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Quantifying Impact on Health Inequality in England: Revised Final Report and Web-Based Calculator

Richard Cookson and James Koh

CHE Research Paper 193

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Background to series

CHE Discussion Papers (DPs) began publication in 1983 as a means of making current research material more widely available to health economists and other potential users. So as to speed up the dissemination process, papers were originally published by CHE and distributed by post to a worldwide readership. The CHE Research Paper series takes over that function and provides access to current research output via web-based publication, although hard copy will continue to be available (but subject to charge).

Acknowledgements

This is an updated version of an unpublished report to the UK National Institute for Care Excellence (NICE) from July 2021. It is based primarily on independent research by the University of York funded by NICE from August 2020 to June 2021 via the Medical Technologies Evaluation Programme (MTEP) and managed by the Centre for Guidelines. The original project was conducted by Richard Cookson and James Koh with advisory input from Susan Griffin, Rita Faria and Fan Yang, and the NICE Project Leads were Lesley Owen and Monica Desai.

Subsequently to the original project a more user-friendly version of the web-based health equity impact calculator was produced (Version 2), with funding from the Wellcome Trust, by Paul Schneider and Richard Cookson in collaboration with Tim Doran. In addition, emerging evidence has suggested that the health opportunity costs of cost-increasing healthcare interventions may not be disproportionately borne by more deprived populations, as was previously thought at the timing of writing the original unpublished report in 2021, and hence equality of opportunity cost may be a reasonable base case assumption. This emerging evidence comes from independent research by the University of York funded by the UK National Institute for Health Research from November 2020 to November 2023 (NIHR 130258, “Unmet Need in Equitable Healthcare Resource Allocation”), conducted by Richard Cookson, Misael Anaya-Montes, Katja Grašič and James Lomas in collaboration with Laura Anselmi, Miqdad Asaria, Ben Barr and Matt Sutton. At the time of writing (September 2023) this evidence remains unpublished.

We are especially grateful to Lesley Owen for her extremely helpful comments on both the original draft report and this revised report, and to Paul Schneider, for this excellent work in coding Version 2 of the calculator. We would also like to thank Susan Griffin, Deborah O’Callaghan and Michael Toolan for helpful comments on the original draft report, James Lomas, Mike Paulden and the NICE officials and advisers we consulted during the original project work in early 2021 (listed in Appendix A) for helpful discussions, and Neil Hawkins and many other colleagues, students and officials who have subsequently provided helpful feedback.

No ethical approval was required.

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Disclaimers

This report has not gone through a formal peer review process. We are publishing it in a long and detailed format to facilitate discussion and comment and to help interested colleagues and students of distributional cost-effectiveness analysis gain a detailed understanding of the web-based calculator and its strengths and limitations.

James Koh was employed by the University of York when providing his contribution to this report. The views expressed in this report do not necessarily reflect those of NICE, where he is currently employed.

The views expressed in this report, and any errors they may contain, are those of the authors and not necessarily those of the NHS, NICE, the Medical Technologies Evaluation Programme, the Wellcome Trust, the NIHR or any of the individuals listed above.

The authors offer no guarantees or warranties of any kind for users of the accompanying web-based calculators. Users are responsible for how they use the calculators, the relevance and accuracy of their own data inputs and assumptions, and how they interpret the findings.

Declared competing interests of authors

Richard Cookson reports grants from the Wellcome Trust for related work received during this study, that he was until the end of 2021 a member of the NHS Resource Allocation Advisory Committee, that he has done work on distributional cost-effectiveness analysis and health inequality for academic, public sector and commercial organisations including paid advisory and educational work for pharmaceutical manufacturers and consultancy firms (Genentech/Roche, GSK, Bristol Myers Squibb, Congentia) that may have an interest in this research.

James Koh reports undertaking paid consultancy/research for pharmaceutical manufacturers that may have an interest in this research.

Corresponding author: Richard Cookson, Centre for Health Economics, University of York, York YO10 5DD, Email: richard.cookson@york.ac.uk

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Centre for Health Economics
University of York
York
YO10 5DD
UK

york.ac.uk/che

Contents

Summary

Background

- *NICE Strategy 2021 to 2026* recognises the important role the National Institute for Care Excellence (NICE) can play in the national drive to reduce health inequalities, defined by the UK Government and the National Health Service (NHS) as unfair differences in health between more and less socially disadvantaged groups.
- Although NICE cannot do much to address wider social and economic causes of health inequalities that lie beyond the control of the NHS, such as inequalities in wealth, education and power, it can try to ensure that its guidance does not increase health inequalities and where possible reduces health inequalities.
- To facilitate a more transparent and concerted approach to reducing health inequalities, NICE could routinely supplement its cost-effectiveness analyses with quantitative analyses of the impact on health inequalities.
- NICE commissioned this project by the University of York to examine the feasibility of doing this routinely in both clinical and public health guideline development and technology appraisal, building on recent methodological advances and NICE's existing strengths in health economic analysis.

Aims

1. To develop a prototype health inequality impact toolkit (comprising a calculator and critical appraisal checklist) that health economists can use to produce and critically appraise simple quantitative estimates of the impact of NICE guidance on health inequalities.
2. To seek feedback from NICE officials and advisers on how this toolkit could potentially be used in practice in different types of guidance at different stages of decision-making.

Calculator Version 1 (Koh): https://shiny.york.ac.uk/nice_equity_tool

Calculator Version 2 (Schneider): https://shiny.york.ac.uk/dceasimple

- The calculator estimates the impact on inequality in quality-adjusted life expectancy at birth (QALE) between five quintile groups of neighbourhoods in England based on the neighbourhood index of multiple deprivation (IMD).
- The IMD includes income, employment, disability, education and skills, crime, housing and service barriers and living environment.
- This provides a general summary measure of impact on health inequality, based on NICE's standard QALY metric, which is comparable across health conditions and provides useful context for more specific health inequality breakdowns by ethnicity, gender, regional deprivation and other social disadvantage characteristics (e.g., rough sleeping, drug use).
- The calculator implements the method known as "simple" or "aggregate" distributional cost-effectiveness analysis (DCEA), using basic inputs from standard cost-effectiveness analysis (the incremental cost and QALY gain per recipient) and data or assumptions about social distributions at four steps in the pathway leading to health inequality impact: the eligible population, uptake, health effects and health opportunity costs.
- The calculator provides a set of "default" distributional assumptions at each step, including a built-in prevalence look-up table to estimate the social distribution of the eligible population, currently based on hospital episode statistics for 2011 for all 3-digit ICD-10 codes and survey data for a handful of risk factors (e.g., smoking), and default assumptions of equal uptake, equal health effects, and equal health opportunity costs.
- It also facilitates sensitivity analysis using alternative assumptions.
- It can also analyse trade-offs between cost-effectiveness and reducing health inequality, by showing the implications for the incremental cost-effectiveness ratio (ICER) of different degrees of concern for reducing health inequality.
- "Triage" DCEA, to gauge whether further analysis is warranted, can be done rapidly based on guestimates of standard cost-effectiveness inputs.
- If "triage" DCEA shows that health inequality impact might be decision-relevant, further analytical time input may be warranted to produce and review a more robust estimate, alongside the process of producing and reviewing standard cost-effectiveness (CEA) evidence, by sourcing and critically appraising bespoke data and expert opinions about inequality in prevalence and other potentially relevant distributional inputs.

- It may also sometimes be worth commissioning a “full” DCEA analysis requiring many weeks of analyst time in conducting de novo cost-effectiveness modelling.

Potential Uses of DCEA Estimates of Impact on Health Inequality

- First, to support the development of supplementary recommendations to increase uptake of cost-effective interventions in socially disadvantaged populations – for example, screening interventions like lung health checks, and interventions with stronger delivery infrastructure in affluent regions, like HIV prevention.
    - Routine and consistent quantification could help NICE do this more consistently between different advisory groups and intervention topics, including technology appraisal as well as guideline development.
- Second, to influence “yes-no” recommendations for interventions that lie close to the appropriate cost-effectiveness decision threshold, both in guideline development and technology appraisal
    - The impact on health inequality will often not be a decision-relevant consideration – for example, the impact might be small for conditions with a flat social gradient in prevalence, or slightly more prevalent in advantaged populations, like colorectal cancer.
    - A substantial positive impact on reducing health inequality might sometimes change a borderline decision from “no” to “yes” – for example, interventions for conditions with unusually steep social gradients in prevalence that are extremely common in disadvantaged populations, like sickle cell disease or Hepatitis C, and new technologies with a disproportionate benefit in disadvantaged populations due to inequality of utilisation and adherence to existing technologies, like more convenient medication for diabetics with poor blood sugar control.
    - Conceivably, a substantial negative impact on increasing health inequality might sometimes change a borderline decision from “yes” to “no” – though in practice this may be rare, since few conditions are substantially more prevalent in advantaged populations, and unequal uptake is usually a reason for re-designing delivery rather than denying access to everyone.
- Third, information on inequality in prevalence, and how this may vary over the life course, can help to frame deliberations on health inequality and add analytical insight and nuance.

- The most straightforward way for NICE to begin using DCEA would be in the context of clinical and public health guideline development, to support more consistent development of supplementary guidance on uptake in socially disadvantaged populations.
- With suitable modification of technology appraisal methods guidance, NICE could potentially also start using this information in the context of technology appraisal, to influence “yes-no” funding decisions about new patented technologies as well as developing supplementary guidance on uptake in disadvantaged populations.
- If health care payers in other countries followed NICE’s lead, use of this information could then potentially start to modify global R&D incentives towards innovating in ways that improve human health and longevity without leaving socially disadvantaged people behind – for example, by re-balancing R&D investment towards conditions disproportionately suffered by disadvantaged populations (e.g. mental illnesses) and finding innovative ways of reducing barriers to uptake among socially disadvantaged populations.

Recommendations

Our main recommendations are that:

1. NICE should pilot the health equity impact calculator, both in clinical and public health guideline development topics and in technology appraisal, to gauge the resources required to use DCEA in practice and learn lessons.
2. NICE should undertake, commission and/or partner in further work to prepare for routine use of DCEA across all NICE activity, including the development of user interface and training materials as well as considering how the outputs would be quality assured and used and impacts on NICE’s ways of working.
3. NIHR should develop guidance on collecting and reporting health inequalities data across all NIHR funded research, and commission long-term research on intersectionality between neighbourhood, ethnic and gender inequalities in health.
4. NICE should work with the Department of Health and Social Care to start developing and piloting modified versions of the calculator to supplement cost-effectiveness analyses used to support decision making by other NHS agencies, for example, the Joint Committee on Vaccination and Immunization, the NHS National Screening Committee, and the Office of Health Improvement and Disparities.

"The COVID-19 pandemic, with its disproportionate impact on those already disadvantaged in society, has brought the issue of health and wider inequalities into sharp focus… We have an important role to play in reducing health inequalities…Although health inequalities are already considered in all aspects of our work, the national drive to improve and protect the public's health and reduce health inequalities post-COVID-19 means we will need to enhance the role we play and strengthen our offer."

NICE Strategy 2021 to 2026
(Published April 2021)

1. Introduction

Background

The development of National Institute for Health and Care Excellence (NICE) guidance routinely involves cost-effectiveness analysis that provides an indication of the likely total population health impact in terms of quality-adjusted life years (QALYs). However, NICE does not routinely quantify the likely impact of its recommendations on unfair differences in health between more and less socially advantaged groups.

Unfair differences in health of this kind are known in the UK as "health inequalities", and that is also the term we use in this report. However, terminology varies. In the USA, the usual term is "health disparities", and the World Health Organization uses the term "health inequities". According to Whitehead and Dahlgren and the World Health Organization, "Three distinguishing features, when combined, turn mere variations or differences in health into a social inequity in health. They are *systematic, socially produced* (and therefore modifiable) and *unfair*." (Whitehead et al., 2006). In practical measurement terms, this means that health inequalities are differences in health between more and less socially advantaged groups – for example, groups defined by socioeconomic status or ethnicity – which display a social gradient whereby socially disadvantaged people systematically tend to have worse health than socially advantaged people.

NICE does already routinely use "equality impact assessments" (EIA) to facilitate compliance with its ethical and legal duties under the Equality Act 2010. For example, the current Centre for Guidelines methods manual requires that EIAs are completed at scoping, development and committee stages. In practice, however,

EIAs are mostly qualitative assessments of potential impact of NICE recommendations on protected characteristics under human rights legislation (i.e. age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, sexual orientation) rather than quantitative estimates of the impacts of NICE recommendations on differences in health between more and less socially disadvantaged groups defined by characteristics such as income, employment, education and skills, crime, housing, and living environment.

Routine quantification using a consistent approach that allows comparisons of the direction and magnitude of health inequality impact between different interventions in different health conditions could help NICE take a more transparent and concerted approach to reducing health inequalities. This could potentially be done at all stages of decision-making, from the earliest stage of topic selection through to scoping, assessment and guidance development and on to implementation support.

Although health inequalities are already considered by NICE and other government bodies, the amount and type of information provided varies considerably and quantitative analysis tends to focus on describing pre-existing health inequalities rather than analysing the expected impacts of interventions on health inequalities. There is no consistent approach to quantifying the direction or magnitude of the impact of interventions on health inequalities in a way that can be compared from one decision topic to another. Furthermore, there is no attempt to identify and articulate the trade-offs that sometimes arise between redistribution of health resources to tackle health inequalities ("equity") and the NICE model of distribution based on investing in the most cost-effective treatment for the whole population ("efficiency") (House of Commons Health Committee, 2009). Routine quantification of impacts on health inequality using a coherent analytical framework could help NICE to start explicitly identifying and articulating these trade-offs.

Routine and consistent quantification is of course only one aspect of the broader challenge of developing consistent deliberative processes for handling health inequality considerations. But it is an important aspect, in which NICE could potentially become a world leader given its analytical firepower and strengths in health economic analysis.

Methods of "distributional" cost-effectiveness analysis (DCEA) now exist for quantitative analysis of health inequality impacts and trade-offs (Cookson et al.,

2020; Cookson et al., 2021b). DCEA allows an intervention to be plotted in the four quadrant “equity-efficiency impact plane”, with the comparator at the origin, which shows whether the intervention lies in the “Win-Win” quadrant (both cost-effective and reduces health inequality), the “Lose-Lose” quadrant (not cost-effective by conventional standards and also increases health inequality) or one of the two “equity-efficiency trade-off” quadrants – “Lose-Win” (not cost-effective by conventional standards but reduces health inequality) and “Win-Lose” (cost-effective but increases health inequality). DCEA also provides analytical tools for quantifying equity-efficiency trade-offs using the concept of health inequality aversion, which specifies the decision maker’s degree of concern for reducing health inequality in terms of their willingness to forgo gains in total health. This can help inform decision makers facing equity-efficiency trade-offs, for example in assessing whether a new medicine in the “Lose-Win” quadrant may be worth funding to help reduce health inequality, or whether a public health prevention programme in the “Win-Lose” quadrant may merit further investment in programme re-design to increase uptake among more disadvantaged populations. A full DCEA involves re-engineering an existing decision analytic model for cost-effectiveness analysis, or designing a new one, to account for differences between more and less socially advantaged groups in intervention needs, uptake, effects and costs. Since this can be resource intensive, a simple version has also been developed (Griffin et al., 2019b; Love-Koh et al., 2019). Simple DCEA is sometimes termed the “aggregate” approach because it takes existing “aggregate” outputs from a standard cost-effectiveness analysis as basic inputs (in particular, incremental costs and QALY gains) and adds simple further distributional modelling on top of that, rather than going “under-the-bonnet“ of the original cost-effectiveness model to do more complicated modelling that involves re-calculating the aggregate costs and health effects through detailed underpinning epidemiological and decision analytical modelling.

In the context of technology appraisal, the main driver of health inequality impact is inequality in the diagnosed prevalence of the condition and consequent inequality in the number of people from different social groups who stand to benefit from the new technology. Introducing a new treatment will usually not change pre-existing social patterns of disease prevalence and diagnosis, but those pre-existing patterns will influence who benefits from the new treatment and hence the health inequality impact. However, in the context of clinical and public health guideline development, it is often also important to consider inequality in intervention uptake within the

eligible population. If need be, simple DCEA can also account for social variation in health effects on people who receive the intervention, if these are clear and substantial. Importantly, simple DCEA also accounts for social variation in health opportunity costs – the health losses due to intervention costs, because scarce resources used to fund the intervention could otherwise be used to improve health in other ways. See later in the report for details on data sources, potential biases and uncertainties, and robustness checks.

To facilitate more systematic and consistent handling of health inequality considerations, it would be useful for NICE to have a health inequality impact "calculator" that allows a quick and simple form of "triage" DCEA to be conducted rapidly for any kind of decision at an early scoping stage of the process, to determine the likely direction and magnitude of health inequality impact and whether this is likely to be decision relevant. Where appropriate, this calculator could also be used at a later stage to facilitate the production and review of simple DCEA estimates of health inequality impact that are sufficiently robust to be used to support coverage decisions. This would allow quantitative estimates of health inequality impact to be used routinely by NICE based on a reasonably comparable set of methods and base case data inputs and assumptions, including sensitivity analysis around alternative inputs and assumptions to assess the degree of uncertainty around the direction and magnitude of impact on health inequality.

If they are to be used in to inform funding decisions and guidance development, estimates of the likely direction and magnitude of health inequality impact would require thorough critical appraisal, interpretation and communication to a wide range of stakeholders, including careful scrutiny of the evidence and assumptions on which it is based and its sensitivity to alternative reasonable assumptions. Hence it would also be useful to have a "checklist" to facilitate critical appraisal and communication of heath inequality impact findings.

Aims of the project

1. To develop a prototype health inequality impact toolkit (comprising a calculator and critical appraisal checklist) that health economists can use to produce and critically appraise quick and simple quantitative estimates of the impact of NICE guidance on health inequalities

2. To seek feedback from NICE officials and advisers on how this toolkit could potentially be used in practice in different types of guidance at different stages of decision-making including topic selection, scoping, guidance development and implementation support.

The aim of this study was to create a working prototype of a health inequality impact toolkit that could potentially be used by health economists to conduct and critically appraise DCEA triage and the production of simple DCEA estimates, to inform NICE's deliberations at topic selection, scoping, committee and implementation stages.

The project was initiated in the context of public health guideline development but broadened during the commissioning process to explore the potential for using the toolkit across the full range of different types of NICE guidance including technology appraisal. It was funded by the MTEP programme with project leads from the public health guideline development.

The resulting prototype calculator, produced in 2021 and coded by James Koh, is a web-based tool at the URL below, and the checklist for critically appraising health inequality impact estimates is in Appendix B.

Calculator Version 1 (Koh): **https://shiny.york.ac.uk/nice_equity_tool**

We subsequently produced a revised and more user-friendly version of the calculator, coded by Paul Schneider, which is at this URL and was produced in 2022 and then updated in 2023.

Calculator Version 2 (Schneider): **https://shiny.york.ac.uk/dceasimple**

How this information might be used

The checklist and calculator could potentially be used at all stages of NICE decision making, both in the process of clinical and public health guideline development and in the process of technology appraisal. It could be used at different stages of decision making as follows:

(1) "Triage" DCEA could be useful at the topic selection and pre-scoping stages, to inform deliberations about the potential relevance, direction and importance of health inequality impacts, based on assumptions about plausible ranges of

incremental costs and health effects from evaluations of similar interventions in the past.

(2) Triage DCEA could also be useful at the scoping stage, to inform deliberations about whether and what further health inequality information is needed, about formulating the review questions, and about whether it is worth investing additional analytical time and resource into producing simple or full DCEA estimates.

(3) Simple or full DCEA could be useful at the assessment and guidance development stage, to help frame deliberations and ensure health inequalities issues are considered at an early stage by providing quantitative background information and pre-existing health inequalities, and to inform deliberations by NICE advisory committees and guideline development groups about the likely direction and magnitude of health inequality impacts. This information could help to justify and support the development of supplementary delivery recommendations to facilitate uptake among socially disadvantaged populations, and it could potentially influence yes-no recommendations (either for or against) in borderline cases where the incremental cost-per-QALY gained lies close to the appropriate cost-effectiveness decision threshold.

(4) Simple or full DCEA could also be useful at the implementation support stage, to inform deliberations about the potential need for additional investments to increase uptake among socially disadvantaged groups and how to take this forward in practice. If such investments would be too costly to recommend without robust evidence, this might also help to catalyse action by NHS agencies other than NICE and further work around effectiveness and cost-effectiveness.

A primer on simple DCEA

This section provides a brief primer on simple DCEA. The methods of DCEA have been summarised in various publications, including introductory level summaries for non-economists as well as advanced texts for specialists, and further information and training resources are available at this website https://www.york.ac.uk/che/research/equity/distributional-cost-effectiveness-analysis/

The basic concept is summarised in this diagram, known as the “equity-efficiency impact plane).

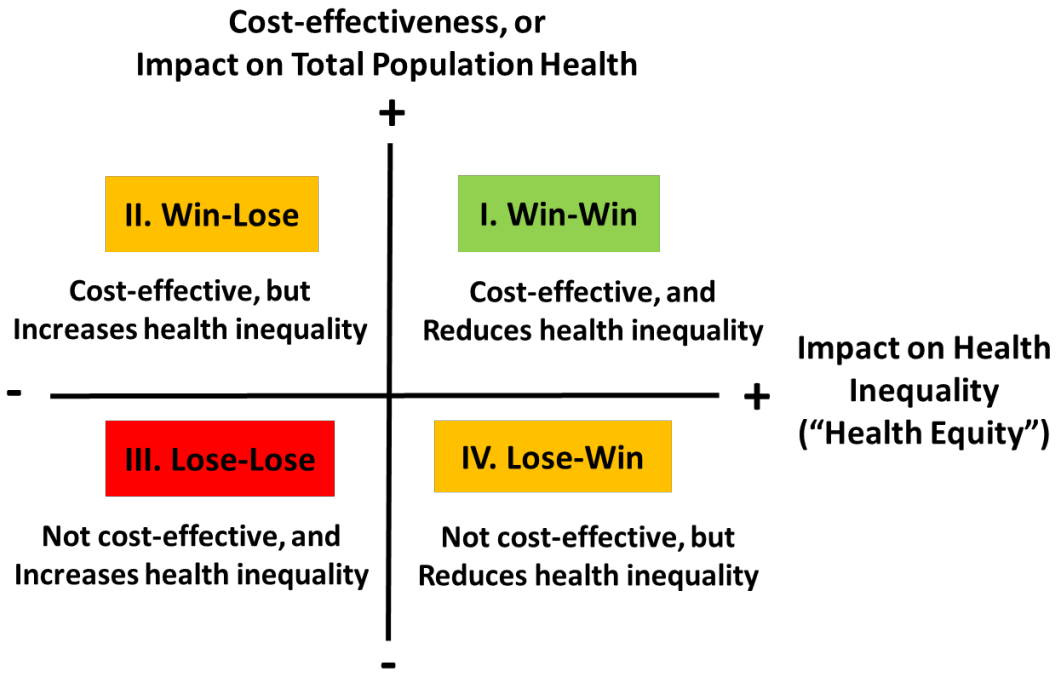


Figure 1: Equity-Efficiency Impact Plane

Standard CEA provides the vertical axis, and DCEA adds the horizontal axis: it quantifies the direction and magnitude of impact on health inequality.

Full DCEA requires careful modelling of the “staircase” leading to intervention impacts on health inequality (Figure 2).

