Baseline risk

From: Key Concepts for assessing claims about treatment effects and making well-informed treatment choices (Version 2022)

3.2b Consider the baseline risk or severity of the symptoms when estimating the size of expected effects.

Explanation

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, consider 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 below). 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 *[Vandvik 2012]*.

Outcome	Relative risk reduction (95% confidence interval)	Risk without aspirin in the next 5 years	Risk difference (95% confidence interval)
Deaths	10% (1% to 18%)	133 per 1,000	13 fewer per 1,000 (1 to 24 fewer)
Strokes	19% (8% to 29%)	135 per 1,000	26 fewer per 1,000 (11 to 39 fewer)
Heart attacks	31% (20% to 40%)	117 per 1,000	37 fewer per 1,000 (23 to 47 fewer)
Serious gastrointestinal bleeds	169% increase (25% to 476%)	15 per 1,000	25 more per 1,000 (4 to 71 more)

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 1,000 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 1,000 in the next **five years**). The relative effect is also slightly lower. The absolute effect is six fewer heart attacks per 1,000 people who take aspirin for 10 years (see table below), compared to 37 fewer per 1,000 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.

Outcome	Relative risk reduction (95% confidence interval)	Risk without aspirin in the next 10 years	Risk difference (95% confidence interval)

Heart attacks	23% (14% to 31%)	27 per 1,000	6 fewer per 1,000 (4 to 8 fewer)
Serious gastrointestinal bleeds	54% increase (30% to 82%)	8 per 1,000	4 more per 1,000 (2 to 7 more)

Basis for this concept

Relative measures tend to be consistent across risk groups, but aren't always *[Deeks 2002 (RS), Engels 2000 (RS), Furukawa 2002 (RS), Schmid 1998 (RS)]*, as illustrated in the above example (see Concept 2.3b). The risk difference can be estimated by applying the relative effect to one or more relevant baseline risks, as illustrated in the tables above. Generally, the benefits of a treatment are less for someone with a low risk of an outcome compared to someone with a high risk. On the other hand, the risk of adverse effects is often the same (although it was not in the example above). Therefore, the benefits and harms of a treatment tend to be more closely balanced for people with a low risk of the condition being treated than for someone with a high risk. The same is true for people with more severe symptoms (e.g., pain or depression) compared to people with less severe symptoms.

Unfortunately, someone's baseline risk is often uncertain. Studies that estimate someone's risk or prognosis and systematic reviews of those studies have been scarce and often of poor quality, but both the quantity and quality of this research has been increasing *[Collins 2014 (SR), Debray 2017 , Matino 2017 (SR), Peat 2014 , Riley 2016 , Skoetz 2019 (SR)]*. Uncertainty in baseline risk estimates and its impact on confidence in absolute estimates of treatment effects are often not considered by guideline developers or systematic review authors *[Iorio 2015 , Spencer 2012]*, as illustrated in the tables above. However, important uncertainty about someone's baseline risk can reduce confidence in absolute effect estimates and increase uncertainty about the balance between the benefits and harms of a treatment *[Iorio 2015 , Spencer 2012]*.

Implications

When making decisions about treatments, consider the estimated baseline risk or the severity of symptoms.

References

Systematic reviews

Collins GS, de Groot JA, Dutton S, Omar O, Shanyinde M, Tajar A, et al. External validation of multivariable prediction models: a systematic review of methodological conduct and reporting. BMC Med Res Methodol. 2014;14:40. https://doi.org/10.1186/1471-2288-14-40

Matino D, Chai-Adisaksopha C, Iorio A. Systematic reviews of prognosis studies: a critical appraisal of five core clinical journals. Diagn Progn Res. 2017;1:9. https://doi.org/10.1186/s41512-017-0008-z

Skoetz N, Goldkuhle M, Weigl A, Dwan K, Labonté V, Dahm P, et al. Methodological review showed correct absolute effect size estimates for time-to-event outcomes in less than one-third of cancer-related systematic reviews. J Clin Epidemiol. 2019;108:1-9. https://doi.org/10.1016/j.jclinepi.2018.12.006

Research studies

Deeks JJ. Issues in the selection of a summary statistic for meta-analysis of clinical trials with binary outcomes. Stat Med. 2002;21(11):1575-600. https://doi.org/10.1002/sim.1188

Engels EA, Schmid CH, Terrin N, Olkin I, Lau J. Heterogeneity and statistical significance in meta-analysis: an empirical study of 125 meta-analyses. Stat Med. 2000;19(13):1707-28. https://doi.org/10.1002/1097-0258(20000715)19:13%3C1707::aid-sim491%3E3.0.co;2-p

Furukawa TA, Guyatt GH, Griffith LE. Can we individualize the 'number needed to treat'? An empirical study of summary effect measures in meta-analyses. Int J Epidemiol. 2002;31(1):72-6. https://doi.org/10.1093/ije/31.1.72

Schmid CH, Lau J, McIntosh MW, Cappelleri JC. An empirical study of the effect of the control rate as a predictor of treatment efficacy in meta-analysis of clinical trials. Stat Med. 1998;17(17):1923-42. https://doi.org/10.1002/(sici)1097-0258(19980915)17:17%3C1923::aid-sim874%3E3.0.co;2-6

Other references

Debray TP, Damen JA, Snell KI, Ensor J, Hooft L, Reitsma JB, et al. A guide to systematic review and meta-analysis of prediction model performance. BMJ. 2017;356:i6460. https://doi.org/10.1136/bmj.i6460

Iorio A, Spencer FA, Falavigna M, Alba C, Lang E, Burnand B, et al. Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients. BMJ. 2015;350:h870. https://doi.org/10.1136/bmj.h870

Peat G, Riley RD, Croft P, Morley KI, Kyzas PA, Moons KG, et al. Improving the transparency of prognosis research: the role of reporting, data sharing, registration, and protocols. PLoS Med. 2014;11(7):e1001671. https://doi.org/10.1371/journal.pmed.1001671

Riley RD, Ensor J, Snell KI, Debray TP, Altman DG, Moons KG, et al. External validation of clinical prediction models using big datasets from e-health records or IPD meta-analysis: opportunities and challenges. BMJ. 2016;353:i3140. https://doi.org/10.1136/bmj.i3140

Spencer FA, Iorio A, You J, Murad MH, Schünemann HJ, Vandvik PO, et al. Uncertainties in baseline risk estimates and confidence in treatment effects. BMJ. 2012;345:e7401. https://doi.org/10.1136/bmj.e7401

Vandvik PO, Lincoff AM, Gore JM, Gutterman DD, Sonnenberg FA, Alonso-Coello P, et al. Primary and secondary prevention of cardiovascular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e637S-e68S. https://doi.org/10.1378/chest.11-2306