6. Formulate the Recommendation noting the Strength of the Recommendation and the Quality of Evidence

(aka putting the Evidence-to-Decision Framework into words)

6.1 Writing the Recommendation

Recommendations are clear, concise and actionable advice on whether to implement the intervention and, if relevant, under what conditions and how. They include five pieces of information:

1. the intervention and what it was compared to;
2. the direction of the recommendation, i.e. for or against the intervention;
3. the specific population of interest, which may also include a specific condition;
4. the strength of the recommendation, i.e. "Strong" or "Conditional"; and
5. the overall quality of evidence and its corresponding symbol, i.e. "Very Low" ⊕⊖⊖⊖, "Low" ⊕⊕⊖⊖, "Moderate" ⊕⊕⊕⊖, "High". ⊕⊕⊕⊕

Most recommendations will be one sentence long. **Consider the following example**: *"For residents at high risk of fractures, we recommend daily supplements of 800 IU to 2000 IU vitamin D_3 (strong recommendation, moderate quality evidence ⊕⊕⊕⊖)"* (5).

Determining the strength of recommendation: Strong recommendations imply **certainty** about the criteria and a clear balance towards either the intervention or comparison. When the review panel is **uncertain** about the balance or when information about the factors that influence the strength of a recommendation is not available, the review panel should be more cautious and in most instances should opt for a Conditional recommendation. Use the following table as a guideline in determining the Strength of the recommendation:

Criteria for each type of recommendation:
Strong recommendation for the intervention – all considerations are strong: high quality evidence, no important uncertainty in patient values, large effect, minimal or no harms, low costs or cost savings.
Conditional recommendation for the intervention – either lower quality evidence, unclear about patients' values (some people, but not all, might want this intervention), smaller effect size, and/or some concerns about side effects or costs.
Conditional recommendation against the intervention – concerns are not extreme: costs, side effects, patients' values. Benefits have low certainty or small estimates of effect. Some people might not want this intervention, but not all. Use wording "suggest" instead of "recommend" (e.g. we suggest not using x, but some may be willing to take/pay [whatever the cost/side effect is]).
Strong recommendation against the intervention – concerns about costs, access, side effects, or inconvenience. Benefits are unclear or there are few. Almost all people would not want this intervention.

Notes:

The strength of the recommendation will determine its wording.

- Strong recommendations use the wording "***We recommend…***"
- Conditional recommendations use the wording "***We suggest***…".

In most situations, recommendations are positively phrased. Thus, in situations where the balance of consequences favours the comparison over the intervention, the recommendation would be "We suggest the comparison not the intervention" rather than "We do not suggest…".

Try to avoid saying "no recommendation" or "no evidence"; instead refer to the problem (e.g. lack of directness if evidence refers to surrogate populations or outcomes). Another possibility is to recommend that an intervention only be used in a research setting (e.g. if there is insufficient evidence to support a decision for or against an intervention or if further research has the potential for reducing uncertainty about the effects of the intervention). In a situation where government guidelines exist (even if based on opinion), a recommendation can be made (e.g.

pregnant women should avoid high mercury fish); cite in the remarks that this is government guidance.

For implications of strong and weak recommendations for patients, clinicians and policy makers, refer to Appendix 10.

The connection between recommendation strength and overall evidence quality: Low quality evidence is rarely tied to strong recommendations and, in general, panels are discouraged from making strong recommendations when evidence quality for critical outcomes is low or very low**.** However, there are five paradigmatic situations in which strong recommendations may be warranted despite low or very low quality of evidence (1). These situations can be conceptualized as ones in which a panel would have a low level of regret if subsequent evidence showed their initial recommendation was misguided. These include:

1. When low quality evidence suggests benefit in a life threatening situation.
2. When low quality evidence suggests benefit and high quality evidence suggests harm or a very high cost
3. When low quality evidence suggests the two options have equivalent benefit, but high quality evidence shows less harm for one option.
4. When high quality evidence suggests the two options have equivalent benefit, and low quality evidence suggests harm in one alternative.
5. When high quality evidence suggests modest benefits and low/very low quality of evidence suggests possibility of catastrophic harm (e.g. applying data from other populations that suggests harm to pregnant women).