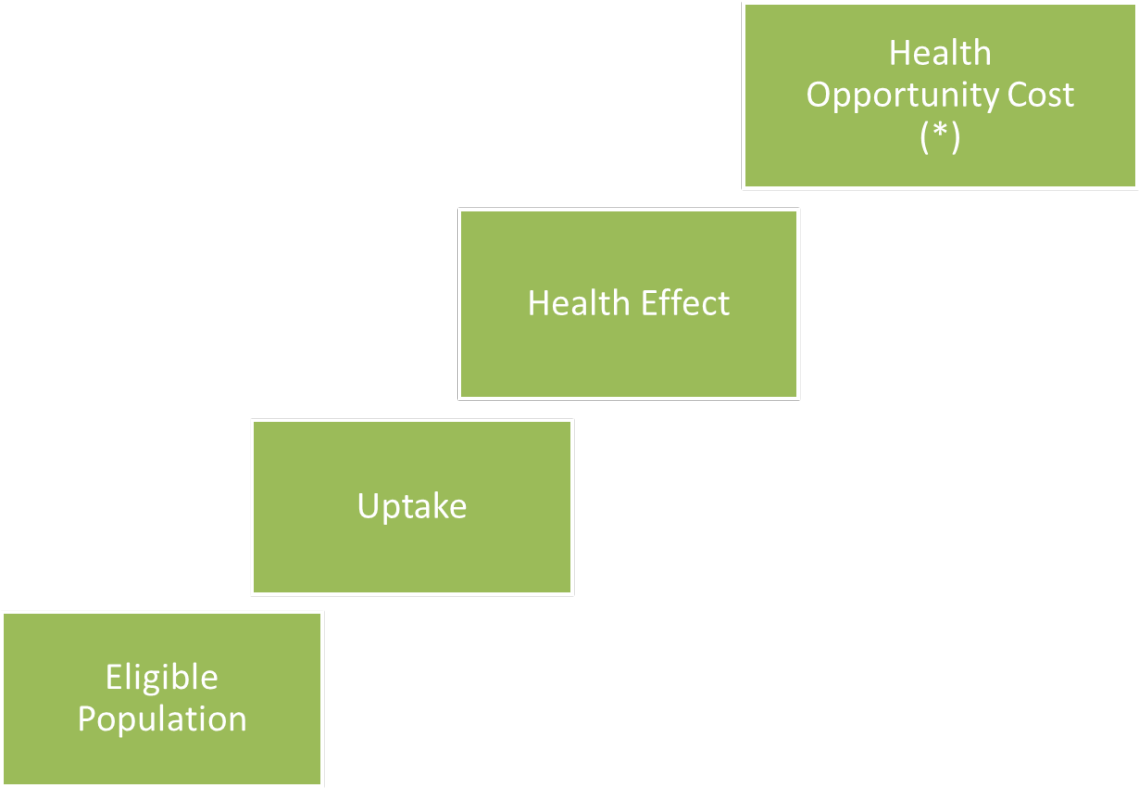


Figure 2: The Staircase Leading to Health Inequality Impact

Note: (*) Health opportunity cost means the health loss due to intervention costs, since scarce resources would otherwise be used to improve health in other ways.

Social variations may arise at different steps on the staircase – and different steps may shift the health inequality impact in different directions. This means that the overall direction and magnitude of health inequality impact may not be immediately obvious or may differ from the intuitive expectations of topic experts – hence the need for systematic analysis. Social variations at each step on the staircase depend not only on the “active ingredient” of the intervention (e.g., a drug, device, or medical procedure) but also on the wider social environment in which the intervention is delivered and used. Hence real-world data on that wider social environment are crucial in estimating the likely impact on health inequality – the information provided by randomised controlled trials (RCTs) alone is not enough. It is increasingly recognised that the same is true for estimating average costs and health impacts, which may differ between trial settings and routine practice for various reasons – most obviously, that trials usually recruit artificially restricted samples of patients who are not representative of the real-world patient population.

Full DCEA models these four steps in detail, based on a detailed underpinning decision analytical model which also re-estimates the standard cost-effectiveness findings. Full DCEA thus also provides a more accurate estimate of cost-effectiveness, by allowing carefully for real-world data on social variations in intervention uptake and health effects. By contrast, simplified DCEA models the four steps in a simplified manner, without re-estimating the underpinning standard CEA findings.

A core data input for simplified DCEA is real world data on the prevalence of the relevant disease(s) or risk factor(s) broken down by neighbourhood deprivation or other equity-relevant social disadvantage characteristics. This data can support inference on the social distribution of the eligible population i.e., how many people can potentially benefit from an intervention in each equity-relevant population group. Further data and assumptions are then needed to estimate further steps along the "staircase of inequality" leading to social differences in health benefits – in particular, differences in uptake (i.e., how many of the eligible population actually receive the intervention), health effects and health opportunity costs. However, estimating the social distribution of population eligibility is a fundamentally important first step in estimating health inequality impacts.

Data on the social distribution of prevalence or intervention eligibility are available for many diseases and risk factors, and in principle could be collected and presented to the relevant officials and advisers at the scoping stage of an assessment process, as part of the standard Equality Impact Assessment (EIA). However, it would also be useful to have a standard set of such data routinely collated and summarised in a comparable format that would provide a useful starting point, facilitate more rapid analysis and allow analysis at earlier topic selection stages.

By exploiting large administrative datasets on hospital activity (e.g., hospital episode statistics HES) primary care (e.g., CPRD) it is possible to create comparable tables of data on how the prevalence of different diseases by ICD-10 code varies by neighbourhood deprivation, age and sex. Data from large surveys such as the Health Survey for England allows this to be supplemented with prevalence data on risk factors such as smoking.

Tabular information that summarises how the prevalence of a standard set of disease categories and risk factors differs by equity-relevant characteristics could

thus be developed and maintained so that it could be applied relatively easily and consistently for simplified distributional cost-effectiveness analysis across the range of topics considered by NICE. This information may not always be precisely relevant – for example, the eligible population may be a specific sub-group of the ICD-10 disease category (e.g., a genetic sub-type or patients resistant to first-line therapy) – but would provide a useful initial indication and starting point for analysis.

This information could then be supplemented as needed by user defined inputs from standard cost-effectiveness analysis and further distributional inputs and assumptions. This would enable analysts rapidly to derive a simple approximate indication of the impact of proposed interventions on social inequality in health.

2. Methods

This methods section uses technical language and is written primarily for health economists and analysts who are familiar with the basic concepts of cost-effectiveness analysis. In what follows we also presume familiarity with the basic concepts of DCEA. We refer the reader to the "primer on DCEA" section earlier in this report, to the OUP handbook of DCEA and two journal articles on simplified DCEA (Griffin et al., 2019b; Love-Koh et al., 2019; Cookson et al., 2020) and to various other introductory and advanced training materials in DCEA which are summarised at this web page: ***https://www.york.ac.uk/che/research/equity/distributional-cost-effectiveness-analysis/***

Data

Underpinning the calculator is a built-in "look-up table" that enables users to select the disease category (3-digit ICD-10 codes) or risk factor (e.g., smoking) most relevant to the health programme under consideration, and automatically estimate the corresponding proportional size of the eligible population by five quintile groups of neighbourhoods in England based on the index of multiple deprivation (IMD). The IMD combines neighbourhood-level information on many different domains of social disadvantage including Income (22.5%) - Employment (22.5%) - Health Deprivation and Disability (13.5%) - Education, Skills Training (13.5%) - Crime (9.3%) - Barriers to Housing and Services (9.3%) - Living Environment (9.3%).

This prototype allows multiple disease categories or risk factors to be selected to provide an overall distribution. However, it does not handle overlaps between two or more different health conditions in a sophisticated way – it simply adds up the condition-specific totals, allowing double counting of people with co-morbidity and multi-morbidity. This is fine when using two or three ICD-10 codes to capture the same basic disease category (e.g., two or three 3-digit codes for different kinds of colorectal cancer) but can generate bias when diverse conditions are selected. One issue is that total prevalence may be over-estimated; a second issue is that the relative shares of prevalence by social group might be inaccurate. The first problem is relatively easy to address by providing a user defined estimate of total prevalence; the second problem is harder to address as it would require analysis of detailed data on multi-morbidity overlaps by social group.

The lookup table in the prototype health inequality impact calculator is based on data that were readily available to the research team: HES data on episode counts from financial year 2010/11 for disease category look-ups by all ICD-10 3-digit codes, and Health Survey for England data for calendar year 2018 for a handful of readily available risk factor look-ups (smoking, obesity, low physical activity, high risk alcohol consumption). Relevant data access permissions and data protection procedures were followed, and we have ensured that the look-up table contains no disclosive information (e.g., counts of less than 5).

Software platform

The calculator is built using R. The online application is developed using Shiny, an R-package that can be used to create a graphical, web browser-based interface that allows users to adjust parameters in an underlying R model without exposure to the source code.

In the calculator, users enter a set of inputs and assumptions that includes the disease area or risk factor, standard cost-effectiveness results and intervention uptake rates. The application then automatically produces a range of graphs and tables summarising the health inequality impacts that can be readily exported into a downloadable report. Example reports are provided in Appendix C.

Underpinning DCEA methods

The simplified DCEA methods underpinning the calculator are described in two academic papers on “aggregate” DCEA (Griffin et al., 2019b; Love-Koh et al., 2019) and full DCEA methods are described in the Oxford University Press handbook of distributional cost-effectiveness analysis (Cookson et al., 2020).

The stages of analysis undertaken within the calculator can be illustrated by the concept of the ‘staircase’ or ‘pathway’ to inequality impact (see Chapter 8 of the DCEA handbook). The pathway describes the steps over the course of disease and treatment in which inequalities may be present, and which may offset or compound one another depending upon the context – inequality impact may be shifted in different directions at different steps; hence the metaphor of a winding ‘pathway’ may be more appropriate than that of a steadily increasing ‘staircase’. Users can enter custom distributions for each step on the ‘Distributional inputs’ tab of the calculator.

The first step identifies differences in the prevalence of the disease or risk factor in the population. These are automatically generated from the look-up tables described above but can also be overwritten by the user. The second step relates to differences in uptake – the proportion of the prevalent population actually expected to receive the intervention. This is the principal input distribution the calculator requires of the user and is by default set at 100% for all groups. The third step characterises inequalities in the health effects of the intervention. Accurate estimation of this stage requires a full DCEA approach that involves de novo cost-effectiveness modelling and re-estimation of the standard cost-effectiveness findings. However, in this simplified approach this step is based on assumptions and rapid evidence review, rather than full DCEA modelling, with the default assumption being no difference between social groups in health effect. The fourth step is to estimate the distribution of health opportunity cost, with the default being the neutral assumption of an equal distribution across social groups.

Evidence on the social distribution of health opportunity costs

The base case assumption about the social distribution of health opportunity costs is important and controversial, since empirical evidence is mixed – as explained below – and this assumption can change the estimated direction of health inequality impact. We recommend a base case assumption of a flat distribution but sensitivity analysis using alternative assumptions involving an "anti-deprived" distribution in which more deprived groups bear larger health opportunity costs.

Current evidence about this question is mixed. To date, the most relevant published studies are by research teams at the University of York - an indirect estimate based on an earlier instrumental variable study (Love-Koh et al., 2020) – and the University of Liverpool - two time series studies of the effects of changes in NHS expenditure on inequalities in amenable mortality age under 75 (Barr et al., 2014; Currie et al., 2019). There is also a direct estimate from an unpublished work-in-progress instrumental variable study currently being led by a team at the University of York in collaboration with teams from Liverpool and Manchester, involving one of the authors of this report (Richard Cookson).

The published studies all found an "anti-deprived" distribution, whereby changes in health care expenditure have a larger absolute impact on health in more deprived populations. This is "anti-deprived" in the sense that it implies more deprived groups will bear larger health opportunity costs when the same amount of expenditure is

displaced from alternative health care uses. However, the work-in-progress study has found a broadly neutral distribution and no evidence that more deprived groups bear larger health opportunity costs – indeed, if anything, the reverse. The findings of the unpublished direct study must be treated with caution because this study has not yet been peer reviewed and published. However, there are reasons for believing that the previous study by Love-Koh and colleagues is likely to be biased in favour of finding an "anti-deprived" distribution, as described below. First, it does not allow for the possibility that people living in deprived small areas may receive a large share of total expenditure than affluent small areas, since they are sicker, but may not receive a larger share of marginal expenditure changes, since they are less able to lobby to protect their own interests when budget are tightened or to extract new benefits when budgets are expanded. Second, it does not allow for the possibility that there may be unequal marginal healthcare productivity, whereby people living in deprived small areas gain smaller health benefits per unit increase in expenditure than people living in affluent small areas due to greater co-morbidity and less ability to co-invest their own time and resources into effective long-term treatment, recovery and prevention – as explained further below. Overall, therefore, we believe that a neutral assumption of an equal distribution of health opportunity cost may be an appropriate default assumption – though with sensitivity analysis around alternative assumptions involving an "anti-deprived" distribution.

The published indirect estimate by Love-Koh et al. 2020 was based on a study by Claxton et al. 2015 combined indirectly with estimates of the social gradient in healthcare utilisation. Claxton et al. 2015 estimated the total health opportunity cost of NHS expenditure using data on local variations in NHS expenditure and mortality data from 2008 stratified by 23 broad disease categories ("programme budgets"). Similar overall estimates are available from more up-to-date data, but they do not stratify by disease categories which is essential for the indirect approach to be applied. Disease group stratification allowed Claxton et al. 2015 to estimate how a 1% decrease in NHS expenditure is likely to be distributed between disease categories (i.e. will they lose more or less than 1%), and also how the QALY loss from a 1% decrease in expenditure varied by disease category (Claxton et al., 2015b). Combining these two estimates, Table 1 in the Love-Koh 2020 paper shows how much health (in QALYs) is lost in each of 23 different broad disease categories from a 1% decrease in NHS expenditure. Love-Koh et al. 2020 then used HES data from 2010 to estimate the social distribution of hospital utilisation (including

emergency and elective hospital episodes) within each disease category and, within that, within each age and gender category. They then assumed that:

1. the social distribution of hospital utilisation is a reasonable indication of the social distribution of NHS expenditure (i.e., disadvantaged people do not tend to have more or less expensive kinds of hospital episodes within each disease-age-gender category, and the distribution of hospital utilisation is similar to the distribution of primary care utilisation – a check was provided for that)

2. the current average social distribution of social expenditure within each disease-age-gender group is a reasonable indication of the marginal distribution of a decrease in expenditure (i.e., future changes will be like present averages), and

3. the marginal productivity of NHS expenditure is the same across different social groups (i.e., equal to the average productivity across all social groups)

The authors then combined these two pieces of information (i.e., estimates of marginal productivity combined with estimates of the social gradient in health care utilisation) to estimate the social distribution of health loss, as explained in Figure 1 in the paper. As highlighted in the Abstract of the paper, the authors estimated that the biggest health losses from displaced NHS expenditure were in disease areas where individuals from more deprived neighbourhoods account for a larger share of health care utilization, namely, respiratory and neurologic disease and mental health.

However, the third assumption is likely to bias the estimates in favour of finding an "anti-deprived" distribution. The marginal productivity of health care expenditure may tend to be lower for more deprived individuals than more affluent individuals, for the reasons set out in the Love-Koh et al. paper and expanded upon in Table 1 (last 2 rows) of this more recent review (Cookson et al., 2021a). This is because socially advantaged patients have fewer co-morbidities and social problems that increase the costs and reduce the health benefits of care and are better able to comply with treatment regimens and secure healthy recovery environments due to greater human and social capital and wealth.

Finally, the study by Currie and colleagues from Liverpool found that the same absolute increase in overall NHS expenditure was associated with larger absolute reductions in mortality in more deprived local authority areas. However, this study focused on avoidable mortality under the age of 75 rather than all-age mortality.

Excluding effects on mortality age 75 and over may tend to under-estimate the health benefits to affluent individuals of increases in health expenditure. This is because affluent individuals are more likely than deprived individuals to survive to age 75 in good health. Hence, among affluent populations, the mortality effects of a marginal change in health expenditure may disproportionately occur at older ages, when affluent populations start to suffer a more substantial burden of morbidity and mortality. A further issue is that this study uses a time series design, which is arguably a less robust way of identifying the causal effect of expenditure on mortality than an instrumental variable approach.

DCEA functionality beyond original papers on "aggregate" DCEA

The calculator adds two simple elements of DCEA functionality that were not included in the original papers on "aggregate" DCEA, by allowing users to make explicit user-defined assumptions about health effects (step 3), and by explicitly separating the estimation of population eligibility (step 1) from the estimation of uptake (step 2) and allowing different inputs and assumptions about each of these three steps. The original papers on "aggregate" DCEA combined steps (1) and (2) by assuming that data on utilisation of existing services for the same condition captures both elements and did not allow for step (3).

The calculator also adds a supplementary way of presenting standard DCEA findings about equity-efficiency trade-offs that has not been used in previous work but may be useful for NICE advisory committees – the equity-weighted incremental cost-effectiveness ratio (ICER) or cost per QALY gained (CQG). This functionality allows users to see how the ICER changes with different social value judgements about the degree of concern for reducing health inequality – known as "health inequality aversion". For interventions with a positive impact on reducing health inequality, stronger health inequality aversion will reduce the (equity-weighted) ICER, making the intervention seem more favourable. For interventions with a negative impact on reducing health inequality, stronger health inequality aversion will increase the (equity-weighted) ICER, making the intervention seem less favourable. The latest version of the calculator (Version 2, 2023 update) also presents the absolute and relative change in ICER after equity weighting, and the corresponding threshold ICER weight. The absolute change in ICER is the weighted ICER minus the unweighted ICER, the relative change in ICER is the absolute change in ICER as a proportion of the unweighted ICER, and the threshold ICER weight is the unweighted

ICER divided by the weighted ICER. The relative change in ICER is related to the threshold ICER weight by the following equation: W = 1 / (1 + R) where W is the threshold ICER weight and R is the relative ICER change. A threshold ICER weight of 1.1 means that the threshold for assessing the unweighted ICER is increased by 10%, so e.g., the customary threshold ICER of £30k would become £33k. For example, imagine the unweighted ICER is £33,000 but equity weighting brings the weighted ICER down to £30,000 which can be considered cost-effective according to a standard ICER threshold of £30,000. Equity weighting thus yields an absolute ICER change of -£3,000 and a relative ICER change of -0.10 (i.e., a reduction of 10% in the ICER). The corresponding threshold weight is 1.11 (i.e., £33,000 divided by £30,000), meaning that the corresponding cost-effectiveness test involves assessing the unweighted ICER of £33,000 against a weighted ICER threshold of £33,000 (i.e., the standard ICER threshold times 1.11).

The standard way of presenting DCEA findings is based on the net health benefit statistic – the equity-weighted net health benefit (NHB) is defined as the equity-weighted incremental health effect minus the equity-weighted incremental health opportunity cost. The equity-weighted ICER is calculated in the same way, except with equity weights applied to opportunity costs expressed in financial terms (i.e., amounts of expenditure, rather than amounts of health foregone). The result is then expressed as an incremental cost-effectiveness ratio rather than a net health benefit. The equity-weighted incremental cost-effectiveness ratio is thus the equity-weighted incremental opportunity cost of displaced health expenditure divided by the equity-weighted incremental health effect. Mathematically, this yields the same results as net health benefit in terms of ordinal rankings of interventions but allows results to be presented in terms of ICERs. This may be a more familiar statistic to some NICE committee members than the concept of net health benefit, though NHB is also commonly reported. Importantly, however, the equity-weighted ICER is not simply the incremental cost per equity-weighted QALY gained. Correct use of direct equity weights requires symmetric application to the distribution of opportunity costs, as well as the distribution of effects, rather than asymmetric application only to the effect side, as explained in Chapter 14 of the DCEA handbook (Cookson et al., 2020). The equity-weighted ICER applies equity weights to the distribution of both costs and benefits and thus remains consistent with the basic principles of DCEA.

Consultation methods

The prototype checklist and calculator were developed through a two-stage iterative process of consultation: (1) face validity checking within the development team and (2) consultation with selected NICE officials and advisers involved in various different types of NICE guidance (see Appendix A). Our consultees included health economists and guidance developers involved in clinical and public health guideline development, technology appraisal and diagnostics guidance, committee members, and senior advisers including former members of NICE board.

We also sought informal feedback from selected other experts and postgraduate students in the UK and overseas. During this process, the tool was tested on a diverse range of exemplars from past NICE guidance, to explore the potential problems, limitations and caveats when using it in practice.

Our consultation explored various issues, including the following questions but also issues raised by NICE officials and advisers:

1. When, how, and by whom can the tool be used?
2. What were the main practical difficulties encountered when using the tool for different types of guidance, and how can they be overcome?
3. When are the default distributional assumptions unsafe?
4. What further improvements in the tool could be made in future research?

3. Results

Overview of the six examples of triage DCEA

This section provides examples of how "triage" DCEA using the health equity impact calculator could be used to at the scoping stage of guideline development and technology appraisal, to determine whether health inequality impact is potentially decision relevant and whether further work is warranted to produce a more robust estimate of health inequality impact. Copies of the detailed output tables and graphs produced by the calculator (2022 version, prior to minor updates in 2023) are provided in Appendix C. There are also published studies providing further examples of quick and simple DCEA estimates as applied to past NICE public health and single technology appraisal guidance (Griffin et al., 2019a; Love-Koh et al., 2019). These examples are quick and simple "triage" DCEA estimates based on readily available data and assumptions, designed for use at an early scoping stage to provide an initial indication of the direction and magnitude of health inequality impact and whether that impact is likely to be decision relevant. To produce more robust DCEA estimates that might potentially be used to modify a funding decision at later stages of guideline development and appraisal would require more work in sourcing more and better data inputs and conducting thorough analysis of uncertainty using alternative assumptions.

The "triage" DCEA examples are as follows:

Example 1. Roflumilast for treating chronic obstructive pulmonary disease in adults with chronic bronchitis (loosely based on NICE TA461 published in 2017 and illustrating a case in the Win-Win quadrant where health inequality impact might have seemed potentially decision relevant at scoping stage but turned out not to be decision relevant at appraisal stage, since the technology was clearly cost-effective anyway)

Example 2. Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency (loosely based on NICE TA709 published in June 2021, illustrating a case where the health inequality impact is too small to be decision relevant)

Example 3. Lung health checks for adults aged 55 to 75 at risk of lung cancer (hypothetical intervention loosely based on published cost-effectiveness analyses of US and UK lung cancer screening trials, and illustrating a case in the Win-Lose quadrant where estimated health inequality impact can support supplementary recommendations on increasing utilisation in socially disadvantaged populations)

Example 4. Crizanlizumab for preventing sickle cell crises in sickle cell disease (loosely based on NICE TA743 published in November 2021, and illustrating a case in the Lose-Win quadrant where estimated health inequality impact can support a positive recommendation for an intervention that is only borderline cost-effective but has unusually high prevalence among socially disadvantaged populations)

Example 5. Hypothetical convenient new medication for poorly controlled type II diabetes (hypothetical intervention and cost-effectiveness estimates, not based on continuous glucose monitoring or estimates from NICE NG28 published in June 2022, illustrating a different kind of case in the Lose-Win quadrant, where the main driver of health inequality reduction is inequality in utilisation of the comparator technology)

Example 6. Olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer (loosely based on NICE TA831 published in October 2022, prior to NICE TA 887 published in May 2023 after a price discount was negotiated, illustrating a hypothetical case in the Lose-Lose quadrant where health inequality impact might conceivably be used to reinforce a negative recommendation alongside lack of cost-effectiveness.)

The first five examples illustrate the following four situations in which DCEA can provide useful information:

A. If the intervention is found to lie in the Win-Win or Lose-Lose quadrant, the estimated impact on health inequality may not be relevant to decision making because it would merely reinforce the standard recommendation based on cost-effectiveness,

B. The estimated impact on health inequality may be too small to influence a decision on funding or delivery,

C. The estimated impact on health inequality may support the development of supplementary guidance on delivery to socially disadvantaged groups – especially but not exclusively in the context of clinical and public health guideline development,

D. The estimated impact on health inequality may support a positive recommendation in favour of an intervention that could potentially change a NICE committee recommendation from a “no” to a “yes” – especially but not exclusively in the context of technology appraisal.

We provide two examples of situation D, illustrating two distinct sub-cases: one where the inequality impact is entirely driven by inequality in prevalence, and one where the impact is also partly driven by inequality in effective utilisation of the comparator intervention.

The sixth example illustrates a further situation in which DCEA information might conceivably be useful:

E. The estimates impact on health inequality might conceivably support a negative recommendation against an intervention that is not cost-effective by conventional standards, as a “negative modifier” that could potentially change a “yes” to a “no”.

