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Probabilistic Analysis: Sensitivity Analysis or Main Result?

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Editorial

According to virtually all published Pharmacoeconomics guidelines, the base case analyses (understood as the main result) must be deterministic. That is, the main result of an economic model (the incremental cost-effectiveness ratio, ICER) is a fixed result and is not subject to any uncertainty analysis. For example, with deterministic base case analysis we can obtain an ICER of 10,000 € per QALY gained with a new drug versus the former, but we do not know what confidence can we accept this result and what is the likelihood that the drug is cost-effective for a certain willingness to pay. The one-way sensitivity analysis, usually presented as tornado diagram is a deterministic analysis very useful to determine which variables of the study drivers of the result are obtained in the base case. According to the NICE guidelines "wherever possible the results of the economic comparisons should be subjected to sensitivity analysis testing. For example, when data are drawn exclusively from clinical trials, 95% confidence intervals can be calculated for cost-effectiveness ratios. When data are drawn from a variety of sources and used in a modelling framework, probabilistic sensitivity analysis is recommended in order to take account of the uncertainty around data values" [1]. According to the ISPOR guidelines "for model-based economic evaluations, parameter uncertainty may be represented for individual parameters in a deterministic sensitivity analysis or across all parameters simultaneously with probabilistic analysis" [2]. The probabilistic sensitivity analysis, typically performed using second order Monte Carlo simulations, gives us an average ICER and, very important, the ICER 95% confidence interval 95% (in the previous example, ICER 95% CI: 9,500-11,200 €) and the probability that the new drug is cost-effective for a certain willingness to pay (for example, 89% for 30,000 € per QALY gained). These results are usually presented in a cost-effectiveness plane and acceptability curve. Therefore, it is clear that the result provides by probabilistic analysis is much more interesting and valid than that obtained from the deterministic analysis. Then, for what reason remains the latter as the main result for economic analysis in the published guidelines? In our opinion, the presentation of results of economic analysis should be done as indicated below. First, the probabilistic analysis (second order Monte Carlo simulation) should not be considered as a mere sensitivity analysis, but as the main study result, providing the average ICER, its 95% CI and the probability of cost-effectiveness of the new drug for different cost-effectiveness thresholds. The fixed deterministic result of ICER should be a secondary analysis, being of greater interest the presentation of the variables that most influence on the result as a tornado diagram. This proposal is not merely formal but, in our opinion, but based on the objectives and weaknesses of cost-effectiveness analysis. This way of presenting the results of cost - effectiveness would give greater clarity and consistency, especially in the case of economic models, which may have a high uncertainty about the values of the variables included. Since this is the main problem of economic models, it is logical that the main result of the study gives a clear answer to the question of uncertainty.

References

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2. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, et al. (2013) ISPOR Health Economic Evaluation Publication Guidelines-CHEERS Good Reporting Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) - explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. Value Health 16: 231-250.