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CURRENT OPINION

The Irish Cost-Effectiveness Threshold: Does it Support Rational Rationing or Might it Lead to Unintended Harm to Ireland's Health System?

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Abstract Ireland is one of the few countries worldwide to have an explicit cost-effectiveness threshold. In 2012, an agreement between government and the pharmaceutical industry that provided substantial savings on existing medications set the threshold at €45,000/quality-adjusted life-year (QALY). This replaced a previously unofficial threshold of €20,000/QALY. According to the agreement, drugs within the threshold will be granted reimbursement, whereas those exceeding it may still be approved following further negotiation. A number of drugs far exceeding the threshold have been approved recently. The agreement only applies to pharmaceuticals. There are four reasons for concern regarding Ireland's threshold. The absence of an explicit threshold for non-drug interventions leaves it unclear if there is parity in willingness to pay across all interventions. As the threshold resembles a price floor rather than a ceiling, in principle it only offers a weak barrier to cost-ineffective interventions. It has no empirical basis. Finally, it is probably too high given recent estimates of a threshold for the UK based on the cost effectiveness of services forgone of approximately £13,000/QALY. An excessive threshold risks causing the Irish health system unintended harm. The lack of an empirically informed threshold means the policy recommendations of cost-effectiveness analysis cannot be considered as fully evidence-based rational rationing. Policy makers should consider these issues and recent Irish legislation that defined cost effectiveness in terms of the opportunity cost of services forgone when choosing what threshold to apply once the current industry agreement expires at the end of 2015.

Key Points for Decision Makers

Ireland is one of the few countries worldwide to have an explicit cost-effectiveness threshold.

The current threshold of €45,000/QALY only applies to drugs, is non-binding, lacks an empirical basis and is probably too high.

The Irish threshold needs to be revised to better account for the opportunity cost of other interventions forgone.

1 Introduction

Rationing healthcare presents profound ethical challenges, but is inevitable due to resource scarcity. Cost-effectiveness analysis (CEA) facilitates the allocation of scarce resources to their most effective use by comparing the benefits of candidate healthcare interventions to their opportunity cost of other services foregone. The standard CEA decision rule employs a cost-effectiveness threshold as a proxy for this opportunity cost. Accordingly, it is important that cost-effectiveness thresholds are set appropriately for both the technical objective of maximising health gain and for the weighty ethical burden placed on

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CEA in informing decisions on which services are provided and which are withheld.

Ireland is one of the few countries worldwide to have an explicit cost-effectiveness threshold. It currently stands at €45,000/quality-adjusted life-year (QALY). The National Institute of Health and Care Excellence (NICE) in England and Wales has an explicit threshold range of £20,000–£30,000/QALY [1], which is approximately €31,000–€47,000/QALY following purchasing power parity (PPP) adjustment. Norway also has an explicit threshold, which is NOK 500,000/QALY (approximately €64,000/QALY following PPP adjustment) [2], although this threshold is considered indicative and is not always adhered to.

The appropriate basis for the cost-effectiveness threshold has been debated extensively [3–6]. The approaches advocated include historical precedent; stated preference willingness-to-pay studies; value of a statistical life estimates; and macroeconomic variables such as GDP per capita [7, 8]. Nevertheless, the approach that is most consistent with CEA's theoretical basis is to determine the threshold with respect to the cost effectiveness of the opportunity cost of interventions foregone to fund new interventions [9, 10]. Notably, this approach has recently been applied in the UK to derive a threshold based on the cost effectiveness of displaced services [11].

This commentary critiques the current Irish cost-effectiveness threshold. The background section explains the current threshold and its origins. The analysis then outlines four reasons why the threshold may not be serving its intended purpose of enhancing resource allocation in the Irish health service. Finally, the discussion section considers some caveats to the critique and outlines what response is required from decision makers.

