Communicating the findings of health technology assessments: Considering uncertainty

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Abstract

Uncertainty is an unavoidable problem when analysing health technology assessment results, which can make decision making difficult. Whilst we have ways of presenting uncertainty for individual outcomes in a systematic review, we do not have a succinct and uncomplicated way to demonstrate the various sources of uncertainty across the clinical, applicability, and economic aspects of an HTA. This article discusses several sources of uncertainty that are present in health technology assessments and highlights certain challenges associated with reporting them. Transparency is key to ensuring that health technology assessments have the greatest utility for decision makers and that trustworthiness in the process is maximised.

Ever since the beginning of clinical research and more recently, health technology assessments (HTA), researchers have been dealing with uncertainty. The Oxford Dictionary defines uncertainty as "The state of not being definitely known or perfectly clear; doubtfulness or vagueness." In health, uncertainty may be due to ignorance or failure, and acknowledgeing uncertainty can be uncomfortable for clinicians.[2] Also, medical research is imperfect, many factors, both known and unknown, and modifiable and fixable, affect the results and impact on how much we can trust them. These uncertainties are not desirable characteristics to associate with big decisions[1] and may sound frightening in relation to health decision making.

Understanding the quality of the research, the limitations to its conduct, and its real world applicability is paramount to good decision making for both patients, carers and for policy and reimbursement decision makers. It is this understanding, interpretation, and application that elevates an HTA beyond its components of systematic review and economic analysis.

The work of HTA can be highly technical and complex, with many factors that contribute to the findings in both the clinical and economic assessments. It is a key task of health technology analysts to be able to identify the "important" results and communicate these effectively. End HTA users are often time-poor and are unlikely to read the complete technical documents associated with a full HTA that includes a comprehensive systematic review and full economic modelling. In Australia, for example, the committee charged with making recommendations for public funding on medical devices and tests (Medical Services Advisory Committee, MSAC) consider as many as twenty new devices at each triannual meeting. The equivalent committee for assessing drugs (Pharmaceutical Benefits Advisory Committee, PBAC) may consider the same number of new drug listings as well as applications for changes to current listings. As producers of HTAs, we understand this and are under increasing pressure to condense our findings into the most succinct form possible, making sure that the important issues are highlighted. Whilst this is mostly achievable when communicating *results*, it is more difficult when it comes to communicating *uncertainty* around those results. This paper will discuss some of the uncertainties that may be present in the clinical and economic components of HTAs and will highlight some of the ways that these uncertainties can be addressed when presenting an HTA.

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Sources of uncertainty

Within the clinical assessment section of an HTA (i.e. the assessment of safety, efficacy, and effectiveness), uncertainty can arise from the type and quality of available evidence. We know that the randomised controlled trial (RCT) is the gold standard of interventional research (such as new medicines or devices). But whilst there are many thousands of RCTs produced every year, there is not always RCT evidence available for the intervention (or population, or comparator) of interest. With new technologies, the evidence base is sometimes immature, with too few large or rigorous studies conducted to ascertain efficacy and safety with any certainty. In other cases, there may be a large body of evidence, but of studies lower on the hierarchy of study design,[3] such as was found in a Canadian HTA of implants for hearing loss.[4] In this HTA, 20 systematic reviews were included, but the vast majority of the primary evidence was from small case series, in which patients were studied before and after the intervention. These types of studies are not as reliable as RCTs, giving lower confidence in the evidence overall. Other evidence bases may demonstrate heterogeneity in uncertainty across distinct parts of the evidence base such as particular outcomes, population sub-groups, or follow-up periods. This can be evident with safety outcomes in particular, where RCTs are often underpowered to detect rare but important adverse events. This was seen in a systematic review of safety outcomes for the human papillomavirus vaccine undertaken for the World Health Organization, where despite the many well-designed and large size RCTs included, rare adverse events were generally not identified.[5] If other information about safety is not available, such as from large observational studies or studies including real world evidence (such as administrative databases from hospitals or

primary care), this can leave a gap in the knowledge about key clinical outcomes.