However, NICE does not currently use “negative modifiers” when developing guidance – for example, end-of-life and severity modifiers are only ever used to support positive recommendations, not negative ones. Furthermore, situation E is likely to be rare in practice, since it is rare to find a substantial “reverse gradient” in prevalence whereby a disease is substantially more prevalent in more socially advantaged groups.

These examples were prepared using version 2 of the calculator (2022, prior to minor recent updates in 2023) by a health economist (Cookson). Each example took about 1 or 2 days of work, which mainly involved time spent reading background medical and epidemiological literature to understand the specific intervention, disease pathway, and decision context, selecting relevant incremental cost and health effect estimates from standard cost-effectiveness studies based on that

background understanding, and writing up the findings. It would take considerably less time for an analyst already working on the topic, who already has that information at their fingertips. Once a suitable incremental cost, health effect, 3-digit ICD-10 code, age range and total eligible population is known, running the calculator just takes a few seconds. So, a health economist who is already familiar with the clinical and epidemiological background and the pre-existing cost-effectiveness evidence, could do DCEA triage more rapidly. The results would be the same using the Version 1 of the calculator (and Version 2 with recent updates) – just with differently formatted output tables and graphs.

Example 1: Roflumilast for treating chronic obstructive pulmonary disease in adults with chronic bronchitis

NICE guidance TA461 published in 2017 (https://www.nice.org.uk/guidance/ta461) recommended Roflumilast, as an add-on to bronchodilator therapy, as an option for treating severe chronic obstructive pulmonary disease in adults with chronic bronchitis, only if: the disease is severe, defined as a forced expiratory volume in 1 second (FEV_1) after a bronchodilator of less than 50% of predicted normal, and the person has had 2 or more exacerbations in the previous 12 months despite triple inhaled therapy with a long-acting muscarinic antagonist, a long-acting beta-2 agonist and an inhaled corticosteroid. The committee considered that this intervention was cost-effective with an ICER of about £25,000 per QALY gained.

The following DCEA triage assumptions were entered into the calculator, based on cost-effectiveness estimates from TA461: incremental cost £3,508; incremental effect 0.14 QALYs; ICD10 code J42: Other chronic bronchitis; age range 16+; cost-effectiveness decision threshold £30,000. This generated a positive impact on reducing health inequality due to a steep social gradient in prevalence. Equity-weighting using a maximum plausible inequality aversion value of 10 would bring the ICER down from about £25,000 to about £22,000, a maximum potential ICER reduction of about £3,000, or 12%.

This intervention therefore lies in the “Win-Win” quadrant of the equity-cost-effectiveness impact plane – it is cost-effective and reduces health inequality. The health inequality impact is therefore not decision relevant in this case, because it merely reinforces a positive recommendation on standard cost-effectiveness grounds.

There is a potential risk of bias in estimating relative prevalence shares since the ICD10 code used includes all people with chronic bronchitis, not just those with severe COPD and recent exacerbations who are eligible for Rofrumilast. However, it is not clear which way the bias would go – i.e., are patients severe COPD more or less likely to be deprived than less severe ones – and this potential bias is not material to our main conclusion that the health inequality impact is not decision relevant in this case.

These DCEA triage findings can also be presented in terms of population health impacts, though that would be more appropriate in a public health context than a technology appraisal context. The population level health inequality reduction is small because the estimated patient population is small. If we use the built-in estimate of 2,533 adults with unspecified chronic bronchitis in England, then the reduction in the population level health inequality gap in England would be about 52 QALYs. To contextualise this figure, the gross population health benefit is 355 QALYs and the net population health benefit, accounting for health opportunity costs, is minus 238 QALYs based on a marginal productivity estimate of £15,000 or plus 58 QALYs based on a marginal productivity estimate of £30,000. Varying the marginal productivity estimate does not change the estimated impact on health inequality, since health opportunity costs are assumed to be evenly distributed.

Example 2: Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency

NICE TA709 published in June 2021 (https://www.nice.org.uk/guidance/ta709) recommended use of Pembrolizumab as an option for untreated metastatic colorectal cancer with high microsatellite instability (MSI) or mismatch repair (MMR) deficiency in adults, only if: pembrolizumab is stopped after 2 years and no documented disease progression, and the company provides pembrolizumab according to the commercial arrangement. The committee considered that ICERs against all relevant comparators were below £20,000 per QALY gained, but cost-effectiveness estimates were commercial in confidence.

The following assumptions were entered into the DCEA calculator, based on guestimates of cost and effect: incremental cost £20,000; incremental effect 1 QALY;

ICD-10 code “C18 Malignant neoplasm of colon”; age range 16+; total eligible population 465 per year based on the NICE resource impact statement. This generated a small negative impact on increasing health inequality due to a reverse gradient in prevalence. However, the maximum potential increase in the ICER with maximum plausible inequality aversion value of 10 was only about £800 pounds or 4% this is not close to being decision relevant.

This illustrates a case where the health inequality impact is too small to be decision relevant.

Example 3: Lung health checks for current or former smokers aged 55 to 75

This is a simple hypothetical DCEA triage example relating to potential future national roll-out of lung cancer screening in England, building on various ongoing local pilot programmes. In the UK, recommendations about national screening programmes are made by the UK National Screening Committee, rather than NICE, but the example is a useful one to illustrate the complications that can arise in relation to preventive programmes when inequality in uptake is important as well as inequality in prevalence. We entered the following assumptions into the DCEA calculator: incremental cost per eligible person invited to screening (i.e., current or former smokers aged 55 to 75) £26; incremental QALY gain 0.00182; risk factor: smoking; uptake proportions from IMD1 (most deprived) to IMD5 (least deprived) 0.1, 0.2, 0.3, 0.4, 0.5; marginal productivity £15,000 per QALY; total eligible population 5,000,000.

This has not yet been formally evaluated by the UK National Screening Programme, so we take basic cost-effectiveness figures from published studies and make various assumptions. We assume that this programme is cost-effective, with an estimated ICER of £14,286 per QALY gained that lies in the middle of the range of published ICERs from around £10,000 from the UKLS model (Field et al., 2016) to £30,000 from the recent PENTAG model (Griffin et al., 2020).

The cost and effect assumptions are based on Table 3 (strategy “S-55-75-3%”) of a published cost-effectiveness study by the Peninsula Technology Assessment Group (PenTAG) that compared a UK-wide programme of one-off lung health checks for current or former smokers aged 55 to 75 versus no screening, delivered according to the same protocol as the UK Lung Screening (UKLS) pilot studies in Liverpool and

Cambridge (Griffin et al., 2020). However, this study potentially under-estimated effectiveness in a UK context since it used effectiveness data from the US National Lung Screening Trial which found smaller effects than the UKLS pilot studies. So we increased the incremental effect by a factor of two (from 0.00091 to 0.00182) to bring the ICER down from about £28,500 to about £14,250, more in line with ICERs from a previous study of the cost-effectiveness of the UKLS pilot studies (Field et al., 2016).

The complicated multi-stage nature of this intervention means there is room for debate about the relevant "eligible population" for calculating incremental costs and health effects There are three populations of interest: (1) the general population age 55 to 75 who are sent a self-assessment letter to check if they are at risk and if so to book a lung health check, (2) the at risk population (current and former smokers) who are eligible for the lung health check (CT scan), and (3) the clinical population screened as positive for lung cancer who are eligible for diagnosis and treatment. We have used the at-risk population eligible for the main component of the intervention i.e., the lung health check. A further complication is that health harms can occur at the lung health check stage (e.g., anxiety), especially for those screened as false positives, and these harms are part of the aggregate-level QALY gain calculation. Teasing out these different factors would ideally require full DCEA analysis based on detailed underpinning modelling, rather than simplified DCEA based on aggregates.

The uptake estimates by IMD group are hypothetical guestimates based on conversations with people involved in the UKLS pilot studies. It is not straightforward to dig out appropriate figures to use, since they are a function of uptake of pre-screening, risk factor prevalence, and uptake of CT scan among invitees. The total eligible population is based on 40% of the England population age 55 to 75 in 2020 (about 12.5 million), where 40% is the England prevalence of current smokers (13.8%) plus the England prevalence of former smokers (26.3%) based on national GP Patient Survey estimates reported by Public Health England.

Under these assumptions, a national lung health check programme in England would generate a negative impact on increasing the population level health inequality gap in England by 294 QALYs. To place that figure in context, the gross population health benefit was 2,288 QALYs and the net population health benefit was just 109 QALYs after accounting for health opportunity costs using a marginal productivity assumption of £15,000 per QALY.

We can also report these findings in terms of ICERs, though that framing is arguably less useful in a public health context than a technology appraisal context and the appropriate decision threshold for screening interventions is a matter for the UK National Screening Committee rather than for NICE. In terms of ICERs, the standard ICER was £14,286/QALY which increased to £16,469/QALY after applying equity-weights based on the maximum plausible health inequality aversion value of 10 – an increase in the ICER of just over £2,000 or 15%.

These DCEA triage findings show that, paradoxically, lung health check programmes may increase health inequality if delivered like the UK Lung Cancer Screening Trial (UKLS) in the early 2010s. Even though the prevalence of lung cancer is higher and rates of early detection lower among more disadvantaged groups, uptake of the UKLS screening pilot was substantially lower. In other words, the "reverse" social gradient in screening uptake (with lower uptake in more deprived groups) is steeper than the social gradient in smoking prevalence (with higher prevalence in more deprived groups) – generating a combined overall pattern of larger health gains in less deprived populations (i.e., a "reverse" social gradient in health gains).

This information could be used to support the development of supplementary guidance for low-cost ways of increasing uptake in disadvantaged populations. It could also be used to recommend and inform the development and evaluation of more costly ways of re-designing lung health check programmes to increase uptake among more disadvantaged populations. For example, experience from lung health check pilots and other vaccination and screening programmes might suggest adding recommendations to use conveniently located mobile screening units in disadvantaged areas, to ask GP practices in disadvantaged areas to send the invitations directly, and to engage local community leaders in the publicity process. Such programmes are currently being tested and could later be evaluated using DCEA once cost, uptake and outcomes data are available comparing such "proportional universal" programmes with "standard universal" programmes.

This situation – i.e., a potentially cost-effective intervention that increases health inequality – is common in both public health and clinical guideline development. Another example suggested by consultees (which we have not evaluated using the calculator) is that HIV service delivery infrastructure is stronger in Brighton and the South of England than in more deprived regions of England. A national recommendation for universal delivery of HIV pre-exposure prophylaxis (PrEP)

would therefore be likely, in practice, to increase uptake and reduce risk of HIV faster among more socially advantaged people than less socially advantaged people. The calculator could potentially be used to support the development of supplementary delivery guidance to start addressing this problem. Justifying costly system-level investments such as the development of new regional infrastructure would first require a new standard cost-effectiveness analysis that carefully examined the costs and health benefits of the proposed investment and might ultimately require action by NHS England rather than NICE. However, consistent quantification by NICE could help to highlight the problem and potentially catalyse appropriate further actions.

Example 4: Crizanlizumab for preventing sickle cell crises in sickle cell disease

NICE TA743 published in November 2021 (https://www.nice.org.uk/guidance/ta743) recommended Crizanlizumab as an option for preventing recurrent sickle cell crises (vaso-occlusive crises) in people aged 16 or over with sickle cell disease only if the conditions in the managed access agreement are followed. The cost-effectiveness estimates used by NICE are commercial-in-confidence so we have guestimated the cost and effect based on CEA evidence from the USA.

The following assumptions were entered into the DCEA calculator: incremental cost £40,000; incremental effect 1 QALY; ICD10 code “D57 Sickle cell disorders”; age range 16+; annual eligible population 500. The eligible population of 500 comes from a NICE resource impact statement about the estimated annual number of people expected to receive this intervention.

This showed a clear positive health inequality impact on reducing health inequality, due to an unusually steep social gradient in prevalence, with the two most deprived groups in England experiencing much higher rates of sickle cell disease than the three more affluent groups. This had a substantial potential impact on the ICER: the standard ICER was £40,000 per QALY gained but this fell to 28,125/QALY after applying equity-weights based on the maximum plausible inequality aversion value of 10 – a potential reduction in the ICER of just under £12,000 or 30%.

In public health terms, this intervention would reduce the population level health gap in England by 246 QALYs, based on an eligible population size of 500 patients and a

gross population health benefit of 500 QALYs. If the intervention were extended to more patients, beyond the managed access scheme, the population level health inequality reduction would be correspondingly larger.

This example therefore illustrates a new health technology in the bottom-right “Lose-Win” quadrant of the equity-cost-effectiveness impact plane – only borderline cost-effective (hence the “Lose” on cost-effectiveness) but a “Win” on reducing health inequality.

Example 5: Hypothetical new convenient medication for poorly controlled type II diabetes

In the context of technology appraisal, imagine a hypothetical new patented medication for diabetes were borderline cost-effective, with an ICER of around £35,000 per QALY gained when offered to people with poorly controlled type II diabetes. Imagine further that this recommendation would have a substantial positive impact on reducing health inequality, since socially disadvantaged people are not only more likely to have diabetes than socially advantaged people but also to have poorly controlled type II diabetes, for example insofar as stressful social and material living conditions may make it harder to overcome the psychological resistance to needle-based insulin therapy that many patients experience.

We entered the following hypothetical assumptions into the DCEA calculator: incremental cost £35,000; incremental effect 1 QALY; ICD10 code "E11 Type II diabetes mellitus”; age range: 16+; uncontrolled proportion from IMD1 (most deprived) to IMD5 (least deprived): 0.2, 0.15, 0.1, 0.05, 0.05. To enter the “uncontrolled proportion” assumptions we used the shortcut of entering these figures into the “uptake proportion” feature of the calculator, since the mathematical calculation is the same. An alternative way of doing this would have been to enter our own customised set of eligibility share estimates for each IMD group along with a customised total population eligibility figure – but that would have required us to do a separate calculation based on information about diabetes prevalence proportions and uncontrolled proportions, or to source separate data about the prevalence of uncontrolled diabetes. These assumptions yielded a standard ICER of £35,000, which fell to £24,493 after equity-weighting using the maximum plausible inequality aversion value of 10 – a fall of £10,500 or 30%. The health inequality impact here is

thus potentially decision relevant, in the sense that it could be a consideration that might help to support a positive recommendation rather than a negative one.

This is another example of a new technology in the “Lose-Win” quadrant, but for a somewhat different reason than the previous case. In the case of Crizanluzimab for sickle cell disease, the positive health inequality impact was driven entirely by inequality in prevalence. In this case, the impact is driven not only by inequality in prevalence but also by inequality in utilisation of the existing comparator technology, meaning that the new technology is especially beneficial for disadvantaged people who are unable to make effective use of the existing comparator technology.

Example 6: Olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer

NICE TA831 published in October 2022 recommend against funding this intervention, but the subsequent NICE TA 887 published in May 2023 (https://www.nice.org.uk/guidance/TA887) recommended in favour of funding it, after a price discount had been negotiated. Specifically, TA887 says that “Olaparib is recommended, within its marketing authorisation, as an option for treating hormone-relapsed metastatic prostate cancer with BRCA1 or BRCA2 mutations that has progressed after a newer hormonal treatment (such as abiraterone or enzalutamide) in adults. Olaparib is only recommended if the company provides it according to the commercial arrangement.”

The cost-effectiveness estimates were commercial in confidence, so we entered guesstimates that aim to mimic a hypothetical initial situation of borderline cost-effectiveness in 2022 before a price discount was negotiated. The guesstimates that were entered into the calculator were: incremental cost £40,000; incremental effect 1 QALY; ICD10 code “C61 Malignant neoplasm of prostate”; eligible population 5,000. This generated an increase in health inequality since prevalence of prostate cancer is higher in more affluent groups. However, the impact is not large – the original ICER of £40,000 increased to £42,412 after applying maximum plausible equity weights, an increase of just under £2,500 or 6%.

This illustrates a hypothetical case in the Lose-Lose quadrant where health inequality impact might conceivably be used to reinforce a negative recommendation alongside lack of cost-effectiveness. However, as mentioned previously, NICE does

not generally use “negative” modifiers and so this might not be a suitable way of using this information.

One consideration in favour of funding this treatment might be end-of-life or severity of illness as measured by individual burden of illness in terms of absolute or proportional QALY loss, since prostate cancer substantially reduces life expectancy and imposes a substantial morbidity burden. However, a conflicting consideration in favour of not funding this treatment might be impact on health inequalities, since this intervention is likely to have a small negative impact on increasing health inequality. How these two competing considerations (severity of illness versus health inequality) are balanced would be a matter for deliberation by the advisory committee and could also be informed by quantitative equity-efficiency and equity-equity trade-off analysis using the calculator. The calculator facilitates this kind of analysis by providing information about how the ICER would change according to different social value judgements about the degree of concern for reducing health inequality.

4. Discussion

In what follows we discuss the main issues raised during the consultation process and our own reflections on them, based on our experience in using the prototype calculator and in seeking feedback from experts. We call this section “Discussion” rather than “Results” since this was a rapid informal consultation process rather than a qualitative research study using formal qualitative research methods, and our findings are somewhat subjective and discursive in nature.

Issues are discussed under the following headings:

1. Using the calculator
2. Finding the data inputs
3. Setting the marginal productivity of alternative resource use
4. Sensitivity analysis around the social distributional of health opportunity costs
5. Setting the inequality aversion parameter
6. Potential biases
7. Issues of communication and interpretation
8. Limitations and potential concerns
9. Options for further work to improve the tool

Using the calculator: where, when, how, by whom?

Where – the potential scope of the calculator

We think the toolkit could potentially be useful as a complement to standard health economic evaluation across most types of NICE guidance, including:

- Clinical Guidelines
- Public Health Guidelines
- Technology Appraisals Guidance,
- Diagnostics Guidance,

- Interventional Procedures Guidance.

It might also be useful for other kinds of guidance, including medical technologies guidance, highly specialised technologies guidance, medicines practice, cancer services, antimicrobial prescribing, and interventions in areas of overlap between health and social care. However, it would not be useful in cases where effectiveness and cost-effectiveness evidence are not available. Furthermore, it would not be useful for social care interventions where the primary outcome of interest is supporting people with activities of daily living rather than improving health measured in terms of quality adjusted life years (QALYs) – though the calculator might still provide useful information when social care interventions are assessed using QALYs or QALY-like metrics, and about the social distribution of prevalence.

In the case of highly specialised technologies, the patient population is typically small and the cost per QALY gained is often very high – typically many times higher than £30,000 pounds per QALY. This means that the net health benefit based on a marginal productivity health opportunity cost threshold of £15,000 will typically be substantially negative due to the high costs per patient, indicating a large net health loss that cannot be turned positive by equity weighting. In such cases, however, health inequality information could still be used by using a weighted ICER approach based on the appropriate decision threshold used for highly specialised medical technologies, which is more like £100,000 per QALY. The total health inequality impact at general population level will be small due to the small patient population; but the health inequality impact relative to population size may nevertheless be worth considering.

When – at what stage in decision making?

We think the checklist and calculator can potentially be used at all stages of decision making, to answer different kinds of question, as follows:

1. At the topic selection and pre-scoping stages, to inform deliberations about the potential relevance and importance of health inequality impacts, based on assumptions about plausible ranges of incremental costs and health effects from evaluations of similar interventions in the past.

2. At the scoping stage, to inform deliberations about what further health inequality information is needed, about formulating the review questions, and about whether it is worth investing additional analytical time and resource into conducting full DCEA.

3. At the assessment and guidance development stage, to inform deliberations by NICE advisory committees and guideline development groups about the likely direction and magnitude of health inequality impacts, about whether special implementation recommendations are needed to address health inequality issues, and about whether health inequality impact could potentially influence a decision (either for or against) in borderline cases where the incremental cost-per-QALY gained lies close to the appropriate cost-effectiveness decision threshold.

4. At the implementation support stage, to inform deliberations about how far it is worth investing additional resources to increase uptake among socially disadvantaged groups, though for costly recommendations it would be necessary first to conduct a new standard cost-effectiveness analysis of supplementary delivery recommendations of this kind.

How – would this influence decisions?

Several consultees asked the question: would this calculator only be used to satisfy the procedural requirement to consider health inequality, or would it also be used to make a substantive difference to NICE decision making? Two different ways of making a substantive difference to decision making were distinguished:

1. Using health inequality impact to justify and support the development of supplementary delivery recommendations about how to increase the uptake of a cost-effective intervention among socially disadvantaged populations. This will often be useful in the context of clinical and public health guideline development but might also sometimes be relevant in the context of technology appraisal; it would also be useful in the context of implementation support.

2. Using health inequality impact as a consideration that potentially influences a yes-no decision about whether or not to recommend a specific intervention that lies on the borderline between being cost-effective and not cost-effective. This could be relevant both in guideline development decisions about specific uses of

existing generic technologies and in technology appraisal decisions about specific uses of new patented technologies.

In relation to (1), the calculator can be used to highlight the potential need for and benefits of equity-oriented implementation support in terms of reducing health inequality. For example, HIV service delivery infrastructure is stronger in Brighton and the South of England than in more deprived regions of England. In the absence of implementation support in deprived regions, a national recommendation for universal delivery of HIV pre-exposure prophylaxis (PrEP) is therefore likely, in practice, to increase uptake and reduce risk of HIV faster among more socially advantaged people than less socially advantaged people. The calculator could potentially be used to calculate the magnitude of the potential health benefit and health inequality reduction from equity-oriented implementation support that improves delivery infrastructure in deprived regions. However, it could not be used to justify substantial additional expenditure in the absence of information about the incremental effects and opportunity costs of that expenditure by social group – especially if the support involves general infrastructure costs with other positive spillover health benefits in reducing delivery costs and increasing the uptake of other HIV services. In such cases, a further CEA study would be needed to provide further evidence, comparing "standard" implementation versus "proportional universal" implementation that devotes additional resources to increasing uptake in disadvantaged groups.

In relation to (2) – i.e., influencing "yes-no" decisions – the calculator can potentially influence decisions in cases of interventions which are borderline cost-effective according to usual standards but have a substantial positive health inequality impact. Interventions with a positive impact may be worth recommending because they reduce health inequality. Examples illustrated earlier in the report include *Example 4 Crizanlizumab for preventing sickle cell crises in sickle cell disease* and *Example 5*: *Hypothetical convenient new medication for poorly controlled type II diabetes.* Conceivably, things might go the other way as well – as illustrated by *Example 6: Olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer.* However, as already discussed, NICE does not use "negative modifiers" in other cases such as end of life and severity weights.

Several consultees suggested that it would seem odd for NICE to spend time and effort developing a systematic approach to considering health inequality impact if this

is never allowed to make any difference to decision making. However, some raised issues about the risk of legal challenge through the appeals process in relation to Technology Appraisal, if health inequality impact were explicitly used as a consideration for or against recommending the funding of costly new technologies. Though on the other hand, there is also a risk that if health inequality impact is only used on an *ad hoc* informal basis in some decisions then there might be legal challenge on that basis as well. Due to this risk, guidance on when and how to use health inequality impact estimates would have to be included in official NICE methods guidance before such estimates could safely be used to inform Technology Appraisal decisions.

A related issue raised by some consultees is whether the legal requirement of procedural consistency would require a "fixed" set of equity weights giving priority to more social disadvantaged groups, based on a specific benchmark value of health inequality aversion, or whether equity weights could be "flexible" i.e., tailored on a case-by-case basis. Announcing a fixed set of equity weights right away would be problematic. We know that the public are concerned to reduce health inequality, and willing to make trade-offs (see discussion later), but evidence about the strength of concern is mixed and it is not clear that concern is the same across all decision contexts. There are at least two relevant precedents for starting with a "flexible" approach before iterating towards more specific quantitative benchmarks: (1) NICE started operating in 1999 with no fixed cost-effectiveness decision threshold and gradually iterated towards more specific benchmarks through experience and precedent, with the conventional £30,000 benchmark for technology appraisal in routine use by 2004 (Rawlins & Culyer, 2004) (2) NICE has used "flexible" equity weights in the past in relation to end-of-life criteria (NICE, 2009), before iterating towards more specific benchmarks such as the current 1.2 and 1.7 threshold weights for different categories of severity of illness (National Institute for Health and Care Excellence, 2022).

By whom?