1.1 Background

Ireland has two primary public bodies with responsibility for CEA. The National Centre for Pharmacoeconomics (NCPE) reviews industry submissions on new drugs. The Health Information and Quality Authority (HIQA) conducts and commissions health technology assessments, primarily of non-drug interventions. The recommendations and advice of both bodies are non-binding and the decision-making authority rests with the Health Service Executive (HSE), the public body with responsibility for delivering state-funded healthcare in Ireland [12, 13]. In the case of drugs, the decision maker is the Products Committee of the HSE's Corporate Pharmaceutical Unit [13]. In the specific case of cancer drugs, the National Cancer Control Programme has its own Technology Review Committee that also assesses new products [14]. Setting the cost-effectiveness threshold is not within the remit of either the NCPE or HIQA.

The formal requirement for CEA of new drugs was introduced as part of a 2006 agreement between the HSE and the Irish Pharmaceutical Healthcare Association (IPHA), a representative body of the Irish pharmaceutical industry in Ireland [15]. For several years following the 2006 agreement, CEAs used a threshold of €45,000/QALY [16]. This threshold was not considered an official or fixed threshold [13, 17], and no basis for its level has been published. The threshold was apparently revised down to €20,000/QALY [18, 19], as from late 2009 this lower threshold began to appear in NCPE reports. There was no official statement on the large threshold reduction, but it presumably was a consequence of the severe budget pressures resulting from Ireland's fiscal crisis, manifest in the reductions in total nominal public health expenditure of approximately 5 % in both 2010 and 2011 [20, 21].

The Irish threshold became explicit for the first time in November 2012 as a result of a renewed agreement between IPHA, the Department of Health and HSE (henceforth *the agreement*) [22]. It was agreed as part of a 3-year service and pricing arrangement that provided gross cost savings of €400M on existing medications, of which €210M would be made available to fund new drugs over its duration [23].

The agreement revised the threshold back to €45,000/QALY. As the agreement only mentions medicines provided under the General Medical Services and Community Drugs schemes, there remains no alternative official statement regarding what threshold applies to non-drug interventions. The agreement states that products not exceeding the threshold are to be adopted, while those exceeding the threshold are not necessarily rejected, but may be put forward for further consideration. The agreement does not explain how the threshold was set or make reference to the opportunity cost of displaced services.

2 Analysis

2.1 No Explicit Threshold for Non-Drug Interventions

The IPHA agreement only applies to drug interventions. Accordingly, the threshold detailed in the agreement does not apply to other non-drug interventions including vaccines, medical devices, surgical procedures and other interventions. The HSE and the Department of Health have not issued any analogous guidance on the decision rules for aspects of care not covered by the IPHA agreement. The lack of an explicit threshold for non-drug interventions despite the existence of the threshold for drugs has been noted by HIQA [24]. Consequently, it is unclear what threshold applies to non-drug interventions.

This lack of clarity is particularly important given that prior to the IPHA agreement the threshold had apparently been revised down to €20,000/QALY. The guidelines for the economic evaluation of health technologies in Ireland are published by HIQA. The current guidelines note that the threshold has varied between €20,000 and €45,000/QALY and require the reporting of the probability of cost effectiveness for both threshold values when assessing cost-effectiveness acceptability curves [12]. Accordingly, it is unclear if the threshold for non-drug interventions has been left at €20,000/QALY or has also been revised back to €45,000/QALY.

In principle, if different classes of interventions are subject to different thresholds, then this raises the possibility of inefficiencies and inconsistencies. For example, if the lower threshold of €20,000/QALY were applied to non-drug interventions, this would create the possibility that funds could be allocated to pharmaceuticals while being withheld from more cost-effective non-drug applications elsewhere. Such allocations would thereby fail to maximise overall health gain from the available budget. They would also prompt equity concerns, as some patients receive the drugs they need, whereas others requiring non-drug interventions of comparable cost effectiveness are denied care.

In practice, there is no evidence that a lower threshold is being applied to non-drug interventions. Three health technology assessments featuring CEAs published by HIQA since the IPHA agreement all mention a €45,000/QALY threshold, indicating that a common threshold is being applied to all interventions [24–26]. Nevertheless, it is still concerning that a threshold has not been made explicit for all interventions: a clear decision rule has been articulated for a class of healthcare interventions backed by the strong proprietary interests of drug manufacturers, but the same clarity has not been provided for other components of healthcare.

