Vaccine 37 (2019) 2831–2837

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Appraising the cost-effectiveness of vaccines in the UK: Insights from the Department of Health Consultation on the revision of methods guidelines

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ARTICLE INFO

Article history:
Received 13 November 2018
Received in revised form 19 March 2019
Accepted 28 March 2019
Available online 15 April 2019

Keywords:
Cost-effectiveness
Economic appraisal
Methods guidelines

ABSTRACT

The UK Department of Health and Social Care recently held a consultation on proposals to revise the methods for the appraisal of cost-effectiveness of vaccines as applied by the Joint Committee on Vaccination and Immunisation (JCVI). This presents a useful opportunity to review the current methods applied by the JCVI and examine the proposals for their improvement. Reviewing such methods is timely as there is mounting evidence that key elements of the health economic appraisal of all healthcare interventions in the UK need to be revised. In particular, there is a need to reassess both the cost-effectiveness threshold used to judge if an intervention is cost-effective and the discount rates used to assess the present value of health gains that occur in the future. Accordingly, we critically appraise the methods and their proposed changes. Overall, the 27 recommendations made within the recent consultation on proposed changes indicate a sensible and carefully considered approach to methods reform. We identify 11 recommendations that deserve further comment or reconsideration. In particular, there are reasons to question the basis for the proposed reduction of the discount rate from 3.5% to 1.5%. We also find that aspects of the current methods for considering uncertainty in the cost-effectiveness of vaccines require revision. Both the discounting and uncertainty analyses recommendations do not appear to be well grounded in economic theory, empirically justified or consistent with the methods set out by the National Institute for Health and Care Excellence.

1. Introduction

The appraisal of cost-effectiveness of healthcare interventions typically follows methods guidelines to ensure both the quality and comparability of analyses. The primary guidelines in England and Wales are those published by the National Institute for Health and Care Excellence (NICE) [1]. The Joint Committee on Vaccination and Immunisation (JCVI) is the statutory advisory body with responsibility for advising the departments of health within the UK on the provision of preventative vaccination and immunisation [2]. The JCVI largely follows the NICE guidelines on economic appraisal, but issues additional guidance within its Code of Practice [2]. These additional guidelines primarily provide supplementary guidance on appraising uncertainty in cost-effectiveness analysis (CEA) and its role in informing approval recommendations.

The Department of Health and Social Care (DHSC) recently held a consultation exercise on possible revisions to the JCVI cost-effectiveness analysis guidelines [3]. The consultation included 27 recommendations for guideline revision which were drafted by the Cost-Effectiveness Methodology for Immunisation Programmes and Procurements (CEMIPP) working group. These recommendations fall under seven principal methodological areas and are reproduced in Appendix Table 1. The CEMIPP working group was first convened by the DHSC in late 2014 and their recommendations were initially published in 2016 [4].

The convening of the CEMIPP working group formed part of a broader initiative under the DHSC's Appraisal Alignment Working Group (AAWG), established in early 2014 to achieve alignment in the methods of economic appraisal of different healthcare interventions [4]. The purpose of this alignment is to enhance comparability of evidence when appraising the cost-effectiveness of different interventions. The principle of achieving consistency within appraisal methods for different classes of interventions that draw resources from the same NHS budget is explicitly recognised by the JCVI in its Code of Practice: "The JCVI has previously decided in principle to follow a similar methodology to National Institute of Clinical Excellence technology appraisals. This ensures consistency

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https://doi.org/10.1016/j.vaccine.2019.03.072
0264-410X/

across these programmes relating to different technologies drawing on the same National Health Service budget. . ." [2]. Furthermore, the JCVI noted that its guidelines should reflect any revisions to NICE's methods [2]. Accordingly, the recent JCVI consultation and the convening of the AAWG both reflect a desire to refine methods guidance while retaining consistency between bodies responsible for appraising cost-effectiveness evidence.

The options for revising the JCVI guidance discussed within the consultation offer useful insight into what aspects of methodology are currently considered candidates for refinement. In this analysis, we review some of the noteworthy options considered within the consultation and comment on their consistency with accepted health economics methods. We critique the proposals in light of established methods and current evidence. The purpose of this critique is to inform the current JCVI deliberations on cost-effectiveness methods and to demonstrate the need for sound and consistently applied evidence appraisal.