6.2 Writing the Remarks

What is the justification for the recommendation, based on the criteria in the framework that drove the decision?

The section should come from information gathered in the EtD Framework and represents the underlying assumptions made by the review panel in forming their recommendation. The remarks are concise and should be written in the active voice. Explicitly state the key criteria used in making the recommendation and, if applicable, which criteria were not considered (e.g. patient values or resources). Consider the following statements for excluded criteria:

- No information on patient values was available in the literature; personal preferences should be discussed with clients individually.
- Patient values associated with <condition> were not examined and should be discussed with clients individually.
- Resource requirement associated with this intervention were not examined and this should be discussed with clients individually.

Example (5):
Recommendations: *For residents at high risk of fractures, daily supplements of 800 IU to 2000 IU vitamin D_3 are recommended (strong recommendation, moderate quality evidence ⊕⊕⊕⊖).*

Remarks: *The recommendation for residents at high risk places a high value on reductions in hip fractures, mortality and falls and a lower value on the resources in long-term care that are required to provide vitamin D supplementation. This recommendation applies to supplementation with D3, as this form may be more accessible because of its lower cost relative to D2. A dose of about 800 IU reduced fractures in people with normal or low 25-hydroxyvitamin D levels and also increased 25-hydroxyvitamin D levels to normal in those with low levels; therefore, 800 IU is recommended. However, the exact dose may depend on the dosing regimen that is available (e.g., a 1000 IU drop or tablet would be acceptable). The benefits of vitamin D supplementation are closely linked to adequate calcium intake, and therefore recommendations for calcium intake should also be applied. The recommended dietary allowance for vitamin D for people older than 70 years is 800 IU daily, and the tolerable upper intake level is up to 4000 IU.*

Additional Tips for Writing Remarks:
The Remarks section replaces the Practice Guidance (PG) section of KPPs. This section should include succinct practice information needed to answer the practice question and guide practitioners. Material used to inform this section should be based on published citations wherever possible. Its content can be derived from the Recommendation and consider the following categories from the EtD framework:

- Priority of problem (for the target audience: client, the public, clinicians, or policy makers; prevalence of the problem)
- Benefits and harms (e.g. weighing the balance between risks and benefits/desirable and undesirable outcomes or consequences(trade-offs))
- Certainty of evidence
- Transparent Values and Preferences (e.g. whether a high or low value is placed on specific outcomes, and for which population groups; lifestyle; culture)
- Resources (e.g. cost, convenience such as market availability of products, burden, effect on human resources, environment)
- Equity, acceptability and feasibility if applicable (e.g. ease of implementation)
- Country specific dietary standards (DRVs), additional considerations about other foods or nutrients
- Short section on relevant background information deemed necessary to provide context for the recommendation.

This section should be written with the expectation that this content will also appear in the related Practice Summary Toolkit, within the Intervention section (in Key Findings, Recommendations and Remarks section) and will be used by dietitians when explaining or discussing the topic with clients, or adapted for education materials such as client handouts.

6.3 Writing the Summary of Evidence

This section, an abstract for the Evidence Profile Table, was created in Step 4, but should be included in the documents sent for panel review.

Example of a Summary of Evidence

"Overall there was moderate quality evidence for benefits and low to very low quality evidence for harms of calcium and vitamin D. We found that vitamin D in addition to calcium probably reduces hip fractures and mortality more than vitamin D alone or calcium alone (Avenell 2009; Bischoff-Ferrari 2012; Murad 2012): for residents at high risk we estimated 15 fewer hip fractures per 1000 (95% CI, 5 to 24 fewer); for residents not at high risk 5 fewer hip fractures per 1000 (95% CI, 2 to 8 fewer); and for all residents, 7 fewer deaths per 1000 (95% CI, 1 to 14 fewer).

