Thinking about the balance between risk and benefit when prescribing

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Framing the way we think
When writing a prescription, we are taught to balance the risks and benefits of each drug prescribed. We think about the risk benefit ratio as if benefits are secured and risks are a shadowy but unlikely eventuality. In fact, benefit is also best thought of as a probability. For example, the potential benefit of amoxycillin for pharyngitis is that, on average, recipients experience a reduction in the number of days of discomfort due to sore throat and fever. The potential harms are expressed as side-effects, a term sharing similarities with the military use of the term ‘collateral damage’ – inconsistent, unpredictable and an unavoidable consequence of a justifiable decision.

Doing the numbers
In order to balance risks and benefits, it is helpful to have information about the probability of getting better without treatment, and information on how much treatment improves the probability of getting better. Similarly, many clinical events thought of as drug side-effects can be seen in patients not given the drug – it is the amount by which they become more likely to happen after giving the drug that provides a means of measuring harm.

In clinical trials, these baseline rates are derived from the control group. If, for example, 80% of patients with a particular illness improve on their own, and 90% improve with an antibiotic, then the difference is 10%. This is known as the risk difference or absolute risk reduction (ARR). The ARR is often expressed as a probability out of one – in this case 10% = 0.1. The number of patients needed to treat (NNT), on average, in order to benefit one patient, is the reciprocal of this number, i.e. 1/0.1, which is 10. The number needed to harm (NNH) is calculated in the same way. The NNH is the number of times one would regard this as an acceptable risk for a valued benefit. However, this also depends on the nature of the benefit and harm: if a patient with a viral runny nose and a scratchy throat develops a Stevens-Johnson syndrome after an antibiotic then this prescription becomes problematic because of the zero potential benefit from the antibiotic, even if Stevens-Johnson syndrome is rare.

Weighting values
Benefits and harms are seldom on the same scale. Treating bacterial pharyngitis reduces the probability of developing rheumatic fever in that individual, and provides a community benefit by reducing streptococcal carriage. Harms may involve many organ systems, and can extend to the community (e.g. increasing prevalence of antibiotic resistance.) Rarely, the harms may be of a much higher order of magnitude, and on a similar metric, making the decision easier – e.g. at 4 or 5 hours after the event, the potential mortality harms of thrombolysis for acute stroke outweigh the potential reduction in infarct sequelae.

Making sense of it all
Withholding highly efficacious medication because of inappropriate concerns about rare potential problems is as detrimental as profligate use of drugs with a narrow gap between benefit and harm. Consider the baseline risk carefully, and avoid overinflating modest benefits. All we can strive for is due diligence – before prescribing, did you and the patient think carefully about whether the possible benefits were worth the foreseeable harms?

Key points
• Attempting to quantify the risks and benefits when prescribing may provide fruitful new perspectives on therapeutic appropriateness.
• It may be difficult to justify unexpected harms that happen after prescribing an agent with very limited or no benefit.
• Potential benefits and potential harms are often on different scales. Patients should be informed about the potential benefits and the potential harms and given an opportunity to contribute their own values to the discussion about the merits of the intervention.