2. Reviewing the consultation

Our analysis of the consultation is laid out as follows. We comment on 11 of the 27 recommendations made by the CEMIPP where we feel important points supporting or contradicting the advice should be noted. These 11 recommendations are marked in Appendix Table 1 within the shaded cells. Our analysis is presented in two sections: the first addresses the six recommendations that we consider to be of primary importance; the second addresses the five remaining recommendations of secondary importance. Within each section we present the recommendations in the order as they appear in the CEIMPP report. As some readers may not be familiar with the context of each recommendation, we provide a brief background to each, including what the current JCVI guidance is. Our analysis also includes some brief commentary, where relevant, on the supporting arguments made in the CEMIPP report.

Our analysis is guided by three principles. The first is that recommendations should be internally consistent, meaning that they should be logically justified given accepted CEA methods. Secondly, recommendations should be supported by empirical evidence where applicable. Finally, recommendations should be externally consistent, meaning that they should be consistent with other resource allocation methods guidance that apply elsewhere within the same health system. As recognised by the CEMIPP report, there can be a tension between the first two principles and the third [4]. In such cases, we suggest that internal consistency and a sound empirical basis take precedent over consistency with other guidelines.

3. Points of primary importance

Recommendation 1.1 states that the JCVI should adopt full economic utility as the scope of benefit only if it is adopted by the AAWG and only as in a trial or shadow mode. The scope of an analysis within CEA relates to what it is that an economic analysis attempts to maximise. The conventional scope of CEA as applied in the UK is a narrow one that considers the costs which accrue to the public health system and attempts to maximise health, as measured by the quality-adjusted life-year (QALY) or some similar measure. This is the current basecase recommendation within NICE guidelines and the 2013 JCVI Code of Practice guidelines explicitly adopt the same perspective [1,2]. A broader perspective that considers utility therefore attempts to maximise the welfare generated by good health [5]. This may include the earnings-related benefits of allowing a worker return to paid employment. Generally, we would expect most interventions to appear more attractive when a broader scope of analysis is employed, as this permits the inclusion of a broader range of beneficial consequences of improved health. Although there is an ostensible appeal to a broader perspective, it recognised by many as being potentially problematic as it can introduce inequitable biases in the allocation of healthcare resources to those with greater earning power [6], such as men and those within the middle years of life.

The JCVI's recommendation 1.1 that the broader scope of full economic utility should only be adopted if it is adopted for all other health economic analyses according to the AAWG review demonstrates a clear appeal to consistency in the appraisal of different types of healthcare interventions. We support this explicit appeal to consistency and strongly endorse the principle that a broader maximand of utility should only be adopted if adopted for all healthcare interventions.

We note that the proposal of a trial of the societal perspective leaves aside the debate as to whether the broader maximand of utility is appropriate. Neither the consultation nor the supporting CEIMPP report appear to endorse the status quo of the QALY as the maximand or the expansion to broader utility. Moving to a maximand of utility would be a fundamental shift from what is currently recommended and does not yet appear to be supported by consensus within the UK health economic research community. Accordingly, adopting a complete switch to a societal perspective would be premature. Also, we believe that some of the consequences of changing methods may still be unforeseen and these will need to be learned through experience. Accordingly, the recommendation that a broader perspective should only be adopted on a trial basis appears prudent.

The CEMIPP report notes that broadening the scope of benefits would require a reduction in the cost-effectiveness threshold [4]. This is a significant and welcome recognition that changes in valuation metrics require accompanying changes in decision rules to achieve consistency with the objective of maximising benefits from finite resources. This can be contrasted with the recent publication of the Second Panel on Cost-Effectiveness in Health and Medicine's guidelines on economic appraisal, which advised that both the health payer and societal perspectives should be applied [7], but failed to explain the implications of different perspectives for the cost-effectiveness threshold.

While achieving consistent modification of the perspective and threshold is welcome, this still leaves questions regarding how the JCVI will resolve divergent policy recommendations under the current standard framework and the trialled societal perspective. There is likely to be pressure to adopt interventions that do not achieve cost-effectiveness under the current perspective, but do under the trialled perspective. Clarity on which perspective will be binding is therefore necessary.

