Key concepts for informed health choices. 3.2: expected advantages should outweigh expected disadvantages

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This is the second of two essays in this series explaining key concepts that can help you make well-informed decisions. In this essay, we explain five considerations about weighing the expected advantages and disadvantages of treatments. Consider:

- Whether the benefits and savings outweigh the harms and costs of acting or not.
- The baseline risk or severity of the symptoms when estimating the size of expected effects.
- How important each advantage and disadvantage is when weighing the pros and cons.
- How certain you can be about each advantage and disadvantage and
- The need for further fair comparisons.

The basis for these concepts is described elsewhere.¹

Weigh the benefits and savings against the harms and costs of acting or not

Individuals, clinicians and policymakers deciding about whether to use a treatment should consider the potential benefits and the potential harms, costs and other advantages and disadvantages of the treatment. When a decision affects many people, it is important to consider the distribution of the advantages and disadvantages, i.e. who will benefit, who will be harmed, who will achieve savings and who will bear the costs.

When the advantages of a treatment clearly outweigh the disadvantages, deciding what to do is relatively easy. For example, for patients who have had a heart attack, stroke or transient ischemic attack, the advantages of low-dose aspirin compared to not taking aspirin (reduced deaths, heart attacks and strokes) are substantially more than the disadvantages (increased serious gastrointestinal bleeds, and minimal inconvenience and cost).² Most people in this situation would choose to take aspirin. On the other hand, when the advantages and disadvantages are closely balanced, deciding what to do can be difficult. For example, for someone 50 years or older without symptomatic cardiovascular disease, aspirin only slightly reduces deaths if taken over 10 years, and a reduction in heart attacks is closely balanced with an increase in serious gastrointestinal bleeds. Some people in this situation would choose to take aspirin, and some would not.

Consider the baseline risk or severity of the symptoms when estimating the size of expected effects

The balance between the benefits and harms of treatments often depends on the baseline risk (the likelihood of an individual experiencing an undesirable event) or on the severity of the symptoms. The balance between the advantages and disadvantages of a treatment is more likely to favour the use of a treatment by people with a higher baseline risk, or more severe symptoms, for example, patients who have had a heart attack, stroke or transient ischemic attack, or have a high probability of dying or having another cardiovascular event in the next five years (see Table 1). Because they have a high baseline risk, aspirin has a large absolute effect (risk difference), despite the relative effect being small to moderate, and the benefits substantially outweigh the harms for someone in this situation.²

On the other hand, for someone 60 years old – without symptomatic cardiovascular disease – who has a low risk of having a cardiovascular event or a gastrointestinal bleed, aspirin has little if any beneficial effect on deaths and strokes. The probability of having a heart attack (27 per 1000 in the next 10 years) is much lower than it is for someone who has had a cardiovascular event and has a high risk (117 per 1000 in the next five years). The relative effect is also slightly lower. The absolute effect is six fewer heart attacks per 1000 people who take aspirin for 10 years (see Table 2), compared to 37...
fewer per 1000 people who take aspirin for just five years. The relative risk increase, the baseline risk without aspirin, and the risk difference for having a serious gastrointestinal bleed are also less for someone who has not had a cardiovascular event and has a low risk of bleeding. Consequently, the benefits and harms of low-dose aspirin are closely balanced for someone in this situation.

Consider how important each advantage and disadvantage is when weighing the pros and cons

Estimates of benefits and harms depend on how much weight people give to treatment advantages and disadvantages. Different people may value outcomes differently and sometimes make different choices because of this. In addition, people usually place more value on outcomes that happen soon than on outcomes that happen years into the future. In other words, the further into the future an outcome (for example, reducing the chance of heart disease or cancer after many years) the more people tend to ‘discount’ its value or importance. The balance between the advantages and disadvantages of treatments may also depend on how much costs and events in the future are discounted.

Consider the example of aspirin to prevent cardiovascular disease in someone 60 years old with a low risk. The main advantage is a reduced risk of having a heart attack. The main disadvantage is an increased risk of having a serious gastrointestinal bleed, as shown in Table 2.2

Although aspirin costs very little, for someone with very little money, this might be another important disadvantage. There is also minimal inconvenience – taking a pill every day for 10 years – but for some people this might be enough of a bother to be another disadvantage. Someone who is more averse to having a heart attack than having a serious gastrointestinal bleed and who is not concerned about the cost or the bother might choose to take aspirin. On the other hand, someone who is more averse to having a serious gastrointestinal bleed and less averse to having a heart attack might choose not