The calculator is for use by analysts (health economists) with (i) training in standard CEA, (ii) experience using standard CEA to inform decision making, and (iii) basic training in "distributional" CEA i.e., sufficient to understand the basic concepts and diagrams used in the calculator. Sourcing suitable CEA data inputs and distributional assumptions requires standard CEA training and experience. And

interpreting and communicating the findings requires training in “distributional” CEA. Depending on the type of guidance, the analyst using the calculator might be based in industry, or NICE, or academia. In Technology Appraisal, for example, the calculator might be used initially by an industry analyst to produce information as part of a submission, then reviewed by a NICE analyst as part of the review group. Whereas in the development of guidelines, the calculator might be used primarily by a member of the NICE secretariat supporting the guideline development group.

Those using the calculator will also need support from a topic expert with specific knowledge about the relevant intervention(s) and health condition(s), to review the selected data inputs and assumptions and avoid errors of interpretation.

The “Health inequality impact report” produced by the calculator is primarily designed for analysts: it provides a concise and complete summary of all the tables and graphs produced and is designed to be readable by a non-specialist. However, it does not provide context-specific interpretations and caveats. It is up to analysts to select the relevant data from the report and present, explain and caveat things for the non-technical audience they are addressing in suitable context-specific ways depending on the policy context, the findings and the audience.

The “checklist” is for use by health economist members of advisory committees, and members of the NICE secretariat, to facilitate critical appraisal of health inequality impact estimates produced by others.

It is possible to communicate the broad outline of health inequality impact findings to non-specialists. However, a firm grasp of the core health inequality impact graphs and statistics, and the strengths and limitations of particular health inequality impact findings, requires familiarity not only with basic concepts of standard CEA but also with some further concepts of DCEA. Some basic training in DCEA would therefore be required by health economists using the calculator and by non-specialists wanting to use health inequality impact findings to support decision making.

How long does it take to use the calculator?

In our experience using the prototype calculator, a quick and simple initial health inequality impact analysis based on distributional assumptions by topic experts can be done in 1 to 2 days, with most of the time spent sourcing appropriate standard CEA inputs and consulting experts. If this analysis indicates that health inequality

impact might potentially be decision relevant, then a more careful analysis would be required that sources real world evidence for the distributional assumptions, rather than relying on “default” assumptions and topic expert opinions and engages in appropriate process of quality assurance. We do not yet know how long that would take – this would require piloting in practice.

The basic tasks involved in creating an initial health inequality impact estimate are (i) selecting and understanding the relevant intervention, comparator and indications, (ii) identifying and accessing the most relevant cost-effectiveness documentation, (iii) digging out the most relevant basic CEA figures from that documentation, and (iv) seeking distributional assumptions from topic experts. Task (iii) can be time consuming because there are often difficult choices to make about which figures to use and how to interpret them. Tasks (i) and (ii) should be fairly straightforward at committee and implementation stages, since relevant confidential internal NICE documentation should already exist. At the topic selection and scoping stages, however, directly relevant documentation may not exist, and it will often be necessary to do a rapid informal literature search to find previous CEA studies of similar interventions, which can then be used to guestimate plausible ranges of incremental cost and QALY gain. There are of course serious risks of bias and error in attempting to predict CEA results without doing the analysis, especially if the relevant effectiveness evidence has not yet been carefully reviewed and critically appraised, but the plausible ranges may nevertheless provide useful information about the degree of uncertainty in the direction and magnitude of health inequality impact. The time taken depends on various factors, and things will be quicker for a health economist who is already familiar with the relevant intervention and its evidence base.

Finding the data inputs

List of data input requirements

Essential information:

1. One intervention, one comparator, and one set of intervention indications (e.g., over 65s with blood pressure, patients with a specific sub-type of epilepsy, patients with type II diabetes with poor blood sugar control on standard treatment)
2. 3-digit ICD-10 code(s) or risk factor indication for the eligible population
3. Age range indication for the eligible population
4. Eligible population size (*)
5. Incremental QALYs gained per recipient
6. Incremental cost per recipient

Desirable additional information about differences by socioeconomic group (**):

7. Differences in uptake by socioeconomic group
8. Differences in health effects by socioeconomic group
9. Differences in health opportunity cost by socioeconomic group

Ideally a published source for each data input should be provided.

Notes:

* The tool will automatically generate a simple estimate of the eligible population size based on 3-digit ICD-code or risk factor and age range. However, this estimate may be inaccurate – for example, it may be an over-estimate if eligibility also depends on more specific indications or an over-estimate if prevalence is under-estimated by our built-in data sources (hospital activity data and routine household surveys). Ideally the eligible population size should be a prevalence-based estimate of the current total number of indicated individuals in England who should be offered the intervention. This may be higher than the actual recipient population size, since uptake may be less than 100%.

** The default assumptions are equal uptake, equal health effect and an equal distribution of health opportunity cost.). Each of these assumptions can be modified, either based on data or expert opinion.

List of potential problems finding data inputs

Total size of the eligible population

We often found it hard to find accurate estimates of the total size of the eligible population, which is subject to considerable uncertainty due to data limitations. Estimates of prevalence often vary substantially due to differences in data sources, methods and interpretations – with patient advocacy groups generally reporting higher estimates than official NHS estimates. And the eligible population is typically smaller than the prevalent population with the relevant condition, in ways that may be hard to estimate, because eligibility often depends on disease sub-type and other characteristics.

Sometimes it was necessary to use an estimate of the recipient population size instead of uptake, from a "budget impact" estimate of the estimated annual uptake of the intervention once it has been fully rolled out. In such cases, the uptake parameters can be set to 100% and the eligible population input parameters re-interpreted as utilisation parameters. The total eligible population will then be set to the total utilisation level, and the proportion of utilisation in each group entered as customised values for the proportion of the eligible population.

Incremental costs and QALYs gained

We found that specific data on incremental costs and QALYs for the relevant decision option is sometimes not available in published NICE guidance. Sometimes it is merely hard to find i.e., buried in a separate technical report or appendix. Sometimes various comparisons are provided (e.g., by both the manufacturers and the NICE secretariat, e.g., in various sensitivity analyses) and it is hard to tell which is the "correct" figure. Sometimes it is not available at all, however, for various reasons:

- Head-to-head incremental cost and QALY comparisons of the new technology against the relevant comparator may not be provided, only incremental comparisons against "do nothing" or an outdated treatment that is less effective than the current standard of care
- The set of decision options and comparisons may be complicated, and so the documentation only describes the overall findings and does not report all the detailed incremental comparisons

- The price paid for a new technology may be commercial in confidence – e.g., due to a patient access scheme – and incremental cost data are not reported to avoid revealing this sensitive information.

If price data are commercial-in-confidence, a solution might be to ensure that any published underpinning information about health inequality impact is suitably restricted so that price data inputs cannot be reverse engineered. The overall health inequality impact and many of the most important data inputs and assumptions could then still be published, without disclosing confidential price information.

Special considerations for particular types of guidance

An issue with diagnostics guidance is that there may be an additional stage in the pathway to inequality: one has to consider not only unequal use of the diagnostic but also subsequent unequal uptake of treatment once a diagnosis has been made. This could be taken into account by modifying the assumption made at the "uptake" step – i.e., by making a combined assumption about uptake of diagnosis and appropriate subsequent treatment. Or it could be taken into account at the "health effect" stage, by allowing for social differences in health benefits for people who are diagnosed with the condition but do not receive appropriate treatment. It may be worth considering an explicit extension to the calculator to incorporate two uptake steps, but there may be diminishing returns to further complication of the calculator rather than conducting bespoke "full" DCEA that models each step in detail.

Setting the marginal productivity of alternative resource use

The calculator draws a clear distinction between two different concepts:

(1) the decision threshold for assessing cost-effectiveness, both before and after equity weighting (the "equity weighted incremental cost-effectiveness ratio" statistic), and

(2) the opportunity cost threshold based on the marginal productivity of alternative resource use, for estimating population level total impacts on health, on health inequality, and on overall social welfare (the "equity-weighted net health benefit" statistic).

Both of these different thresholds are required inputs for the health inequality impact calculator. The decision threshold is used for assessing incremental cost-

effectiveness ratios whereas the marginal productivity estimate is used for assessing population total net health benefit, which is often a useful further statistic to consider from a public health perspective. The appropriate decision threshold value for the incremental cost per QALY at which an intervention is normally considered cost-effective without requiring special justification is an issue of social value judgement, which NICE typically sets at different starting levels for different kinds of guidance product. By contrast, the marginal productivity of alternative resource i.e., the marginal cost of producing a QALY from alternative use of resources is an empirical (factual) matter. The marginal productivity of alternative resource use depends on the decision context and, in particular, whether opportunity costs primarily fall on NHS budgets or local authority budgets (or, in rarer cases, primarily on central government budgets in other policy sectors such as education). The current best estimate of the marginal cost of producing a QALY from alternative use of NHS resources, based on analysis of NHS health outcomes and expenditure data, is about £13,000 pounds with a range from £5,000 to £15,000 (Claxton et al., 2015a; Lomas et al., 2019). By contrast, typical estimates in the context of preventative public health expenditure funded by central government and local authority budgets are much lower – more like £3,000 pounds (Masters et al., 2017).

The Department of Health and Social Care has recommended using a marginal productivity figure of £15,000 in its Impact Assessments. This is stated in a working group report dated 20 July 2016, entitled "Review of Cost-Effectiveness Methodology for Immunisation Programmes & Procurements" (CEMIPP). https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/683872/CEMIPP_report_2016__2_.pdf

Paragraph 70 of this report states that “The working group noted that on the basis of the programme of work by the York researchers, the DH is now recommending that the opportunity costs of spending from the NHS budget, in terms of displaced health, are estimated using a figure of £15,000 per QALY. To arrive at this figure, the York estimate *[Claxton et al. 2015, denominated in 2008 prices]* was adjusted with the GDP deflator to £14,803 in 2014/15 prices. For convenience, and for the time being, the DH recommends that this figure is rounded to £15,000 per QALY for use in DH Impact Assessments.” [*Clarification text in italics added*].

In the light of this DHSC recommendation, we have used £15,000 as the default value of marginal productivity in the web calculated i.e., the estimate of £15,000 as in

standard health impact assessments by the DHSC that focus on total population health impact.

The cost-effectiveness decision thresholds used by NICE in practice are usually substantially higher than £15,000. The "NICE Principles" website states that "Interventions with an ICER of less than £20,000 per QALY gained are generally considered to be cost effective. Our methods manuals explain when it might be acceptable to recommend an intervention with a higher cost-effectiveness estimate" https://www.nice.org.uk/about/who-we-are/our-principles

This benchmark decision threshold of £20,000 per QALY gained applies primarily to clinical, public health and social care guideline development, which focuses on the use of existing generic technologies. In the context of technology appraisal, which focuses on the use of new patented technologies, interventions with an ICER less than £30,000 are generally considered to be cost effective, with additional justification required for going beyond this. And higher decision thresholds are applied in special cases, such as conditions with a high degree of severity of illness and highly specialised technologies. An independent research study of 240 NICE TAs published up to 31 December 2011 found that, on average, the decision threshold for technology appraisal was in practice closer to £40,000 (Dakin et al., 2015).

The appropriate cost-effectiveness decision thresholds used by NICE to determine whether different kinds of intervention should be recommended as cost-effective uses of public funding are a matter of social value judgement for the NICE Board and Executive and the Secretary of State for Health, and ultimate responsibility lies with the UK Prime Minister on behalf of the general population of England and Wales. Evidence about marginal productivity is one relevant consideration but there are other relevant considerations including maintaining public confidence.

There are also various potential justifications for the use of different standard decision thresholds from one decision context to another. For example, NICE considers high severity of illness as a relevant justification for going beyond the usual threshold, and a substantially higher threshold is also usually deemed appropriate for patients with rare conditions who are in need of highly specialised technologies. NICE may also wish to use a higher threshold in the context of technology appraisal than in guideline development to allow for the wider benefits of

industrial innovation including potential future price decreases once patent protection expires, if these are not elsewhere accounted for in the cost-effectiveness calculation.

The assumption about marginal productivity entered into the health inequality impact calculator is only used to make factual estimates about total population health impact and how this varies by social group. This has no direct bearing on the normative question of what decision threshold should be used by the advisory committee. A "low" marginal productivity assumption in the calculator is consistent with a "high" decision threshold – the two concepts are different.

The assumption about marginal productivity will however have important implications for the estimates of total population health impact and health inequality impact. A lower marginal productivity assumption will reduce total health opportunity costs and hence increase the (net) total population health benefit of an intervention. It may also change the magnitude and direction of population level total health inequality impact.

Sensitivity analysis around the social distributional of health opportunity costs

The default assumption in the calculator is that the health opportunity costs of NHS expenditure are equally distributed across social groups, based on the evidence and reasoning described above in the Methods section. Given the mixed nature of the evidence and the high degree of uncertainty around this assumption, however, we recommend conducting sensitivity analysis around alternative assumptions. There is a particular need for sensitivity analysis around this assumption when evaluating public health and social care interventions, as discussed further below in the section on potential biases, since existing evidence on this matter relates almost exclusively to health care expenditure.

The default assumption is primarily based on a direct regression-based estimate from an unpublished work-in-progress study by the University of York, together with further evidence and reasoning that suggests that a previous indirect estimate by Love-Koh et al. (2020) may have over-estimated the social gradient in opportunity costs. The calculator provides two options for conducting sensitivity analysis: a "moderate" and "steep" social gradient in health opportunity costs. The "steep" option implements the indirect estimates from Love-Koh et al. (2020); while the

“moderate” option lies halfway between the default neutral assumption and the Love-Koh et al. (2020) indirect estimates.

The tool does not currently have the functionality to implement an assumption of “anti-affluent” health opportunity costs falling disproportionately on more affluent groups, since we are not aware of evidence suggesting that this may be a reasonable assumption. However, it would be a simple matter to add this functionality to the tool.

Setting the inequality aversion parameter

The calculator uses a default maximum plausible inequality aversion parameter value of 10 for the purpose of making comparisons of the magnitude of health inequality impact across decision topics and assessing whether the magnitude is relatively small, as explained further below. However, the appropriate parameter value for the purpose of assessing trade-offs between cost-effectiveness and health inequality impact and evaluating whether an intervention is worthwhile is a normative matter that we believe would have to be decided flexibly on a case-by-case basis through advisory committee deliberations, rather than being fixed in advance. Empirical estimates from surveys of the public vary considerably (see references below) and there are ongoing academic controversies about how health inequality aversion should be defined and measured. Case-by-case flexibility would allow custom and practice benchmarks to evolve over time, and to be informed by more robust and accurate empirical estimates as research continues.

There is ongoing research to improve methods for estimating health inequality aversion, and one aspect of this is to distinguish more clearly between value judgements about different causes of variation – potentially requiring more than one kind of inequality aversion parameter. There are also long-standing academic controversies about the nature of ethical concern for health inequality. For example, some ethicists and economists argue that concern for health inequality should be re-formulated and broadened beyond current UK and WHO definitions to include concern for “pure” all-cause variation in realised health between individuals. All-cause health variation includes condition-related variation in health between people with the same level of social disadvantage but different health conditions. However, others argue that condition-related variation in health should continue to be handled separately under the heading of “severity of illness”.

Our current thinking about what counts as “low”, “middle” and “high” benchmark values for health inequality aversion is informed by the current range of values found in surveys of the general public, which range from “low” values of around 1 to “high” values of 11 (Costa-Font & Cowell, 2019; McNamara et al., 2020). Almost all surveys find evidence of public concern for reducing health inequality, and hence a parameter value above 0 (which implies no concern for health inequality). So far, however, the “low” parameter values have tended to come from studies of “pure” all-cause health inequality aversion rather than studies of aversion to “unfair” health inequality associated with social disadvantage.

A “low” benchmark parameter might be 1, corresponding to an additional weight of about 19% on health gains and losses to the worst-off group (IMD1) compared with the best-off group (IMD5).

(A technical note for health inequality measurement experts. These five groups are defined as quintile groups based on neighbourhood deprivation. Due to the steep social gradient in health, deprivation group rank always corresponds to health group rank – for example, the worst-off group is always worst-off in terms of both deprivation and health-adjusted life expectancy at birth. Hence, we can safely treat health group rank and social group rank as being the same, without worrying about conceptually possible cases where the two might come apart. For example, we can use a single health inequality aversion parameter based on a univariate health distribution to represent health inequality aversion, rather than requiring a more complicated bivariate functional form that explicitly models concern for social status related inequality in health).

A “mid-range” benchmark parameter might be 2.5, corresponding to an additional weight of about 54% on health gains and losses to the worst-off socioeconomic group (IMD1) compared with the best-off group (IMD5).

Finally, a “high” benchmark parameter might be around 11, estimated by a University of York survey of the English general population (Robson et al., 2017). This corresponds to an implied additional weight of about 576% to health gains and losses for the worst-off (IMD5) compared with the best-off (IMD1). To avoid spurious precision, in the calculator we use the simple round number of 10 as our “high” benchmark parameter for the highest plausible health inequality weights.

Importantly, the figures cited above are implied QALY weights for social groups and not implied cost-effectiveness threshold weights for interventions (see the earlier Methods sub-section on “DCEA functionality beyond the original papers on “aggregate” DCEA”). The implied threshold weight for health inequality is always much lower than the implied QALY weight for the worst-off deprivation group, since the NHS is a universal service that provides health care interventions for the whole general population of individuals from across the social spectrum, rather than funding interventions exclusively for people from the worst-off deprivation group. So, the implied threshold weight is a function of the proportion of people from each deprivation group who receive the intervention, as well as the QALY weights applied to each group. So long as an intervention is not received exclusively by people in the most deprived fifth, therefore, the threshold weight for the intervention will be lower than the QALY weight for the most deprived fifth. In practice, in crude simulations conducted using the data on inequality in prevalence embedded in the calculator, the highest threshold weight we encountered when using a high inequality aversion parameter of 10 was about 1.4 – which is considerably lower than the implied threshold weight of 1.7 used by NICE for severity weighting.

Other surveys using different designs have estimated “low” and “mid-range” values and research is ongoing: there is considerable variation between studies as well as considerable individual heterogeneity in the value judgements made by different citizens. All we can say for sure based on current evidence is that the “average” (median) citizen in England (and other countries where surveys have been conducted) is concerned about reducing health inequality and has a health inequality aversion parameter above zero.

We use a default “high” inequality aversion parameter value of 10 in the toolkit, as a useful benchmark for the purpose of making “triage” assessments about whether health inequality could possibly be decision relevant. However, for decision making purposes a social value judgement would need to be made about a suitable benchmark, along with sensitivity analysis around different value judgements.

Potential biases

The calculator makes default distributional assumptions about four steps on the staircase of inequality:

1. Eligible population (proportion of total general population, summing to 1)

2. Uptake (proportion of eligible population, so that 1 = full uptake)

3. Health effect (proportion of average effect, so that 1 = average)

4. Health opportunity cost (proportion of total health opportunity cost among the general population, summing to 1)

The default assumptions about (1) are based on built-in prevalence look-up tables, using data from hospital episode statistics (for disease prevalence) and household surveys (for risk factor prevalence).

For (2) and (3) the default assumption is an equal social distribution (i.e., 1 for all social groups).

For (4) the default assumptions are that health opportunity costs are equally distributed

When are these default assumptions likely to be misleading, and in what direction might the bias lie?

1. Eligible population

The two main potential biases in our current disease prevalence estimates based on HES data are: (1) counting numbers of inpatient hospital episodes rather than numbers of people, which potentially over-estimates prevalence by double counting people with more than one hospital episode during the year, and (2) not counting people with the health condition who did not attend hospital during that financial year, which potentially under-counts prevalence for long-term conditions usually managed in primary and community care, such as dementia and diabetes. HES data on hospital activity are only able to count a non-random sample of the prevalent population who were admitted for inpatient hospital treatment during the measurement period, due to acute exacerbations of the relevant long-term health condition or for treatment of other conditions. This will under-estimate the total prevalent population and, in addition, this non-random sample is likely to be less healthy and more deprived than the full prevalent population. Nevertheless, the proportional distribution by social group within this non-random sample may still be a reasonable approximation of the proportional distribution within the full prevalent population, even though the absolute levels are under-estimated. The levels can

then be fixed by entering a more accurate user estimate of the total eligible population, based on external sources of data.

A better source of routine prevalence data for long-term conditions usually managed in primary and community care would be the Clinical Practice Research Datalink (CPRD) which provides detailed patient-level primary care data for a large but non-random sample of primary care practices in England, which can then also be linked to HES data. HES alone is fine for acute conditions and long-term conditions usually managed in secondary care such as cancers; and arguably better than CPRD insofar as HES captures the whole population whereas CPRD itself is a non-random sample of the general population. Though on the other hand there is a case for using a single source of data for all disease categories – including conditions usually managed in both primary and secondary care – to ensure a level playing field. These issues will need to be explored in further research to improve the underpinning data for the calculator.

2. Uptake

There is often no data on the distribution of uptake, and so assumptions may be required. It may be possible to apply data from other similar kinds of interventions (e.g., one kind of screening or vaccination programme may be expected to have similar uptake differentials to another, if the type of programme is similar involving similar barriers to uptake). There is a conservative tendency to make no adjustment if there are no data on which to base the adjustment. However, this may bias the analysis against disadvantaged groups, by assuming that uptake will be equal across disadvantaged groups when in fact uptake is likely to be lower in more disadvantaged groups. So, it may be useful to explore different assumptions in "what if" scenario analysis, so see how much difference this makes to the health inequality impact calculation.

3. Health effect

The calculator uses the incremental QALY gain per recipient as its standard measure of health effect, taken from a prior cost-effectiveness study. The default assumption is no difference in health effect, though as with uptake it is important to consider whether this default assumption is likely to under- or over-estimate health inequality impact and to check whether alternative plausible differences make a large difference to the direction of health inequality impact. The distribution of health effect

can be modelled using full DCEA, but that is a resource-intensive exercise that explicitly accounts for the complex interactions between:

1. social differences in condition-specific baseline risk, which tend to yield larger health benefits for more disadvantaged populations, and

2. social differences in short-term and long-term competing mortality risks, co-morbidities, adherence and recovery environment, which tend to yield smaller health benefits for more disadvantaged populations.

In some cases, it may be clear which of these two effects is likely to dominate, without doing full DCEA modelling. In most cases, however, the balance of effects is likely to be unclear and the calculator default assumption of an equal social distribution of health effects may be a reasonable base case assumption.

4. Health opportunity cost

The main issue here arises for public health and social care interventions funded outside the NHS, via national or local government budgets. In this case, the default assumption of £15,000 for the marginal productivity of resource use may be too high but the default assumption of an equal distribution may be reasonable. There is a case for using a "pro-deprived" distribution for public health and social care expenditure funded outside the NHS, on the grounds that disadvantaged populations are especially likely to need and use public health and social care services. On the other hand, it may be that, at the margin, reductions and increases in local authority expenditure tend to focus on non-statutory types of funding that tend to benefit more socially advantaged people (e.g., libraries, leisure centres) rather than statutory services that tend to benefit socially disadvantaged people (e.g. child and adult social care). If so, the social distribution of health opportunity costs might be relatively flat. Clearly, however, it is important to conduct sensitivity analysis using alternative assumptions, and this is an important topic for future research.

Issues of communication and interpretation

Health inequality aversion and equity weights

There are various challenges around communications with stakeholders including government agencies, pharmaceutical industry, patient groups and the public. One issue, for example, relates to communications around health inequality

weights. Health inequality threshold weights are typically smaller than severity threshold weights. For example, with an inequality aversion parameter of 10, which as discussed earlier is our default maximum plausible parameter value based on current evidence, health inequality threshold weights go up to a maximum of 1.4 and are usually much smaller than that. By comparison, NICE uses a specific formula for severity weighting with positive categorical threshold severity weights of 1.2 and 1.7. However, a health inequality aversion parameter of 10 also imply theoretical patient level QALY weights that are much higher – up to 5 – which might appear politically unacceptable when quoted out of context. Addressing this challenge would require careful messaging to explain the difference between the practical technology-level weights applied to NICE recommendations about whether a technology should be funded by the NHS for all patients, and the theoretical patient-level weights that can be derived by taking the theory to its logical extreme but would never be applied in practice by NHS clinicians making decisions about individual patients.

