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**Comparing health inequality impact magnitudes across disease interventions**

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**Supplementary Information (Word Document, included in submission)**

**Research data (Data file, not included in journal submission)**

Stata .dta file with simulation results for hospital admissions data on 1,336 diseases plus a code look-up table for the 155 mapped primary care conditions. Will be made available through a data repository.

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**Abstract**

**Objectives**

To compare and communicate magnitudes of health inequality impact across interventions for different diseases.

**Methods**

By rescaling the slope index of inequality, we measured health inequality impact as change in the total predicted gap in quality-adjusted life-years (QALYs) between the least and most socially disadvantaged groups. Use of linear regression predictions accounted for effects on intermediate groups. We reported the impact relative to health opportunity cost (HOC) to facilitate comparison across interventions with varying scale and unit costs. We illustrated with aggregate distributional cost-effectiveness analyses of hypothetical treatments for 1,336 diseases in England. We approximated benefit shares for neighbourhood deprivation quintile groups using disease-specific hospital admissions. We tested between-group equality using generalised linear regression and constructed uncertainty intervals using Monte Carlo simulation. We assumed equal HOC and benefit-cost ratio (BCR) of one, with alternative scenarios in sensitivity analysis.

**Results**

Health inequality impacts ranged from -33.1% of HOC (inequality-increasing) to +45.3% (inequality-decreasing), and were ≤ -5% for 1.6% of diseases, ≥ 5% for 41.8% and ≥ 20% for 1.6%. The impact was positively associated with the BCR and decreased when the poor were assumed to incur proportionately more HOC.

**Conclusions**

Health inequality impacts can be compared using change in the total predicted QALY gap between least and most socially disadvantaged groups, as a proportion of health opportunity cost. For technology appraisal in England, a health inequality impact below 5% of health opportunity cost might be classified as small, 5-10% as medium, and above 10% as large.

**Keywords**

Cost-effectiveness analysis, distributional cost-effectiveness analysis, equity, equity-efficiency trade-off, health inequality, inequality, slope index of inequality, deprivation, social factors

**Statements and Declarations**

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**Key points for decision-makers**

* Comparison of magnitudes of health inequality impact across interventions for different diseases is required to identify cost-effective investments in health inequality reduction.
* We show how to make these comparisons based on change in the total predicted quality-adjusted life-years gap between the least and most socially disadvantaged groups, as a proportion of health opportunity cost.
* We illustrate by comparing health inequality impacts of hypothetical treatments for 1,336 diseases in England.
* In the context of technology appraisal in England, a health inequality impact below 5% of health opportunity cost might be classified as small, 5-10% as medium, and above 10% as large

1. **Introduction**

Distributional cost-effectiveness analysis (DCEA) evaluates the health inequality impact of an intervention as well as its cost-effectiveness [1]. It can inform trade-offs between equity and efficiency, the prioritisation of socially disadvantaged groups that also face worse health prospects, and the design of interventions to increase uptake among those groups. It may even incentivise development of technologies that disproportionately benefit the same groups. However, it is hard to compare magnitudes of health inequality impact between interventions for different diseases and to communicate those magnitudes to decision-makers and stakeholders who may be unfamiliar with inequality indices [2]. Addressing this challenge is important to ensure DCEA delivers transparent and usable quantification of the health inequality reduction achievable through an investment that goes beyond qualitative information on the direction of any health inequality impact.

DCEA usually focuses on impact on health inequality between social groups. Reducing that inequality is an important health policy objective [3] that can stem from public concern about groups that are both disadvantaged socially (or economically) and more likely to suffer illness and premature death [4]. These groups are often categorised by indicators of social disadvantage, such as area deprivation or ethnicity, that are routinely available in health datasets, allowing group health to be compared using a generic measure, such as quality adjusted life expectancy at birth (QALE). This population average is insensitive to an intervention for a specific patient group. For example, a gain of 1 quality adjusted life year (QALY) to each of 1,000 patients potentially benefiting from an intervention would increase QALE by 0.000017 in a population of 60 million people. The impact on a between-group difference in QALE would be even smaller, and a tiny fraction of the baseline difference, which is around 11 QALYs between the least and most socially disadvantaged groups in England, for example [5]. The health inequality impact of an intervention depends on the number of people who can potentially benefit from it (scale) and the incremental cost per recipient (unit cost) as well as inequalities in intervention eligibility, uptake, effect and health opportunity cost from unrealised interventions competing for the same resources [1]. Cost is relevant because the magnitude and distribution of the health opportunity cost contribute to the net impact on health inequality. We therefore need a way of making even-handed comparisons of health inequality impact between interventions of different scale and unit cost.

This paper aims to show how to compare and communicate the magnitudes of health inequality impact across interventions for different diseases. It makes three main contributions. First, it shows how to re-scale intervention-induced change in the slope index of inequality [6] to estimate impact as the change in the gap in predicted health between least and most socially disadvantaged groups, while taking into account effects on middle groups. Second, it allows for the scale and unit cost of an intervention by reporting health inequality impact relative to health opportunity cost. Third, it illustrates the potential range of these impacts for hypothetical new treatments for 1,336 diseases, using data on all hospital admissions in England, together with appropriate analysis of uncertainty and sensitivity to key assumptions.

1. **Health inequality impact metrics**

## **2.1 Health inequality**

DCEA studies often stratify a general population into groups ranked in order of social disadvantage, and measure health inequality by the health gap between the least and most disadvantaged groups. For example, Fig. 1 shows the estimated gap in total QALYs between least and most deprived quintile groups in England, based on neighbourhood deprivation.

1. **Average QALYs by deprivation quintile**

11.1 QALY deficit per person in   
most deprived quintile group

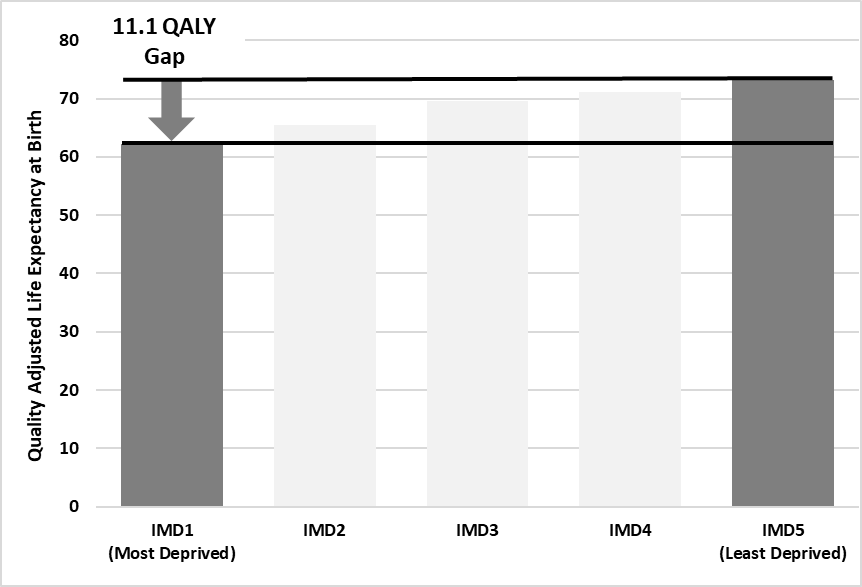
×

11.5m persons in that group

=

**128m QALY gap**

**b) Gap in total QALYs**



**Fig. 1 Gaps in average and total quality adjusted life years (QALYs) between deprivation quintile groups in England, 2023**

*Notes:* Based on Office of National Statistics mid-year population of England estimate for 2023 of 57m and estimates of quality adjusted life expectancy (QALE) by Index of Multiple Deprivation (IMD) quintile group in 2017-2018 [5]. QALE estimates are 62.2, 65.5, 69.5, 71.1 and 73.3 for the most to least deprived groups, respectively.

This approach ignores health of the middle groups. It would miss any health inequality impact of an intervention resulting from effects on the health of these groups. To avoid this limitation, we use the slope index of inequality (SII) [6], which is the estimated gap in *predicted* health between the extremities of the population ordered by social disadvantage. It is estimated from a linear regression of the mean health of social disadvantage group *j,* h*j,* on the cumulative fractional rank of that group*, Rj*:

where , is the health of individual *i* in group *j* of size *nj*, , is the general population size, and is an error term. The groups are ordered in decreasing social disadvantage. For example, if there were five equally sized groups, their fractional ranks would be 0.1, 0.3, 0.5, 0.7 and 0.9 from the most to least disadvantaged. The ordinary least squares (OLS) estimate of is the SII. This is a measure of health inequality. Eq. (1) is not a model of health determination. It is a device to calculate the inequality measure – a descriptive statistic.

The gap in *total* predicted health between the least and most disadvantaged groups is

*GAP =*

where and are the OLS estimates of the respective parameters. This is the difference between the mean predicted health of the least disadvantaged group scaled by its size and the respective scaled mean predicted health of the most disadvantaged group. If the groups are equally sized, such that , then (2) collapses to the SII scaled by the population size and a proportionately factor determined by the number of groups:

(3)

For example, if there are five equally sized groups (as in our illustrative application), then . This measure can be estimated directly as the OLS slope coefficient from a regression as (1) but with either multiplication of the left-hand-side variable by or division of the fractional rank by that scaling factor.[[1]](#footnote-1)

Fig. 2 shows the *GAP* in total predicted QALYs between the least and most deprived fifths of the population of England in 2023.