An important caveat to the concerns about the lack of a non-drug threshold is that not all non-drug interventions are currently subject to CEA in Ireland. All new pharmaceuticals seeking reimbursement must undergo an assessment by the NCPE. There is no mandatory parallel CEA assessment process for drugs provided by hospitals, vaccines, medical devices, surgical procedures and other interventions. Only some will be subject to a formal CEA as part of a HIQA health technology assessment. So while 45 drugs have undergone a full submission review at the NCPE from the start of the current IPHA agreement to date, three interventions have been referred to HIQA for assessment over the same period. Similarly, while cost-effectiveness evidence is now being reviewed as part of the national clinical guidelines development programme conducted by the National Clinical Effectiveness Committee [27], there is apparently no binding decision framework regarding cost effectiveness as part of this process.

2.2 The Threshold Resembles a Price Floor

The threshold is conventionally interpreted as the upper bound on the cost per QALY that should be funded [10, 28]. In principle, adopting interventions with incremental cost-effectiveness ratios (ICERs) exceeding the threshold results in net harm to the health system, as more health is foregone than gained. However, since the Irish threshold in principle ensures reimbursement for interventions within it and does not provide a binding constraint to those exceeding it, the threshold appears less of a price ceiling and more of a price floor.

The potential for little positive net health benefit to accrue to health systems when manufacturers price to the threshold has been noted previously [9]. If the threshold functions as a price floor, then there is *no* scope for accruing positive net benefit and only a weak constraint on interventions that impose net harm on the health system.

In practice, that the Irish threshold resembles a price floor rather than ceiling may matter less. The agreement stipulates that products granted reimbursement should be funded at the lesser of either the approved submitted price or a European reference price, so there is some scope for positive net benefit if the reference price is lower than the threshold price. Furthermore, while the ICERs on approval are typically not published, there is evidence that manufacturers are submitting prices below threshold in some instances. For example, apixaban and nalmefene have been assessed and recommended for adoption with ICERs of €11,000/QALY and €7800/QALY, respectively [29, 30].

While some products are apparently being priced below the threshold, there are also drugs that the NCPE have not been able to recommend due to a failure to demonstrate cost effectiveness, which nevertheless have been adopted by the HSE. Some have ICERs far exceeding the threshold; for example, cabazitaxel, vemurafenib and pertuzumab at €110,000/QALY, €123,000/QALY and €203,000/QALY, respectively (note that the effective ICERs of these interventions may be somewhat lower as a result of price reductions secured as part of patient access schemes, although the extent of any discounts are not published) [31, 32]. So, while the threshold might not function as a price floor in practice, the approval of ICERs in excess of the threshold draws attention to the remaining issue of the lack of a stated price ceiling. Unlike the UK threshold range, the Irish threshold lacks an upper bound. Furthermore, the reasons for acceptable exceptions to the threshold are not justified: either ex ante, in terms of guidelines detailing the criteria according to which ICERs above the threshold are acceptable, including explicit weights to quantify the extent of any breach of the threshold; or ex post, in terms of documentation of the approvals decisions made by the

Corporate Pharmaceutical Unit or the National Cancer Control Programme Technology Review Committee.

2.3 Lack of Empirical Basis

Neither the current threshold nor its unofficial predecessors have been justified by empirical evidence, either of opportunity cost or willingness to pay. This lack of an empirical basis for the threshold presents a profound challenge to the notion of CEA as a tool of evidence-based policy making. While the costs and effects of candidate interventions are carefully appraised by experts at the NCPE and HIQA, this evidence only represents half of the decision problem, as there is no evidence regarding the opportunity cost of candidate interventions. Without evidence of the opportunity cost, the resulting policy guidance cannot be truly considered evidence-based and it leaves it disconcertingly unclear whether current reimbursement decisions are enhancing the health system.

Although the lack of an empirical basis for the threshold is a profound problem, it is not unusual given practice elsewhere. Most countries do not employ explicit thresholds at all and the most notable example of an explicit threshold as used by the NICE in England is also not supported by evidence [33].