Population health perspective

One communication challenge is that the health inequality impact calculator presents information from a population health perspective, rather than the usual patient level perspective that is more familiar to clinical staff and stakeholders. The population health perspective is familiar to public health experts but not to most clinical experts and stakeholders. Most NICE staff and stakeholders are used to seeing data on effectiveness and cost-effectiveness presented at the patient level (focusing on the "average" patient), with less attention paid to the total size of the eligible population or the total population health impact.

NICE methods guidance also endorses a clear separation between cost-effectiveness and total budget impact – if there is robust evidence that an intervention is cost-effective, NICE committees can make a strong recommendation even if it would be costly to implement. Nevertheless, the total budget impact of guidance is examined by the resource impact team at NICE. In a guideline, a recommendation that will cost more than £1m/year to implement is considered to have a "significant" impact and must have economic evidence to support it (https://www.nice.org.uk/About/What-we-do/Into-practice/resource-impact-assessment). Resource impact is estimated for each of the first 5 years of implementing the guideline in England after its publication. It is defined as

“significant” if it is more than £1 million per year for a single recommendation, or £5 million per year for the whole guideline.

It is not possible to re-frame health inequality impacts at patient level since health inequality is fundamentally a general population concept – it is about differences in health between social groups within the general population, not about the health of an “average” patient, nor about differences only within a specific patient population.

However, it would be possible to re-frame the vertical axis of the equity-efficiency impact plane in terms of cost-effectiveness rather than population health impact. This might be a useful alternative way of presenting findings about cost-effectiveness and health inequality impact on the same diagram and is worth exploring in future research and future versions of the toolkit.

Opportunity cost and net health benefit

The equity impact tool builds on the health economic concepts of “health opportunity cost” and “net health benefit” which are not familiar to all NICE staff and stakeholders.

Political issues

Given the political sensitivity of the topic of health inequalities, there are obvious political risks to NICE in seeking to adopt a more consistent and transparent approach. A particular challenge is the issue of political asymmetry which NICE always faces between saying “yes” (generating stakeholder approval) and “no” (generating stakeholder disapproval). Stakeholder responses to information on health inequality impact will vary depending on whether or not it supports their favoured intervention. Using health inequality impact as a justification to fund an intervention is likely to generate favourable stakeholder reactions, while using health inequality impact as a justification not to fund an intervention is likely to generate unfavourable stakeholder reactions.

Another challenge with a political dimension is how to communicate the concept of “health inequality aversion” clearly to public audiences, without over-simplifying in ways that generate political controversy. There are obvious risks of politically motivated misrepresentation. For example, opponents might misrepresent NICE as claiming that poor lives matter more than rich lives, or that deprived people should

receive better care than affluent people. This also relates to potential concerns about means-testing and social discrimination, which are discussed earlier in the report in the Introduction section.

Limitations and potential concerns

Consultees generally supported the idea that NICE should start routinely producing and using quantitative health inequality impact information. However, they also pointed out various limitations of the calculator and raised various concerns about the potential use of health inequality impact information in decision making.

Some of the main limitations are as follows.

- The tool focuses on neighbourhood-level deprivation and so does not directly address health inequalities relating to ethnicity, gender or vulnerable groups such as rough sleepers. However, it does provide a general summary measure of health inequality impact and a useful starting point for bespoke analysis of more specific health inequality impacts. IMD combines data on multiple domains of neighbourhood deprivation including income, employment, disability, education and skills, crime, housing and service barriers, and living environment.

- The tool does not bypass the need for credible estimates of incremental cost and health effect from standard cost-effectiveness analysis: it a quick and simple "add-on", not a substitute. It therefore does not solve the long-standing methodological challenge of how to produce credible model-based estimates of the effects and cost savings of complex, system-level interventions that have not been evaluated using well-designed RCTs or quasi-experiments, such as investments in workforce, capital and delivery infrastructure. Without credible estimates, the tool therefore cannot justify high-cost system-level investments to increase uptake in socially disadvantaged populations – though it can help to flag the problem and highlight the need for better evidence and modelling of specific proposed investments.

- Health inequality impact estimates would require different levels of quality assurance for different purposes, with the highest level required for estimates used to influence "yes-no" decisions. Initial quick and simple "triage" estimates of health inequality impact can be produced rapidly based on guestimates of cost

and effect. However, thorough quality-assurance would require longer, to source real-world evidence for the distributional assumptions and subject those assumptions to careful scrutiny by experts and stakeholders.

Some of the main potential concerns were as follows.

- Should NICE stick to cost-effectiveness and leave health inequality concerns to other NHS and public sector agencies that have more control over NHS delivery infrastructure and the wider non-NHS social determinants of health, and hence potentially can play a larger role in reducing health inequalities?

- Should NICE stick to health inequalities activities relating to tackling discrimination and improving diversity and inclusion in the workplace, as a large and influential employer, rather than the health inequality impact of its guidance?

- The health inequality impact of a new technology depends on disease prevalence and other external real-world factors beyond the control of the manufacturer, so why should the manufacturer be credited or penalised for the impact?

- Does using health inequality impact information involve means-testing and discrimination against socially advantaged patients?

- Would using health inequality impact information leave NICE exposed to risk of successful legal challenge and/or damaging political controversy?

These concerns cut across all types of NICE guidance but are especially salient in the context of technology appraisal. We discuss these four concerns in turn below.

Leaving health inequalities to other government agencies

Other government agencies can do more than NICE to address wider social and economic causes of health inequalities that lie beyond the control of the NHS, such as inequalities in wealth, education and power. And other NHS agencies can do more than NICE to address basic inequalities in the NHS delivery infrastructure that can lead to social inequalities in health care access and outcomes, such as geographical inequalities in funding and workforce and inequalities in funding and esteem between mental health and physical health.

However, NICE guidance does have impacts on health inequalities – sometimes reducing health inequalities but sometimes increasing them. Individually, these impacts may appear small when compared with the total magnitude of health inequality and the impacts on health inequality of decisions made by other branches of government involving larger sums of money. Cumulatively, however, many small impacts over time can add up to large impacts.

Furthermore, trade-offs sometimes arise between redistribution of health resources to tackle health inequalities ("equity") and the NICE model of distribution based on investing in the most cost-effective treatment for the whole population ("efficiency") (House of Commons Health Committee, 2009). Given the new national drive to reduce health inequalities, it is therefore incumbent upon NICE to try to ensure that as far as possible its guidance does not increase health inequalities and where possible reduces health inequalities, as reflected in the NICE five-year strategy. Continuing to focus exclusively on cost-effectiveness would mean that NICE remains part of the problem rather than part of the solution.

Focusing on tackling discrimination and improving workplace diversity and inclusion

NICE is a large and influential employer both locally and nationally and there is indeed a strong case for NICE to play a leading role in tackling discrimination and improving diversity and inclusion in the workplace. In addition, however, NICE's recommendations to the NHS and wider public services also have important, cumulative long-term impacts on health inequality, as described above.

Furthermore, NICE can also play an influential role in tackling health inequality by pioneering new methods for analysing health inequality impacts. NICE has the opportunity to punch above its weight and pave the way for other public organisations to follow suit, given its analytical firepower and strengths in the kinds of health economic and decision modelling needed to estimate health inequality impacts.

Health inequality impact is not the responsibility of the intervention manufacturer

This concern was sometimes phrased as the idea that a negative health inequality impact is not a "fault" of the intervention, and sometimes as the idea that health inequality impact (negative or positive) is not an "internal" property of the underlying technology or active ingredient of the intervention (such as a pharmaceutical

compound or clinical device) that can be fully evaluated in a laboratory or randomised controlled trial (RCT) without reference to the external real-world context in which the intervention will be used. It is indeed true that health inequality impact is not an "internal" property of the intervention. Health inequality impact in routine clinical practice, like effectiveness and cost-effectiveness in routine clinical practice, depends crucially on disease prevalence and other aspects of the external wider real-world context in which the intervention will be used. An example might be the introduction of the same new diabetes treatment technology in a high-income country such as the UK, where diabetes is more prevalent among socially disadvantaged populations, versus a low or middle-income country context where diabetes is currently still more prevalent among wealthy populations. The health inequality impact might differ from one country to another, due to the different socio-economic and epidemiological context of utilisation, even though the underlying technology or active ingredient is the same. The health inequality impact thus emerges through interactions between the "internal" properties of the intervention and the "external" real-world context in which the intervention is used.

However, it seems strange to stipulate that the external real-world context is not relevant when making public funding decisions and that public officials are only allowed to consider information from laboratory studies and RCTs when making public funding decisions. That restriction does not apply to any UK government agency involved in making public funding decisions. It is also clearly inconsistent with NICE's processes and ways of working – NICE devotes considerable resources to considering non-RCT forms of evidence, intelligence and stakeholder opinion about the real-world context. NICE does not just consider "efficacy" in the context of a clinical trial but also effectiveness and cost-effectiveness in the context of routine real-world clinical practice.

The health benefits expected in routine practice often differ from the health benefits measured in RCTs, since trial settings differ in many important respects from real-world settings, including patient case-mix, provider delivery, and wider social context. The same is also true of costs. Average cost and total budget impact both depend crucially on the relevant health care delivery environment and may differ substantially from the costs observed in RCTs. Hence when assessing cost-effectiveness NICE often considers a wide range of different types of real-world evidence, intelligence and stakeholder opinion that go well beyond RCT evidence.

Means-testing and social discrimination

We do not propose using information on health inequality impact in ways that involve means-testing or social discrimination. Instead, we propose using this information in ways that are consistent with the founding principles of the NHS as a universal public health service that provides health care to all citizens on the basis of need, regardless of their financial means or social background.

Concern that using information on health inequality impact would involve discrimination against socially advantaged patients is based on a misunderstanding. The NHS founding principle of need-based distribution already gives an innocuous form of indirect, population-level priority to socially disadvantaged groups, because socially disadvantaged groups tend to have greater health needs than socially advantaged groups (Cookson et al., 2021a). Producing and using quantitative estimates of health inequality impact would perhaps make this innocuous form of social prioritisation more explicit. However, it would not make this more invidious or unethical and would not make derogatory terms like “discrimination” more applicable.

NHS services are need-tested, but there is no means-testing or direct, individual-level social discrimination. NICE uses cost-effectiveness as its main criterion for assessing need, and the cost-effectiveness test is routinely applied both between different interventions (some interventions are cost-effective while others are not) and within the same intervention (some uses of the intervention are cost-effective, and others are not). NICE often recommends that an intervention is only cost-effective when offered to specific patient sub-groups who meet specific need criteria – for example, that a costly new treatment should only be offered to patients who do not respond well to standard treatment. However, individual patients with the same needs are always entitled to receive the same NHS care, no matter whether they are rich or poor, black or white, male or female.

Socially disadvantaged groups within the general population tend to have greater needs for health care than socially advantaged groups, because they tend to suffer more illnesses and comorbidities earlier in their lives. Health needs are socially patterned – they are associated with social characteristics within the general population. NHS need testing thus implies an innocuous and indirect form of population-level social “discrimination” – in the sense that socially disadvantaged groups receive more health care resource inputs than socially advantaged groups,

because they need more health care resource inputs. Though since the term "discrimination" carries negative ethical connotations, a more ethically neutral term such as "prioritisation" is more appropriate in this case.

The distinction between invidious, direct, individual-level social discrimination versus innocuous, indirect, population-level social prioritisation also applies to NICE recommendations about the delivery and implementation of cost-effective interventions, as well as to NICE recommendations about which interventions are cost-effective for which patient sub-groups. For example, uptake of screening tends to be lower in socially disadvantaged groups, suggesting that disadvantaged groups have greater needs for implementation support to access screening services. It may therefore be appropriate to recommend increasing uptake in disadvantaged groups by using mobile screening services and placing them in convenient locations for disadvantaged populations – an innocuous form of social prioritisation. However, it would not be appropriate to refuse entry to a mobile screening unit to a socially advantaged individual – an invidious form of social discrimination.

In clinical applications, the inequality impact calculator would therefore only be used to inform population-level decisions about which interventions to fund on a universal basis for which need-based subgroups. It would not be used to inform potentially discriminatory individual-level decisions about funding the same intervention for socially disadvantaged individuals but not socially advantaged individuals. The relevant questions, for which health inequality impact analysis may useful, are which need-tested interventions to prioritise for universal funding and how to re-design the delivery of interventions to reduce inequalities of access and outcome favouring socially advantaged groups.

Legal challenge and political controversy

In the context of technology appraisal, using information about health inequality impact without clear methods guidance could potentially expose NICE to risk of successful legal challenge against its recommendations on procedural grounds. To avoid this risk, NICE would need to revise its methods guidance for technology appraisal to set out the relevant analytical principles, methods and processes before using information about health inequality impact in the context of technology appraisal.

There are also obvious risks of political controversy in seeking to address health inequalities in a more transparent and consistent manner, given the politically sensitive and controversial nature of this topic.

Options for further work to improve the tool

Improving the disease category prevalence look-up tables
A priority is to develop disease category look-up tables based on CPRD data on primary care. This would provide more accurate estimates of prevalence for conditions usually managed in primary and community care.

There may also be a case for going down to 4-digits of the ICD code rather than 3, to enable more precise estimates in some cases, though this would raise issues of small numbers and data disclosure (counts below 5 cannot be included in a publicly available version of the tool).

The current prototype disease category look-up tables are based on HES data from 2010. Updating this data will be problematic until at least mid to late 2023, however, since ongoing Covid-19 disruptions mean that current social patterns of hospital utilisation may differ substantially from long-run “steady-state” patterns. Paradoxically, therefore, past patterns of hospital activity may provide a better guide to the social patterning of disease prevalence than current patterns.

Updating the disease category look-up tables based on hospital episode statistics (HES) is unlikely to be worth doing until hospital activity returns to a more stable long-term pattern. A steady-state pattern is unlikely to re-emerge until financial year 2022/23 at the earliest, or perhaps even later than that to allow for a period of atypical “catch-up” activity to clear backlogs of need. Lags in data production and access mean that quality-controlled HES data for a financial year is typically not available until about six months after that financial year ends in April. Preliminary hospital data would potentially be available earlier than that, though this data is not fully quality controlled and cannot readily be accessed by academic units without going through costly data access procedures.

The purpose of the look-up tables is to provide a proxy indicator of social variation in disease prevalence which then acts as a proxy indicator of the pattern of social

variation in intervention eligibility. The aim is not directly to ascertain expected social variation in utilisation of the intervention, since social variation in uptake is handled separately. However, insofar as social patterns of utilisation are influenced by Covid-19 disruptions this will influence estimates of disease prevalence based on utilisation.

Expanding the risk factor prevalence look-up tables

The prototype look-up table for the social distribution of risk factors only covers 4 risk factors, based on Health Survey for England data. The coverage could be expanded and updated, by using a broader range of data from different surveys. Ideally this work would be conducted in collaboration with analysts from Public Health England, who collect and analyse this kind of data routinely.

Expanding the risk factor look-up tables using survey data on disease prevalence would be relatively straightforward. This may involve collaboration with analysts from the Office of Health Improvement and Disparities (OHID) who regularly analyse survey data on disease prevalence and produce breakdowns by various categories including neighbourhood level deprivation (IMD). At the time of writing, OHID do produce publicly accessible inequality breakdowns of various kind – for example, as part of the "fingertips" toolkit (https://fingertips.phe.org.uk/profile/inequality-tools), and further breakdowns produced by analytical teams working on specific health conditions. Unfortunately, however, the underpinning data are not published in a suitably detailed format (i.e., at a sufficiently fine-grained geographical level together with age, sex breakdowns) for the purpose of our look-up tables. However, it may be possible for analysts to supply at least some of the necessary underpinning data. The core risk factor data set would be collected from a single source: Health Survey for England (HSE), which would have the benefit of comparability. However, it might be useful to check with specialist analytical teams working on specific health conditions to see if additional useful age-gender-IMD breakdown data for England is available on additional risk factors not available in the core HSE dataset. This would also require iteration with public health colleagues at NICE to discuss which non-HSE risk factors are important to include if possible.

Other equity-relevant variables:

Geographical deprivation, urban-rural, North-South

In principle, the tool could be expanded to provide further breakdowns by larger scale geographies, such as region, urban-rural or North-South group, if that were deemed useful. However, this would generate technical issues: (1) increasing complexity of data visualisation with many more sub-groups (e.g., adding urban-rural would double the number of groups to 10), and (2) handling small numbers problems. Small numbers of problems might arise for some disease categories or risk factors when sub-dividing them further, potentially resulting in more unstable and reliable estimates and in some cases a greater need for supressing counts below 5.

Furthermore, since NICE is responsible for providing national guidance, it may not be appropriate for NICE routinely to pay close attention to geographical variations in resource allocation, instead leaving these issues to other NHS agencies and initiatives such as the NHS Resource Allocation Formula.

Gender

Technically, it would be fairly straightforward to add gender to the tool – though raising the same issues of complexity of data visualisation and small numbers problems as for North-South.

Substantively, however, a drawback with adding gender is that gender inequalities in health are complicated and when life expectancy and quality of life data are combined there is overall little or no overall gender inequality in quality adjusted life expectancy at birth. Women have a higher life expectancy at birth than men but lower health-adjusted quality of life. When these data are combined, women overall have a similar health adjusted life expectancy at birth to men. This is discordant with wider patterns of gender inequality and discrimination in society, including patterns of inequality in health care: overall, women tend to receive worse quality health care in some though not all areas of care. So to analyse gender inequalities in health care one needs to use more specific health metrics and not the general summary metric of quality-adjusted life expectancy at birth. So, there is a case for leaving gender out of the health inequality impact tool and instead separately examining issues of gender inequality in health care.

Ethnicity

Providing equity breakdowns by ethnicity would be technically challenging and would require commissioning substantial further methodological research before this could

be added to the equity impact calculator. Data recording on ethnicity is improving, but neither the data nor our understanding of it are currently good enough to add ethnicity to the calculator.

We therefore recommend using the tool as a general starting point for examining health inequality impact, and then conducting further bespoke analysis of ethnic inequalities as appropriate.

In principle, it would be possible to use individual-level HES data on ethnicity to refine the in-built lookup-table in the calculator and produce IMD-ethnicity subgroup breakdowns by a handful of broad ethnic groups as well as ICD-10 code and IMD quintile group. There are 18 recommended ethnic group categories in England and Wales from the 2011 Census, and various ways of grouping these together to create a handful of broad ethnic groups – for example, the five broad categories of "White, Mixed, Asian, Black, Other" (https://www.ethnicity-facts-figures.service.gov.uk/style-guide/ethnic-groups). It might be possible routinely to provide separate data on inequality in prevalence by these five ethnic groups, with no analysis of interaction with IMD quintile group, and routinely present this data separately from the DCEA analysis.

However, integrating ethnicity into the DCEA analysis would be problematic without substantial further research. There would be risks of misleading estimates of ethnic variations in the prevalence of specific condition, with "quick and simple" findings varying in potentially puzzling and misleading ways for different conditions. There would also be further small number problems and costs due to the additional data security burdens of linking sensitive individual-level data on ethnicity to neighbourhood-level data on deprivation.

The fundamental methodological problem that would need resolving is how to handle intersectionality and the puzzling findings that often arise due to grouping together importantly different ethnic groups (e.g. the broad category "Asian" groups together "Indian", "Pakistani", "Bangladeshi", "Chinese" and "Any other Asian background") and aspects of ethnicity (e.g. country of birth, nationality, language, skin colour, national/geographical origin, religion) and in failing to allow for important interactions with other aspects of social disadvantage such as socioeconomic status, gender, occupation, education and others. A major recent study of ethnic inequalities in

health in the UK using data on nearly 1.5 million GP Patient Survey respondents aged 55 years and older concluded that “Area-level social deprivation and individual socioeconomic status are important determinants of health, and intersect with gender, ethnic group, and other personal characteristics, such as immigrant status or religion, resulting in complex moderation or exacerbation of disadvantage among different subgroups... An improved understanding of the mechanisms that underlie these intersecting layers of disadvantage will be important for informing the development of policy interventions and should be a priority for future research.” (Watkinson et al., 2021).

The challenge is partly a matter of limitations in data and methods, partly a matter of limited scientific knowledge, and partly a matter of limited expertise in these complex intersectionality issues among the UK health analytical community. Basically, the UK health data and research infrastructure was not designed with ethnicity in mind. Although things are improving - and may now start to improve further and faster following the Black Lives Matters movement – data on ethnicity remain substantially more limited and harder to access than data on IMD.

IMD is available at general population level in almost all health datasets, and almost always yields simple and plausible results that are easy to understand: it splits the population into five equally sized quintile groups which almost always yields the same kind of simple monotonic social gradient in health. This makes IMD amenable to "quick and simple" analysis - the risk of finding puzzling social gradients with an implausible sign or magnitude on important coefficients of interest is low.

However, disentangling ethnicity from IMD is challenging given current data, methods, knowledge and expertise. There are substantial risks in conducting "quick and simple" analysis of ethnicity, which often produces results that are implausible and would require time-consuming further investigation before being presented to decision makers or released for public consumption. This further investigation is often not practical due to time and analytical capacity constraints and sometimes not even technically feasible due to data limitations. Associations often appear to have the "wrong" sign because crucially important issues of intersectionality have been ignored. So, there is a substantial risk that "quick and simple" analysis of ethnicity could produce puzzling and potentially misleading findings that can generate unnecessary and unhelpful misunderstanding and public controversy.

Taken together, this means that adding ethnicity would likely be a substantial additional understanding requiring substantial new methods development work up front and substantial additional analytical capacity and expertise from NICE to interpret the findings and investigate and defuse puzzling findings with the "wrong" sign - i.e., somewhat spoiling the point of providing “quick and simple" analysis.

Further methodological development and feasibility work would therefore be required before we can be confident that ethnicity can be handled robustly and gauge the scale of the task and the resources required to add ethnicity to this tool.

Interactions between health inequality, time and discounting

Further methodological research may be warranted to consider the interactions between health inequality and the discounting of future health benefits and costs. How does the discount rate influence the health inequality impact? Are health inequality impacts generally larger or smaller for interventions involving long-term treatment lasting longer than one year? Currently the calculator does not explicitly discount future health benefits and costs. Our current recommendation is therefore to use discounted incremental costs and QALY gains as the base case CEA inputs.

Further research on opportunity cost

Further research is needed to estimate the distribution of health opportunity cost from national and local government expenditure (of different kinds). Further research is also needed to critique the existing estimates of the health opportunity cost of NHS expenditure and provide alternative estimates.

5. Recommendations

1. We recommend piloting the use of the calculator in NICE decision making across a wide range of different types of guidance, with support from experts in DCEA. This will help to determine the resource required to undertake this work and impact on committee time. It will also help to iron out teething problems and develop experience, facilitating the development of official NICE guidance on methods for assessing health inequality impact. In cases where there is a risk of legal challenge, the piloting could focus on a "realistic" setting out with the decision making process – for example, Technology Appraisal committee members could be shown health inequality impact information about a technology immediately after they have made their final determination, and asked to scrutinise the information and give feedback on how it could be improved and used in future cases. This piloting will need to be carefully planned and adequately resourced, with close involvement and support from experts in DCEA.

2. We also recommend that NICE should undertake, commission and/or partner in further work to prepare for routine use of DCEA across all NICE activity, including the development of user interface and training materials as well as considering how the outputs would be quality assured and used and impacts on NICE's ways of working. This might include further work on exploring the accuracy and reliability of estimates of inequality in disease and risk factor prevalence from different data sources. There may also be value in improving the built-in data within the calculator used for the purpose of "triage" DCEA – for example, updating the time period, going down to 4-digit rather than 3-digit ICD level for disease categories, and/or adding primary care disease category estimates from analysis of CPRD data. However, updating the built-in data would be costly and time consuming, especially for disease prevalence data from large and complex administrative datasets, due to time-consuming data access paperwork, substantial data access fees, and substantial specialist data analyst time costs. So the value of updating this data needs to be weighed against the risks and costs of delay. The built-in data for triage DCEA purposes can never be fully authoritative, and to produce simple and full DCEA estimates that support important expenditure decisions there will always be a need for bespoke data analysis and sensitivity analysis using alternative sources of data. So an alternative might be to use existing data for "triage" DCEA purposes and use bespoke data on a case-by-case basis as required – for example, in a technology

appraisal context companies could be asked to source their own bespoke data on disease prevalence, and in a public health guideline development context the guideline development group could be asked to source their own bespoke data on risk factor prevalence.