A graph of a graph showing a line of sloped gap

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**Fig. 2 Gap in predicted QALYs between deprivation quintile groups in England, 2023**

Notes: The grey and black arrows indicate gaps in quality-adjusted life expectancy at birth (QALE) and predicted QALE, respectively. Multiplication of each by the group population size gives the respective gaps in total QALYs.

Supplementary Note (SN) 1 explains how to scale up the SII to measure inequality as the deficit in the predicted health of all individuals compared with that of the most socially advantaged. This is potentially useful where there are many population strata and the most and least disadvantaged groups are small and unequally sized. However, this measure not as transparent as the predicted health gap between least and most disadvantaged groups, and it harder to sense check against the gap in observed health. Furthermore, the predicted health gap can still be calculated in such cases, and it may be possible to combine sub-groups into least and most disadvantaged groups of approximately equal size.

## **2.2 Health inequality impact**

The health inequality impact of an intervention can be measured by the induced change in *GAP.* This measures the intervention-generated narrowing or widening of the difference in total predicted QALYs between least and most socially disadvantaged groups. Sensitivity to health effects on intermediate groups gives this measure of inequality impact an advantage over of the change in the raw difference in total (observed) QALYs between the two extreme groups.

We assume that DCEA simulation modelling has estimated the health benefit, health opportunity cost and net health benefit by social group, each in QALYs.[[2]](#footnote-2) Discounting can be undertaken after estimation of the health inequality impact. This is appropriate if policy concern is with inequality in health, rather than inequality in discounted health. The latter can be substantially smaller when health is measured as QALE.

SII measures absolute health inequality – it is invariant to the addition of a constant to the health of all groups (or individuals). The *GAP* measure inherits this property. Consequently, the health inequality impact captured by the change in this measure can be estimated from the scaled SII of the incremental net health benefit (NHB) generated by an intervention. The average NHB of group *j* is the difference between its mean health (QALYs) with and without the intervention, . This is the average health gain to group *j* from the intervention net of the average health opportunity cost incurred by that group.

Health inequality without and with the intervention could be estimated by the respective SII obtained from two linear regressions,

(4)

where is the fractional rank of group j under intervention scenario *t.* OLS estimates of and are the SII without and with the intervention, respectively. Provided the intervention does not change the (social disadvantage) ranks, , the health inequality impact can be estimated directly from a regression of the group-average NHB on the fractional rank:

The OLS estimate of is the difference in the SII between the intervention and no intervention scenarios – a measure of health inequality impact in QALYs per capita.

The change in the gap in total (not per capita) predicted health () is equal to the gap in total predicted net health benefits (*GAP-NHB*). Assuming the intervention also does not change the group sizes, this is

where ^ indicates OLS estimates of the respective parameters. In the case of equally sized groups, this reduces to

(7)

That is, the scaled SII of the intervention’s average NHB measures its impact on inequality in total health (QALYs). We label this the *health inequality impact*.

Table 1 illustrates calculation of this measure for a hypothetical treatment for sickle cell disease in England. We report the impact as , such that a positive number indicates a reduction in inequality. To facilitate comparison between interventions differing in scale and unit cost, we propose also reporting the impact as per unit of health opportunity cost (last row of the table).

**[Table 1 Health inequality impact of hypothetical sickle cell intervention in England, QALYs](#_Manuscript_Figures_and)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| [Social disadvantage group (j)](#_Manuscript_Figures_and) | [Total Health Benefit (THB)](#_Manuscript_Figures_and)[a](#_Manuscript_Figures_and) | [Total Health Opportunity Cost (THC)](#_Manuscript_Figures_and)[b](#_Manuscript_Figures_and) | [Total Net Health Benefit (TNHB = THB - THC)](#_Manuscript_Figures_and) | [TNHB](#_Manuscript_Figures_and)[j](#_Manuscript_Figures_and) [-TNHB](#_Manuscript_Figures_and)[5](#_Manuscript_Figures_and) | [c](#_Manuscript_Figures_and) |
| [1 –Most](#_Manuscript_Figures_and) | [180](#_Manuscript_Figures_and) | [133](#_Manuscript_Figures_and) | [47](#_Manuscript_Figures_and) | [155](#_Manuscript_Figures_and) | [174](#_Manuscript_Figures_and) |
| [2](#_Manuscript_Figures_and) | [167](#_Manuscript_Figures_and) | [133](#_Manuscript_Figures_and) | [34](#_Manuscript_Figures_and) | [142](#_Manuscript_Figures_and) | [130](#_Manuscript_Figures_and) |
| [3](#_Manuscript_Figures_and) | [87](#_Manuscript_Figures_and) | [133](#_Manuscript_Figures_and) | [-46](#_Manuscript_Figures_and) | [62](#_Manuscript_Figures_and) | [87](#_Manuscript_Figures_and) |
| [4](#_Manuscript_Figures_and) | [41](#_Manuscript_Figures_and) | [133](#_Manuscript_Figures_and) | [-92](#_Manuscript_Figures_and) | [16](#_Manuscript_Figures_and) | [43](#_Manuscript_Figures_and) |
| [5 - Least](#_Manuscript_Figures_and) | [25](#_Manuscript_Figures_and) | [133](#_Manuscript_Figures_and) | [-108](#_Manuscript_Figures_and) | [0](#_Manuscript_Figures_and) | [0](#_Manuscript_Figures_and) |
| [Mean](#_Manuscript_Figures_and) | [100](#_Manuscript_Figures_and) | [133](#_Manuscript_Figures_and) | [-33](#_Manuscript_Figures_and) | [75](#_Manuscript_Figures_and) | [87](#_Manuscript_Figures_and) |
| [Health Inequality Impact (HIC), -∆GAP](#_Manuscript_Figures_and) | | | |  | [174](#_Manuscript_Figures_and) |
| [HIC relative to health opportunity cost,](#_Manuscript_Figures_and) [d](#_Manuscript_Figures_and) | | | |  | [0.261](#_Manuscript_Figures_and) |

*[Notes:](#_Manuscript_Figures_and)*

1. [Total health benefits are simulated on the simple assumptions of 1 QALY benefit per recipient and a total of 500 recipients with severe sickle cell disease receiving the intervention annually. Health benefit breakdowns by social group categorised by neighbourhood deprivation index quintiles are simulated using prevalence inequality alone, assuming no inequality in uptake or effect. We estimate prevalence inequality using primary care data from 2018, with shares of 35.92%, 33.49%, 17.34%, 8.15%, and 5.10% from the most to least deprived groups, respectively. We assume that each group has a general population size of about 11.5m summing to a total England population size of about 57.7m, which was the UK Office for National Statistics estimate for 2023.](#_Manuscript_Figures_and)
2. [Health opportunity costs are estimated based on a cost per recipient of £40,000, a health opportunity cost transformation rate (](#_Manuscript_Figures_and)*[k](#_Manuscript_Figures_and)*[) of £30,000 per QALY, and a flat gradient in health opportunity costs, see SN S4.](#_Manuscript_Figures_and)
3. [is the predicted total net health benefit for social advantage group](#_Manuscript_Figures_and) *[j](#_Manuscript_Figures_and)* [from regression (5) scaled up by the population group size. is from Eq. (6), with group](#_Manuscript_Figures_and) *[j](#_Manuscript_Figures_and)* [in place of group 1.](#_Manuscript_Figures_and)
4. [This row gives the health inequality impact as a proportion of the total health opportunity cost over all groups.](#_Manuscript_Figures_and)
5. **Illustrative application**

We used the *ΔGAP* measure to illustrate the potential range of health inequality impacts of *hypothetical* new treatments for 1,336 diseases in England. We simulated impacts by estimating inequality in disease prevalence by social group using published data on hospital admissions and assuming no inequality by social group in treatment uptake, long-term health effect and health opportunity cost. We conducted scenario analysis of sensitivity to assumptions about distribution of opportunity costs and the benefit-cost ratio of simulated interventions.

## **3.1 Data**

Our main simulation was based on all inpatient (including emergency) hospital admissions in England in 2011/12 [7, 8].[[3]](#footnote-3) We used Hospital Episodes Statistics (HES) data on 1,336 International Classification of Disease 10 (ICD-10) 3-digit disease codes [9]. We excluded censored data for 143 very rare diseases and ICD-10 Chapters 20 to 22 for external factors (e.g. accidents) and special codes. We used the percentage share of all disease-specific admissions attributable to each social group as a simple estimate of the share of health benefit to each group*.* In effect, we assumed that use of the new, hypothetical treatment for the disease would be proportional to existing hospital admissions for that disease and that each patient would get the same long-term health benefit per unit of expenditure. These assumptions may tend to over-estimate impacts.

We used quintiles of a neighbourhood index of multiple deprivation (IMD) [10] to stratify the population into five equally sized groups from most deprived to least deprived. Admissions were categorised by these groups.

