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CURRENT OPINION

Revision of Ireland's Cost-Effectiveness Threshold: New State-Industry Drug Pricing Deal Should Adequately Reflect Opportunity Costs

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Abstract

Ireland's cost-effectiveness threshold is currently €45,000 per quality-adjusted life-year (QALY). It has previously been determined by periodic agreements between the State and a pharma industry lobby body. A new deal is due in July 2021 and it is therefore timely to re-examine Ireland's threshold, how it is set and transparency around adherence to it. Previous research has noted a series of problems with the threshold, including that it is likely too high relative to the opportunity cost of unmet need within Ireland's health system. This means reimbursement at the threshold may do net harm to population health. The high threshold may also mean the Irish health system is failing to satisfy existing legislation on healthcare resource allocation. Recent COVID-19-related pressures on healthcare capacity and public spending appear to increase the urgency for an evidence-based revision of threshold to better reflect opportunity costs within the Irish healthcare system. Despite these problems, the prospects for reform of the threshold do not appear strong as the political and institutional incentives may favour the status quo. At the very least, the State should provide greater transparency regarding how the threshold is set and adhered to. A potential reform for consideration in the longer run could include a partial abandonment of thresholds in favour of an auction process to achieve the lowest cost per QALY from new drug interventions.

Key Points for Decision Makers

Ireland's cost-effectiveness threshold has previously been set by periodic agreements between the State and the pharmaceutical industry and a new deal is due in July 2021.

Ireland's current threshold of €45,000/quality-adjusted life-year appears to exceed opportunity costs, which suggests it may need to be moderated to provide a better balance between spending on new drugs relative to those interventions that currently exhibit considerable unmet need.

Ireland's Department of Health needs to demonstrate leadership in reforming the threshold to ensure decision rules are determined by a fair and consistent appraisal of evidence rather than commercial and political interests.

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1 Introduction

Ireland is one of few countries with an explicit cost-effectiveness threshold, with Thailand, England and Wales being other current examples [1]. Ireland's threshold for pharmaceutical interventions currently stands at €45,000/quality-adjusted life-year (QALY) [2]. It has been determined as part of a pricing and supply deal periodically agreed between the State and a pharmaceutical lobby organisation. The current agreement is due for renewal by July 2021, so it is timely to re-examine the Irish threshold, the process by which it is set and the issue of drug price transparency.

This commentary assesses the threshold and related issues using a broad policy perspective, taking account of technical health economic considerations and political and institutional incentives. While this article is primarily intended for those interested in the performance of the Irish health service, it should also serve as a more general examination of the policy considerations around cost-effectiveness thresholds in systems with collective financing of healthcare. Furthermore, although this article primarily addresses the threshold that applies to new drugs in Ireland, it also examines the closely associated issue of

the threshold for non-drug interventions. The article first outlines the system for health economic appraisal in Ireland and the role of thresholds within it. It then describes the background of previous pricing agreements before giving the context of the Irish health system regarding public and private financing and waiting lists and previous criticism of the threshold. Against this backdrop, this manuscript revisits the relevance of waiting lists, considers transparency regarding public spending and the political and institutional context around reform of the threshold. Finally, it considers some particular COVID-19-related pressures before making suggestions for changes to the threshold and processes for setting it.

1.1 The Cost-Effectiveness Threshold and Health Economic Appraisal in Ireland

The conceptual role of cost-effectiveness thresholds in guiding decision makers to the efficient allocation of scarce healthcare resources is well established [3]. The approach most consistent with the standard objective of maximising health gain from an exogenously determined budget is commonly termed the 'supply-side' conception of the threshold [4]. Under this, the threshold should correspond with optimal alternative use of funds [5], typically referred to as the opportunity cost. Subject to several assumptions [4], approving interventions with incremental cost-effectiveness ratios (ICERs) below the threshold should add to net population health. Conversely, approving interventions with ICERs above the threshold is anticipated to yield less health gain from the newly approved intervention in comparison to the opportunity cost of health foregone by not spending on more efficient interventions. Similarly, setting the cost-effectiveness threshold in excess of the true opportunity cost means that new approvals may diminish rather than enhance population health [3, 4]. Setting the threshold too low relative to opportunity costs would result in the health system spending too little on new, more efficient interventions. It is therefore important that the cost-effectiveness threshold corresponds appropriately to opportunity costs.