Recommendation 2.1 states that vaccines should be evaluated on an incremental basis, as is explicitly recommended by NICE and reflected in the JCVI Code of Practice [1,2]. Incremental analysis in the context of CEA relates to the need to compare each intervention to its next best comparator, rather than to doing nothing or the usual standard of care. This is because we wish to appraise what is the additional health gain achieved between alternative intervention strategies for the additional expenditure required [8]. Appropriate incremental comparison has to be conducted carefully, as many interventions can be made to appear more cost-effective if relevant comparators are omitted [9].

The JCVI's recommendation that comparisons should be incremental is uncontroversial, as this has long been recognised as the appropriate approach in CEA [10]. Despite this, the recommendation still deserves comment for two reasons. The first is that what constitutes an appropriate incremental comparison can be somewhat complicated in the context of infectious diseases. This is because outcomes are not necessarily independent between alternative risk groups. For example, the effectiveness of broadening the scope of a vaccination programme needs to assess the benefits

of incrementally expanding coverage rather than independently assessing the benefit of vaccinating each group relative to no vaccination. Secondly, the JCVI has considered non-incremental analyses in the appraisal of two population-wide vaccination programmes in recent years. An analysis relating to meningitis B vaccination considered the cost-effectiveness of providing immunisation to different recipient groups without considering the costs and effects under a standard incremental analysis [11]. More recently, the JCVI assessment of the cost-effectiveness evidence on extending human papillomavirus vaccination to boys included an analysis comparing vaccinating boys and girls to no vaccination, unlike the standard comparison of vaccination of boys and girls relative to girls only (which was considered in the base case analysis) [12]. Accordingly, since the correct incremental analysis of costs and effects has not always been conducted in JCVI deliberations in the past, we believe the consultation document is right to emphasise the need to observe it in the future.

Recommendation 3.1 states that health and healthcare costs should be discounted at 1.5%. Discounting is the procedure used in health economics to account for what is known as time preference [13]. Time preference is the desire to enjoy good things sooner rather than later. Discounting reduces the value of both costs and health effects that occur in the future relative to those that occur in the present. The application of discounting typically leads to higher (less cost-effective) cost-effectiveness ratios. Interventions that have long lasting effects that occur long in the future, such as vaccination, are particularly sensitive to discounting. Future costs and effects are typically discounted at rates between 5% and 1.5%, depending on the different national guidelines [14]. Lower discount rates typically lead to lower cost-effectiveness ratios (interventions appear more cost-effective).

The JCVI's recommended rate of 1.5% represents a significant reduction on the standard 3.5% currently recommended by NICE (and therefore adopted by the JCVI) [1]. Reducing the discount rate could have a profound effect on the cost-effectiveness of many vaccinations. Specifically, the reduction could greatly increase the chance that vaccines would be found to be cost-effective at current prices, or, more likely, could greatly increase the prices at which vaccines remain cost-effective.

A reduction in the discount rate appears appropriate given recent theory and empirical evidence on discounting [15]. Notably, the rate recommended within the consultation is consistent with a recent revision of the Canadian discount rate for costs and health effects, which was also reduced to 1.5% [16].

While the CEMIPP's recommended 1.5% discount rate appears to be more appropriate than the existing 3.5% rate, we question the basis on which the recommendation has been made. The proposed revision is not based on the research that informed the Canadian reduction, but rather takes its guidance from the recently revised HM Treasury Green Book [17]. While the Green Book is ostensibly the most relevant domestic guidance, we note a number of reasons for caution with this source. The Green Book itself does not reference recent research on discounting with CEA, but instead justifies a lower discount rate for health based on a claim that diminishing marginal utility of growing wealth does not apply to health. This claim is not supported by standard health economic theory or by consensus within the cost-effectiveness research community. In summary, the JCVI's recommendation of discounting at 1.5% is arguably the right recommendation for the wrong reasons. Accordingly, we urge a reconsideration of the evidence base for discounting before guidelines are revised.

Recommendation 3.2 states that a higher discount rate of 3.5% should apply to non-health related costs. Whether the same discount rate should be applied to health gains as to costs has been long debated within health economics [13]. The application of a lower discount rate to health effects has been advocated as a way of accounting for a growth in the value of health over time [18]. It is, however, notable that recommendation relates to something somewhat different that has not be widely advocated before. In particular, it is recommending a different discount rate for costs that fall outside of the scope conventionally considered within the health payer perspective.

