The implications of a weak recommendation are:

- For patients—most people in your situation would want the recommended course of action, but many would not
- For clinicians—you should recognise that different choices will be appropriate for different patients and that you must help each patient to arrive at a management decision consistent with her or his values and preferences
- For policy makers—policy making will require substantial debate and involvement of many stakeholders.

As clinicians become more aware of variability in patients’ values and preferences, they are turning to structured decision aids to facilitate the decision making process.¹ A strong recommendation indicates that use of a decision aid is unnecessary—almost all informed patients will make the same choice. A weak recommendation indicates that a decision aid could be useful.

Managers of healthcare systems are becoming increasingly interested in ensuring the quality of care. Guidelines help managers to differentiate practices that constitute quality of care from others that are discretionary. GRADE provides clear guidance on these matters: The management options associated with strong, but not with weak, recommendations are candidates for quality criteria. When a recommendation is weak, discussing with patients and families the relative merits of the alternative management strategies may become a quality criterion.

Four key factors determine the strength of a recommendation

The first key determinant of the strength of a recommendation is the balance between the desirable and undesirable consequences of the alternative management strategies, on the basis of the best estimates of those consequences (table 1). Consider, for instance, the use of antenatal steroids in women destined to deliver an infant prematurely. Administration of steroids to mothers decreases the risk of infant respiratory distress syndrome with minimal side effects, inconvenience, and costs. Advantages of steroid administration hugely outweigh the disadvantages, indicating the appropriateness of a strong recommendation.

When advantages and disadvantages are closely

**strong and weak recommendations provide specific guidance**

GRADE’s binary classification of strength of recommendations provides clear direction to patients, clinicians, and policy makers. The implications of a strong recommendation are:

- For patients—most people in your situation would want the recommended course of action and only a small proportion would not; request discussion if the intervention is not offered
- For clinicians—most patients should receive the recommended course of action
- For policy makers—the recommendation can be adopted as a policy in most situations.

The implications of a weak recommendation are:
balanced, a weak recommendation becomes appropriate. Consider, for instance, patients with atrial fibrillation at low risk of stroke. Warfarin can reduce that low risk even further, but adds inconvenience and an increased risk of bleeding. The right choice under such circumstances is likely to differ between patients.

The second determinant of the strength of a recommendation is the quality of the evidence. If we are uncertain of the magnitude of the benefits and harms of an intervention, making a strong recommendation for or against a particular course of action becomes problematic. For instance, graduated compression stockings have an apparent large effect in reducing deep venous thrombosis in people making long plane journeys. The randomised trials from which the estimate of effect comes were, however, seriously flawed—the techniques for measuring deep venous thrombosis were not reproducible, and the studies were unblinded. Despite the apparent large benefit, use of stockings warrants only a weak recommendation.

The third determinant of the strength of a recommendation is uncertainty about, or variability in, values and preferences. Given that alternative management strategies will always have advantages and disadvantages, and thus a trade-off exists, how a guideline panel values benefits, risks, and inconvenience is critical to the strength of any recommendation.

Consider the subject of preventing strokes in patients with atrial fibrillation. Warfarin, relative to no antithrombotic therapy, reduces the risk of stroke by approximately 65% but increases the risk of severe gastrointestinal bleeding. Devereaux and colleagues asked 63 physicians and 61 patients how many suggestions to change their lifestyle. The alternative, heparin, eliminates the risk to the child. The benefit, however, comes with disadvantages of pain, inconvenience, and cost. Clinicians’ experience is that women overwhelmingly place a high value on preventing fetal complications. Thus, despite its disadvantages, a strong recommendation for heparin substitution is warranted.

The final determinant of the strength of a recommendation is cost. Cost is much more variable over time and geographical areas than are other outcomes. Drug costs tend to plummet when patents expire, and charges for the same drug differ widely across jurisdictions. In addition, the resource implications vary widely. For instance, a year’s prescription of the same expensive drug may pay for a single nurse’s salary in the United States and 30 nurses’ salaries in China.

Thus, although higher costs reduce the likelihood of a strong recommendation in favour of an intervention, the context of the recommendation will be critical. In considering resource allocation, guideline panels must therefore be specific about the setting to which a recommendation applies.

**Strong recommendations may not be important from all perspectives**

If the consequences of the choice are relatively unimportant, some patients may not bother with even strong recommendations. This is particularly likely if they are faced with many new drugs or many suggestions to change their lifestyle.

When setting priorities, governments and public health officials must also consider factors beyond the strength of a recommendation. These include the prevalence of the health problem, considerations of equity, and the potential for improvement in quality of care, all of which will have an impact on the population health gain of an intervention.

**Determinants of strength of recommendation**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balance between desirable and undesirable effects</td>
<td>The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted.</td>
</tr>
<tr>
<td>Quality of evidence</td>
<td>The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted.</td>
</tr>
<tr>
<td>Values and preferences</td>
<td>The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted.</td>
</tr>
<tr>
<td>Costs (resource allocation)</td>
<td>The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted.</td>
</tr>
</tbody>
</table>
SUMMARY POINTS

The strength of a recommendation reflects the extent to which we can be confident that desirable effects of an intervention outweigh undesirable effects. GRADE classifies recommendations as strong or weak. Strong recommendations mean that most informed patients would choose the recommended management and that clinicians can structure their interactions with patients accordingly. Weak recommendations mean that patients’ choices will vary according to their values and preferences, and clinicians must ensure that patients’ care is in keeping with their values and preferences.

Strength of recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, quality of evidence, variability in values and preferences, and resource use.

Endpiece

Two kinds of surgery

Surgical operations are of two kinds—those that benefit the patient and those that kill him.

Abu al-Qasim Khalaf bin ‘Abbas el-Zahrawi, also known as Albucasis (940-1013)