Ireland has a well-established cost-effectiveness appraisal process for new drugs seeking reimbursement, which has been described previously [6, 7]. In short, pharmaceutical manufacturers seeking reimbursement must submit evidence regarding the expected costs and effects of their products to the National Centre for Pharmacoeconomics (NCPE) for appraisal. The NCPE issues recommendations to decision-making units within the Health Service Executive (HSE) [8]. The HSE is the State body responsible for the delivery of publicly funded health services in Ireland. The NCPE's role in appraising new medicines has evolved since its establishment in 1998 and much of the context for its recommendations is laid out in the 2013 Health Act [7, 9]. Responsibility for the appraisal of non-drug interventions lies primarily with the Health Information and Quality Authority (HIQA), often at the request of the Department of Health or HSE [6]. HIQA's remit, including its role in conducting cost-effectiveness analyses, is established under the 2007 Health Act [10].

The NCPE's recommendations are, in part, explicitly informed by comparisons of ICERs relative to Ireland's €45,000/QALY threshold. This threshold does not formally apply to non-drug interventions [2], though in practice HIQA cite both €20,000/QALY and €45,000/QALY as thresholds in their assessments of non-drug interventions [11, 12]. The exact status of these thresholds in informing HIQA's advice remains unclear [2].

A relevant feature of cost-effectiveness analysis (CEA) in Ireland is the lack of formalised exceptions to the standard threshold. The UK uses a threshold range rather than a point threshold, leaving five explicitly stated but unquantified additional criteria that can influence the probability of approval [13]. Additional formalised exceptions to the standard UK threshold include the End of Life criteria; the two iterations of the Cancer Drugs Fund; non-standard discounting guidelines; and the Highly Specialised Technologies criteria [13–17]. Notably, all these exceptions have attracted pointed criticism from health economists and others [15–19]. Other examples of departures from point thresholds include various forms of severity weighting in the Netherlands, Sweden and Norway [20–22].

1.2 Irish Pharmaceutical Healthcare Association (IPHA) and Drug Pricing Deals

The Irish Pharmaceutical Healthcare Association (IPHA) is an industry lobby body that represents the interests of manufacturers of patented medicines in Ireland. IPHA has negotiated periodic industrial agreements with the Irish State on the pricing and supply of medicines for decades [23]. The 2006 IPHA agreement established the requirement for cost-effectiveness analysis of pharmaceutical interventions prior to reimbursement but did not specify a cost-effectiveness threshold [7, 24]. The two most recent deals in 2012 and 2016 both state what cost-effectiveness threshold should be used in pharmaceutical reimbursement decisions in Ireland [25, 26].

The negotiating parties acting on behalf of the State in such deals have typically included the Department of Health and, since its inception in 2005, the HSE. The HSE has frequently exhibited cost overruns, value for money in health expenditure has been repeatedly questioned and there have been renewed concerns regarding growth in pharmaceutical expenditure [27–30]. The 2016 deal also included the

Department of Public Expenditure and Reform (DPER). DPER is a government department established following the global fiscal crisis and part of its remit is to pursue sustainability in public spending.

A notable development between the 2012 and 2016 deals was the 2013 Health Act. It, among other provisions, established the legislative basis for cost-effectiveness analysis in Ireland. Schedule 3, Part 3(b) states that the HSE "shall have regard to the cost-effectiveness of meeting health needs by supplying the item concerned rather than providing other health services" [9]. This requirement of the HSE to "have regard" to opportunity costs does not appear binding in that it does not oblige the HSE to reject interventions with benefits less than those of services foregone. Furthermore, the Act does not explicitly mention cost-effectiveness thresholds. Despite that, the legislation clearly interprets cost effectiveness in terms of the opportunity cost of other interventions foregone. As such, the intent of the legislation is consistent with the broadly accepted principle within CEA that the threshold should represent the opportunity cost of other healthcare interventions foregone.

A minor change between the 2012 and 2016 deals is that the earlier agreement clearly stated a new medicine's price should be the lower of either an international reference price (with respect to an aggregate of prices in Austria, Belgium, Denmark, Finland, France, Germany, the Netherlands, Spain and the UK) or a price found acceptable according to the threshold [25]. The 2016 deal is less clear as although it also mentions both international referencing pricing (to an expanded basket also including Greece, Italy, Luxembourg, Portugal and Sweden) and the requirement that prices meet the conditions for cost effectiveness, it does not unambiguously state that the agreed price should be the lower of the two [26].