The current NICE guidelines (by extension, those adopted by the JCVI) do not recommend the explicit quantitative appraisal of non-health costs [1]. Accordingly, at present there is no explicit recommendation regarding how such non-health costs should be discounted. The recommendation for such non-health related costs would presumably only apply in analyses that employ the broader trialled societal perspective. This recommendation again appears to be based on the Treasury Green Book recommendations. For the same reasons as above, using the Green Book recommendations appears incompatible with the most recent CEA methods research. Furthermore, it is likely that the application of different discount rates to different categories of outcomes is likely to result in unintended consequences that make the interpretation of cost-effectiveness evidence less clear. We note the difficulties that can arise when different discount rates are applied to costs and health effects in multi-cohort models [19], which are exactly the type required to appraise infectious diseases [13]. We believe similar problematic effects will be observed when different rates are applied to health and non-health outcomes.

We add further caution to the recommendation for different discount rates for non-health related consequences. A clear decision framework needs to be articulated regarding the maximand of the societal perspective before the appropriate discount rate can be specified. This is because current discounting theory derives discount rates from the decision rules employed [20]. Therefore, clarity on decision rules must be achieved before a theoretically consistent recommendation on discounting can be made.

Recommendation 7.2 recommends reducing the cost-effectiveness threshold to £15,000/QALY. The cost-effectiveness threshold is the decision rule commonly used in CEA to decide if an intervention represents sufficient value for money for approval or not [5]. While there have been many arguments advanced on how best to determine the cost-effectiveness threshold [21], the view that is arguably most consistent with the standard objective of CEA of maximising health from scarce healthcare resources is that the threshold should represent a proxy of the opportunity cost of other health interventions foregone [22]. While CEA has been practiced for decades, it is only recently that concerted efforts have been made to base the threshold on empirical evidence of the opportunity cost [21].

Current NICE guidelines state that interventions should be considered at a cost-effectiveness threshold range of £20,000-£30,000/QALY, with additional factors required to justify reimbursement as the upper bound of this ranges is approached [1]. The JCVI Code of Practice indicates that an intervention's most plausible ICER should be compared to a threshold of £20,000/QALY [2], which indicates a somewhat stricter threshold. The JCVI, however, also note an uncertainty criterion (described below) which uses the upper bound of NICE's threshold range of £30,000/QALY [2]. Accordingly, while the threshold range does not appear to be applied identically between the two bodies, the JCVI have clearly used NICE's threshold range to inform their guidance.

The recommendation that the threshold be reduced to £15,000/QALY is supported in the consultation report with reference to recent empirical estimates of the opportunity cost of health foregone within the NHS [23]. While the Claxton et al. estimate is only one attempt to estimate the opportunity cost within the health system, it must be remembered that the £20,000–30,000/QALY threshold range currently recommended by NICE and referenced by the JCVI is not supported by any empirical evidence

[24,25]. Therefore, while more evidence to support the threshold would be desirable, the proposed revision represents a clear improvement over the current arbitrary benchmark.

Although reducing the threshold is consistent with recent empirical evidence, a notable difficulty (of which the JCVI are apparently aware) is that there is no apparent commitment by NICE to make a similar reduction. A unilateral threshold reduction by the JCVI without a similar change by NICE would then place potential vaccine recipients at disadvantage relative to other patients. This could then lead the irrational and inefficient situation whereby the health system would not be willing to prevent certain illnesses, but would be willing to spend more to treat them as they emerge. How this inconsistency is best resolved is unclear. It is arguably the responsibility of other bodies to bring their thresholds in line with emerging evidence rather than the JCVI's obligation to wait for them. Accordingly, we support the JCVI's decision to recommend a reduction despite the lack of consensus with NICE.