3. We recommend not attempting to expand the calculator to provide automated outputs examining impacts on more specific health inequalities, such as ethnic and gender inequalities in health. Instead, we recommend using the general health inequality impact by IMD deprivation group as a starting point that facilitates bespoke consideration of specific health inequality impacts relating to ethnicity, gender and other aspects of social disadvantage. This can help to focus attention and data-gathering efforts on the question of how far other important health inequality impacts on specific populations are likely to differ from the general health inequality impact. The potential for NICE guidance to have special impacts on ethnic and gender inequality in health care access and quality – different from the general socioeconomic impacts estimated by the tool – can then be examined separately using other sources of quantitative or qualitative information. Issues of diversity and inclusion in NHS workplaces (including NICE) can also be discussed separately if relevant to a decision about a specific intervention.

4. We also recommend not expanding the calculator to examine regional disadvantage as well as socioeconomic disadvantage based on neighbourhood deprivation. The two concepts are closely correlated and adding many regional disadvantage sub-groups would substantially complicate the calculator with risks of information over-load and small number problems. This would also raise conceptual and policy challenges about potential overlap between the remits of NICE and the NHS resource allocation formula. Currently, the primary remit of NICE is to develop national guidance applicable across all regions, and the NHS has other mechanisms for addressing health inequality concerns related to geographical resource allocation – for example, the unmet need and health inequality adjustments to the geographical resource allocation formula.

5. To improve the evidence base for health inequalities analysis, we recommend that the NIHR should develop guidance on collecting and reporting health inequalities data across all NIHR funded research, and should also commission a substantial piece of research to better understand the complex patterns of

intersectionality between ethnic, gender and socioeconomic inequalities in health and health care utilisation, to inform the development of various types of health inequality analysis needed to support the work of NICE and other NHS agencies, including the NHS resource allocation formula.

6. We also recommend that NICE work with the Department of Health and Social Care to start developing and piloting modified versions of the calculator to supplement cost-effectiveness analyses used to support decision making by other NHS agencies, for example, the Joint Committee on Vaccination and Immunization, the NHS National Screening Committee, and the Office of Health Improvement and Disparities.

Appendix A: List of NICE Officials and Advisers Consulted

Guideline Development

Clinical

Helen Cross, UCL, Clinical Topic Expert Member of NICE Guideline Committee on Epilepsy

Elizabeth Kay, Peninsula Dental School, Chair of NICE NGA Guideline Committee on Epilepsy

Arjune Sen, Oxford Epilepsy Research Group, Clinical Topic Expert Member of NICE Guideline Committee on Epilepsy

Public Health

Robbie Currie, London Borough of Bexley, Public Health Topic Expert Member of NICE Public Health Advisory Committee E - Reducing sexually transmitted infections

Kathryn Faulkner, Cambridgeshire CC & Peterborough City Council, Core Member of NICE Public Health Advisory Committee E - Reducing sexually transmitted infections

Judith Hooper, Core Member of NICE Public Health Advisory Committee E - Reducing sexually transmitted infections

Centre for Guidelines

Technical Support

James Hawkins, National Guidelines Alliance, Health Economist at NICE National Guidelines Alliance

Sophia Kemmis Betty, National Guidelines Centre, Health Economist at NICE National Guidelines Centre

Bhash Naidoo, NICE, Senior Technical Adviser (Health Economics), Centre for Guidelines

Joshua Pink, NICE, Technical Adviser (Health Economics), Centre for Guidelines

Commissioning Managers

Victoria Axe, NICE, NICE Guideline Commissioning Manager, Centre for Guidelines

Catrina Charlton, NICE, NICE Guideline Commissioning Manager, Centre for Guidelines

Clifford Middleton, NICE, NICE Guideline Commissioning Manager, Centre for Guidelines

Nick Staples, NICE, NICE Guideline Commissioning Manager, Centre for Guidelines

Technology Appraisal

Advisory Committee

Amanda Adler, NICE, Chair of NICE Technology Appraisals Committee

Rita Faria, University of York, Health Economist Member of NICE Technology Appraisals Committee

Technical Support

Richard Diaz, NICE, Technical Adviser (Health Economics) - leading the modifiers work, Technology Appraisals

Ian Watson, NICE, Senior Technical (Health Economics), Centre for Guidelines

Diagnostics Advisory Committee

Neil Hawkins, University of Glasgow, Health Economist Member of NICE Diagnostics Advisory Committee

Other Senior Advisory Roles for NICE

Martin Cowie, Imperial College London, Former NICE Non-Executive Director

Anthony Culyer, University of York, Founding Vice-Chair of NICE.

Hugh McIntyre, Acting Medical Adviser to the NICE Board.

Peter Littlejohns, Founding Clinical and Public Health Director of NICE, 1999-2012.

Mark Sculpher, University of York, Former member of various NICE advisory committees (technology, public health, diagnostics) and chair of methods task group

Allan Wailoo, University of Sheffield, Director of NICE Decision Support Unit

Appendix B: Checklist for Critical Appraisal of Health Inequality Impact Estimates

Main One Page Checklist

1. **Basic cost-effectiveness inputs.** Are the 7 basic cost-effectiveness inputs appropriate and have they been clearly justified? (i) Intervention and comparator; (ii) Indicated health condition; (iii) Indicated age range; (iv) Eligible population size; (v) Incremental costs; (vi) Incremental QALYs, (vii) marginal productivity of alternative resource use.

2. **Inequality in health benefits.** Have appropriate and clearly justified assumptions been made about the direction and magnitude of social differences at each step in the staircase of inequality?

   – Eligibility (what proportion of people are eligible for this intervention)

   – Uptake (what proportion of eligible people will receive this intervention)

   – Health effect (will the health effect differ from the average health effect)

3. **Inequality in health burdens.** Have appropriate and clearly justified assumptions been made about the distribution of health opportunity costs by social group, taking into account whether the main costs fall on the NHS budget or elsewhere (e.g., local government, national government, families, businesses)?

4. **Sensitivity analysis.** Is it clear how far the direction and magnitude of impact on health inequality varies according to alternative plausible cost-effectiveness inputs and distributional assumptions?

5. **Inequality in non-health outcomes.** Has appropriate consideration been given to differences in non-health benefits and burdens by social group? E.g., carer non-health burdens, child development, employment, education, crime, wellbeing

6. **Equity-efficiency trade-offs.** Has appropriate consideration been given to potential trade-offs between improving total health and reducing health inequality, including if appropriate sensitivity analysis of recommendations to changes in the inequality aversion parameter?

7. **Equity-equity conflicts.** Has appropriate consideration been given to potential conflicts between reducing health inequality and other equity concerns such as prioritising severely ill patients? E.g., funding life-extending end-of-life treatments may sometimes increase health inequality, if the costs fall on more cost-effective services that benefit more socially disadvantaged populations

8. **Specific populations.** Has appropriate consideration been given to whether impacts on specific disadvantaged populations may differ substantially from the general impact predicted by neighbourhood deprivation alone? E.g., regional deprivation, ethnicity, gender, disability, rough sleeping, drug use, imprisonment, other vulnerable and excluded populations

More Detailed Supplementary Questions

1. Have the intervention(s) and the comparator been clearly described?

2. Have all the indications for the eligible population been listed?
   e.g., age range, disease sub-type, further eligibility criteria [This is crucial for estimating both QALY gains and social distributions]

3. Has a user estimate of the eligible population size been provided?

4. Is the eligible population like to be substantially different to the built-in estimate based on hospital data or risk factor surveys?

5. Is there substantial potential for bias in the base case user estimate of incremental cost and QALY gain? (e.g., Do cost-effectiveness estimates from reputable models differ by a factor of 2 or more?)

6. Is there substantial scope for disagreement about the appropriate marginal productivity assumption in this decision context? (e.g., for local authority expenditure a threshold below £15,000 may be appropriate). Do plausible changes in marginal productivity change the direction of health inequality impact?

7. Is there likely to be substantial bias in the built-in default estimates of the social distribution of the eligible population? If so, can a less biased estimate be provided?

8. Has a user assumption about the social distribution of uptake been provided? Is it based on data or opinion? Is there substantial scope for expert disagreement about this assumption?

9. Is it reasonable in this context to assume no social difference in effectiveness? If not, has a user assumption been provided? Do disadvantaged recipients have more capacity to benefit than others (e.g., due to greater severity or risk) or less (e.g., due to worse adherence, co-morbidity or life expectancy)?

10. Is it reasonable to use the NHS base case estimate of the social distribution of health opportunity cost? (e.g., Does the funding come from local government rather than the NHS). If not, has a user assumption been provided? Is there substantial scope for disagreement about the shape of the distribution?

11. Is there an unusual (non-monotonic) shape to the net health benefit distribution? If so, is the direction of health inequality impact ambiguous?

12. Does the level of health inequality aversion change the recommended decision? If so, what is an appropriate health inequality aversion parameter in this context?

Appendix C: Further Details on the Triage DCEA Examples

This appendix provides further details of the six DCEA triage examples summarised in the report, by reproducing the report tables and graphs generated by the health equity impact calculator (Version 2, 2022).

Example 1:

Roflumilast for treating chronic obstructive pulmonary disease in adults with chronic bronchitis

Equity impact report

2023-05-21

This report was generated by entering user-defined assumptions into a health inequality impact calculator (https://shiny.york.ac.uk/dceasimple) produced by the University of York. The University of York offers no guarantees of any kind for the results produced.

The following analysis compares **Rofrumilast** against **Standard**. This first page summarises the main results; the user-defined assumptions are listed on the next page; and further pages show various graphs.

***Table 1**: Main model results*

Net health inequality benefit	**52 QALYs**
Incremental Cost-Effectiveness Ratio (ICER)	**£25,057/QALY**
Incremental Net Monetary Benefit (INMB)/recipient	**£692**
Incremental net health benefit (INHB)	**58 QALYs**
Equity-weighted ICER	**£22,168/QALY**
Equity-weighted INMB/recipient	**£1,239**
Equity-weighted INHB	**106 QALYs**
Decision threshold	**£30,000**
Marginal productivity	**£30,000**
Atkinson parameter	**10**

***Table 2**: Distributional results*

	IMD1	IMD2	IMD3	IMD4	IMD5	Total
Share of the eligible population	27%	23%	18%	18%	15%	100%
Uptake	100%	100%	100%	100%	100%	
Inc. QALY/recipient	0.14	0.14	0.14	0.14	0.14	
Share of health opportunity costs	20%	20%	20%	20%	20%	100%
Recipients (in 1,000s)	1	1	0	0	0	3
Recipients (share)	27%	23%	18%	18%	15%	100%
Intervention benefits (QALYs)	94	81	64	64	52	355
Opportunity costs (QALYs)	59	59	59	59	59	296
Net health benefit (QALYs)	35	22	4	4	-8	58

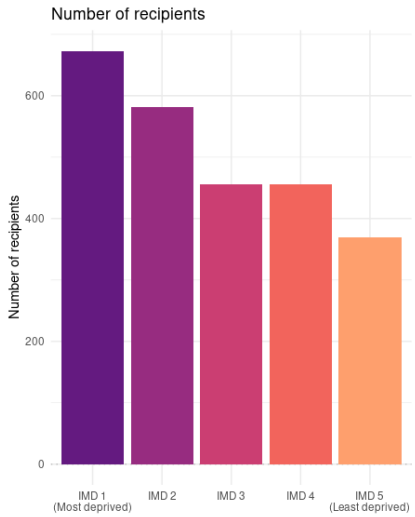
Inputs

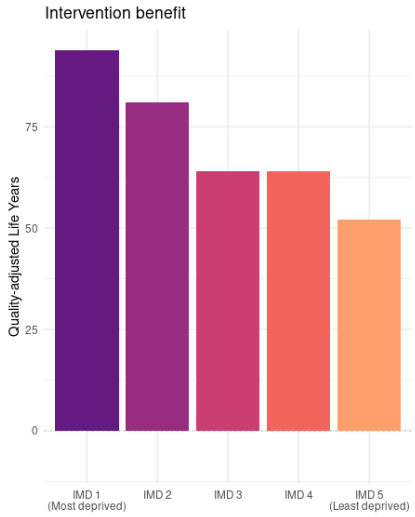
This section summarises the user-defined assumptions used to create the results and plots.

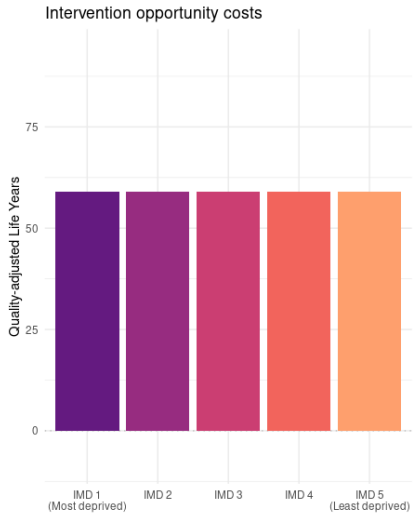
***Table 3**: Input parameters*

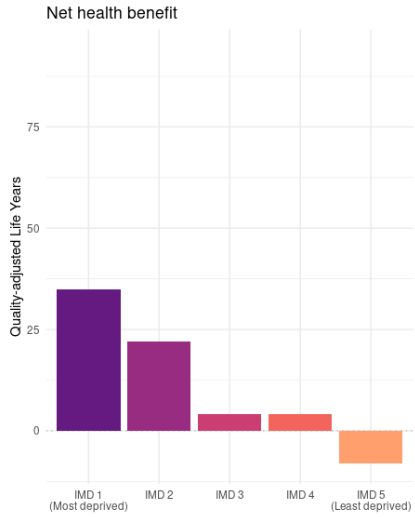
Variable	Value
Intervention name	Rofrumilast
Comparator name	Standard
Incremental QALYs	0.140
Incremental cost (£)	3,508
Intervention type	Disease population
Intervention disease category (ICD-10)	J42
Age range	16; 100
Eligible population	2,533
Uptake (%) in IMD1 (most deprived)	100
Uptake (%) in IMD2	100
Uptake (%) in IMD3	100
Uptake (%) in IMD4	100
Uptake (%) in IMD5 (least deprived)	100
Effectiveness in IMD1 (most deprived)	1.000
Effectiveness in IMD2	1.000
Effectiveness in IMD3	1.000
Effectiveness in IMD4	1.000
Effectiveness in IMD5 (least deprived)	1.000
Share of eligible population IMD1 (most deprived)	0.266
Share of eligible population IMD2	0.229
Share of eligible population IMD3	0.180
Share of eligible population IMD4	0.180
Share of eligible population IMD5 (least deprived)	0.146
Health opportunity cost distribution	flat
Marginal productivity	30,000
Atkinson inequality aversion value	10
Decision threshold (£)	30,000

Distributional health impact

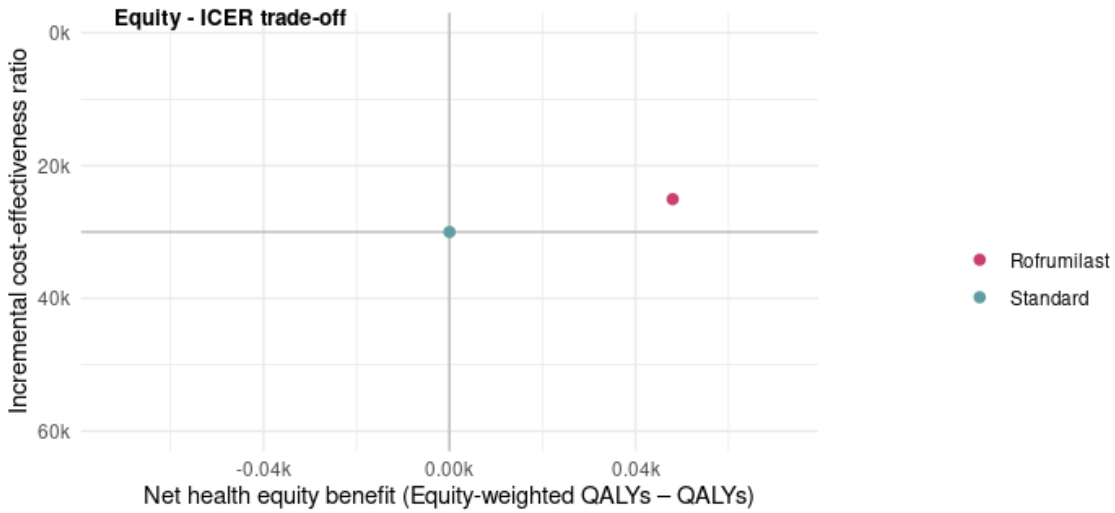


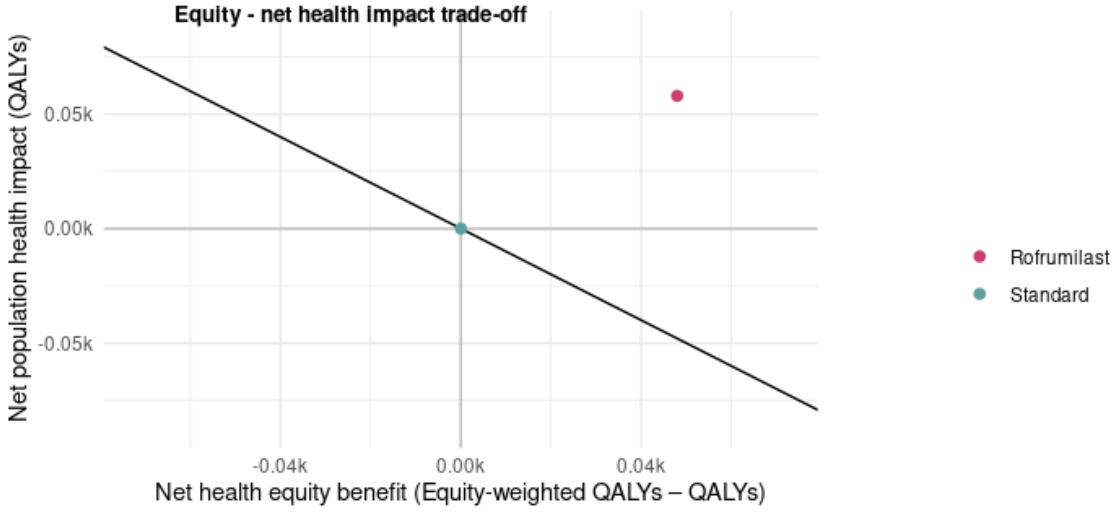


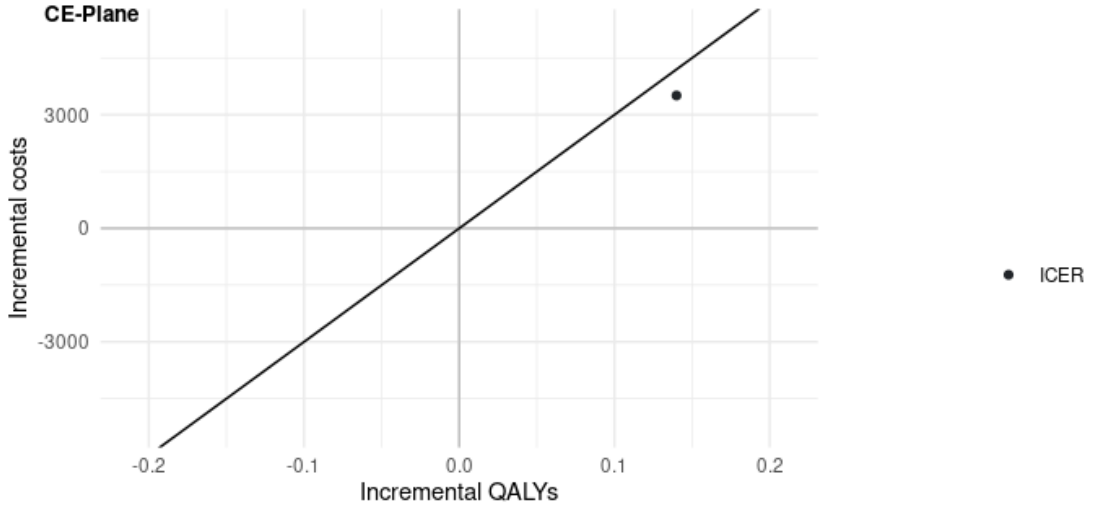




Equity & efficiency







Example 2

Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency

Equity impact report

2023-05-21

This report was generated by entering user-defined assumptions into a health inequality impact calculator (https://shiny.york.ac.uk/dceasimple) produced by the University of York. The University of York offers no guarantees of any kind for the results produced.

The following analysis compares **Pembrolizumab** against **Standard**. This first page summarises the main results; the user-defined assumptions are listed on the next page; and further pages show various graphs.

***Table 1**: Main model results*

Net health inequality benefit	**-23 QALYs**
Incremental Cost-Effectiveness Ratio (ICER)	**£20,000/QALY**
Incremental Net Monetary Benefit (INMB)/recipient	**£10,000**
Incremental net health benefit (INHB)	**155 QALYs**
Equity-weighted ICER	**£20,870/QALY**
Equity-weighted INMB/recipient	**£8,749**
Equity-weighted INHB	**138 QALYs**
Decision threshold	**£30,000**
Marginal productivity	**£30,000**
Atkinson parameter	**10**

***Table 2**: Distributional results*

	IMD1	IMD2	IMD3	IMD4	IMD5	Total
Share of the eligible population	18%	18%	21%	21%	22%	100%
Uptake	100%	100%	100%	100%	100%	
Inc. QALY/recipient	1	1	1	1	1	
Share of health opportunity costs	20%	20%	20%	20%	20%	100%
Recipients (in 1,000s)	0	0	0	0	0	0
Recipients (share)	18%	18%	21%	21%	22%	100%
Intervention benefits (QALYs)	85	82	99	99	100	465
Opportunity costs (QALYs)	62	62	62	62	62	310
Net health benefit (QALYs)	23	20	37	37	38	155

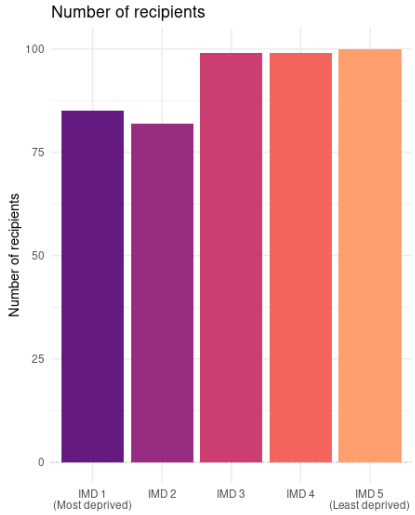
Inputs

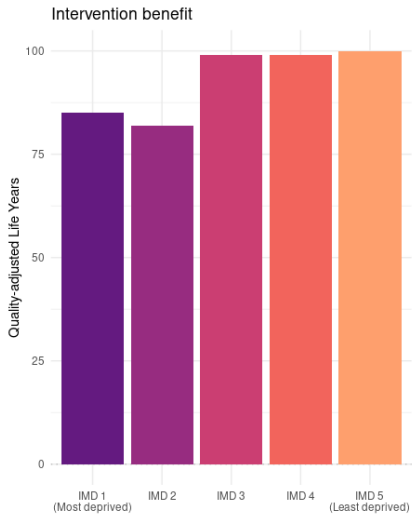
This section summarises the user-defined assumptions used to create the results and plots.