Another minor change is the introduction of what is described as the 'decision authority level table' in the 2016 deal. It stipulates two thresholds of €20,000/QALY and €45,000/QALY and three different net budget impact categories [26]. This means approvals of new medicines with higher costs per QALY or greater budget impact must be made at higher levels within HSE management. Ultimately however, the lower €20,000/QALY threshold appears to have little relevance, as clearly any decision can be simply elevated for consideration at a higher level of authority.

1.3 Access to Public Health Services

Ireland's public-private mix in healthcare provision and the chronic problems of access to elective services in the public system provide relevant context for questions of suitability of the current Irish threshold. Ireland operates a tax-funded healthcare system that is free at the point of use for roughly one third of the population [31], with eligibility largely determined by income but supplemented with specific health-related entitlements. Free services include primary and hospital care and prescription medications subject to capped prescription charges. The remainder of the population can use public services but face capped co-payments. Approximately 43% of the Irish population purchase private medical insurance with varying degrees of coverage [32], enabling access to care both from private providers and private care provided within public services.

Large waiting lists for elective care in the public system form part of the incentive to purchase private insurance. Those privately insured can often gain faster access to services than public patients [33]. This includes diagnostic services, even though the patient may go on to receive the necessary therapeutic care within the public system [31]. Whyte et al. has shown that holding private health insurance is associated with a lower probability of waiting 3 months or more for both inpatient and outpatient care relative to those without private insurance [31]. Connolly and Wren find a quarter of survey respondents reporting an unmet health need in Ireland cite waiting lists as a cause [34]. Recent work providing comparable estimates of waiting lists shows Ireland lags behind other high-income western European countries for hip replacements, knee replacements and cataract removal [32]. Brick and Connolly note in particular that Ireland demonstrates substantially longer waits compared with the UK [32].

1.4 Previous Critiques of the Irish Threshold

Brick et al. queried if the €45,000/QALY threshold is at the appropriate level, drew attention to breaches of the threshold and questioned if it should be set by negotiations with industry rather than be determined independently by the State [35]. More recently, O'Mahony & Coughlan critiqued the threshold, noting four problems: it only applies to drugs, it represents a price floor not a ceiling, it is not based on evidence of the opportunity cost of health forgone and is likely too high [2]. That analysis noted that three common elective surgical interventions with notably large waiting lists in Ireland—hip replacement, knee replacement and cataract removal—were all highly cost effective according to UK estimates, with cost-effectiveness ratios ranging from £2000 to 5600/QALY. It also noted that an empirical estimate of the threshold in the UK of approximately £13,000/QALY is considerably lower than the current Irish threshold. While O'Mahony and Coughlan caution on drawing direct comparisons between Ireland and the UK, they noted the similarities between the two countries in terms of per capita income and health spending. Gorecki echoed concerns that the Irish threshold may be too high, stating that drugs likely consume an excessive share of public spending [36]. Recent

work by Chen et al. also found that many of the interventions with the largest waiting lists in Ireland had cost-effectiveness estimates substantially below the current threshold [37].

2 Analysis

While the threshold agreed within the previous IPHA deals only applies to drugs, the requirement of the 2013 Health Act that the HSE gives regard to the opportunity cost of other interventions means, in principle, the cost effectiveness of drugs and non-drug interventions ought to be linked. Assuming there are no special characteristics of drugs that warrant spending more per unit of health gain achieved compared with other interventions, then a rational allocation of resources implies a common threshold should apply to both drug and non-drug interventions.

The observation made by O'Mahony and Coughlan and Chen et al. that highly cost-effective interventions are currently subject to long waiting lists in Ireland is certainly not conclusive evidence that the threshold should be reduced. Nevertheless, I contend it is suggestive that a reduction in the threshold to facilitate a reallocation of resources to services exhibiting considerable unmet need would be beneficial. I argue there are several factors that reinforce the relevance of waiting lists in the Irish context. The waits for some interventions within the Irish system are not trivial and extend beyond what might be necessary to co-ordinate supply with unpredictable demand. For example, Brick and Connolly report that waits of 9 months or more were experienced by over 30% of patients receiving hip replacements and cataract removals and approximately 45% of those receiving knee replacements [32]. Not only will patients experience diminished quality of life during such waits, their eventual outcomes may be inferior as treatment delay has been found to lead to worse outcomes for some interventions including hip and knee replacements [38]. Furthermore, the long waits are just one manifestation of the unmet need within the Irish health system. Much of the health need for such elective services is ultimately met by private expenditure, primarily through health insurance. This private activity represents health need that is not met by the public system. Finally, it is also worth noting that waiting times appear to be a particular weakness of the Irish health system. Ireland ranked last out of 35 European nations both on an aggregated score of waiting times in general and on the specific measure of wait times for elective surgery [39].