Recommendation 7.6 relates to uncertainty analysis. A commonly used method of representing uncertainty in CEA is the cost-effectiveness acceptability curve (CEAC), which is derived from an exploration of uncertainty within decision analytics models through the process of probabilistic sensitivity analysis (PSA) [26,27]. CEACs represent the proportion of PSA iterations from an analysis in which a given intervention strategy is found to be the most cost-effective. Current NICE guidelines advise that CEACs can be used to represent uncertainty, but do not stipulate a decision rule regarding what level of uncertainty is acceptable and what is not [2]. The JCVI's current Code of Practice provides additional guidance beyond what NICE requires. It outlines that the Department of Health needs to be "almost sure" that purchasing a vaccine will yield a net health benefit. It suggests that no more than 10% of PSA iterations can exceed a cost-effectiveness threshold at £30,000/QALY [2]. Accordingly, we can see in the existing guidance, the JCVI is more prescriptive regarding the handling of uncertainty and provides a quantitative framework for understanding how its risk aversion applies to reimbursement decisions. The JCVI guidance on uncertainty analysis is explicitly caveated with an explanation that the 10% rule is not a hard decision rule, but is more a starting point for discussions on the topic of uncertainty.

Recommendation 7.6 is to retain the JCVI's current uncertainty criterion, but with a minor reduction of the threshold such that no more than 10% of PSA iterations can exceed a threshold of £25,000/QALY. The CEMIPP report states that the reduction in the threshold used in the suggested uncertainty criteria is to reflect the reduction in the baseline cost-effectiveness threshold made in recommendation 7.2.

Despite the JCVI's qualification that the uncertainty criterion is not a strict rule, we suggest it is problematic for a number of reasons. The first is that there is no clear rationale to impose a risk preference if, in principle, we expect decision makers to be risk neutral [28]. Secondly, even if, in practice, decisions makers are risk averse, there is no clear framework within CEA for determining an appropriate quantitative response. Basing a decision criterion on the proportion of PSA iterations that are not cost-effective has been criticised previously as only reflecting the probability of error and not reflecting the gravity of that error [29]. A further problem is that the probability of error is contingent on the number of strategies compared in an analysis [30]. Accordingly, this means the JCVI's uncertainty metric is somewhat arbitrary. Similarly, the amount of uncertainty within the analysis is likely to be highly contingent on the time horizon used, especially if the discount rate is reduced. Finally, since NICE does not impose a similar uncertainty criterion, vaccine manufacturers may need to absorb large compensating cost-reductions to reduce the risk of error that do not apply to manufacturers of other interventions. In summary, even if the uncertainty criterion is not used strictly, it appears to be arbitrary in a number of respects and inconsistent with the approach to uncertainty used by NICE.

4. Points of secondary importance

Recommendation 3.4 states that long term impacts not amenable to the discounting paradigm should be explicitly noted and assessed as part of the overall cost-effectiveness considerations. In general, discounting is considered applicable to all outcomes in cost-effectiveness analysis. Nevertheless, there have been suggestions that this could be problematic, as it could lead decision makers to place insufficient value on the benefits or costs of very significant future events. In particular, there have been debates within the climate change literature around the point that applying commonly used discount rates could provide very little incentive to take costly, but necessary measures to avoid future disaster from global warming [31].

The CEMIPP report does not explain the rationale for exempting certain outcomes from discounting in any great detail, but it does briefly relate it to the prospect of eradicating disease [4]. Although not stated explicitly, the implication seems that the open-ended stream of benefits that would stem from eradication should be treated differently from other health gains. If this is a fair interpretation of the recommendation, then it is problematic. There is no clear reason why an open-ended stream of benefits should not be discounted while finite streams are. Indeed, it is relevant to note that the sum of a discounted infinite series of future values has a finite value. As such, discounting may prove a useful way of appropriately balancing the benefit of eradication against the healthcare needs of current populations. The practical import of this point is likely to be limited, however, as examples of eradication are likely to remain exceptions unfortunately.

Recommendation 4.1 relates to the choice of the time horizon applied within a CEA. In CEAs of non-infectious diseases, a time horizon equivalent to the lifetime of one patient cohort is usually sufficient to capture all meaningful consequences [13]. In the case of infectious disease control, there are reasons to consider longer horizons, as herd immunity effects may take decades to accumulate. In such cases, simulation analyses with multiple overlapping birth cohorts are required to simulate the long term effects of an intervention. Some analyses may simulate as many as 60 or 100 consecutive birth cohorts. Although the need for such extended time horizons are recognised in the literature, they are not explicitly mentioned in the existing JCVI Code of Practice or current NICE guidence.

