

Benefit, risk and harm

Andrew Herxheimer, Emeritus Fellow, UK Cochrane Centre, Oxford, UK

Whenever we choose a treatment, we do so because we believe that on balance it will help the patient – that is, the advantages outweigh the disadvantages. Common decisions have been made many times before, and are embedded in traditions, guidelines and formularies, but there are still many situations that require an individual ‘benefit/risk evaluation’ or determination of the ‘benefit:risk ratio’. Unfortunately these widely accepted terms muddle thought.

The confusion arises because benefits and risks in the ordinary uses of the words have completely different dimensions. A benefit is a material or experiential good ‘thing’, while a risk is a ‘probability’, the chance that something bad will happen. The asymmetry is clear. We should therefore be weighing **benefit** against **harm**, and the probability of benefit against the probability of harm. In doing that we should consider the kinds of benefit and harm, their chance of occurring, their magnitude and importance (primarily to the patient), as well as their timing and duration.

The idea of a benefit:risk ratio is especially wrong, because very often, the benefit and the risk are not of the same nature, and no one can really ‘weight’ them. One can ask populations about how many days, weeks or years of their life they would exchange to get rid of this or that handicap, but such comparisons are very fragile, and such enquiries are rare.

With the oral contraceptive pill we are left comparing a benefit such as making love with no fear of getting pregnant (tomorrow) with a risk of venous thrombosis or myocardial infarction (15 to 25 years in the future). Doctors should not take such decisions unless the case is very clear: it is the population or individual patients who should decide for themselves.

Two brief illustrations

Adjuvant tamoxifen after mastectomy for breast cancer

Benefits: Five years’ treatment reduced the recurrence rate in women with oestrogen receptor positive tumours from 38% to 23%, with a corresponding improvement in survival.¹

Harms: Five years’ treatment increased the risk of endometrial cancer, over 10 years causing about two extra deaths per 1000 women treated. Premenopausal women have bone loss (1.4% per year). There is an increased risk of thrombosis.¹ Anti-oestrogen adverse effects include hot flushes, nausea and vomiting in up to 25% of patients, less commonly vaginal dryness or itching, dry skin, deepening of the voice.

Comment: Whether treatment beyond five years adds to the benefit is not yet clear.

Controlled trials are designed to assess expected benefits, while harmful effects are mostly unexpected and noted only incidentally and unsystematically. This asymmetry is inherent in reports of trials, and leads to a bias that is insufficiently recognised.

A thorough evaluation of benefits and harms can be complicated and difficult, not least because they vary greatly with different drug dosages and regimens. In the absence of reliable estimates of the probabilities and the relative magnitudes of benefits and harms a meaningful evaluation is impossible.

What are the implications for practice? I think that in our roles as clinicians, members of formulary or guideline committees, or regulators, we must try to be much more specific when we consider the benefits of treatments and the kinds of harm they may do. We also need to consider the probabilities of those benefits and harms. If we can explain to each other how we weigh up the pluses and minuses for a particular intervention, then we will also be able to explain and discuss them more clearly and easily with patients. In that process we will come to understand better what our patients want and what they fear. When they too can weigh the pros and cons of treatments, they can better contribute to the therapeutic choice and are more likely to be content with it.

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REFERENCE

1. Early Breast Cancer Trialists’ Collaborative Group. Tamoxifen for early breast cancer: an overview of the randomised trials. *Lancet* 1998;351: 1451-67.

E-mail: Andrew_Herxheimer@compuserve.com

Tolterodine 2 mg twice daily for symptoms of unstable bladder

Benefits: During four weeks’ treatment, only 9% of patients had no or minimal bladder problems. On average patients voided 25 mL urine per micturition instead of 12 mL on placebo, and had one fewer incontinence episode every three days.

Harms: Headache. Anticholinergic effects – dry mouth, dry eyes, somnolence, nervousness, impaired accommodation, constipation, urinary retention; incidence stated as ‘>1–0.1%’. All wear off when the drug is stopped.

Comment: A minimally effective, but rather troublesome drug – hardly worth using.