2.1 Opportunity Costs in a Legal Context

The absence of an empirical basis in the opportunity cost of health foregone for the current threshold means it can be questioned if the outgoing 2016 IPHA deal agreed by the State meets the requirements of the 2013 Health Act. Although the 2016 deal explicitly cites the 2013 legislation, including the specific provisions of Schedule 3, Part 3, it does not describe how the specified thresholds correspond to opportunity costs or any evidence regarding them. So although the 2013 Act does not impose a binding requirement on the HSE to apply a threshold, it is unclear how the thresholds specified by the 2016 IPHA deal enable the HSE to meaningfully 'have regard' to the opportunity cost of other services as required by the legislation.

2.2 Transparency and Accountability Regarding Public Spending

Not only is the level of the current threshold questionable, but there are also broader concerns of transparency regarding both the process for setting the threshold and adherence to it. Although the relevant legislation clearly recognises cost effectiveness in terms of opportunity costs, the two most recent IPHA deals did not document the process for deciding the threshold or the issues considered by those who agreed it. It is notable that a parameter which, in principle at least, informs hundreds of millions of euro of public spending annually is agreed behind closed doors without external oversight. This is especially so given initiatives towards greater government transparency, including on public spending, led by DPER as part of the international Open Government Partnership initiative that Ireland joined in 2014 [40, 41].

It is unclear if the cost-effectiveness threshold has been the subject of any research by the Department of Health, DPER or the Irish Government Economic Evaluation Service (IGEES) in recent years in anticipation of renewing the IPHA deal. While IGEES have published reports on the health system [42], some of which mention the IPHA deals [43, 44], none mention the cost-effectiveness threshold. Similarly, I am not aware of any published documents substantively addressing the topic by the other bodies mentioned. Although, of course, an absence of published work is not evidence that the issue has not been considered.

There is also limited transparency on the cost effectiveness of interventions on adoption. In the case of non-drug interventions when assessed by HIQA, it will often be clear if adoption of an intervention has been advised despite exceeding the threshold. This is because the complete cost-effectiveness evidence is typically published in a detailed health technology assessment and, except for vaccines, there usually is little or no scope for post-decision confidential price discounts. For example, HIQA advised the provision of surveillance strategies for women at high risk of breast cancer that exceeded the €45,000/QALY threshold [45]. The same clarity usually does not apply to drugs as the reimbursed prices typically remain confidential [46]. The

prices and cost-effectiveness ratios publicly available in NCPE summary documents relate to prices on application not approval. Furthermore, this cost-effectiveness summary information is only published for those interventions subject to a full assessment by the NCPE, not those solely subject to the Rapid Review pathway [6]. Further transparency concerns arise when we consider the potential application of managed-entry agreements that may condition aspects of reimbursement with price-volume agreements, budget caps or agreements based on observed treatment effectiveness [47]. Such mechanisms may make it uncertain what the effective price per QALY achieved is, even to those privy to confidential pricing information.

While price confidentiality is an understandable condition to commercial negotiations given manufacturers' interests in other markets, it prohibits any meaningful oversight of adherence to the current threshold [2]. Previous research has attempted to examine factors influencing drug reimbursement and aspects of appraisal but have not been able to use actual reimbursed prices [8, 46]. It is therefore impossible for parties external to the HSE to determine how often the threshold is breached or to what extent. In turn, this makes it impossible to judge the practical relevance of the threshold.