## **3.2 Methods**

The health inequality impact can be estimated in two steps. First, calculate the total net health benefit for each group as a proportion of the total health opportunity cost across the population (*THC*):

where *,* and are the total health benefit and health opportunity cost for group *j*, respectively, , and . The benefit-cost ratio, is the inverse of the incremental cost-effectiveness ratio (*ICER*) multiplied by the marginal rate of transformation from expenditure to health, *k*.

Second, regress on a rescaled group cumulative fractional rank, (see footnote 1):

The OLS estimate of is : the health inequality impact relative to the health opportunity cost. That is, the impact of the intervention on the gap in total predicted QALYs between the least and most disadvantage groups per QALY of health opportunity cost. Multiplying this measure by 1m / *k* gives the inequality impact per million monetary units of expenditure.

Given we estimated health inequality impacts for 1,336 disease interventions, to reduce computation time we took a short cut to the second step. Using Eq. (8) and the linearity of regression (9):

where GAP(*Xj*) is the scaled SII of variable estimated by the slope coefficient from a convenient regression like Eq. (9) for that variable. This allows us to focus on simulating and for each disease, and then making a simple linear transformation based on two parameters that are assumed constant across all hypothetical interventions: BCR and Given the assumption of equal uptake and equal treatment effects across groups, is determined by a group’s hospital utilisation share for the disease, which is assumed to correspond to its prevalence share.

Since the data include repeat hospital admissions within a year and more disadvantaged groups have higher rates of repeat hospitalisation, admissions shares may overestimate prevalence count shares of these groups. We adjusted for this potential bias by using primary care data on 12m patients from 1406 general practices that provide more accurate estimates of prevalence by deprivation group for 155 health conditions that can be matched to a subset of the 1,336 disease categories in the HES data used in the analysis [11]. For these 155 diseases, we estimated health inequality impact from the primary care data and from the hospital admissions data. Then, we regressed the first set of estimates on the second (separately for positive and negative inequality impacts) and used the fitted regression to predict an adjusted inequality impact from the hospital-admissions estimate for all 1,336 diseases (see SN 4). The adjusted estimates are our baseline health inequality impacts.

## **3.3 Base case assumptions**

Our base case assumptions were, for each intervention, a) equal treatment effects across social groups, such that group health benefit shares equal group utilisation shares, which equal group disease prevalence count shares, b) equal health opportunity cost shares across groups, , and c) a BCR of 1. The latter implies that each intervention is (just) cost-effective; *ICER* = *k.* The BCR influences the health inequality impact since a larger health effect per unit of cost generates a larger health inequality impact (per unit of cost), all else equal.

We assumed *k =* £30,000, in line with the technology appraisal decision threshold used by the National Institute for Health and Care Excellence (NICE). We interpret this as a context-specific health opportunity cost transformation rate that allows both for future long-term price decreases and for the rebate paid by the pharmaceutical industry to ensure that pharmaceutical cost growth in the UK is capped (see SN2). In this context, a BCR of 1 corresponds to both the ICER and *k* equal to approximately £30,000, although it can also fit cases with lower values of both parameters.

## **3.4 Uncertainty intervals and scenario analysis**

Given our base case assumptions of no social inequalities in uptake, treatment effect and opportunity cost, the estimated health inequality impact of each disease-intervention is entirely attributable to inequality in prevalence count shares, which is captured by the scaled SII for those shares. We used Monte Carlo simulation to calculate uncertainty intervals around this scaled SII. We took 1,000 random draws from five group-specific Poisson distributions, with each event rate set to the observed admissions rate (number of admissions divided by population size) of the respective deprivation group. For each draw, we computed the scaled SII and used the percentile method to construct the 95% uncertainty interval. We used that interval to test the null of no social inequality in the prevalence of the respective disease.

We used group-level generalised linear models (Poisson with log link) of admissions counts to conduct two other tests of equality. The first regressed admissions on group indicators and tested equal admission shares of the most and least deprived groups. The second regressed admissions on fractional group ranks and tested significance of the (exponentiated) rank coefficient. We produced a *conservative* set of inequality impacts in which the impact of an intervention was set to zero if the null of no inequality in prevalence of the respective disease was not rejected by any of the three tests at the 5% significance level.

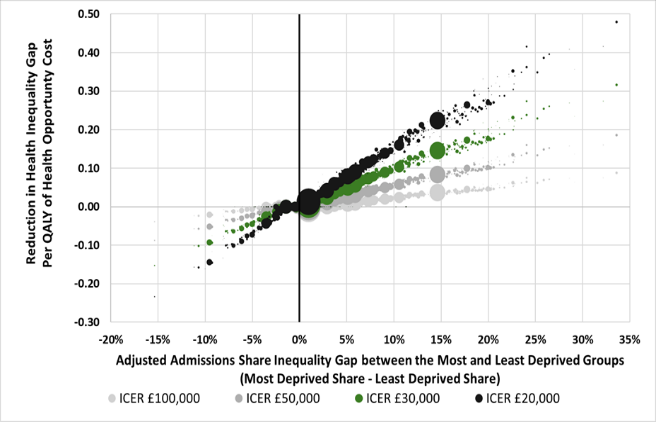
We conducted sensitivity analysis using alternative BCRs of 1.5, 1, 0.75, 0.6 and 0.3. These values correspond to ICERs of £20,000, £30,000, £40,000, £50,000 and £100,000, respectively, if the health opportunity cost transformation rate (aka “threshold”) used for monetising health effects (*k*)is assumed equal to £30,000. We also conducted sensitivity analysis with respect to the assumption of equal health opportunity costs by considering three alternative scenarios in which cost shares were skewed a) slightly toward more deprived groups (22%, 21%, 20%, 19% and 18%, for the most to least deprived groups), which we label *slight pro-poor*, b) moderately in the same direction (24%, 22%, 20%, 18% and 16%), aka *moderate pro-poor*, and c) slightly in the other direction (18%, 19%, 2%, 21% and 22%), aka *slight pro-rich*. See SN5 for the rationale for these scenarios. With unequal health opportunity costs, the BCR has an indirect influence on the inequality impact because the distribution of net health benefits depends on the magnitudes of health benefits and opportunity costs.

## **3.4 Results**

For diseases *d* = 1, 2, …, 1,336, Fig. 3 plots the simulated health inequality impact per QALY of health opportunity cost of the respective hypothetical intervention, , against inequality in prevalence count shares between the most and least deprived groups. The latter is proxied by inequality in admission shares adjusted for repeat hospitalisation bias in the same way as the simulated health inequality impact (SN 4). The base case (in green) assumes a BCR = 1 – corresponding to an ICER = £30,000, assuming a health opportunity cost transformation rate of that value – and equal incidence of those costs across groups. Panel a. shows scenarios differing in cost-effectiveness, while Panel b. shows different health opportunity cost incidence scenarios (SN5).

In the base case, potential health inequality impacts across the 1,336 disease codes ranged from a reduction in the gap in total predicted QALYs between the least and most deprived fifths of the population equal to 45.3% of the respective health opportunity cost of the treatment (F11: mental and behavioural disorders due to use of opioids) to an increase in the gap of 33.1% (L36: other acute skin changes due to ultraviolet radiation). The inter-percentile range of the inequality impacts relative to health opportunity costs was from a gap reduction of 32.2% to a gap increase of 5.9%, and the inter-quartile range was from a gap reduction of 11.9% to zero impact (corresponding to a non-significant gap reduction of 2.6%). Impacts did not differ significantly from zero for 23.4% of diseases. Gap reductions (relative to cost) were ≥ 5% for 41.8% of diseases, ≥ 10% for 16.5%, ≥ 15% for 6.2% and ≥ 20% for 1.6%. Gap increases were ≥ 5% for 1.6% of diseases and ≥ 10% for 0.4%.

a. **By incremental cost-effectiveness ratio b.** **By health opportunity cost incidence**

**A graph showing the growth of an individual

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**Fig. 3** **Proportionate health inequality impact against inequality in prevalence count shares between most and least deprived groups for 1,336 diseases, England 2011**

*Notes:*The y-axis shows health inequality impact as a proportion of health opportunity cost, -ΔGAP / THC, for each disease intervention. The x-axis shows, per disease, inequality in prevalence count shares between the most and least deprived groups. Prevalence shares estimated by hospital admissions shares adjusted for repeat hospitalisations. Figure only shows impacts significantly different from zero using 95% uncertainty intervals. In Panel a., we assumed equal health opportunity costs across groups and show results for benefit-cost ratios (BCRs) of 0.3, 0.6, 1 and 1.5, respectively, corresponding to ICERs of £100,000, £50,000, £30,000 and £20,000, respectively, assuming a health opportunity cost transformation rate of £30,000. This panel excludes one extreme outlier – L56: Other acute skin changes due to ultraviolet radiation – with a base-case impact of -0.33. In Panel b., we fix the BCR at 1 and show results for four health opportunity cost incidence scenarios (see SN 5).

