits and harms, consideration placed on patient values & preferences or required resources. **See Step 6 for more information on the remarks that accompany a recommendation.**				
Subgroup considerations	Directive Question: *What, if any subgroups were considered and what, if any specific factors should be considered in relation to those subgroups?* Explanation: A concise summary of the subgroups that were considered and any changes to the recommendation.				
Optional: Implementation considerations (if equity, acceptability and/or feasibility were considered)	Directive Question: *What should be considered when implementing the intervention, including strategies to address concerns about equity, acceptability and feasibility?* Explanation: Key considerations, including strategies to address concerns about equity, acceptability and feasibility, if any of these criteria were considered by the panel				
Monitoring and evaluation.	Directive Question: *What indicators should be monitored? Is there a need to evaluate the impact of the option?* Explanation: Consider important indicators that should be monitored if the recommendation is implemented.				
Research priorities	Directive Question: *Are there any important uncertainties in relation to any of the criteria that are a priority for further research?* Explanation: Any research priorities				