2.4 Likely to be Excessive

While NICE's threshold also lacks an empirical basis, the IPHA agreement came at a time when initial estimates of an empirically informed threshold for the UK were being made with reference to the opportunity cost of displaced services [34]. Although the methods used in this recent work have already prompted debate and the estimates vary widely depending on the assumptions made [11, 35, 36], the central estimate of £13,000/QALY (approximately equivalent to €20,000/QALY, PPP adjusted) is significant as it is markedly lower than current thresholds.

The British and Irish health systems differ in many ways, so it would be mistaken to assume that the same threshold should necessarily apply. Indeed, the Claxton et al. estimates are specific to the particular patterns of displacement observed in the UK [11]. However, there are also many similarities between the two countries, not least in terms of per capita income and health spending, so estimates from the UK could be considered broadly indicative of what should apply in Ireland. Therefore, the recent UK estimate naturally prompts concern that the Irish threshold may be excessive. Indeed, that the empirical threshold estimate is much lower than that currently employed previously prompted the Economic and Social Research Institute, Ireland's primary independent public policy research body, to question if the current threshold is appropriate [37]. Similarly, HIQA have also noted that the UK empirical threshold estimate is considerably lower than €45,000/QALY [24].

While the UK empirical threshold estimate is informative when considering the appropriate threshold for Ireland, there is arguably more directly relevant evidence available from within the Irish health system in the form of unmet need. In part, this unmet need is reflected by the long waiting lists for some services [38]. The examples of waiting lists for the three common elective surgical procedures of hip replacement, knee replacement and cataract removal were 1639, 1293 and 8491, respectively, as of August 2015, of which 40, 46 and 53 % were for waits of 6 months or more [39]. A recent comparison of waiting times in OECD countries showed that the median waiting times for these three procedures were between two to three times longer in Ireland than in Sweden [40]. Recent cost-effectiveness estimates for each of these examples from the UK shows them to be highly cost effective, with ICER estimates of approximately £2100/QALY, £5600/QALY and £2000/QALY for hip replacement, knee replacement and cataract removal, respectively [41–43]. That such highly cost-effective interventions lack timely access in Ireland gives reason to question whether the threshold should be maintained at its current level.

3 Discussion

That Ireland's threshold is explicit for at least some interventions is arguably a good thing. Thresholds can bring transparency to decision making and promote fairness in the allocation of resources [44]. Although thresholds have recognised theoretical and practical shortcomings [7, 45], they are probably better than employing no clear decision rule at all. Nevertheless, the benefits of CEA will only be realised if thresholds are set appropriately and implemented correctly.

The purpose of CEA is to balance the identified benefits of adopting new interventions with the often unidentified costs of care foregone elsewhere. A high or seemingly generous threshold stands to benefit recipients of new interventions, but these benefits will be more than outweighed by the costs of health foregone if the threshold is too high. The result is at best a perpetuation of inefficiency and at worst a net harm to the health system [46, 47]. However, if thresholds are not subject to careful examination, then the risk is that inefficiencies and net harms will go unnoticed and unchecked. Therefore, the level and scope of cost-effectiveness thresholds need to be considered carefully to avoid systematic harm to the health system.

Any critique of thresholds needs to acknowledge that cost effectiveness is not the only decision criterion. Rather, cost effectiveness is one part of the broader health technology assessment process that must consider clinical, ethical and social concerns as well as the practical constraints of budget impact and legal issues [12]. Indeed, the approval of interventions with ICERs above the threshold is itself evidence that factors other than cost effectiveness are important within the decision process. Nevertheless, thresholds remain centrally important to the balancing of a range of important factors between intervention recipients and those patients bearing the inevitable opportunity cost. Indeed, the presence of other factors influencing decisions does not obviate the need to set the threshold appropriately or to carefully consider whether breaching it is justified or not.

