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CORRESPONDENCE

HIQA's Perspective on the Challenges Posed by Evaluations of Screening Programs: A Reply

Teljeur et al. [1] recently replied to a critique of the Health Information and Quality Authority's (HIQA's) decision to publish average cost-effectiveness ratios (ACERs) as incremental cost-effectiveness ratios (ICERs) in a health technology assessment (HTA) [2]. The reply raises important questions about the attitude of Ireland's HTA authority toward simulation analysis and merits further comment.

HIQA published a HTA of breast screening for women at elevated risk of breast cancer that reported ICERs estimated on the basis of each simulated screening strategy relative to no screening [3]. The critique noted that such ratios are more commonly known as ACERs and have long been recognized as an inappropriate basis for the efficient health care resource allocation [2]. HIQA replied with four principal points: 1) the body that commissioned HIQA's HTA, the National Cancer Control Programme, was seeking to standardize screening in a way that was no less effective or more costly than the current practice; 2) using data on diagnostic test performance rather than mortality reductions creates uncertainties, and ideally it would be preferable to use long-term mortality data; 3) test performance characteristics estimates in the model were primarily from studies with screening intervals of 12 months, and thus simulation estimates for other screening intervals for which there is less test performance data are less reliable; and 4) the absence of supporting data meant that some strategies were not considered acceptable to clinicians (presumably those on HIQA's HTA expert review group) [1].

Regarding point 1, specifying a constraint that any new service must be at least as effective as the status quo is arbitrary and may inhibit a HTA from identifying the most cost-effective strategy. Nevertheless, it may be necessary to accept that decision makers might have objectives that deviate from both the goal of maximizing population health and the assumption typical in cost-effectiveness analysis (CEA) that the health of all people is treated equally.

The question of the appropriate objective of the CEA is, however, primarily the responsibility of the decision maker rather than HIQA as the analyst. Moreover, HIQA has not explained why the existence of an alternative policy objective justifies reporting ACERs as ICERs. Indeed, there appears to be no good reason why choosing strategies at least as effective as the status quo merits departing from the correct presentation of ICERs according to their conventional definition. On the contrary, if policymakers wish to privilege certain patient groups by departing from standard CEA recommendations, then it seems ever more important that the cost-effectiveness implications of such decisions be made plain and that this is best achieved by adhering to the conventional definition of the ICER.

Points 2 to 4 made in HIQA's reply relate to the reliance on simulation modeling rather than trial evidence. HIQA makes a number of fair points regarding the challenges of combining multiple sources of data of varying quality and completeness on different interventions and the resulting uncertainty in costs and effects estimates. The HTA considered various combinations of imagining modalities (mammography alone, magnetic resolution imagining [MRI] alone, and mammography and MRI combined) at screening intervals of 1 and 2 years. HIQA's reply explains that there is more uncertainty relating to the performance of certain modalities (MRI alone) and screening intervals (2 years) because of less supporting trial evidence. Indeed, it is true that a lack of direct, long-term evidence of the effectiveness of each and every possible screening strategy does contribute uncertainty to the optimal choice. Consequently, there may be more uncertainty in the costs and effects estimates of some strategies than others. It also follows that the ICERs between strategies might be more uncertain than the ACERs relative to no screening. Nevertheless, this does not overcome the fact that ACERs are not the correct measure of cost-effectiveness to use.

We must remember that the policy choice is between different screening alternatives rather than necessarily between each screening alternative and doing nothing. Although the absolute uncertainty in the costs and effects estimates of some strategies might be greater than others, the pertinent source of uncertainty to consider is not attached to each strategy alone, but relates to the incremental choice between strategies. We cannot escape uncertainty regarding the optimal policy by selectively ignoring certain strategies. Excluding relevant strategies from the calculation of ICERs on the grounds of uncertainty runs counter to the International Society for Pharmacoeconomics and Outcomes Research and the Society for Medical Decision Making recommendations that the choice of comparators should not be determined by the availability and quality of data, but rather that all feasible strategies should be considered [4]. Furthermore, we must acknowledge that presenting ACERs as ICERs provides a measure of cost effectiveness that is necessarily biased, because ACERs are typically less than correctly estimated ICERs. In brief, an understandable preference for greater certainty does not justify presenting biased, incorrect estimates.

I now move on to the more general point regarding the status of modeling evidence, which is the primary motivation for this letter. This relates to the statement in HIQA's reply that reads "An assessment that recommends screening strategies for which the only evidence of efficacy or effectiveness has been generated by a modeling exercise lacks external validity and therefore may be of little or no use to a decision maker and undermine the

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credibility of HTA" [1]. This statement was made in the context of a lack of direct, long-term trial evidence regarding certain screening modalities. It implies a distinction between strategies that are sufficiently well supported by evidence to be considered in analysis and those that are not. This is a very significant statement for a HTA agency to make, because it appears to cast doubt over potentially a very large amount of simulation evidence used in health care resource allocation.