2.3 Political and Institutional Context

The prospects for the adoption of an evidence-based threshold and consistent adherence to it depend in part on the political context in which CEA is applied. Previous authors have examined the reasons why health economic evidence has had an apparently modest impact on policy and emphasise the potential for divergence between the objectives of health economists and policy makers [48, 49]. Bate et al. note that it is important for health economists to understand the policy context in which health economic evidence is going to be used and to understand the pragmatic considerations around policy making [50]. Understanding this context is important if we wish to have a realistic appraisal of the possibility of greater fidelity to the principles of CEA in healthcare spending. Cost effectiveness is something politicians and others will espouse in the abstract [51], but is often rejected in particular instances when the intervention of interest is rejected. This is especially likely with elected decision makers. Achieving improving health services and value for money is a perennial goal, yet politicians will naturally wish to avoid withholding specific interventions for identifiable patients when the patients that benefit from more efficient resource allocation remain unidentified.

The incentives for politicians to confront the inappropriate threshold are weak. A more equitable and efficient threshold would be lower, leading to more new drugs being rejected, which will be politically costly. It may be more electorally advantageous to allow the status quo to persist, as voters may be inured to waiting lists. Furthermore, improving public services will likely be an expensive task for government. Recent estimates of the annual cost of reducing Ireland's public waiting lists to more manageable levels by Brick and Keegan stand at €183–212 million per annum and approximately €60 million thereafter once current excessive waiting lists have been addressed [52]. Ireland's mix of public and private provision effectively splits the electorate's interests regarding reform. Wealthier voters with the ability to purchase insurance may see their interests better served with a continuation of the status quo whereby they use private insurance to secure access to elective care rather than supporting reforms that require increased taxation to improve access for both them and the uninsured. Indeed, perceptions of the health vote as the apocryphal fiscal 'black hole' may create expectations that the health system cannot effectively convert increased taxation into better access for all [53].

There is also an important institutional context to consider alongside CEA's political environment. Ireland's health economic infrastructure is growing. There are increasing numbers of health economists and related specialists trained to doctoral level, in part thanks to the Health Research Board's Structured Population Health-services Research Education (SPHeRE) programme. Both the NCPE and HIQA's health technology assessment directorate have expanded their staff. Health economic analysis now forms part of the National Clinical Effectiveness Committee's deliberations on service provision. Two health economists sit on Ireland's recently convened National Screening Advisory Committee. PhD health economists are also employed at the Economic and Social Research Institute (ESRI) and DPER.

While growth in health economics capacity is welcome, it does not necessarily translate into efficient service provision. We should not comfort ourselves simply with the fact that more health economic analyses are being conducted. Interventions have been recommended for adoption or have been adopted despite being found to be cost ineffective [11, 35, 54]. Indeed, increased knowledge of the health economic performance of the health systems might actually elicit concern, as it becomes increasingly clear where we fail to achieve good value for money despite improving CEA evidence.

It is therefore relevant to consider where Ireland's health economic capacity is concentrated and what incentives it has to support reform. The Irish State's health economic expertise is largely concentrated at the NCPE and HIQA. The division of responsibility for drug and non-drug appraisals between the two bodies means that neither has an overarching responsibility for achieving balance between drug and other spending. Neither body has a role regarding health policy that would encompass the threshold's level. Unless commissioned to do so, attempts by either institution to critique

the threshold or the mechanisms for setting it could justifiably be interpreted as a breach of their remit and risk criticism from the Department of Health and politicians alike. Conversely, while responsibility for setting an appropriate threshold lies with the Department of Health, it currently lacks the same concentration of health economic expertise. This imbalance of remit with expert capacity arguably militates against a cohesive initiative from the State towards fair and efficient rationing.

Further insights into the incentives and prospects for reform of the threshold are offered by examining some of the political and institutional considerations together. The technocratic perspective that resource allocation should follow a fair and consistent application of rules can conflict with democratic processes which are subject to lobbying, media attention and an understandable yet asymmetric empathetic focus on patients of interest and insufficient appreciation for opportunity costs. A question then is to what extent can elected decision makers refrain from interfering with technocratic processes by circumventing rules on fair allocation. Experience in Ireland with the approval of cost-ineffective drugs such as pembrolizumab and ivacaftor following apparent political intervention indicates that politicians will sometimes overrule technical processes [55, 56]. Similar experiences with cost-ineffective drugs abroad show that Ireland is not alone in its reimbursement processes being susceptible to political pressure [57].