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**Table 1.** Probability of an event with and without aspirin in the next five years for someone with a high baseline risk.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative risk reduction (95% confidence interval)</th>
<th>Risk without aspirin in the next five years</th>
<th>Risk difference (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>10% (1% to 18%)</td>
<td>133 per 1000</td>
<td>13 fewer per 1000 (1 to 24 fewer)</td>
</tr>
<tr>
<td>Strokes</td>
<td>19% (8% to 29%)</td>
<td>135 per 1000</td>
<td>26 fewer per 1000 (11 to 39 fewer)</td>
</tr>
<tr>
<td>Heart attacks</td>
<td>31% (20% to 40%)</td>
<td>117 per 1000</td>
<td>37 fewer per 1000 (23 to 47 fewer)</td>
</tr>
<tr>
<td>Serious gastrointestinal bleeds</td>
<td>169% Increase (25% to 476%)</td>
<td>15 per 1000</td>
<td>25 more per 1000 (4 to 71 more)</td>
</tr>
</tbody>
</table>

*Based on Vandvik et al.*

**Table 2.** Probability of an event with and without aspirin in the next 10 years for someone with a low baseline risk.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Relative risk reduction (95% confidence interval)</th>
<th>Risk without aspirin in the next 10 years</th>
<th>Risk difference (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart attacks</td>
<td>23% (14% to 31%)</td>
<td>27 per 1000</td>
<td>6 fewer per 1000 (4 to 8 fewer)</td>
</tr>
<tr>
<td>Serious gastrointestinal bleeds</td>
<td>54% increase (30% to 82%)</td>
<td>8 per 1000</td>
<td>4 more per 1000 (2 to 7 more)</td>
</tr>
</tbody>
</table>

*Based on Vandvik et al.*
to take aspirin, especially if they were concerned about the cost or the bother.

**Consider how certain you can be about each advantage and disadvantage**

The certainty of the evidence (the extent to which the research provides a good indication of the likely effects of treatments) can affect peoples’ treatment choices. For example, someone might decide not to use or to pay for a treatment if the certainty of the evidence is low or very low. How ‘certain’ the evidence is depends on the fairness of the comparisons, the risk of being misled by the play of chance, and how directly relevant the evidence is. Systematic reviews provide the best basis for these judgements and based on these judgements, should report an assessment of the certainty of the evidence. Unexplained inconsistencies in effect estimates from different studies can also affect the certainty of the evidence.

The use of hydroxychloroquine (HCQ) and chloroquine (CQ) to treat COVID-19 illustrates the importance of considering the certainty of the evidence when making decisions about treatments. On 28 March 2020, the U.S. Food and Drug Administration (FDA) issued a letter granting an Emergency Use Authorization for use of HCQ and HQ for treating COVID-19, and the use of HCQ and HQ surged. The letter did not describe the evidence underlying the decision. It stated that the authorisation was supported by recommendations “for treatment of hospitalized COVID-19 patients in several countries, and a number of national guidelines” based on “limited in-vitro and anecdotal clinical data in case series”. By June, controlled trials had shown that the FDA guidelines had been misleading – no beneficial effects on morbidity or mortality had been detected. On 15 June, the FDA revoked the Emergency Use Authorization. A systematic review published in April 2021 included 14 unpublished trials (1308 patients) and 14 publications/preprints (9011 patients). It found that HCQ increased deaths in COVID-19 patients, and no benefit of chloroquine had been demonstrated.

**Consider the need for further fair comparisons**

There is always some uncertainty about the effects of treatments. If that uncertainty affects decisions that are important to people, the uncertainty should be reduced by further fair comparisons whenever possible. Individuals should consider participating in those fair comparisons when they are uncertain about which alternative to choose because of uncertainty about the effects of the alternatives. Participating in a fair comparison is a good hedging strategy when there is important uncertainty about effects. Moreover, people in fair comparisons sometimes fare better than people outside of fair comparisons. In addition, the results of fair comparisons can help to generate reliable information on which to base future decisions.

Willingness to contribute to the collective good and to help others is commonly thought to be the key motivating factor for participation in randomised trials. However, although willingness to help others might incline people towards participation, participation may be conditional, to some extent, on expectations of personal benefit. For example, a study interviewed people about their motivation to participate in a trial of surgery compared to medical management of gastroesophageal reflux (heartburn and regurgitation caused by stomach contents regurgitating into the oesophagus – the tube connecting the mouth and stomach). It found that people invited to participate viewed:

- recruitment appointments as an opportunity for learning and review,
- participation as potentially offering access or faster access to surgery and
- participation as offering careful monitoring.

Participants reported that being inclined to help others predisposed them towards trial participation, but considerations of the implications of trial participation for them personally also influenced decisions about participation. For the people who agreed to be randomised, trial participation seemed to be a win–win situation – one in which they could both help others and benefit (or at least not be harmed) personally.

**Implications**

- Always consider the balance between advantages and disadvantages of treatments.
- When making decisions about treatments, consider the estimated baseline risk or the severity of symptoms.
- Consider how important each treatment advantage and disadvantage is when choosing a treatment.
- Consider the certainty of the evidence when choosing treatments.
- Consider advocating for and participating in fair comparisons of treatments when there are
important uncertainties about the effects of the treatments.

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References


