References


4. TreeAge Pro. Williamstown, MA: TreeAge Software.


36. Freemantle N. Interpreting the results of secondary end points and subgroup analyses in clinical trials: should we lock the crazy aunt in the attic? BMJ. 2001 Apr 21,322(7202):989-91.


58. Freemantle N. Interpreting the results of secondary end points and subgroup analyses in clinical trials: should we lock the crazy aunt in the attic? BMJ. 2001 Apr 21,322(7202):989-91.


[1] (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ref32) Please note that, although not explicit on this diagram, the health needs of the family or whānau of the person receiving the treatment, and of wider society will be taken into consideration during our decision making process. This Factor is detailed in the Supporting Information that can be found on the PHARMAC website at www.pharmac.govt.nz/medicines/how-medicines-are-funded/factors-for-consideration/supporting-information/.

[2] (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ref22) Refer to Table 12: Reporting of Cost-Utility Analysis Results in Chapter 11 for further details on information to include in a CUA report when describing the disease, patient population and treatment options.


[5] (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ref21) The p value is the probability that an observed effect is due to sampling error; therefore, it provides a measure of the strength of an association. This section uses p values to notionally define statistical significance; however, it is noted that confidence intervals may better summarise the strength and precision of the effect estimate.

[6] (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ref6) Effect sizes with p values close to but not reaching statistical significance will be due to either one of two circumstances: (1) the effect is strong but the confidence interval is wide, because numbers of events, etc, are small; or (2) the effect is weaker but the confidence interval is narrower. In either case the p value being close to 0.05 means that the 95% confidence interval will only just include the value of 1.0 (ie a small but statistically significant chance that there is no effect). When deciding whether to still include such clinical events: (1) a strong effect will take precedence over a weaker effect; (2) a strong effect (wide confidence limits) means the effect is likely to be clinically important, being limited by insufficient power (where ‘absence of evidence is not evidence of absence’) (18 (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ref18)). Conversely, a weak effect with narrower confidence limits is unlikely to be clinically important (ie greater confidence but a negligible effect on outcomes).

[7] (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ftnref7) To help determine whether events are clinically significant, outcomes should be examined to determine whether their association with treatment is likely to be causal. Key criteria for determining causal associations include (19 (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ftnref12)): temporality (ie the cause must precede the effect); strength of association; consistency between different populations and different study designs; and a dose-response relationship (ie increased exposure is associated with an increased biological effect).

[8] (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ftnref6) For composite endpoints to be valid, the results of the individual endpoints of composite measures reported by clinical trials should be reported (20 (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ftnref2)). The number of individual endpoints should be minimised to preferably no more than three or four (21 (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ftnref12)). Component non-fatal endpoints should be measured appropriately, with the use of a blinded endpoints committee, a core laboratory, or both (21 (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ftnref12)), and analysis of non-fatal events should take into account competing risks. For information on the assessment of composite outcomes, please refer to the PBAC Guidelines for preparing a major submission (22 (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ftnref2)).


[10] (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ftnref2) Patient subgroups may have different responses to treatment or magnitudes of benefit. These subgroups may be defined by age, gender, other demographic factors, disease-related factors (symptom complexes, severities), comorbidities, or intractability and factors affecting treatment effectiveness. The degree of breakdown depends upon the complexity of the targeting decisions to be made. Some situations will require many subgroups, others just the overall group.

[11] (https://www.pharmac.govt.nz/medicines/how-medicines-are-funded/economic-analysis/pfpa/references/#ftnref7) Relevant statistical tests of interaction include the chi-square test using the Q statistic in an individual trial or the Cochran Q statistic across the pooled result, and the 12 statistic with its 95% uncertainty interval.

Subgroup treatment effects in a trial with no overall treatment effect are said to be usually superfluous subgroup salvages of otherwise indeterminate (negative) trials (33).

DALYs are expressed in terms of years of life lost due to premature death and years lived with a disability of specific severity and duration.

HYEs incorporate individual preference structures over a complete path of health states (rather than discrete health states).

This included negative values for health states considered to be worse than death (47). Survey results indicated that respondents can and do evaluate some health states as worse than death, and the study authors recommended the systematic inclusion of these states to describe a more complete range of preference values (48).

Logical inconsistency was defined as "when a state that 'in logical terms' is unambiguously less severe than another is assigned a lower value" (46).