Supplementary Fig. S1 shows histograms of significant positive and negative health inequality impacts, respectively. Supplementary Fig. S2 gives a plot like Fig. 3a but with health inequality impact in monetary units and using a lower value of the assumed expenditure-health transformation rate. Supplementary Fig. S3 shows simulations of health inequality impact based on primary care disease prevalence data for health conditions.

Table 2 reports impact quantiles and cut-offs that may be useful to normatively categorise impact magnitudes as “large”, “medium” and “small”, with sensitivity around alternative BCRs. Supplementary Table S1 shows the corresponding estimates without adjustment for repeat hospitalisation bias in the admissions-data estimates. Supplementary Figs. S4 and S5 provide further information to assess impact magnitude: a plot of prevalence inequality and ICER for different thresholds of impact and impacts before and after the adjustment for repeat hospitalisation. Finally, simulation results for all 1,336 3-digit disease categories together with a code look-up table for our 155 mapped primary care conditions are available on request.

**Table 2: Percentage of disease interventions achieving different levels of proportionate health inequality impact given different levels of cost-effectiveness, England 2011**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **BCR 1.5** | **BCR 1** | **BCR 0.75** | **BCR 0.6** | **BCR 0.3** |
|  | **ICER £20,000** | **ICER**  **£30,000** | **ICER £40,000** | **ICER**  **£50,000** | **ICER £100,000** |
|  | **Minimum positive impact achieved by top percentage groups** | | | | |
| **Top 1%** | 0.33 | 0.22 | 0.17 | 0.13 | 0.07 |
| **Top 2.5%** | 0.27 | 0.18 | 0.13 | 0.11 | 0.05 |
| **Top 5%** | 0.24 | 0.16 | 0.12 | 0.10 | 0.05 |
| **Top 10%** | 0.19 | 0.13 | 0.09 | 0.08 | 0.04 |
| **Top 20%** | 0.13 | 0.09 | 0.07 | 0.05 | 0.03 |
| **Top 25%** | 0.11 | 0.08 | 0.06 | 0.05 | 0.02 |
| **Top 30%** | 0.10 | 0.07 | 0.05 | 0.04 | 0.02 |
|  | **Minimum negative impact achieved by bottom percentage groups** | | | | |
| **Bottom 1%** | -0.09 | -0.06 | -0.05 | -0.04 | -0.02 |
| **Bottom 2.5%** | -0.06 | -0.04 | -0.03 | -0.02 | -0.01 |
| **Bottom 5%** | -0.03 | -0.02 | -0.02 | -0.01 | -0.01 |
| **Bottom 10%** | -0.01 | -0.01 | -0.01 | -0.01 | 0.00 |
|  | **Percentage with positive impact above this level** | | | | |
| **Above 0.30** | 1.6% | 0.1% | 0.0% | 0.0% | 0.0% |
| **Above 0.20** | 8.7% | 1.6% | 0.3% | 0.0% | 0.0% |
| **Above 0.15** | 16.5% | 6.2% | 1.6% | 0.4% | 0.0% |
| **Above 0.10** | 30.2% | 16.5% | 8.7% | 4.0% | 0.0% |
| **Above 0.05** | 54.3% | 41.8% | 30.2% | 21.8% | 4.0% |
|  | **Percentage with negative impact below this level** | | | | |
| **Below -0.10** | 0.7% | 0.4% | 0.1% | 0.1% | 0.1% |
| **Below -0.5** | 2.9% | 1.6% | 0.7% | 0.6% | 0.1% |

*Notes:* The minimum impact cut-offs show the minimum proportionate health inequality impact required to join the relevant percentage group. The percentages show the percentage of all disease interventions with impacts above or below the stated cut-off value for proportionate health inequality impact. An adjustment is applied for repeat hospitalisation bias, as described in the methods section.

# **Discussion**

## **4.1 Summary of findings**

We proposed a metric for reporting the health inequality impact of an intervention evaluated by distributional cost-effectiveness analysis (DCEA). It is the change in the gap in total predicted health (QALYs) between least and most disadvantaged social groups, which is calculated by re-scaling the intervention-induced change in the slope index of inequality (SII), a standard measure of social inequality in health. Equivalently, the metric is the scaled SII of the intervention’s total net health benefit. Division by the health opportunity cost of the intervention incurred across the population gives the health inequality impact per QALY of that cost. Measurement of inequality impact by change in the gap in *predicted* health between the top and bottom groups ensures sensitivity to (net) effects on intermediate groups.

Our illustrative application to hypothetical, equally effective interventions for 1,336 disease categories in England reveals that if all interventions had a benefit-cost ratio of 1, then the health inequality impact would range from a reduction in the (predicted) QALY gap between the least and most deprived fifths of the population equivalent to 45.3% of the population-wide health opportunity cost to an increase in the gap equal to 33.1% of the cost, assuming the health opportunity cost is distributed evenly over all social groups. The range of health inequality impacts becomes narrower if a less favourable benefit-cost ratio (lower cost-effectiveness) is assumed. Positive health inequality impacts (inequality-reducing) become smaller and negative impacts (inequality-increasing) become larger in magnitude if more deprived groups – who use more healthcare, generally, and so may benefit more from alternative investments – are assumed to incur a larger share of health opportunity costs.

## **4.2 Strengths and limitations**

The main strengths of our proposed measure of health inequality impact are that (1) it is in QALYs, (2) it captures effects on all social groups and yet has an intuitive interpretation as a gap change, (3) it can be calculated from the distribution of net health benefits without needing to simulate the baseline distribution of health, (4) it is based on a widely used measure of health inequality, and (5) it can be sense-checked against the change in the gap in QALYs (not predicted QALYs), which is even more readily understood by non-specialists but, importantly, loses strength (2). Another potentially appealing feature for decision-makers is that the measure can be applied consistently across interventions in different disease areas without requiring case-by-case selection of parameters or models. A caveat is that some may consider it limiting to impose the same value judgements about aversion to inequality that are implicit in the SII derived from a linear prediction model.

The measure can be reported as a proportion of the health opportunity cost, facilitating comparison between interventions of different scale and unit cost. Health opportunity cost provides a more stable denominator for this purpose than net health benefit, which can be negative and close to zero. It is a more useful denominator than the total health benefit since it focuses more directly on efficiency in reducing health inequality. Over a series of decisions, choosing interventions with larger reductions in health inequality per unit of cost will lead to a larger total health inequality impact for the same expenditure. We suggest reporting health inequality impact by the reduction in QALY gap per unit of cost rather than by the cost per QALY gap reduction. This is because the latter is potentially misleading – it looks like a conventional ICER but is not.

The main limitations of the measure derive from those of the SII that underpins it. First, the measure uses predictions from a linear regression of health (or net health benefits) on fractional social disadvantage group ranks. Some studies fit a non-linear relationship when it appears to fit the data better, and then obtain a non-linear SII [6]. In the context of DCEA, this would leave scope for overfitting and the subjective choice of specification to yield favourable results, and it would impede comparability across interventions [12]. This study proposes a measure of inequality impact that can be readily interpreted and consistently applied in DCEA. The objective was not to find the best fitting statistical description of health differences across social groups. All inequality indices, including the SII, rest on assumptions about the nature and degree of inequality aversion [13, 14]. The choice of index is essentially normative, not empirical. For these reasons, and to take advantage of the above-mentioned strengths, we recommend a measure derived from the linear SII together with assessment of the extent to which a linear specification fits the data in any application and the sense-check mentioned in strength (5).

Second, we measure impact on *absolute* inequality in the form of change in a health gap between groups. This can differ from the impact on relative inequality based on change in a health ratio. Given that CEA aims to maximise the amount of health produced from constrained resources, considering impacts on differences in health levels is the most immediate distributional extension – and the most easily bolted onto the CEA toolkit. Furthermore, absolute inequality reduction is a tougher test than relative inequality reduction in this context. An intervention could reduce relative inequality by having a proportionately larger, positive effect on the health of more socially disadvantaged (less healthy) groups, and yet the absolute health improvement can be larger for less disadvantaged groups. Providing equal health benefits to all groups will reduce relative inequality. Reducing absolute inequality requires larger health benefits to more disadvantaged groups. The possibility that an intervention can have a negative absolute health inequality impact – increasing that inequality – and a positive relative inequality impact can be checked using a relative inequality measure. Decision-makers must judge whether a reduction in relative inequality is sufficient to justify an investment or if justification requires a reduction in absolute inequality of a certain magnitude, which can be assessed with reference to our proposed measure.

Our illustrative application that aimed to provide a range of potential health inequality impacts of effective new treatments across many diseases in England also has limitations. First, we only use 3-digit ICD disease classification codes, whereas many new technologies focus on more fine-grained disease classification and clinical sub-groups. It is possible that a more granular analysis of disease categories would reveal larger and smaller inequality impacts. Hence, we may underestimate the range of potential impacts. Second, our assumption of equal uptake and long-term treatment benefit by social group may not hold for all new treatments. Again, this may cause underestimation of the range of impacts. Interventions with lower uptake or smaller benefits for socially disadvantaged groups may increase health inequality, and so we may underestimate negative inequality impacts. A third limitation is our use of data on hospital admissions rather than prevalence. There is potential for overestimating positive impacts and underestimating negative impacts when using hospital admissions data due to more frequent repeat admissions in more disadvantaged groups. We addressed this issue by comparing impact estimates using prevalence inequality in 2018 and admissions inequality in 2011 for a matched sample of 155 primary care conditions. We found substantial bias – positive impacts were overestimated by nearly 39% on average and negative impacts were underestimated by nearly 18%. We applied a simple adjustment to correct for this bias. However, we cannot be sure how reliable this estimate of bias is, especially at high levels of inequality, since there are relatively few matched conditions with high levels of prevalence inequality. We report unadjusted results in Table S1, which show a higher range of positive impacts but a lower range of negative impacts.