The uses and limitations of modeling have been assessed in the context of cancer screening [5]. It is widely recognized that a direct assessment of all relevant alternatives using mortality outcomes is infeasible in the context of cancer screening, because the size of trials and the length of follow-up required are prohibitive [6]. Accordingly, the commonly accepted approach is to combine what limited trial and other data are available from various sources regarding various outcomes in a simulation model [5]. There will always be a variation in the level of evidence supporting different strategies, because some will have more parameters that can be directly observed from trials, whereas others will rely more on inference. Clearly, it would be mistaken to believe that there is some clear, discrete distinction between strategies that are supported by trial evidence and others that are not; in reality, the potential strategies will lie on a continuous spectrum between those largely supported by direct evidence and those more reliant on simulation evidence.

It is undeniably difficult to determine at what point on that continuum does simulation cease to be an acceptable basis for resource allocation. Indeed, any attempt to determine that point is open to the charge of imposing an arbitrary threshold. Consequently, HIQA is in the unenviable position that no matter where they draw that line, they will be open to criticism.

There remain four more points to note regarding HIQA's rejection of certain strategies. The first relates to the problem that considering only those strategies that have considerable supporting trial evidence is likely to lead to biased cost-effectiveness estimates. Although the primary strategies of interest might be supported by trial evidence, the exclusion of other strategies may deprive an analysis of comparator strategies against which we typically compare to estimate ICERs. It is likely that untrialed comparator strategies will be typically of lower intensity than the trialed primary strategies of interest, because they may use single test modalities and longer screening intervals. The exclusion of such simulated comparators will likely lead to the systematic underestimation of ICERs.

The second point relates to the role of clinicians in determining which strategies are sufficiently supported by evidence for inclusion. There is always likely to be a tension between a clinical perspective that may tend to focus primarily on the candidate recipients of the intervention under consideration as opposed to the broader perspective used by health economists, which also considers the health of those patients who will bear the opportunity cost of funding decisions. Health economists might be concerned if clinicians involved in the HTA process as members of the expert review group are apparently able to veto the inclusion of certain strategies. Indeed, although HIQA points out that the inclusion of certain strategies could compromise the credibility of a HTA from a clinical perspective, it should also be recognized that the exclusion of certain strategies can conversely compromise the HTA's credibility from a cost-effectiveness perspective.

Third, it is important to ask what are the implications of HIQA's stance on the exclusion of strategies with respect to other cancer screening HTAs published by HIQA before and since [7,8]. In particular, it is worth noting that fecal-based immunochemical tests have never been assessed in randomized controlled trials [9], but were subject to a correct incremental analysis when included in HIQA's 2009 HTA of colorectal cancer screening [7]. An obvious question of consistency arises when some HTAs feature multiple testing modalities with alternative screening intervals that were subject to the correct incremental comparisons in a way that the strategies in the breast screening HTA were not.

Finally, in noting that decisions would ideally be made with long-term outcome data rather than surrogate outcomes, HIQA's reply states that some HTA agencies do not accept diagnostic test accuracy as evidence of effectiveness (although HIQA does not cite which agencies) [1]. HIQA did not make it clear whether they endorse this position. Although there may be an apparent appeal to a perspective that places primacy on longer term outcomes such as mortality reductions, we must remember that modeling is adopted precisely because we do not have the benefit of all such data. We choose to model because we believe it brings advantages over relying on the limited comparisons of trial outcomes. We must remember to balance the benefits of modeling when rightly considering its limitations.

Overall it is unclear how to best interpret HIQA's choice of excluding certain simulated strategies. It could be seen as a very broad repudiation of modeling methods in general and a strong preference for only intervention strategies supported primarily by trial evidence. This would be troubling because it is difficult to adequately assess most screening strategies without at least some simulation analysis for the reasons described earlier. It would both severely limit the range of strategies that could be considered and, importantly, curtail the basis for incremental analysis of cost effectiveness. A more benign interpretation is that HIQA's statement does not constitute a dismissal of modeling methods and that it simply reflects an aversion to heavy reliance on model estimates that are only indirectly supported by empirical data. Which interpretation is closer to the truth remains unresolved.

In conclusion, HIQA has apparently attempted to justify the presentation of ACERs as ICERs on the basis of two primary arguments: 1) the decision maker had a specific objective that differed from simple health maximization and 2) certain strategies carry considerable uncertainty and therefore can be excluded from incremental analysis. Neither argument provides a sound justification for presenting ACERs as ICERs. More broadly, HIQA's comments on the unacceptability of strategies with effectiveness estimates that rely more on simulation analysis rather than trial data cast doubt over the standing of modeling in resource allocation in Ireland. Establishing the boundaries of what constitutes acceptable evidence is admittedly not easy, but further debate would usefully clarify the appropriate use of HTA modeling in health resource allocation.

James F. O'Mahony, PhD
Centre for Health Policy and Management
School of Medicine
Trinity College Dublin
Dublin, Ireland

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