Of course, an RCT is not a guarantee for quality. RCTs are subject to methodological bias, which results in uncertainties in the findings. In fact, well-designed and executed observational studies can be more trustworthy than poorly designed and executed RCTs. It is very common for the evidence base in an HTA to contain more than one study type, and for the quality across the outcomes – and the studies – to be mixed. The tasks of understanding the sources of uncertainty and interpreting their importance across the body of evidence in these types of HTA is challenging.

Understanding uncertainty can be compounded within economic analyses undertaken for HTA as the multiple inputs into economic models can have varying levels of uncertainty. The incremental cost effectiveness ratio (ICER), a measure of the extra cost associated with a unit of extra benefit, commonly a quality-adjusted life-year, is now the preferred metric for decision making in many jurisdictions, but this approach often relies on a number of assumptions to estimate the health gain and the utilities associated with various health states, and to extrapolate over time. Uncertainty in economic models is typically explored through scenario and sensitivity analyses, for example where the smallest and largest plausible estimates for model inputs are tested to see the impact on the results.[6] The uncertainty around various aspects of these models can be described in different ways, but it is safe to say that these highly complex and extremely technical analyses can be difficult for non-economists to grasp. Again, we rely on the analyst to help the reader understand where the uncertainty lies and how it impacts the result.

Uncertainty can also arise through applicability. Applicability refers to the ability of a new technology to fit into the existing landscape of clinical practice, infrastructure, and policies. To show applicability, the evidence base requires assessing the technology and intervention within the population and setting appropriate for its intended use. This may include considering clinical and demographic factors in the study the populations, including the disease spectrum, and technology delivery. Applicability uncertainty may be extrapolated to more pragmatic issues: Does the technology require specific workforce training or accreditation? What equipment is required, and can it be housed within existing infrastructure? Can all people who will be eligible to receive the technology access it? Is there likely to be "leakage", i.e. uptake of the technology by

Table 1. Issues to consider when reporting results of HTA

Concept	Description
Clinically important effects	Distinguish between clinically important and statistically significant effects; statistical uncertainty can be unrelated to the intervention, whereas clinically important effects are more likely to be related to the intervention
Patient-relevant outcomes	Prioritise the reporting of findings in patient-relevant outcomes when considering safety and effectiveness, and prioritise direct outcomes over surrogate outcomes
Compounding uncertainty in economic models	Consider that uncertainty in the clinical (and other) evidence used in any economic modelling will also have an impact on the results and could be multiplied when several uncertain inputs are used. If appropriate, best- and worst-case scenarios can be helpful as they are easily understood.
Case of no or insufficient evidence	Be explicit about where there is no evidence; where there is insufficient evidence (and why); and, where there is heterogeneity across the evidence base, e.g. some outcomes are uncertain and some are more certain. This helps decision-makers understand where the limitations are.
Recipients	Consider the differences between the needs of policy makers or funders (for whom the HTA is designed) and the needs of consumers, especially with regard to language and use of statistics.
Visual representations	Where appropriate, results can be presented visually. There is no standard way of visually representing uncertainty, but some ideas include a traffic light system or a thermometer-style measure (cold=uncertain, warm=more certain)

people it is not intended for? Some of the time, assessors can only provide their best guess about implementation, but it is this contextualisation of "evidence" that makes HTA such an essential tool to decision making.

Communicating results in an HTA

As illlustrated, interpreting the results of an HTA is complex. Knowing that the end users are not always able to digest a full technical report – which can run to hundreds of pages – the assessor must therefore summarise the results accurately and succinctly. Specifically, this often means using dot points, summarising in tables or figures, and making tough decisions about what information should go "up front" in a report.