Recommendation 4.1 states that an indefinite time horizon should be used in analyses and that the effects of varying the horizon should be considered in sensitivity analyses. Such a lengthy timescale would permit models to accrue herd immunity effects that might be censored by shorter time horizons. As such, we support the use of extended time horizons. Nevertheless, it is worth considering what the consequences of extending the time horizon may be for the JCVI's proposed uncertainty criterion mentioned above. The certainty that an intervention is cost-effective might decline as the period of analysis is extended over a long period. The JCVI may need to consider how to resolve such inconsistencies.

Related to the issue an infinite time horizon, it is notable that the CEMIPP report does not mention issues of patent expiry and the entrant of newer patent protected competing interventions over the life span of the intervention [32]. While the appraisal of the full herd immunity effects may require a model that considers five or six decades of implementation, patent expiry or obsolescence typically arrives within two decades. Accordingly, we suggest these issues are likely to be of greater quantitative significance and practical relevance than the adoption of an infinite horizon. While there currently appears no clear or cogent way to

consider these pragmatic aspects of pricing and use, the JCVI may wish to support research on how they should be best managed in the future.

Recommendation 6.2 relates to the incorporation of "peace of mind" benefits. This relates to ascribing a value to knowing that one is protected against disease because of inoculation. Such a proposal is controversial as it ascribes a value over and above the benefit of reducing disease burden itself, but relates to a concern about that burden. Peace of mind benefits are not typically included in economic analyses presently.

We strongly support the evident caution shown in the recommendation that research is needed on incorporating "peace of mind" benefits and the advice against including such benefits until strong evidence for their inclusion can be shown. We note the mention in the CEMIPP report that such benefits could equally be claimed for the knowledge that treatment is available should one fall ill [4]. Furthermore, it is important to remember the principle that claims for including additional benefits for given interventions need to be considered carefully, especially when these might also apply to the opportunity cost: the displacement of other health care services to fund new interventions might diminish the "peace of mind" currently enjoyed by other patients elsewhere within the health system.

Recommendation 6.3 states that the JCVI should take care recording and presenting value judgements when applying differential weights to outcomes. While the standard approach within CEA is to value all health gains equally, some exceptions have been applied. Most notably in the case of the JCVI, it permitted the application of a quality of life adjustment factor (QAF) of three in the case of an analysis of meningitis B vaccine because the recipients were children [11]. This effectively valued the health of the recipients in that case at three times that of other patients.

We strongly support recommendation 6.3, but would suggest going further by requiring decision makers explicitly acknowledge that, by applying differential weights, they are valuing the health of some individuals more than others. For example, in the case of meningitis B vaccine, we suggest decision makers would be obliged to make a statement such as "the committee endorses the QAF in this analysis, such that we consider the health of one child to be worth that of three adults". We believe that such an explicit acknowledgement of differential weights might clarify the ethical challenges of weighing the health of some people more than others.

Recommendation 6.6 notes that the JCVI should monitor methods developments in other bodies regarding differential weighting of health losses and health gains. As mentioned above, the standard analysis applied within CEA is to value the health of all equally, meaning that the health gains of all individuals as measured by QALYs carry equal weight, irrespective of age, gender, disease or type of intervention. This approach has be modified (or eroded) to a degree by a small number of exceptions. One has been the up weighting of health gains at the end of life [33], another more recent exception has been the acceptance of higher thresholds for highly specialised treatments [34]. One particularly relevant exception was the acceptance by NICE for lower discount rates for certain interventions that provided very long term health gains, on the condition that these were achieved through a therapeutic rather than a preventative effect [35]. This example is notable, as there is typically neutrality regarding prevention versus cure, with the QALY gains from each being valued equally. While such departures from standard methods have had their vociferous critics, they largely remain the exception. The statement that the JCVI will closely monitor such developments elsewhere demonstrates that it has an awareness of the exceptions that have made in certain cases.

It is notable that Recommendation 6.6 itself does not endorse any departure from the standard equity position with CEA. Moreover, it clearly does not advocate a greater weight for the prevention of health loss rather than its therapeutic restoration. Moreover, the JCVI Code of Practice explicitly states there is reason to prioritise prevention over cure [2]. We believe the JCVI's position is appropriate, as any differential weighting could result in perverse consequences such that there might be a policy preference for strategies that save fewer lives through prevention than could have been saved through cure. More broadly, we would encourage decision makers to critically examine claims for exceptions from standard methods based on evidence of human heuristics as opposed to a rational deliberation of the principles involved.