We found vitamin D and calcium supplementation likely has little or no effect on vertebral fractures with only 2 fewer vertebral fractures per 1000 (95% CI, 44 fewer to 61 more). The effect is similar with vitamin D only, but a reduction may be likely with calcium only (49 fewer per 1000: 95% CI, 99 fewer to 19 more)(Avenell 2009; Murad 2012). Calcium, or vitamin D with or without calcium, probably has little to no effect on the incidence of nonvertebral fractures (Avenell 2009; Bischoff- Ferrari 2012; Murad 2012), quality of life (Grant 2005) or muscle strength (Muir The data for falls were not precise (wide confidence intervals including the possibility for benefit, no effect and harm) and the effects were not consistent when the rate or risk of falls was measured (Cameron 2012; Gillespie 2012; Murad 2011; Reid 2006). However, vitamin D and calcium, or vitamin D alone may reduce falls. This is important because one-third of all falls may result in an injury and every fifth injurious fall may result in treatment outside the patient's own setting (Nurmi 2002). There were no data on pain, anxiety, mobility and activities of daily living performance in relation to calcium and vitamin D.

With respect to minor and major adverse events, vitamin D or calcium supplements probably increase mild or serious gastrointestinal events to a similar extent, approximately 8 per 1000 more (95% CI, 0 to 17 more) (Avenell 2009). Gastrointestinal symptoms or difficulties taking calcium tablets may contribute to poor adherence (Grant 2005; Reid 2006). The evidence suggests slightly more cases of hypercalcaemia (5 more per 1,000: 95% CI, 1 fewer to 18 more) and renal insufficiency or calculi (3 more cases per 1000: 95% CI, 0 to 6 more) with vitamin D (D_2 or D_3) with calcium (Avenell 2009). The evidence for greater myocardial infarctions with supplementation of calcium >=1000 mg in community-dwelling individuals is uncertain as it is not consistent with the reductions in mortality (Avenell 2009), and the confidence intervals around the estimates include no effect, and the possibility of appreciable harm (Bolland 2010; Bolland 2011; Elamin

2011).
Subgroup analyses from systematic reviews found that there may be little or no difference in rates of fractures or falls by type of vitamin D (D_3 or D_2) (Avenell 2009; Levis 2012; Murad 2011); that there may be greater benefits with vitamin D >792 IU (actual intake in most studies was between 792-844 IU), but no difference with < or >1000 mg Ca, and there are inconsistent effects when vitamin D is given in large monthly or annual doses (Bischoff-Ferrari 2012; Bischoff-Ferrari 2009). Analyses did find that vitamin D may have greater effects in reducing falls (Gillespie 2012; Murad 2011) and fractures in people with low vitamin D status (Bischoff-Ferrari 2012). Autier 2012 (Autier 2012) also found that approximately 800 IU daily over several months can increase serum vitamin D levels to 'normal' levels in people with initial vitamin D deficiency (e.g. <= 25 nmol/L)." (5)

6.4 Writing the Evidence to Decision Summary

The Evidence to Decision Summary follows the Remarks section and supports it by providing even more information on the factors that were considered when making the final recommendation. Think of this section as an abstract for the Evidence-to-Decision Table; translate the key points from the table into paragraph form using plain language. This section should not be longer than two to three paragraphs in length.

6.5 Revising based on Reviewers' Comments

The recommendations and remarks along with the Evidence Profile Table and Evidence to Decision framework will be sent to reviewers along with the International Review Panel questionnaire (see Appendix 11).

6.6 Recommended Readings / Resources for Formulating Recommendations

- Chapter 6. In: Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE Handbook. Updated October 2013. Full text available from: http://www.guidelinedevelopment.org/handbook/