## **4.3 Conclusions and implications**

Impacts on health inequality can be compared between interventions for different diseases in a way that is grounded in the slope index of inequality, the strengths and limitations of which are well-understood by specialists. We envisage that intuitive interpretation of our proposed measure of inequality impact as a between-group health gap reduction will appeal to decision-makers aiming to evaluate the return on investments in inequality reduction and to compare them across interventions for a wide array of diseases.

We hope our illustrative DCEA league table findings for England are useful in gauging the approximate range of health inequality impacts per unit of opportunity cost that might be expected from new treatments in different disease areas. They may also help assess what might count as a sufficiently large and important impact to merit careful consideration in decision making, with the potential to influence reimbursement and pricing decisions. Rather than setting magnitude thresholds purely on the basis of inequality in prevalence, or on health inequality impact relative to health benefit, we believe that a more appropriate approach is to focus on health inequality impact relative to health opportunity cost. The net magnitude of reduction in health inequality, after allowing for opportunity costs as well as benefits, depends not only prevalence inequality but also on the ICER. For example, a prevalence inequality gap of 15% yields an impact on reducing health inequality of about 15% if the ICER is £30,000, but only about 10% if the ICER is £45,000, 7.5% if the ICER is £60,000 and 5% if the ICER is £90,000.

One simple approach to classifying impact magnitudes, for example, might be to assess an impact per unit of opportunity cost as *small* if it is less than 5%, *medium* if it is 5% to 10%, and *large* if it is more than 10%. We found that new interventions with an ICER of £30,000 (i.e. a benefit-cost ratio of one) would only yield large impacts for about 16.5% of disease categories, falling to 8.7% with an ICER of £40,000, 4.0% with an ICER of £50,000, and zero with an ICER of £100,000 or more. The proportions of interventions likely to meet these and other cut-offs can be seen in Table 2 and Fig. S5.

We refrain from drawing policy conclusions about the actual health inequality impacts of specific interventions since our analysis was based on old and approximate data as well as strong assumptions about cost-effectiveness, uptake, and long-term health effect. For example, the disease chapter league table in Table S2 should not be interpreted as suggesting that interventions for newborn children (the top category) will always reduce health inequality more than interventions for cancer (the bottom category, with inequality-increasing impacts on average). Investing in early diagnosis of cancer might conceivably help to reduce health inequality even more than investing in improved treatment of newborn conditions, if it is more cost-effective and if it disproportionately benefits socially disadvantaged populations due to their higher rates of late diagnosis. This in turn will depend crucially on rates of uptake of the early diagnosis intervention in different groups, which will depend on the specific details of the intervention. We also refrain from generalising our findings outside England and hope that researchers will conduct similar analyses in other countries.

# 

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**Comparing health inequality impact magnitudes across disease interventions**

**Supplementary Information**

**Page**

Supplementary Figures 28

Supplementary Tables 33

Supplementary Note 1: Health Deficit 35

Supplementary Note 2: Standard Cost-Effectiveness Metrics and Thresholds 37

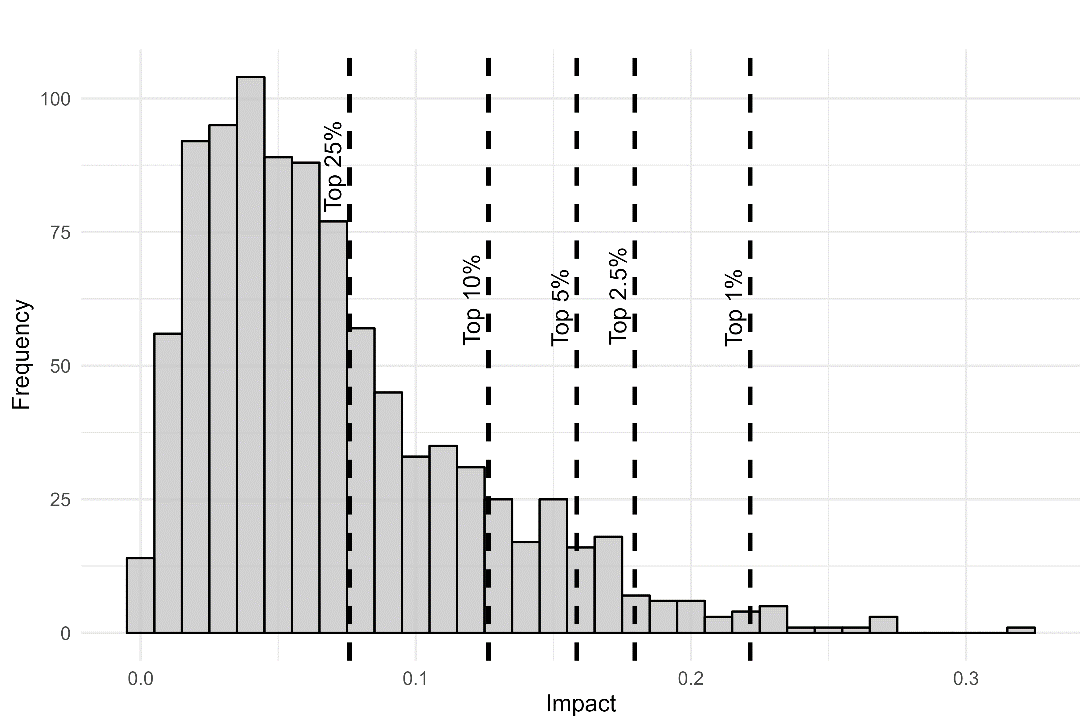
Supplementary Note 3: Recap on Distributional Cost-Effectiveness Analysis 40

Supplementary Note 4: Adjustment for repeat admission bias 43

Supplementary Note 5: Health opportunity cost scenarios for England 46

**Supplementary Figures**

Panel A: Positive Impacts

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Panel B: Negative Impacts

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# **Fig. S1 Histograms of significant positive and negative health inequality impacts, England 2011**

*Notes:* Histograms of health inequality impact per QALY of health opportunity cost, -ΔGAP / THC. Impact is estimate assuming a benefit-cost ratio of 1 and with inequality in prevalence count shares estimated from admissions data with adjustment for repeat hospitalisation bias. Vertical dashed lines are quantiles of base case health inequality impact. For example, disease interventions in the top 1% achieve positive impacts of at least 0.22. We include only impacts that are significantly different from zero (p-value < 0.05). Extreme low outlier (L56) excluded.

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**Fig. S2 Health inequality impact per million pounds of expenditure on existing treatments against inequality in prevalence count shares between most and least deprived groups for 1,336 diseases, England 2011**

*Notes:* The y-axis shows health inequality impact (-ΔGAP) per million pounds of expenditure on existing treatments for each disease intervention. We assumed a health opportunity cost transformation rate of £15,000 instead of £30,000 used in the baseline estimates (Fig. 3). The lower transformation rate is more appropriate for evaluating existing treatments. The x-axis shows, per disease, inequality in prevalence count shares between the most and least deprived groups. Prevalence shares estimated by hospital admissions shares adjusted for repeat hospitalisations. Figure only shows impacts significantly different from zero using 95% uncertainty intervals. We assumed equal health opportunity costs across groups and show results for benefit-cost ratios (BCRs) of 0.3, 0.6, 1 and 1.5, respectively, corresponding to ICERs of £50,000, £25,000, £15,000, £10,000 and £5,000, respectively, given a health opportunity cost transformation rate of £15,000. Excluded one extreme low outlier – L56: Other acute skin changes due to ultraviolet radiation