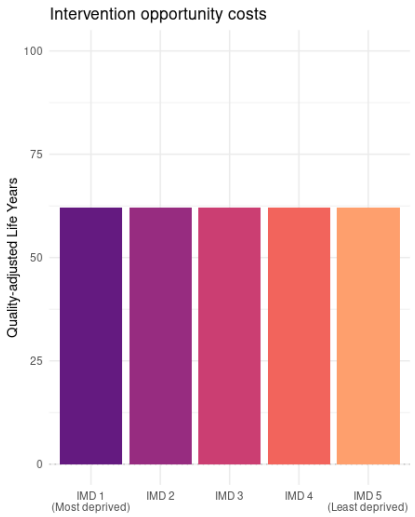
***Table 3**: Input parameters*

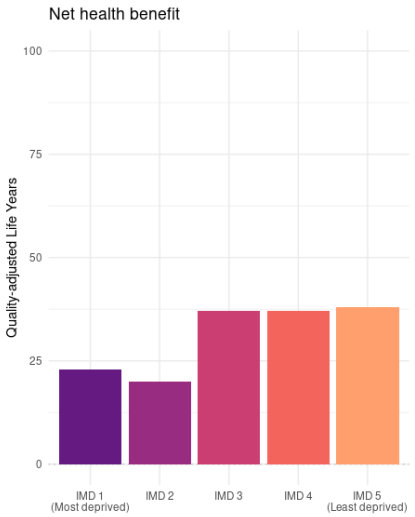
Variable	Value
Intervention name	Pembrolizumab
Comparator name	Standard
Incremental QALYs	1.000
Incremental cost (£)	20,000
Intervention type	Disease population
Intervention disease category (ICD-10)	C18
Age range	16; 100
Eligible population	465
Uptake (%) in IMD1 (most deprived)	100
Uptake (%) in IMD2	100
Uptake (%) in IMD3	100
Uptake (%) in IMD4	100
Uptake (%) in IMD5 (least deprived)	100
Effectiveness in IMD1 (most deprived)	1.000
Effectiveness in IMD2	1.000
Effectiveness in IMD3	1.000
Effectiveness in IMD4	1.000
Effectiveness in IMD5 (least deprived)	1.000
Share of eligible population IMD1 (most deprived)	0.183
Share of eligible population IMD2	0.175
Share of eligible population IMD3	0.213
Share of eligible population IMD4	0.213
Share of eligible population IMD5 (least deprived)	0.215
Health opportunity cost distribution	flat
Marginal productivity	30,000
Atkinson inequality aversion value	10
Decision threshold (£)	30,000

Distributional health impact

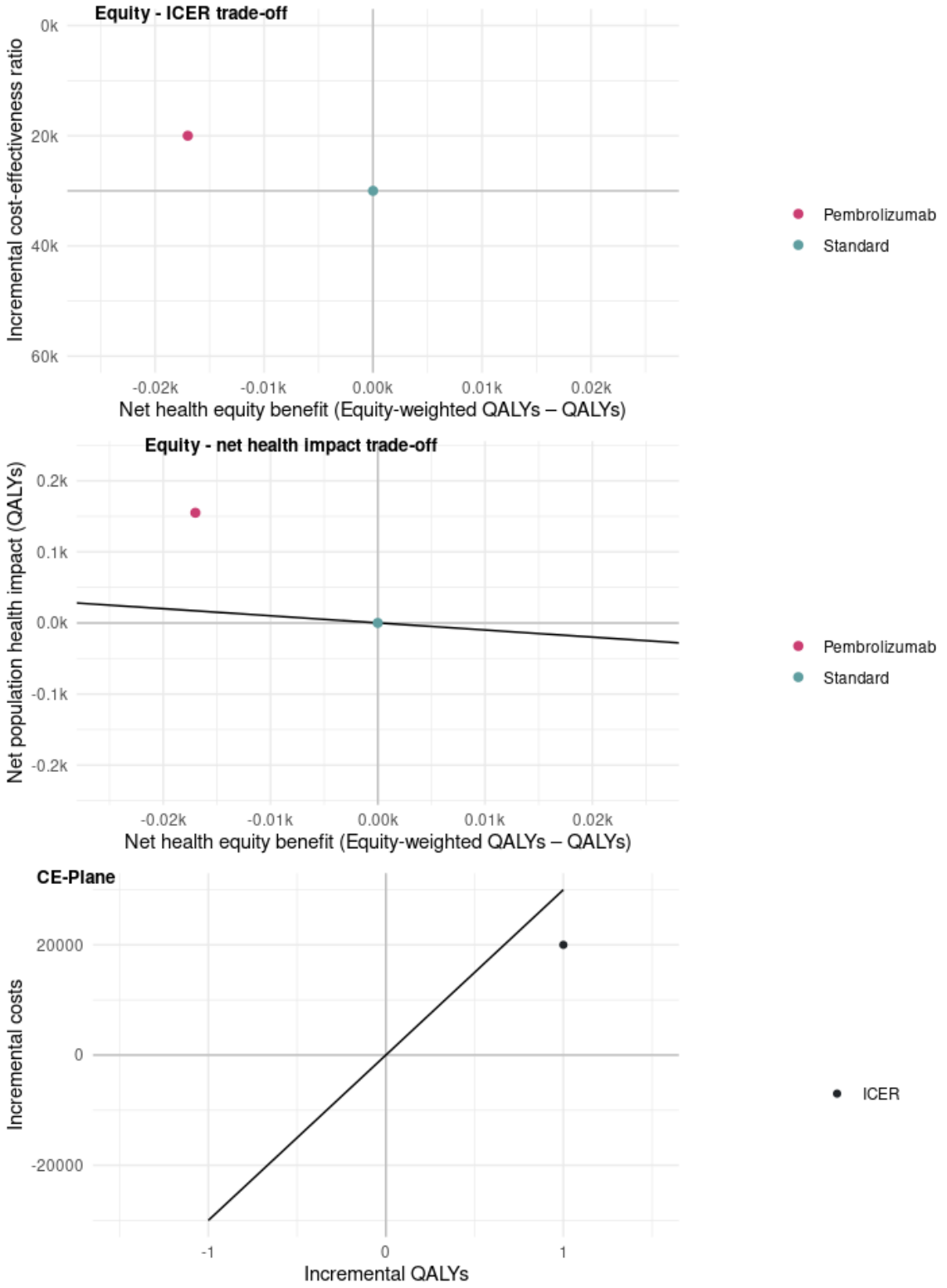








Equity & efficiency



Example 3:

Lung health checks for current or former smokers aged 55 to 75

Equity impact report

2023-05-22

This report was generated by entering user-defined assumptions into a health inequality impact calculator (https://shiny.york.ac.uk/dceasimple) produced by the University of York. The University of York offers no guarantees of any kind for the results produced.

The following analysis compares **Lung health checks** against **No screening**. This first page summarises the main results; the user-defined assumptions are listed on the next page; and further pages show various graphs.

***Table 1**: Main model results*

Net health inequality benefit	**-294 QALYs**
Incremental Cost-Effectiveness Ratio (ICER)	**£14,286/QALY**
Incremental Net Monetary Benefit (INMB)/recipient	**£29**
Incremental net health benefit (INHB)	**109 QALYs**
Equity-weighted ICER	**£16,469/QALY**
Equity-weighted INMB/recipient	**£21**
Equity-weighted INHB	**-195 QALYs**
Decision threshold	**£30,000**
Marginal productivity	**£15,000**
Atkinson parameter	**10**

***Table 2**: Distributional results*

	IMD1	IMD2	IMD3	IMD4	IMD5	Total
Share of the eligible population	33%	21%	19%	15%	12%	100%
Uptake	10%	20%	30%	40%	50%	
Inc. QALY/recipient	0.002	0.002	0.002	0.002	0.002	
Share of health opportunity costs	20%	20%	20%	20%	20%	100%
Recipients (in 1,000s)	165	209	289	299	294	1,257
Recipients (share)	13%	17%	23%	24%	23%	100%
Intervention benefits (QALYs)	301	381	526	544	536	2,288
Opportunity costs (QALYs)	436	436	436	436	436	2,179
Net health benefit (QALYs)	-135	-55	91	108	100	109

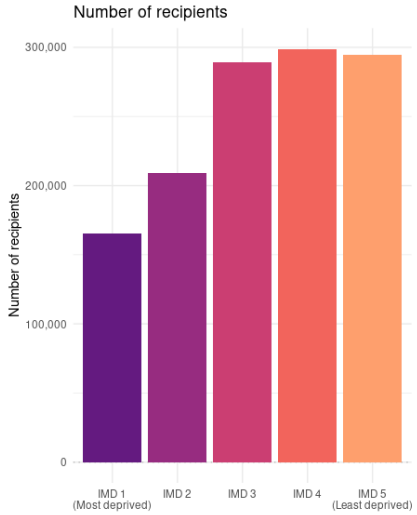
Inputs

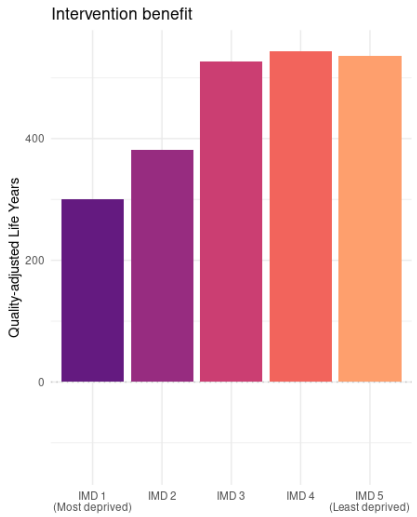
This section summarises the user-defined assumptions used to create the results and plots.

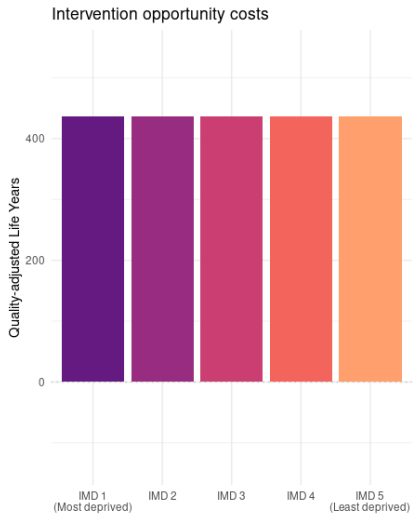
***Table 3**: Input parameters*

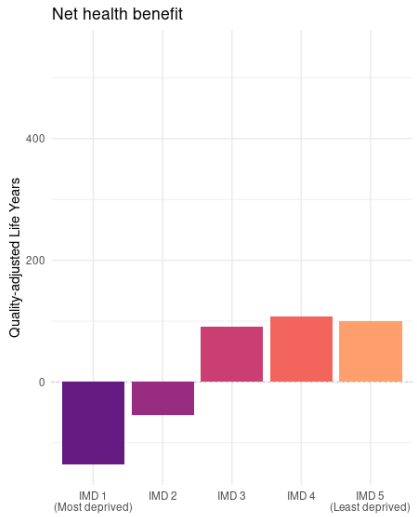
Variable	Value
Intervention name	Lung health checks
Comparator name	No screening
Incremental QALYs	0.002
Incremental cost (£)	26
Intervention type	Risk factor population
Intervention risk factor	Smoking
Age range	0; 100
Eligible population	5,000,000
Uptake (%) in IMD1 (most deprived)	10
Uptake (%) in IMD2	20
Uptake (%) in IMD3	30
Uptake (%) in IMD4	40
Uptake (%) in IMD5 (least deprived)	50
Effectiveness in IMD1 (most deprived)	1.000
Effectiveness in IMD2	1.000
Effectiveness in IMD3	1.000
Effectiveness in IMD4	1.000
Effectiveness in IMD5 (least deprived)	1.000
Share of eligible population IMD1 (most deprived)	0.331
Share of eligible population IMD2	0.209
Share of eligible population IMD3	0.193
Share of eligible population IMD4	0.149
Share of eligible population IMD5 (least deprived)	0.118
Health opportunity cost distribution	flat
Marginal productivity	15,000
Atkinson inequality aversion value	10
Decision threshold (£)	30,000

Distributional health impact

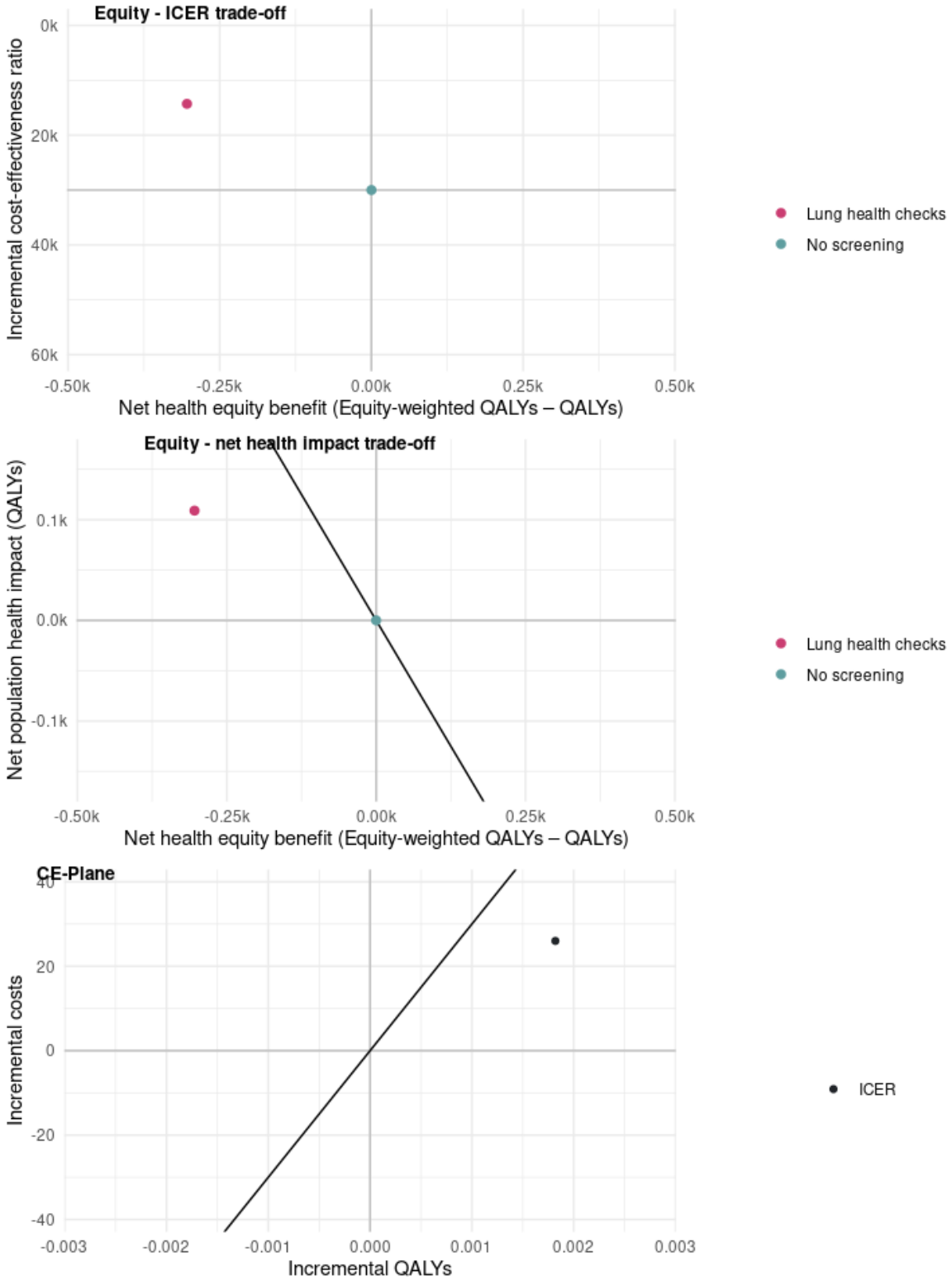








Equity & efficiency



Example 4:

Crizanlizumab for preventing sickle cell crises in sickle cell disease

Equity impact report

2023-03-20

This report was generated by entering user-defined assumptions into a health inequality impact calculator (https://shiny.york.ac.uk/dceasimple) produced by the University of York. The University of York offers no guarantees of any kind for the results produced.

The following analysis compares **Crizanluzimab** against **Standard.** This first page summarises the main results; the user-defined assumptions are listed on the next page; and further pages show various graphs.

***Table 1**: Main model results*

Net health inequality benefit	**246 QALYs**
Incremental Cost-Effectiveness Ratio (ICER)	**£40,000/QALY**
Incremental Net Monetary Benefit (INMB)/recipient	**£-10,000**
Incremental net health benefit (INHB)	**-166 QALYs**
Equity-weighted ICER	**£28,125/QALY**
Equity-weighted INMB/recipient	**£2,667**
Equity-weighted INHB	**43 QALYs**
Decision threshold	**£30,000**
Marginal productivity	**£30,000**
Atkinson parameter	**10**

***Table 2**: Distributional results*

	IMD1	IMD2	IMD3	IMD4	IMD5	Total
Share of the eligible population	39%	38%	8%	8%	6%	100%
Uptake	100%	100%	100%	100%	100%	
Inc. QALY/recipient	1	1	1	1	1	
Share of health opportunity costs	20%	20%	20%	20%	20%	100%
Recipients (in 1,000s)	0	0	0	0	0	0
Recipients (share)	39%	38%	8%	8%	6%	100%
Intervention benefits (QALYs)	197	188	42	42	30	499
Opportunity costs (QALYs)	133	133	133	133	133	665
Net health benefit (QALYs)	64	55	-91	-91	-103	-166

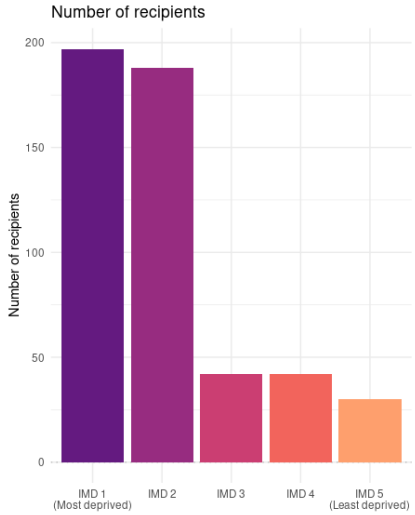
Inputs

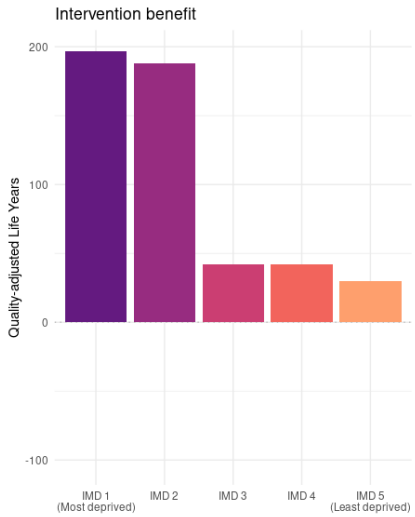
This section summarises the user-defined assumptions used to create the results and plots.

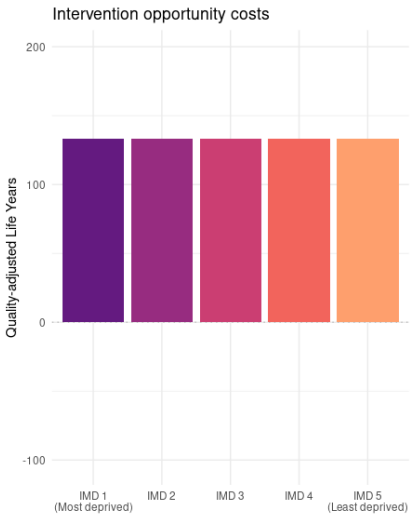
***Table 3**: Input parameters*

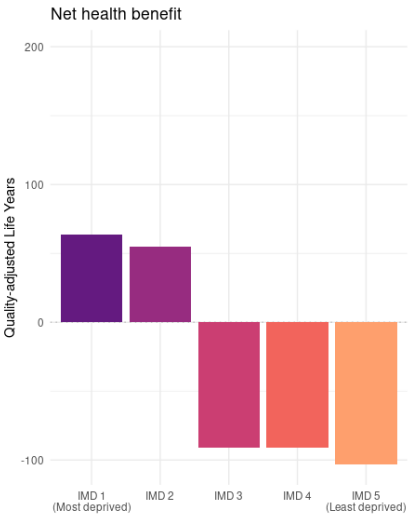
Variable	Value
Intervention name	
Comparator name	
Incremental QALYs	1.000
Incremental cost (£)	40,000
Intervention type	Disease population
Intervention disease category (ICD-10)	D57
Age range	16; 100
Eligible population	500
Uptake (%) in IMD1 (most deprived)	100
Uptake (%) in IMD2	100
Uptake (%) in IMD3	100
Uptake (%) in IMD4	100
Uptake (%) in IMD5 (least deprived)	100
Effectiveness in IMD1 (most deprived)	1.000
Effectiveness in IMD2	1.000
Effectiveness in IMD3	1.000
Effectiveness in IMD4	1.000
Effectiveness in IMD5 (least deprived)	1.000
Share of eligible population IMD1 (most deprived)	0.393
Share of eligible population IMD2	0.377
Share of eligible population IMD3	0.085
Share of eligible population IMD4	0.085
Share of eligible population IMD5 (least deprived)	0.060
Health opportunity cost distribution	flat
Marginal productivity	30,000
Atkinson inequality aversion value	10
Decision threshold (£)	30,000

Distributional health impact

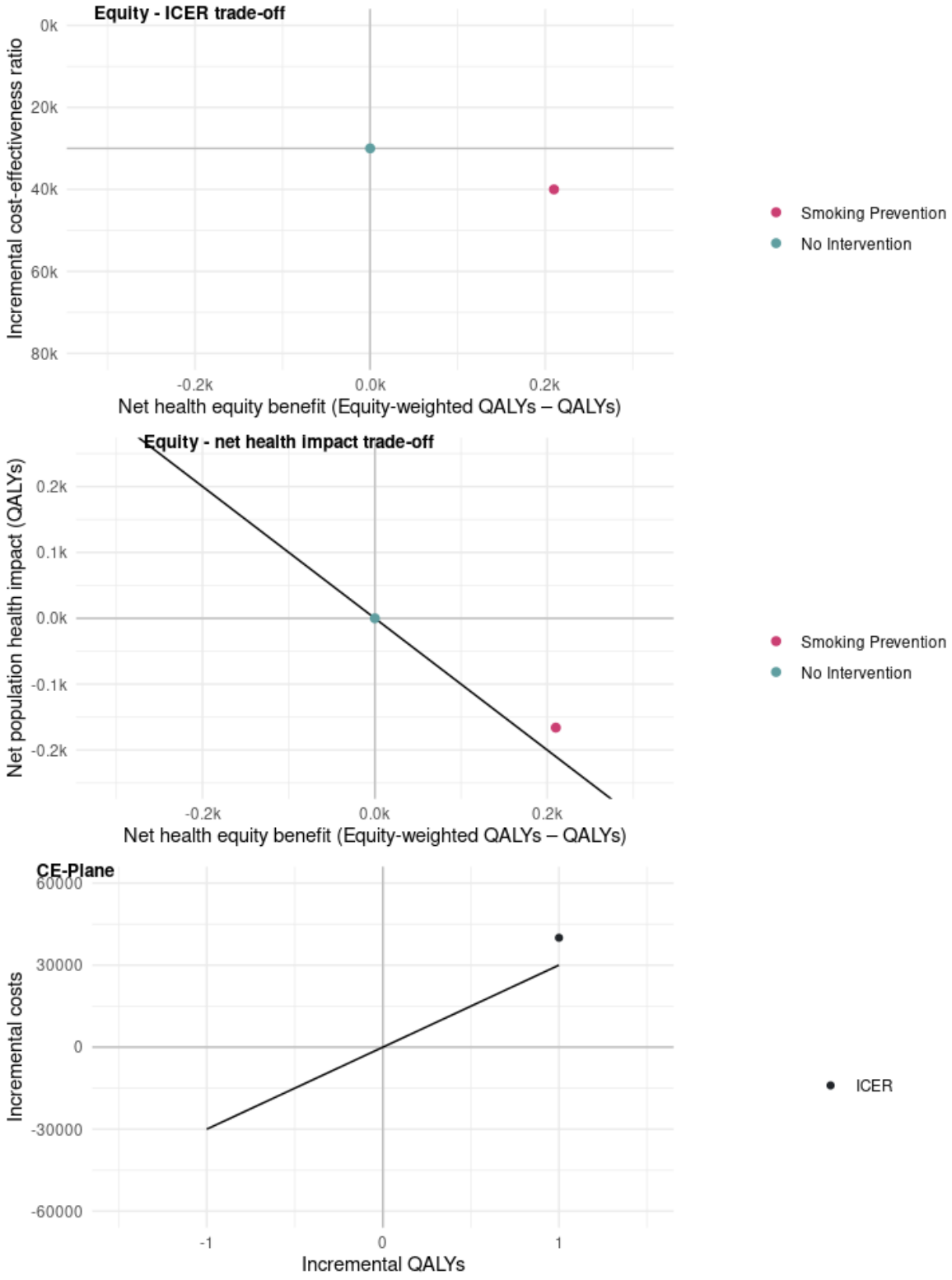








Equity & efficiency



Example 5:

Hypothetical new convenient medication for poorly controlled type II diabetes

Equity impact report

2023-05-22

This report was generated by entering user-defined assumptions into a health inequality impact calculator (https://shiny.york.ac.uk/dceasimple) produced by the University of York. The University of York offers no guarantees of any kind for the results produced.