If politicians are unwilling to distance themselves from such decision making and support independent, technocratic processes, then a question is how firmly should technocrats push back in an attempt to address the weaknesses in fair allocation that arise from democratic pressures. For example, the head of the NCPE has urged politicians not to deviate from the standard drug reimbursement process [58]. Other such efforts could include attempting to achieve greater transparency on breaching thresholds, greater scrutiny of the process to set the threshold and engaging with the public on the need for fair and consistent resource allocation. A difficulty with such activities is that they blur the lines between strengthening technocratic processes and advocacy which might invite conflict with political, commercial and professional interests and thereby compromise career prospects. Furthermore, recommending that cost-ineffective care is withheld from identifiable groups will likely attract hostile media and public attention. Such efforts are also time consuming. Accordingly, the incentives for technocrats to confront political interference appear weak.

The weak incentives for both reform of the threshold and enhanced transparency around reimbursement contrast with those for industry. IPHA has a clear interest in maintaining the current threshold rather than seeing any attempt to balance it more accurately with the opportunity cost. Moreover, evidence indicates that IPHA is an active lobbyist. The record of lobbying activity reported under the provisions of the Regulation of Lobbying Act shows IPHA engaged with 110 unique individuals over 78 different occasions on a range of issues in the reporting period from September 2015 to December 2020 [59]. The individuals lobbied include members of the Dáil and Seanad (lower and upper houses of the Irish Parliament, respectively), members of the European Parliament, government ministers and senior civil servants. It seems relevant to ask how concerted the State's countervailing efforts are to protect the interests of patients bearing the opportunity of new drug therapies.

2.4 Impact of COVID-19

Previous critiques of the Irish threshold have questioned whether the threshold is too high. These concerns arose before the advent of COVID-19. The pandemic has had two important effects relevant to the cost-effectiveness threshold. The most obvious has been its impact on health services. COVID-19 directly consumed much of the available health system capacity throughout 2020 and early 2021 and led to the cancellation of many services. Accordingly, waiting lists have grown, further exacerbating the problems of unmet need. By mid-2020, waiting lists for inpatient and outpatient care had increased sharply [32]. The consequences of sustained service disruptions will clearly be both an additional accumulated demand for an already underperforming health system to address, but also potentially a more demanding case burden as some needs will have grown more acute.

In addition to the direct impact on health services, the pandemic has also required large increases in State spending, both within the health budget and in public spending overall. Overall government spending in 2019 is reported as €67.2 billion, of which €18.4 billion was public expenditure on health, €2.2 billion of which was on pharmaceuticals, representing just under 12% of total health spending [60]. An additional €14.1 billion of overall COVID-19-related spending was allocated for 2020, of which €2.0 billion was on health [60]. This additional spending will only be temporary and will be attenuated through borrowing; nevertheless, the sums involved are large and represent a significant additional fiscal burden.

These combined system capacity and budget challenges make it ever more difficult to sustain a case for continuing with the current threshold. While the accumulation of unmet need might be predominantly for non-pharmaceutical interventions, the rational allocation of resources according to efficacy means that demand pressures in one aspect of health spending ought to have implications on the appropriate levels of spending elsewhere within the health system. The dual impact of meeting substantial further accumulations of unmet need while eventually achieving spending reductions appears to create greater urgency for a threshold

that more appropriately balances resources between drug and non-drug interventions.

2.5 Other Considerations

2.5.1 Threshold as Subsidy

A previous examination of the Irish cost-effectiveness perspective speculated that maintenance of a high threshold could be rationalised as a subsidy to the pharmaceutical sector [2]. The sector is a key employer and exporter for Ireland and it is conceivable that enterprise-oriented elements of government might wish to retain generous reimbursement as a way of supporting the sector without explicitly breaking European state aid rules. This is one conceivable reason why a common threshold might not necessarily apply to both drug and non-drug interventions. If a high drug-specific threshold was maintained for this reason it presumably would never be confirmed by government. That, however, does not render the issue moot. The possibility of such a form of subsidy then prompts questions of whether it is an effective or efficient form of support. While Ireland has a large pharma sector, not all manufacturers who supply the Irish health system have significant operations in Ireland. It also seems relevant to ask whether the same high threshold should be extended to non-drug care. Arguments regarding equity of access to equally cost-effective care would suggest so, but this then would implicitly increase the overall cost to public spending of maintaining such a form of subsidy.