**a. By incremental cost-effectiveness ratio b. By health opportunity cost incidence**

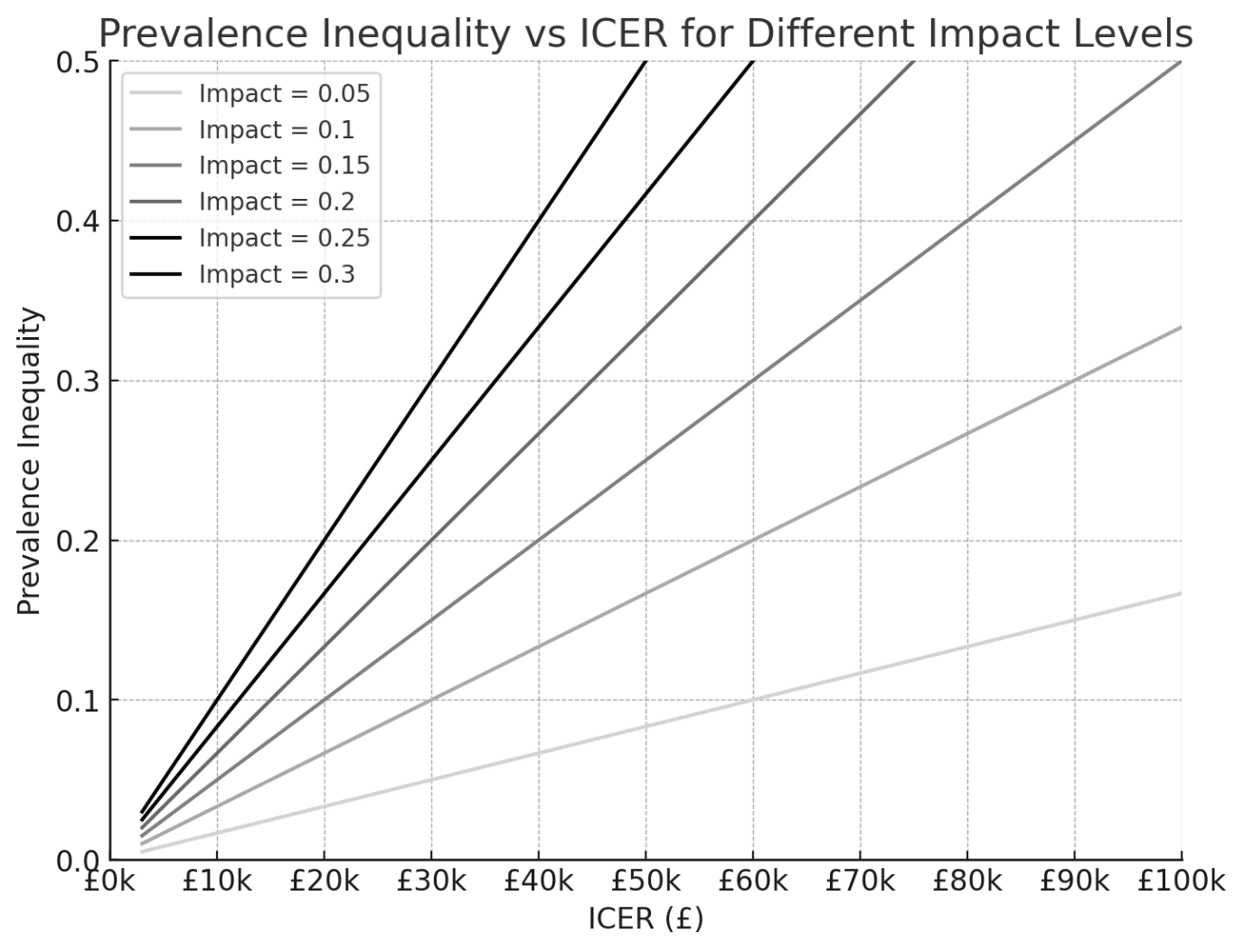
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AI-generated content may be incorrect.

**Fig. 3 Proportionate health inequality impact against inequality in prevalence count shares between most and least deprived groups for 205 primary care conditions, England 2011**

*Notes:* The y-axis shows health inequality impact as a proportion of health opportunity cost, -ΔGAP / THC, for each condition intervention. The x-axis shows, per condition, inequality in prevalence count shares between the most and least deprived groups. Impact and prevalence shares estimated using primary care data from 1406 general practices in Clinical Practice Research Datalink Aurum (CPRD). Figure only shows impacts significantly different from zero using 95% uncertainty intervals. In Panel a., we assumed equal health opportunity costs across groups and show results for benefit-cost ratios (BCRs) of 0.3, 0.6, 1 and 1.5, respectively, corresponding to ICERs of £100,000, £50,000, £30,000 and £20,000, respectively, assuming a health opportunity cost transformation rate of £30,000. In Panel b., we fix the BCR at 1 and show results for four health opportunity cost incidence scenarios (see SN 5).



# **Fig. S4 Prevalence inequality and ICER necessary to achieve different magnitudes of health inequality impact as a proportion of health opportunity cost**

*Notes:*Each line represents a different size of health inequality impact, as specified in the legend. Health inequality impact is measured as the reduction in predicted health inequality gap per QALY of health opportunity cost, -ΔGAP / THC. Prevalence inequality is measured as the predicted gap in disease prevalence share between the most and least deprived fifths of the population. The health opportunity cost transformation rate is assumed to be £30,000, so that an ICER of £30,000 represents a borderline cost-effective intervention with a benefit-cost ratio of 1. Less cost-effective interventions require higher levels of prevalence inequality to achieve the same impact on reducing health inequality.

Panel A: Before Adjustment

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Panel B: After Adjustment

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**Fig. S5 Histograms of health inequality impacts without and with adjustment of prevalence estimates for repeat hospitalisation bias**

*Note:* Histograms of health inequality impact per QALY of health opportunity cost, -ΔGAP / THC. Impact is estimate assuming a benefit-cost ratio of 1 and with inequality in prevalence count shares estimated from admissions data. In Panel a., there is no adjustment for repeat hospitalisation bias. In Panel b., there is adjustment using the procedure described in SN4. Vertical dashed lines are quantiles of base case health inequality impact. For example, disease interventions in the top 1% achieve positive impacts of at least 0.22. We include only impacts that are significantly different from zero (p-value < 0.05). Extreme low outlier (L56) excluded.

**Supplementary Tables**

**Table S1 Percentage of disease interventions achieving different levels of proportionate health inequality impact given different levels of cost-effectiveness, without adjusting for repeat hospitalisation bias England 2011**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **BCR 1.5** | **BCR 1** | **BCR 0.75** | **BCR 0.6** | **BCR 0.3** |
|  | **ICER £20,000** | **ICER**  **£30,000** | **ICER £40,000** | **ICER**  **£50,000** | **ICER £100,000** |
|  | **Minimum positive impact achieved by top percentage groups** | | | | |
| **Top 1%** | 0.48 | 0.32 | 0.24 | 0.19 | 0.10 |
| **Top 2.5%** | 0.40 | 0.26 | 0.20 | 0.16 | 0.08 |
| **Top 5%** | 0.35 | 0.24 | 0.18 | 0.14 | 0.07 |
| **Top 10%** | 0.28 | 0.19 | 0.14 | 0.11 | 0.06 |
| **Top 20%** | 0.20 | 0.14 | 0.10 | 0.08 | 0.04 |
| **Top 25%** | 0.18 | 0.12 | 0.09 | 0.07 | 0.04 |
| **Top 30%** | 0.16 | 0.11 | 0.08 | 0.06 | 0.03 |
|  | **Minimum negative impact achieved by bottom percentage groups** | | | | |
| **Bottom 1%** | -0.09 | -0.06 | -0.04 | -0.04 | -0.02 |
| **Bottom 2.5%** | -0.06 | -0.04 | -0.03 | -0.02 | -0.01 |
| **Bottom 5%** | -0.04 | -0.02 | -0.02 | -0.01 | -0.01 |
| **Bottom 10%** | -0.01 | -0.01 | 0.00 | 0.00 | 0.00 |
|  | **Percentage with positive impact above this level** | | | | |
| **Above 0.30** | 8.6% | 1.3% | 0.1% | 0.0% | 0.0% |
| **Above 0.20** | 20.3% | 8.6% | 2.4% | 0.7% | 0.0% |
| **Above 0.15** | 33.6% | 17.2% | 8.6% | 3.2% | 0.0% |
| **Above 0.10** | 51.0% | 33.6% | 20.3% | 14.1% | 0.7% |
| **Above 0.05** | 71.5% | 60.3% | 51.0% | 41.8% | 14.1% |
|  | **Percentage with negative impact below this level** | | | | |
| **Below -0.10** | 0.7% | 0.1% | 0.1% | 0.1% | 0.0% |
| **Below -0.5** | 3.1% | 1.6% | 0.7% | 0.5% | 0.1% |

*Notes:* The minimum impact cut-offs show the minimum proportionate health inequality impact required to join the relevant percentage group. The percentages show the percentage of all disease interventions with impacts above or below the stated cut-off value for proportionate health inequality impact. No adjustment is applied for repeat hospitalisation bias.