5. Discussion

We support the initiative demonstrated by the JCVI to revise its CEA guidance. In particular, we agree with the proposals to reduce both the discount rate and the cost-effectiveness threshold. While we believe the JCVI are right to reduce the discount rate to 1.5%, we think the wrong evidence base has been used to inform this change. We feel the JCVI should be commended for recommending a reduction in the cost-effectiveness threshold, even though a similar commitment has not yet been made by NICE. We suggest that the JCVI reconsider its current uncertainty criterion and the proposed revision, both of which appear problematic.

Public consultations on cost-effectiveness methods, such as that undertaken by the DHSC and JCVI, are welcome. They are important for eliciting views from experienced analysts which may avoid unintended consequences of changes to economic evaluation methods. The recent JCVI consultation can be contrasted with the limited consultation undertaken by the Second Panel on Cost-Effectiveness in Health and Medicine, which resulted in confused discounting recommendations that failed to make the best use of existing theoretical and empirical research [36]. Both the CEIMPP report and the DHSC consultation provide carefully considered documents that elucidate many of the relevant issues. This demonstrates that the issues have been considered and the importance of good methods guidance is appreciated. We hope this commentary will inform debates over methods revision, both by the JCVI and NICE. We look forward to a similarly open and constructive consultation exercise from NICE when its methods guidelines are next considered for revision.

While the JCVI's methods guidelines are primarily of significance to UK vaccination policy, there is a broader international significance to the JCVI's revision of vaccination-specific guidelines. NICE's appraisal guidelines are among the most detailed worldwide and offer a clear template for adaptation for other countries to follow. Analogously, the JCVI's advice has global significance, as most other countries do not issue specific additional advice for such interventions. Accordingly, both the content of the recommendations themselves and the broader process of open consultation and refinement are useful examples for other jurisdictions.

Declaration of interest

None.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A

See Table 1.

Table 1
CEMIPP report recommendations.

1	**Perspective on costs and outcomes**
1.1	JCVI should adopt, or trial in shadow mode, full economic utility as the scope of impacts to be assessed within evaluations if and only if this is the recommended "best practice approach" for archetypal evaluations selected by the AAWG.
1.2	Case-by-case selection (by the manufacturers, by JCVI or by modelling teams) of impacts to be considered should be avoided to promote consistency across evaluations and fairness to those whose benefits would be displaced (concerning whom bespoke analysis is intrinsically more difficult).
1.3	JCVI or DH should commission an infographic or other summary relating to the displaced benefits that can be used to inform discussions held by JCVI given the intrinsic difficulty of assessing the impact of specific factors upon the displaced.
2	**Incremental analysis of all relevant comparators**
2.1	Evaluations of immunisation programmes should be conducted on an incremental basis.
2.2	The options to be compared should be clearly described and justified. Careful attention should be given to ensuring that the programme configurations compared comprise the range of options (including the status quo) among which the best is likely to be found, for instance including options where a new dose is added and an existing dose is removed.
2.3	JCVI should be asked to advise on the clinical and scientific aspects of the options. Public health experts should be asked to advise on practicalities of implementation and vaccine availability.
3	**Discounting**
3.1	Health impacts (benefits and the displacement effects of expenditure) should be discounted at 1.5%.
3.2	Any non-health benefits and costs outside the health system, included in evaluations, should be discounted at 3.5%.
3.3	These rates should not change within the period of analysis (discussed in the next section).
3.4	Long term impacts not amenable to this discounting paradigm should be explicitly noted and assessed as part of the overall cost-effectiveness considerations.
4	**Time horizon of the evaluation**
4.1	Immunisation programmes should be evaluated using an indefinite timescale and, as a sensitivity test, an analysis should be undertaken to highlight the extent to which the estimated cost-effectiveness is influenced by this choice of discount rate and time horizon.
4.2	Decision makers should be advised on how to interpret the difference between the two sets of results and the role of the QALY gains and losses in the far future in the difference between the results.
4.3	While review of procurement methodology is beyond the remit of this working group, the Department should give consideration to how uncertainty regarding cost-effectiveness, and specifically sensitivity analyses should be included in the procurement methodology.

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