2.5.2 Should We Use a Threshold at All?

Much of this discussion is from the standard CEA perspective, which contends that population health will be maximised through the operation of a cost-effectiveness threshold. The assumptions required to support that position are not likely to apply in reality [61]. Using a known, explicit reservation price as a threshold may not maximise health, but could yield zero net health gain, as all the benefits of new interventions are capitalised into prices by suppliers [62]. Furthermore, the standard CEA perspective assumes fungibility of resources across all healthcare interventions, whereas in practice funds tend to be hypothecated to specific classes of spending. For instance, Irish healthcare spending makes drug-specific allocations, portions of which are further earmarked for the reimbursement of new drugs [23].

If funding is hypothecated for pharmaceutical spending in general and on new drugs in particular, then it might be better to partially abandon the threshold in favour of an auction approach that considers multiple candidate interventions within a series of periodic spending rounds. It could award reimbursement to interventions in rank order of cost per QALY until the funding within each round is exhausted. Drugs not approved could form part of the panel for the next funding round. Suppliers therefore have an incentive to bid their prices down to receive funding and compete against suppliers of other interventions for other indications. A threshold may still be required to provide an upper bound of what will be reimbursed if there are too few candidate interventions within any individual funding round to achieve cost effectiveness. Moreover, a threshold would still be required for non-drug interventions reimbursed outside the auction.

An auction system might require considerable forward planning to arrange panels of candidate interventions over multiple funding rounds and would likely take longer than the current process. Careful consideration would need to be given to this and other potential disadvantages of such an auction process relative to the status quo. While sophisticated auction processes have been most well documented in the context of selling public assets such as mobile phone network licences [63], they can also be applied to public procurement. The potential for substantially increased capture of welfare by the State in the form of lower drug prices seems worth exploring. This option, however, is only a tentative proposal and as such is clearly beyond the scope of the forthcoming price negotiations.

2.6 What Must Change?

The primary suggestion for a new cost-effectiveness threshold for Ireland is that it needs to be referenced in some meaningful way to opportunity costs within the healthcare system. This seems necessary if the HSE is to fulfil its obligations under the 2013 Health Act. This commentary argues that better reflecting opportunity costs probably requires a threshold reduction. It seems this would be best achieved by the State determining the appropriate threshold itself, rather than in negotiation with IPHA, as suggested by Brick et al. [35].

Whatever decisions are made in the coming months regarding a new threshold, it is necessary that the evidence and deliberations around this are published by the Department of Health. If Ireland's reimbursement process applies greater weights to health related to certain patients, intervention types, diseases or levels of disease severity, then such criteria should be made explicit. Furthermore, any preference weights should be supported by evidence underpinning preferential weighting.

A previous critique of the Irish threshold published 5 years ago noted the challenges of making an empirical estimate of opportunity costs to support an evidence-based threshold [2]. More supply-side threshold estimates have been published internationally since then [4, 64], but no clear consensus on the appropriate methods for estimating opportunity costs has yet emerged. Irish decision makers may therefore be forgiven for not identifying an appropriate

evidence base for the threshold to date. The cost effectiveness of services subject to waiting lists arguably represents an important starting point that is particularly relevant to the Irish context. Research on informing a threshold on such a basis could capitalise on recent work by the ESRI on waiting times and estimates of the costs of reducing them [32, 34, 52].

A medium-term objective beyond the forthcoming agreement includes greater price transparency regarding products on adoption. This is necessary to provide accountability regarding the allocation of resources and reveal to what extent the threshold is meaningfully applied. Price transparency need not compromise commercial confidentiality. Annual reports could publish aggregated information on the incremental cost-effectiveness ratios and budget impacts of approved interventions to conceal the price and cost of individual products, yet still broadly indicate the level of adherence to the threshold and related budget consequences.

3 Conclusion

This commentary contends that Ireland's current cost-effectiveness threshold lacks an appropriate evidence base and likely exceeds opportunity costs. A threshold that exceeds opportunity costs of unmet needs risks harming Ireland's health system. The persistence of a threshold that is not supported by evidence of opportunity costs is increasingly unacceptable and an appropriate evidence-informed threshold that facilitates balance between pharmaceutical spending with other services is needed. Concerted effort may be required by the State to support reform, as the incentives to counter industrial interests appear weak for both politicians and technocrats. It now seems necessary for the Department of Health to take leadership on setting an appropriate threshold. If it succeeds, Ireland can look forward to the benefits of fair and consistent application of CEA.

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Conflict of interest JFOM declares that he has no conflict of interest.

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