# **Table S2 Health inequality impact by broad ICD-10 disease chapter, England 2011**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Broad disease category**  **(ICD 10 chapter)** | **Disease category share of total** | **S1 share of disease category**  **(Most Deprived)** | **S5 share of disease category**  **(Least Deprived)** | **Difference in share**  **(S1 - S5)** | **Health Inequality Impact As Proportion of Opportunity Cost** |
| Newborn Conditions | 1.5% | 35.9% | 16.9% | 19.0% | 12.8% |
| Mental Health Disorders | 6.3% | 27.7% | 15.7% | 12.0% | 7.9% |
| Birth Defects | 0.8% | 28.9% | 18.0% | 10.9% | 5.8% |
| Pregnancy and Childbirth | 5.1% | 25.4% | 17.2% | 8.2% | 4.8% |
| Infectious Diseases | 1.7% | 24.1% | 18.0% | 6.1% | 2.1% |
| Lung Diseases | 7.3% | 23.7% | 17.8% | 5.9% | 1.7% |
| Injuries and Poisonings | 4.3% | 23.8% | 18.3% | 5.5% | 1.9% |
| Hormonal and Metabolic Disorders | 7.7% | 22.7% | 18.0% | 4.7% | 0.6% |
| Other Symptoms and Findings | 11.7% | 23.1% | 18.5% | 4.6% | 0.8% |
| Blood and Immune Disorders | 1.6% | 22.9% | 18.3% | 4.6% | 0.5% |
| Skin Diseases | 2.0% | 22.4% | 18.5% | 3.9% | 0.1% |
| Neurological Disorders | 2.3% | 22.2% | 18.7% | 3.5% | 0.6% |
| Ear Disorders | 0.7% | 21.7% | 19.2% | 2.5% | -1.6% |
| Digestive Diseases | 10.3% | 21.4% | 19.2% | 2.2% | -0.9% |
| Urinary and Reproductive Diseases | 6.1% | 21.0% | 19.0% | 2.1% | -1.6% |
| Heart and Vascular Diseases | 16.3% | 20.9% | 19.2% | 1.6% | -1.9% |
| Musculoskeletal Disorders | 7.6% | 20.5% | 19.5% | 1.0% | -2.1% |
| Eye Disorders | 2.6% | 19.5% | 20.2% | -0.6% | -2.0% |
| Cancers | 3.9% | 19.2% | 21.0% | -1.8% | -3.7% |
| Total | 100.0% | 23.5% | 18.5% | 5.0% | 1.3% |

*Note:* This table includes 19 disease chapters from ICD-10, ranked in order of potential health inequality reduction by threshold weight, but excludes chapters 20 to 22 which cover external causes (e.g. accidents) and special codes. Shares of hospital admissions are used to approximate treatment uptake shares. We assume a flat health opportunity cost, a cost-benefit ratio of 1 (e.g. an ICER of £30,000 divided by a health opportunity cost transformation rate of £30,000) and no difference in long-term benefit between patients from different social groups. The shares and impact are adjusted for repeat hospitalisation bias as described in the methods section. We include only significant impacts.

**Supplementary Notes**

# **Supplementary Note 1. Health Deficit**

The aggregate of the health gaps between the least socially disadvantaged group and all other groups provides a measure of health inequality we label the *health deficit*. This can be calculated by summing the observed between-group health gaps – the simple health deficit. A modelled version is calculated by scaling the slope index of inequality (SII) – the difference between the predicted health of the least and most disadvantaged individuals – by the general population size (N):

(S1) Modelled health deficit = SII × N × 0.5.

This metric, which is also known as the *population attributable risk* (Cookson et al. 2016; Schlotheubeur et al. 2022), can be visualised as the area of a triangle with width equal to N and height equal to the SII in group mean health, as shown in Fig. S6.

**A graph of a sloped graph

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=

**400m QALY deficit**

13.9 QALYs (slope index of inequality)

×

57.7m individuals in England

×

0.5

**(b) Total QALY Deficit**

1. **Average QALY Deficit**

# **Fig. S6** **Health inequality deficit, England 2023**

*Note:* Based on England ONS mid-year population estimate for 2023 of 57.7m, and England QALE estimates for 2017-2018. The QALE estimates are based on quality adjustment using EQ-5D-5L, reported in Love-Koh et al. (2023), Table 2.

The modelled deficit is larger than the simple deficit because the gap in predicted health between the least and most socially disadvantaged individuals is larger than the gap in observed mean health between the least and most disadvantaged groups (Fig. S7). With five equally sized groups, as in our illustrative example, the modelled deficit is 3.125 (= 0.5 / 0.16) times larger than the GAP in total predicted health between least and most disadvantaged groups given by Eq. (2) in the main manuscript.

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**Fig. S7 Modelled versus simple health inequality deficit, England 2023**

*Note:* The simple deficit is the white area below the horizontal black line times general population size. The modelled deficit is the area of the triangle times general population size.The data source is Love-Koh (2023)

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# **Supplementary Note 2. Standard Cost-Effectiveness Metrics and Thresholds**

The incremental cost-effectiveness ratio (ICER) test for the cost-effectiveness of a health intervention is:

where *C* is the total incremental cost for all recipients, *HB* is the total incremental health benefit in QALYs, and is the decision threshold ICER value for assessing cost-effectiveness. This can be converted into a net health benefit test for general population health improvement by replacing with the health opportunity cost transformation rate, *k,* representing the marginal rate of transformation between expenditure and health, to yield Health opportunity costs arise because resources are diverted towards benefiting the recipient population and away from alternative uses that would have generated health benefits among the general population. The health opportunity cost transformation rate is used to estimate health opportunity costs by transforming costs into foregone health benefits. The health opportunity transformation rate (i.e. the marginal change in expenditure required for one unit of health effect) is the inverse of the marginal productivity of expenditure (i.e. the health effect of a marginal change in expenditure). Each unit of additional expenditure on the recipient population, C*,* imposes *k* units of forgone health benefits among the general population, hence the population health opportunity cost is *C / k.* We can express this as a net health benefit (NHB) test:

The NHB test says that population health is improved if the net health benefit – i.e. the total health benefit, *HB*, minus the total health opportunity cost, *C / k –* is greater than zero. The population NHB statistic tells us how many QALYs are gained or lost overall by the programme, after allowing for both health benefits and health opportunity costs.

We can also express these tests in per recipient terms, by dividing B and C by the total number of recipients, N, to get the incremental cost per recipient, *c,* and the incremental health benefit per recipient, *c.* The recipient level NHB test then becomes This tells us that the health benefit per recipient must be greater than the health opportunity cost per recipient. The test could also be expressed per member of the general population – what one might call “citizen level” net health benefit – as , where *N / P* is the ratio of the number of recipients to the number of people in the whole general population. However, this is likely to be a small number that is hard to interpret since the recipient population is likely to be considerably smaller than the general population. Fr example, the general population of England is more than 50 million while the corresponding size of the recipient population is sometimes only a few thousand people. In practice, therefore, NHB is usually reported either in population level or recipient level terms.

Different assumptions about the decision threshold and health opportunity cost transformation rate are appropriate in different contexts, depending on the objectives of the relevant decision-making organisation and the nature of the relevant funding system (e.g. is it reasonable to assume that funding comes from an exogenous general health care budget or are things more complicated in important ways). In practice, is typically higher than *k,* meaning that the ICER decision threshold test for cost-effectiveness is typically more favourable towards a programme than the NHB test for population health improvement. For example, in England the current NICE decision threshold for new health technologies of around £30,000 is about twice the current best estimate of the basic health opportunity cost transformation rate based on the marginal productivity of general health care expenditure, of not more than £15,000. In the context of decision making about new patented technologies, however, it may be reasonable to adjust the basic health transformation rate upwards – closer to the level of the decision threshold – to allow for two specific considerations. First, the long-term cost of introducing a new technology may be lower than the estimated cost, due to long-term price reductions once the technology loses patent protection (Woods et al. 2024). Second, the net financial cost to the public purse may be lower than the estimated cost if wider national policies are in place to control branded pharmaceutical expenditure growth, such as the UK “Voluntary scheme for branded medicines pricing, access and growth” (VPAG) which caps expenditure growth via an industry-wide system of rebates.

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**Information about the VPAG system of pharmaceutical rebates in the UK at:**

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<https://www.gov.uk/government/publications/2024-voluntary-scheme-for-branded-medicines-pricing-access-and-growth>

# **Supplementary Note 3. Recap on Distributional Cost-Effectiveness Analysis**

This note reviews the basic conceptual framework, terminology, and notation used for distributional cost-effectiveness analysis (DCEA) (Cookson et al. 2020), building on the standard CEA metrics reviewed in SN2. Like CEA, DCEA adopts a general population perspective that considers not only health benefits for intervention recipients but also health opportunity costs borne by the general population. It therefore aims to estimate the impact on health inequality within the general population, not just within the recipient population. Like CEA, it also adopts a standard measurement approach to facilitate systematic comparison of health impacts and value for money between different programmes of intervention for different recipients of different ages with different diseases. This can help reduce the risk of capriciously and inefficiently spending far too much on reducing health inequality in some cases, and far too little in others, without having any clear idea of how much health inequality reduction is being purchased or whether re-allocating that expenditure would deliver a larger overall reduction in health inequality.

Establishing a standard measurement approach for doing DCEA routinely in a specific country or by a decision-making agency requires establishing at least five building blocks for standardisation: (1) a standard social advantage classification system for dividing the general population into groups, (2) a standard measure of the health of each social advantage group that allows comparisons between the health impacts of interventions for different recipient populations of different ages with different health conditions, (3) a standard approach to estimating the share of health opportunity cost falling on each social group, with a benchmark and plausible range, (4) a standard summary measure of the direction and magnitude of health inequality impact, and (5) a standard approach to assessing the relevance and importance of health inequality impact as a decision-making consideration, which may or may not involve explicit health inequality weighting with a benchmark and plausible range of values.