The following analysis compares **Hypothetical new medication for diabetes** against **Standard**. This first page summarises the main results; the user-defined assumptions are listed on the next page; and further pages show various graphs.

***Table 1**: Main model results*

Net health inequality benefit	**39,273 QALYs**
Incremental Cost-Effectiveness Ratio (ICER)	**£35,000/QALY**
Incremental Net Monetary Benefit (INMB)/recipient	**£-5,000**
Incremental net health benefit (INHB)	**-13,361 QALYs**
Equity-weighted ICER	**£24,493/QALY**
Equity-weighted INMB/recipient	**£7,869**
Equity-weighted INHB	**21,114 QALYs**
Decision threshold	**£30,000**
Marginal productivity	**£30,000**
Atkinson parameter	**10**

***Table 2**: Distributional results*

	IMD1	IMD2	IMD3	IMD4	IMD5	Total
Share of the eligible population	25%	22%	18%	18%	16%	100%
Uptake	20%	15%	10%	5%	5%	
Inc. QALY/recipient	1	1	1	1	1	
Share of health opportunity costs	20%	20%	20%	20%	20%	100%
Recipients (in 1,000s)	34	23	12	6	5	80
Recipients (share)	42%	28%	15%	8%	6%	100%
Intervention benefits (QALYs)	33,698	22,702	12,369	6,184	5,216	80,169
Opportunity costs (QALYs)	18,706	18,706	18,706	18,706	18,706	93,530
Net health benefit (QALYs)	14,992	3,996	-6,337	-12,522	-13,490	-13,361

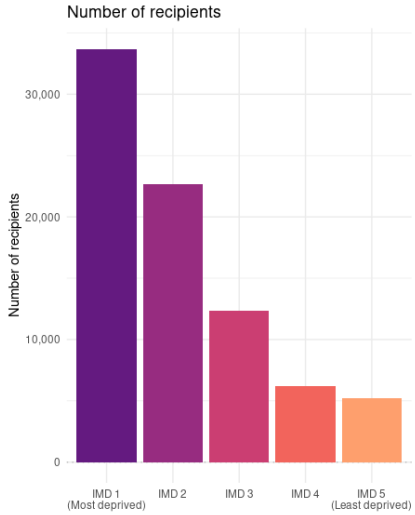
Inputs

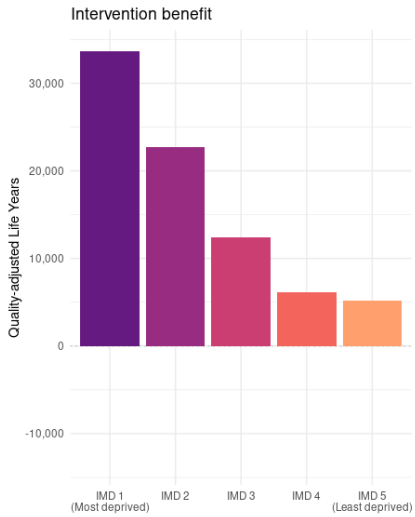
This section summarises the user-defined assumptions used to create the results and plots.

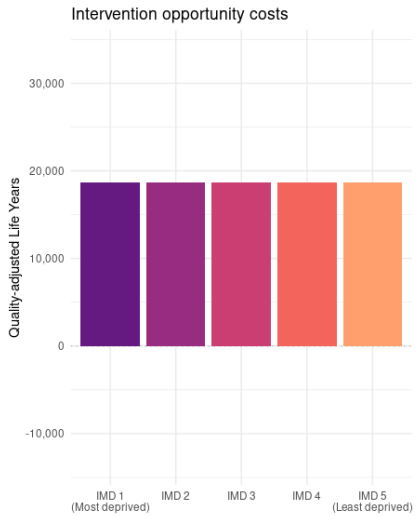
***Table 3**: Input parameters*

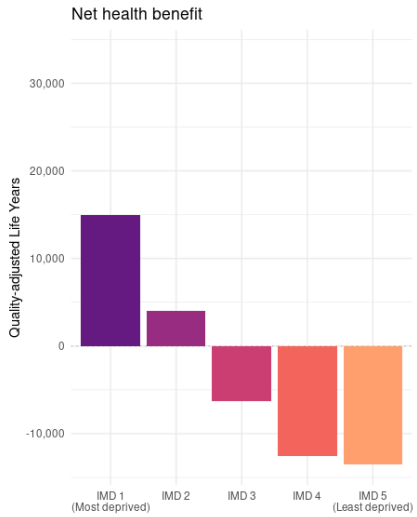
Variable	Value
Intervention name	Hypothetical new medication for diabetes
Comparator name	Standard
Incremental QALYs	1.000
Incremental cost (£)	35,000
Intervention type	Disease population
Intervention disease category (ICD-10)	E11
Age range	16; 100
Eligible population	671,545
Uptake (%) in IMD1 (most deprived)	20
Uptake (%) in IMD2	15
Uptake (%) in IMD3	10
Uptake (%) in IMD4	5
Uptake (%) in IMD5 (least deprived)	5
Effectiveness in IMD1 (most deprived)	1.000
Effectiveness in IMD2	1.000
Effectiveness in IMD3	1.000
Effectiveness in IMD4	1.000
Effectiveness in IMD5 (least deprived)	1.000
Share of eligible population IMD1 (most deprived)	0.251
Share of eligible population IMD2	0.225
Share of eligible population IMD3	0.184
Share of eligible population IMD4	0.184
Share of eligible population IMD5 (least deprived)	0.155
Health opportunity cost distribution	flat
Marginal productivity	30,000
Atkinson inequality aversion value	10
Decision threshold (£)	30,000

Distributional health impact

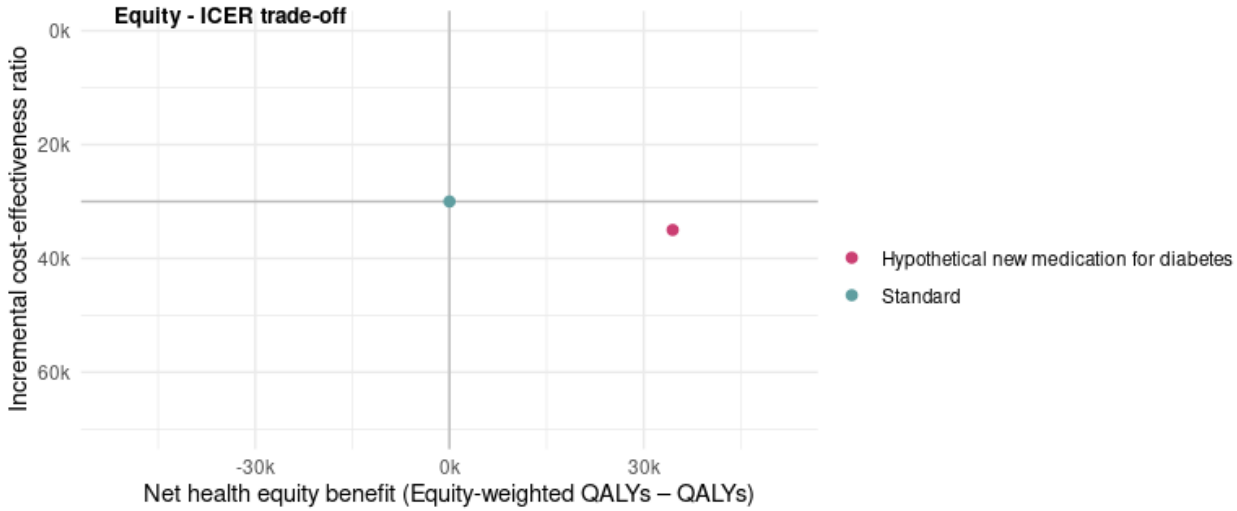


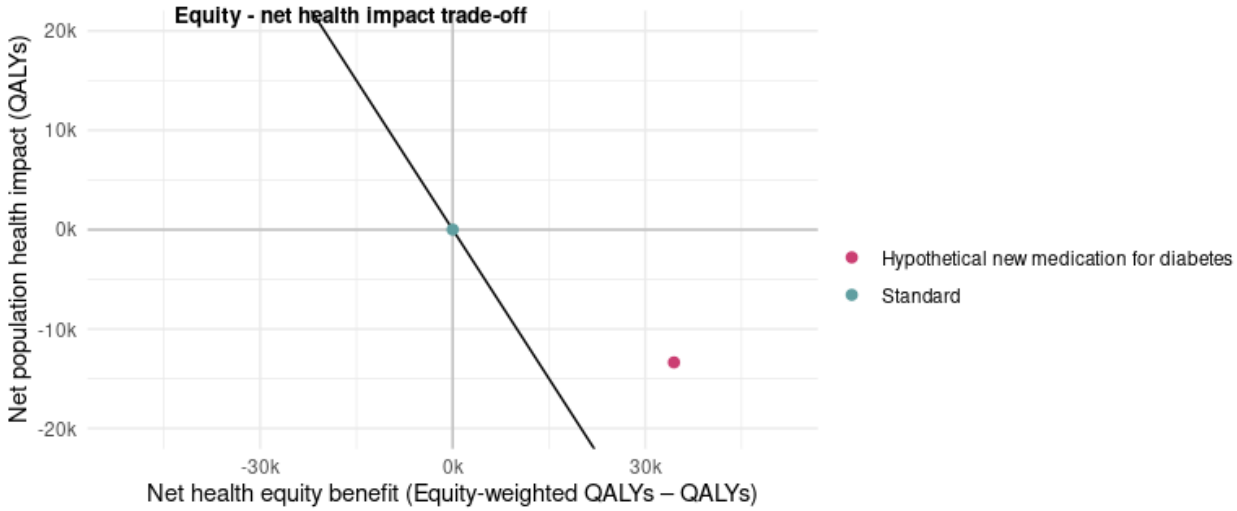


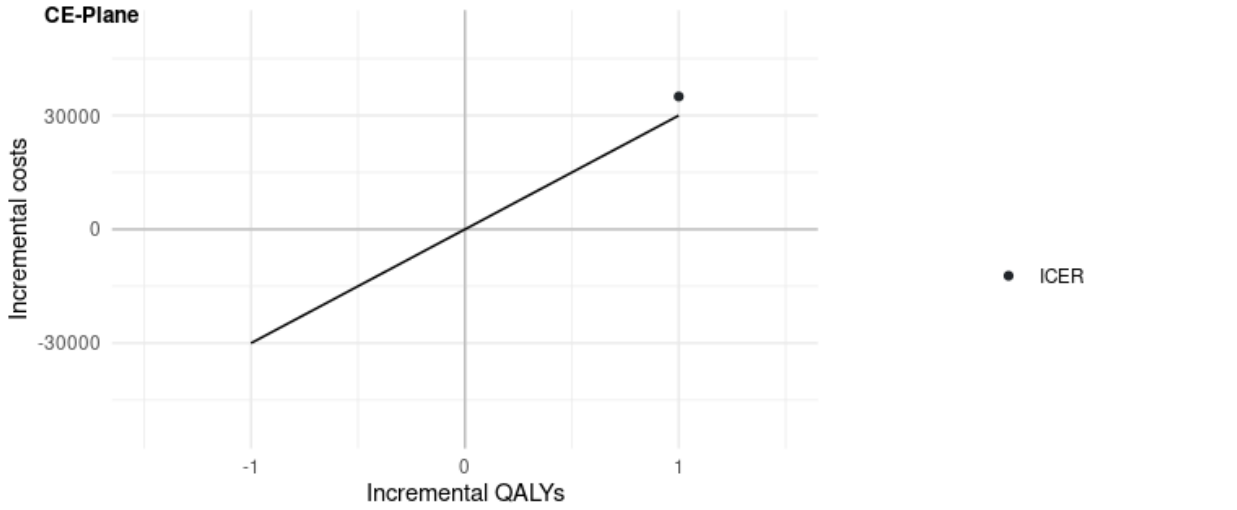




Equity & efficiency







Example 6:
Olaparib for previously treated BRCA mutation-positive hormone-relapsed metastatic prostate cancer

Equity impact report

2023-05-22

This report was generated by entering user-defined assumptions into a health inequality impact calculator (https://shiny.york.ac.uk/dceasimple) produced by the University of York. The University of York offers no guarantees of any kind for the results produced.

The following analysis compares **Olaparib** against **Standard**. This first page summarises the main results; the user-defined assumptions are listed on the next page; and further pages show various graphs.

***Table 1**: Main model results*

Net health inequality benefit	**-685 QALYs**
Incremental Cost-Effectiveness Ratio (ICER)	**£40,000/QALY**
Incremental Net Monetary Benefit (INMB)/recipient	**£-10,000**
Incremental net health benefit (INHB)	**-3,400 QALYs**
Equity-weighted ICER	**£42,412/QALY**
Equity-weighted INMB/recipient	**£-11,706**
Equity-weighted INHB	**-4,053 QALYs**
Decision threshold	**£30,000**
Marginal productivity	**£30,000**
Atkinson parameter	**10**

***Table 2**: Distributional results*

	IMD1	IMD2	IMD3	IMD4	IMD5	Total
Share of the eligible population	18%	17%	22%	22%	22%	100%
Uptake	100%	100%	100%	100%	100%	
Inc. QALY/recipient	1	1	1	1	1	
Share of health opportunity costs	20%	20%	20%	20%	20%	100%
Recipients (in 1,000s)	2	2	2	2	2	10
Recipients (share)	18%	17%	22%	22%	22%	100%
Intervention benefits (QALYs)	1,801	1,700	2,234	2,234	2,232	10,201
Opportunity costs (QALYs)	2,720	2,720	2,720	2,720	2,720	13,601
Net health benefit (QALYs)	-919	-1,020	-486	-486	-488	-3,400

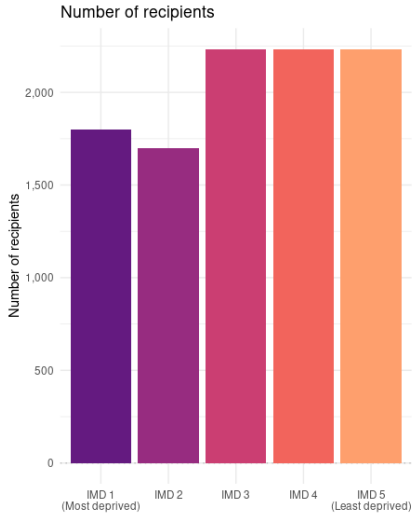
Inputs

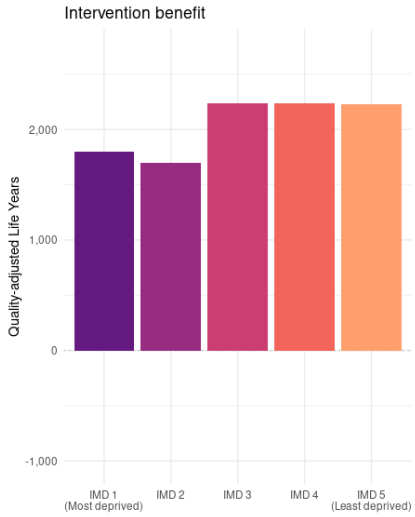
This section summarises the user-defined assumptions used to create the results and plots.

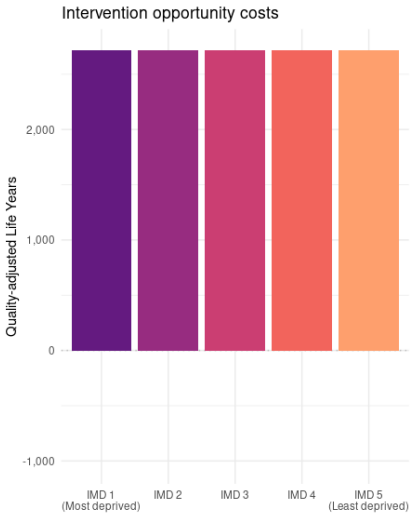
***Table 3**: Input parameters*

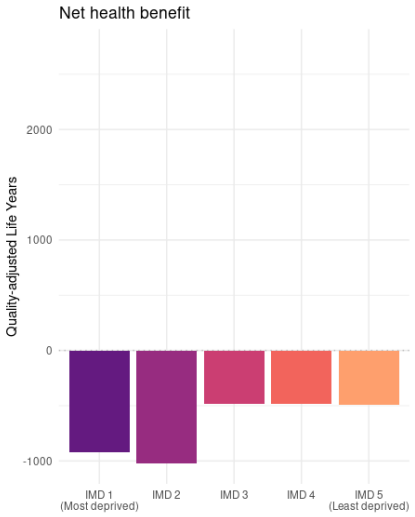
Variable	Value
Intervention name	Olaparib
Comparator name	Standard
Incremental QALYs	1.000
Incremental cost (£)	40,000
Intervention type	Disease population
Intervention disease category (ICD-10)	C61
Age range	16; 100
Eligible population	10,200
Uptake (%) in IMD1 (most deprived)	100
Uptake (%) in IMD2	100
Uptake (%) in IMD3	100
Uptake (%) in IMD4	100
Uptake (%) in IMD5 (least deprived)	100
Effectiveness in IMD1 (most deprived)	1.000
Effectiveness in IMD2	1.000
Effectiveness in IMD3	1.000
Effectiveness in IMD4	1.000
Effectiveness in IMD5 (least deprived)	1.000
Share of eligible population IMD1 (most deprived)	0.177
Share of eligible population IMD2	0.167
Share of eligible population IMD3	0.219
Share of eligible population IMD4	0.219
Share of eligible population IMD5 (least deprived)	0.219
Health opportunity cost distribution	flat
Marginal productivity	30,000
Atkinson inequality aversion value	10
Decision threshold (£)	30,000

Distributional health impact

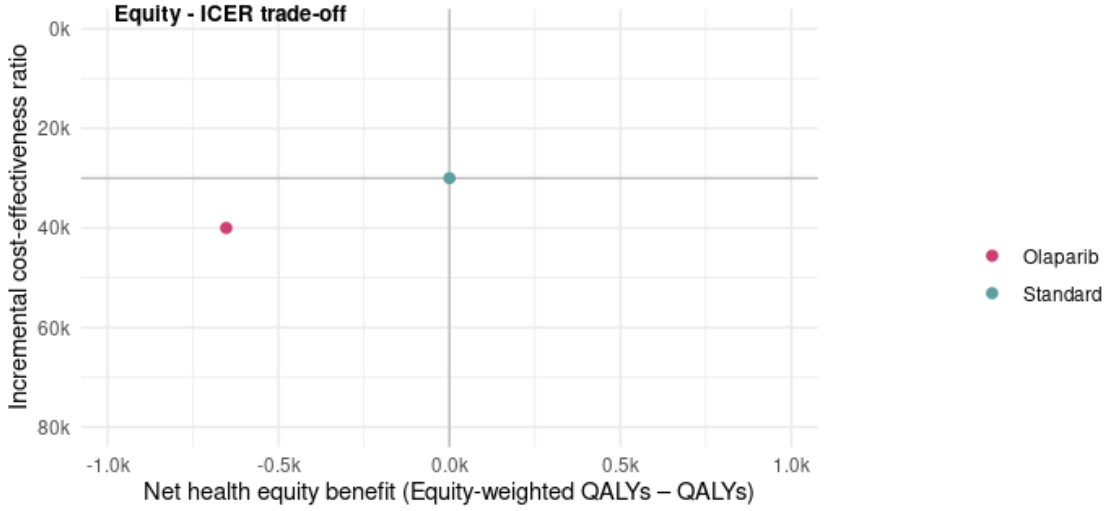


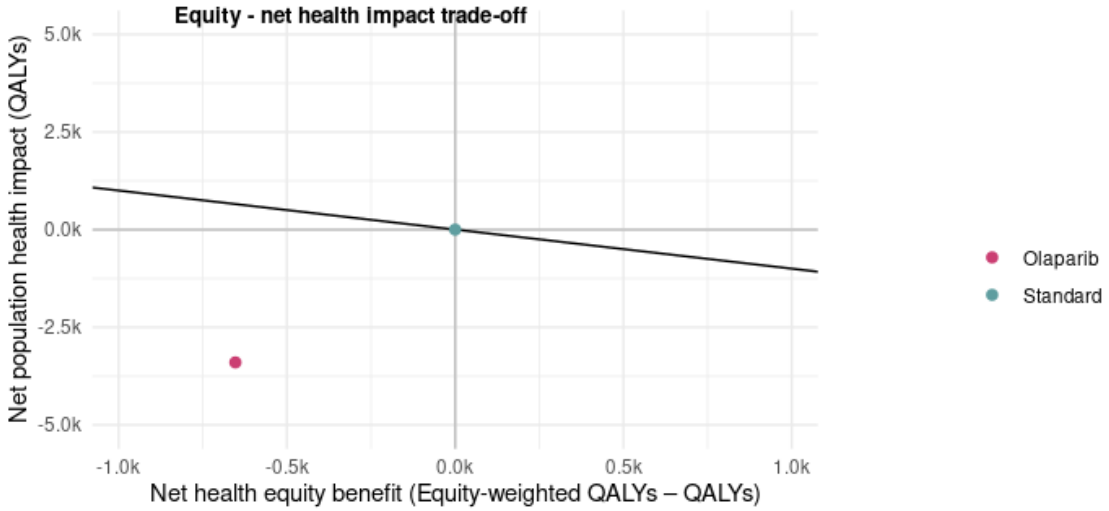


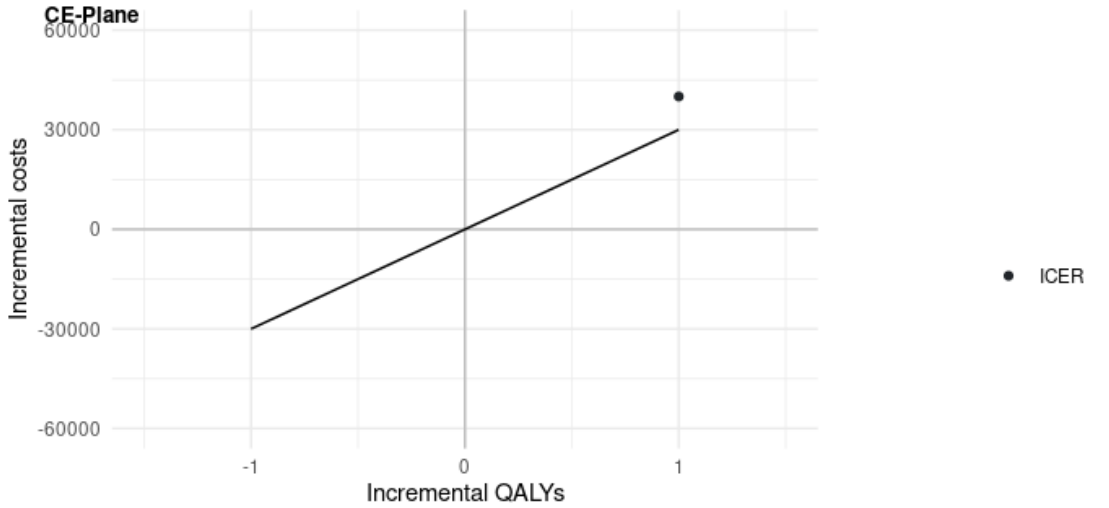




Equity & efficiency







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