While many of the problems with the current threshold could be resolved by revising it in accordance with evidence of the cost effectiveness of services forgone, questions regarding how binding the threshold should be will remain. The current NICE decision rules embody a notable degree of flexibility, as the threshold is a range in which a number of explicitly stated factors also influence the probability of approval [1]. Similarly, there are special criteria for end-of-life care that permit interventions with ICERs beyond the threshold range [48]. Moreover, analyses of NICE's decisions indicate that the effective threshold range is higher than that explicitly stated [49, 50]. Furthermore, the UK provides separate funding for some cancer treatments that fail to demonstrate cost effectiveness [51]. Opinions differ on whether thresholds should be 'hard' or 'soft' [52], and although full consideration of this debate is beyond the scope of this article, it remains appropriate to ask just how 'soft' the Irish threshold should be. While some flexibility is likely to be supported by health economists and will probably remain a pragmatic political necessity, it is important that the threshold does not become too soft as to become meaningless.

Unfortunately, it is impossible to judge just how soft the Irish threshold is at present, as much of the relevant data is not published (due to understandable constraints of commercial confidentiality). In the interests of promoting confidence in the decision process, a revision of the threshold could be accompanied by the annual publication of aggregated data on the cost effectiveness of recently adopted interventions, with the number of interventions with ICERs falling within categories defined by various multiples of the threshold; for example, ranging from 0.5 to 4+. This reporting would complement existing work by the NCPE quantifying the aggregate savings achieved as a result of price negotiations following the initial rejection of cost-ineffective interventions [53].

The critique presented here is based on the assumption that a common threshold should be applied to all interventions. It is important to acknowledge that the 2012 agreement provided very large savings on existing medications. Those defending the current threshold might understandably point to these savings as justification for the threshold's drug-only scope. Similarly, a drug-only threshold may be defended on the grounds that the pharmaceutical sector is a key employer and exporter for the Irish economy. A generous threshold could be an expedient means of supporting an industry that avoids European state-aid rules. Neither rationalisation of a drug-only threshold fits readily within the standard CEA framework and it is therefore difficult to appraise their justification.

Another caveat is that the importance of the threshold should not be overstated. Concerns of budget impact and political acceptability may still dominate value in many instances and it would be naïve to assume that an appropriately revised threshold would necessarily result in efficient resource allocation.

The concerns raised in this article are especially timely as the current IPHA agreement is due to expire at the end of 2015. Moreover, recent legislation on the pricing of medical goods enacted since the current agreement began has defined cost effectiveness in terms of the opportunity cost of services forgone, thereby providing legal recognition for an important principle in CEA [54]. Accordingly, a thorough reappraisal of the threshold and its basis is now due.

The recent legislation may now require decision makers at the Department of Health and HSE (and the experts that advise them) to explicitly reflect the opportunity cost of services foregone when setting a threshold. There is insufficient time to make a complete empirical threshold estimate for Ireland by the expiry of the current agreement at the end of 2015. Nevertheless, a commitment in principle to a future revision of the threshold in accordance with an empirical estimate of the opportunity cost would be welcome. Indeed, even if there is no explicit legal necessity to do so, we suggest there is a strong moral imperative given the large number of patients currently enduring long waits for services in the public health system. Similarly, a revised threshold would also help demonstrate a firm commitment to value for money to other government departments, including Finance and Public Expenditure and Reform.

The problems with the current threshold identified here are not all unique to Ireland. Indeed, as mentioned above, almost all other countries with established CEA infrastructure lack explicit thresholds in the first instance. In addition, even the most advanced work to date on estimating a threshold based on opportunity cost is still in its relative infancy. Therefore, establishing appropriate empirical thresholds remains a novel challenge for all countries, not just Ireland.

4 Conclusion

This article has identified four problems with the current Irish cost-effectiveness threshold, chief among them are the lack of an empirical basis and that the threshold is probably too high. There is an urgent need to reappraise the threshold given the forthcoming expiry of the current pricing agreement. Substantial unmet healthcare needs and recent legislation mean that decision makers and their expert advisors need to reflect opportunity costs in a revised threshold. Although revising the threshold to reflect opportunity costs will certainly present analytical challenges, there are reasons to be hopeful. The recent work on the empirical threshold in the UK provides a useful template for such research in Ireland. Furthermore, Ireland already has the necessary CEA institutional infrastructure and expertise in the form of HIQA and the NCPE.

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Compliance with Ethical Standards

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