How can a STRONG recommendation be based on VERY LOW quality evidence?
Background

- Grading of Recommendations, Assessment, Development and Evaluation (GRADE) is a widely used rating system.

- Several COG-endorsed supportive care guidelines have used the GRADE approach.

GRADE classifies Recommendations as STRONG or WEAK and Quality of the Evidence* as VERY LOW, LOW, MODERATE or HIGH.

*Reflects the level of confidence that the estimate of an intervention’s effect is correct.
<table>
<thead>
<tr>
<th>Quality of the body of evidence</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High 🟢🟢🟢🟢</td>
<td>We are very confident that the true effect lies close to that of the estimate of the effect</td>
</tr>
<tr>
<td>Moderate 🟢🟢🟢🟢</td>
<td>We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different</td>
</tr>
<tr>
<td>Low 🟢🟢🟢🟢</td>
<td>Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect</td>
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<tr>
<td>Very Low 🟢🟢🟢🟢</td>
<td>We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect</td>
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<table>
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<tr>
<th>Strength of Recommendation</th>
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<tbody>
<tr>
<td>Strong</td>
<td>Most people would want and should receive the recommended course of action. The recommendation can be adapted as a policy in most situations.</td>
</tr>
<tr>
<td>Weak</td>
<td>There is a need for substantial debate and involvement of stakeholders in policy making. The majority of people would want the recommended course of action, but many would not. Clinicians should be more prepared to help patients to make a decision that is consistent with their own values.</td>
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In this module we explain how a **STRAONG GRADE GUIDELINE RECOMMENDATION** can be based on very low / low quality evidence and how to integrate such recommendations into your practice.
GRADE recommendations: A balance of factors

Possible factors:
- Benefits and Harms
- Quality of the Evidence
- Values
- Acceptability
- Feasibility
- Equity
- Costs

For

Against

The world's childhood cancer experts
Because GRADE incorporates separate judgments of evidence quality and strength of recommendation…

High quality evidence does not necessarily lead to a strong recommendation

and

Low quality evidence does not always lead to a weak recommendation
If after weighing all factors, the guideline panel is **very certain** that desirable effects outweigh undesirable effects, they will make a strong recommendation.
GRADE example: Should oral direct thrombin and factor Xa inhibitors be used in pregnancy for women requiring anticoagulation?

Weighing the factors:

- *High certainty (i.e. high quality evidence) of similar effects of different anticoagulants*
- # However, there is low quality evidence (i.e. low certainty of the effect) suggesting potential harm to the unborn infant with oral direct thrombin and factor Xa inhibitors

For Against

High certainty of similar benefits between different anticoagulants*

Uncertain but potential for harm to unborn infant from specific anticoagulants: oral direct thrombin and factor Xa inhibitors*
The guideline panel therefore made a **STRONG recommendation against** the use of oral direct thrombin and factor Xa inhibitors in pregnancy.

**This means:**
Almost all women would not want to use oral direct thrombin and factor Xa inhibitors supplements in pregnancy and clinicians should not prescribe it in this setting.

- **For**
  - High certainty of similar benefits between different anticoagulants*

- **Against**
  - Uncertain but potential for harm to unborn infant from specific anticoagulants: oral direct thrombin and factor Xa inhibitors*
## Implications for practice

<table>
<thead>
<tr>
<th>Implications</th>
<th>Strong recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>For patients</td>
<td>Most individuals in this situation would want the recommended course of action, and only a small proportion would not. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.</td>
</tr>
<tr>
<td>For clinicians</td>
<td>Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.</td>
</tr>
<tr>
<td>For policy makers</td>
<td>The recommendation can be adopted as policy in most situations.</td>
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</table>

Source: [http://www.gradeworkinggroup.org/](http://www.gradeworkinggroup.org/)
Want to learn more about GRADE?
Visit: https://cebgrade.mcmaster.ca/training/

Acknowledgement:
Example courtesy of Dr. Nancy Santesso, GRADE group