In recent years primary research communication, has gained from the advent of visual abstracts and now, influential, international journals such as the BMJ and JAMA routinely publish them. Visual abstracts are not intended to replace reading the full article but to attract the reader's interest. Usually, they summarise methods and results, but rarely study limitations. They are also a useful means of communicating medical research on social media. Ramos and Concepcion (2020) reported that social media posts with visual abstracts had higher engagement rates than posts without pictures or than other types of visual post (such as tables or graphs from the study).[7] Whilst this engagement is desirable, the authors also acknowledge that the succinct nature of a visual abstract could lead to misinterpretation and oversimplification of the study results. Oversimplification is a major risk when presenting the results of an HTA if the uncertainty associated with the results is not communicated.

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A key way of communicating uncertainty in the clinical component is to use GRADE (Grades of Recommendation, Assessment, Development, and Evaluation).[8] This tool, designed for guideline developers, enables assessors to appraise the quality of the evidence by outcome, taking into account factors such as the risk of bias in the included studies, inconsistency, and publication bias. In the US, the Agency for Healthcare Research and Quality have a similar tool.[9] Although GRADE is widely used, it is not without its issues, particularly around automatic downgrading of observational studies. Moreover, although it can provide information about strength of evidence for individual outcomes, it does not provide an overall assessment of the intervention, taking into account all the possible benefits and harms. In HTA, findings need to be communicated across a range of desirable and undesirable outcomes and decisions made on whether the benefits of an intervention outweighs the harms, within the context of the proposed clinical setting.

The key aspect of all forms of communication of results is transparency. This is especially true for uncertainty, as it is more difficult to communicate and understand than simple "results".

Considerable work has been done to assess the best way to present results, especially to patients, but the best way to communicate any uncertainty associated with those results is much more difficult and has not been studied extensively. Uncertainty in findings may or may not influence decisions, but it always needs to be considered. Being clear, direct, and comprehensive in describing the findings of an HTA is vitally important to both the utility of the work and to its trustworthiness. The documentation of all methods (such as the choice of inputs for economic models, reasons for downgrading or upgrading of evidence) and their justification is essential to ensure that end users are properly informed for decision making.

Comprehensive explanations can rarely be summarised in dot points, however – and herein lies the issue. How do we communicate the important aspects of uncertainty in an HTA in a way that is succinct but understandable? Tools like GRADE use a visual representation of solid and hollow circles to illustrate certainty for individual outcomes. When considering a whole HTA (with clinical, applicability and economic outcomes) a succinct visual tool is needed to express the heterogeneity of uncertainty across all parameters. Today, there is no standard method for representing uncertainty, and further research is required to determine a suitable method. Some ideas include a visual representation of uncertainty, such as a traffic light system, alongside key results, or using different colour or font text for different levels of uncertainty. This could be especially helpful for interpreting the results of economic analyses.

On the other hand, we need to be careful that we do not fall into the trap of oversimplifying results. HTAs are complex and technical, and explanations that provide adequate transparency can be necessarily lengthy. We need to strike a balance between thorough reporting of results – including uncertainty – and summaries that are useful and accurate.

Some of the issues to consider when communicating results of an HTA are explained in Table 1. This list is by no means exhaustive but may provide a starting point for medical writers to think about how they can contribute to transparency and the understanding of the limitations of an evidence base.

HTAs are an increasingly important tool in decision making worldwide, and their methodology has developed, and continues to develop, alongside this growth. To ensure the greatest utility and to encourage trust in HTA, we must continue to work towards complete transparency when reporting all aspects of the HTA. Policy makers and funders also need to be transparent in their decision-making processes. As HTAs are often read only in summary form, medical writers need to carefully consider how uncertainty associated with the findings in abridged versions of reports is conveyed. Uncertainty does not need to be a sign of weakness, and an acknowledgement that it exists and a description of how it has been approached add credibility to research. As the battle against misinformation and mistrust in science rages on, it has never been more important to be transparent and trustworthy.

Disclaimers

The opinions expressed in this article are the author's own and not necessarily shared by her employer or EMWA.

Conflicts of interest

The author declares no conflicts of interest.

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