DCEA produces standard health inequality impact breakdowns of (1) health benefit, (2) health opportunity cost, and (3) net health benefit. The total health benefit for group *i* is:

where *si* is the proportional share of general population health benefit received by group *i* and *HB* is the total health benefit. The total health opportunity cost borne by group *i* is:

where *pi*is the proportional share of total health opportunity cost borne by group i*, C* is the total cost of the programme, and *k* is the marginal rate of transformation between financial cost and health opportunity cost. Each unit of additional expenditure on the recipient population, C*,* imposes *k* units of forgone health benefits among the general population, hence total health opportunity cost, *HOC,* is *C / k.*

The total net health benefit for group *i* is:

Differences between social groups in the proportional share of general population health benefit, *si*, depend not only on differences in group size but also on differences along the “staircase” to health inequality impact, including (1) the prevalence of the condition, (2) the uptake of the intervention, and (3) the long-term health effect of intervention. In the context of new medical treatments in a country with universal health coverage, the main driver is often (1) since inequality in prevalence is often larger than inequality in the uptake and long-term health effect of new treatments. By contrast, in the context of preventive services the main drivers are often (2) and (3), since there are often large inequalities in both the uptake and the long-term health effect of preventive services. Though this will depend on the context and there can be substantial inequalities in both the uptake and long-term health effects of new health technologies, even in countries with universal coverage.

Simple or “aggregate” DCEA starts with aggregate cost-effectiveness results and then does simple further modelling to estimate distributional breakdowns within the general population by social advantage group (Love-Koh et al. 2019). Full DCEA starts by modelling the distributional breakdowns and then aggregates things back up to the general population level to generate the cost-effectiveness results (Cookson et al. 2020). Full DCEA is a more comprehensive and resource-intensive approach that yields more accurate estimates of *HB, C* and *si*.

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# **Supplementary Note 4. Adjustment for repeat hospitalisation bias of prevalence**

Repeat hospitalisation within a year is more common in more deprived groups, and so admission shares tend to overestimate prevalence shares of these groups. This will tend to upwardly bias hospital-admissions estimates of prevalence inequality for diseases that have higher prevalence in more deprived groups and downwardly bias respective estimates for diseases with higher prevalence in less deprived groups. If unaddressed, this would bias our estimates of health inequality impact since we assume that health gains from an intervention to each group are proportionate to the group’s share of the prevalence count for the respective disease.

To adjust for this potential bias, we used primary care data on 12m patients from 1406 general practices (in the Clinical Practice Research Datalink Aurum) that provide more accurate estimates of prevalence by social deprivation group for 155 health conditions that can be matched to a subset of the 1,336 disease categories in the HES data used in the analysis (Wang et al. 2024). For each of the 155 matched disease categories, we made two estimates of health inequality impact (-*ΔGAP*): one from the hospital admissions data and the other from the primary care data. We then used ordinary least squares to estimate linear regressions of the primary care data estimate on the hospital admissions data estimate. We estimated separate regressions for diseases with a positive hospital-admissions estimate of health inequality impact (-*ΔGAP* > 0, i.e. inequality reducing) and for those with an estimated negative inequality impact using the hospital admissions data.

Fig. S8 shows the regression estimates and scatter plots of the health inequality impact estimates.

a. Positive impacts b. Negative impacts

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# **Figure S8: Health inequality impacts for 155 disease conditions – primary care estimates against hospital admissions estimate**

*Notes:* Base case health inequality impacts as a proportion of health opportunity cost, -ΔGAP / THC. Y-axis shows estimates obtained using primary care data from 1406 general practices in Clinical Practice Research Datalink Aurum (CPRD). X-axis gives estimates obtained using admissions data from Hospital Episode Statistics (HES). Panel a. includes diseases with a positive HES estimate of health inequality impact (inequality reducing, -ΔGAP > 0). Panel b. includes diseases with a negative HES estimate of inequality impact. Regression lines are from linear ordinary least squares regressions of CPRD-based impact estimate on HES-bases impact estimate. Slope and intercept coefficients were significantly (p-value < 0.05) different from zero in both regressions. The Pearson correlation coefficients were 73% (R-squared 0.53) for the positive impacts and 65% (R-squared 0.42) for the negative impacts.

In both cases (positive and negative inequality impact), the two sets of estimates are positively and reasonably strongly correlated (Pearson correlation coefficient: 0.73 and 0.65 for positive and negative inequality impact diseases, respectively). As expected, using hospitalisation data tended to overestimate magnitudes of reductions in inequality that disadvantage more deprived groups. This is seen in Panel a. of Fig. 8, which includes diseases for which the hospital admissions data estimates positive health inequality impact (= inequality reduction). The regression line is everywhere below the diagonal, which indicates the tendency toward overestimation of prevalence using hospitalisation (HES) data.

Panel b. includes diseases for which the hospital-admissions estimate of inequality impact is negative (= inequality increasing). In this case, there is less support for the prediction that the admissions data would underestimate the magnitude of the inequality impact. The regression line crosses the diagonal at about -0.4, indicating that a hospital-admissions estimate of inequality impact less (more) than this value is predicted to understate (overstate) the inequality increase that would be obtained with more accurate prevalence data.

We used the two regressions and the hospital-admissions estimates of health inequality impact for all 1,336 diseases to predict the impact for each disease that would be estimated from more accurate prevalence data not biased by repeat hospitalisations. These predictions are our adjusted estimates of health inequality impact used as the baseline estimates. For hospital-admissions estimates of positive health inequality impact, the regression slope is 0.72 and the intercept is -0.01 (both significant at the 5% level). Application to a disease intervention with a hospital-admissions estimate of inequality impact equal to 0.10 (= 10% of health opportunity cost) gives an adjusted impact of 0.10 × 0.72 – 0.01 = 0.062. That is, the estimated reduction in inequality achievable by the intervention is 3.8 percentage points (38%) lower after adjusting for bias in the estimated social gradient in disease prevalence.

If we ignore the small intercept, the adjustment lowered inequality impact by about 28% (1 - 0.72) on average over disease interventions estimated (based on admissions data) to reduce inequality. For diseases interventions with hospital-admissions estimates of negative inequality impact, the regression slope and intercept are 1.22 and 0.01, respectively. Ignoring the intercept, the adjusted estimate of the inequality impact is about 22% larger (1.22 – 1) on average over those interventions. Putting things the other way around, before adjustment, positive inequality impacts were overestimated by about 39% ((1 / 0.72) – 1) and negative inequality impacts were underestimated by about 18% ((1 / 1.22) – 1), on average.

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# **Supplementary Note 5. Health opportunity cost scenarios for England**

The incremental health opportunity cost (*HOC*) of a decision intervention compared with an alternative can be estimated as *C / k*, where *C* is the incremental cost and *k* is the health opportunity cost transformation rate. The health opportunity cost borne by social disadvantage group *j, HOCj*, is *HOC×pj*, where *pj* is the percentage share of total health opportunity cost borne by group *j*.

The appropriate base case assumption and range of sensitivity analyses around health opportunity cost shares depends on the decision-making context. Table S3 shows four scenarios relevant in the context of decisions about cost-increasing health technologies and programmes in England.

**Table S3**. Scenarios for share of health opportunity costs by social deprivation group

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Most deprived | 2nd most deprived | Middle | 2nd least deprived | Least deprived |
| 1. Flat | 20% | 20% | 20% | 20% | 20% |
| 1. Slight pro-poor | 22% | 21% | 20% | 19% | 18% |
| 1. Moderate pro-poor | 24% | 22% | 20% | 18% | 16% |
| 1. Slight pro-rich | 18% | 19% | 20% | 21% | 22% |

*Note*. Social deprivation is measured by the index of multiple deprivation (IMD). Groups are quintile groups of this index.

Our main estimates assumed a flat gradient with an equal 20% of HOC incurred by each group. In the slight pro-poor scenario the more deprived groups incurred a slightly larger share of HOC. The rationale is that these groups may be expected to benefit slightly more than average from alternative investments that may be sacrificed to release resources sufficient to implement the index disease intervention (given a fixed overall budget). The moderate pro-poor scenario skews HOC even more toward the more deprived groups. This is a simplified version of a simulated HOC shares distribution of 24.3%, 21.3%, 21.2%, 17.8% and 15.4% from the most to least deprived groups, respectively, based on overall hospital utilization in England (Cookson et al. 2020, Excerise 9). It is less skewed toward the more deprived groups than in another simulated HOC distribution because it is based on geographic (North-South) rather than sex stratification (Love-Koh et al. 2020). In the slight pro-rich scenario, HOC are skewed slightly in the other direction, with a larger share incurred by the less deprived groups. The pro-poor and pro-rich scenarios yield smaller and larger positive health inequality impacts, respectively, compared with the baseline flat scenario.

**Why not use a steep gradient based on overall hospitalization rates?**

Love-Koh et al. (2020) made indirect inferences about the gradient in health opportunity costs over deprivation groups using data on overall rates of inpatient hospital utilization in England 2012-13, including emergency admissions. However, the steep pro-poor gradient in overall hospital utilization observed in this study was primarily driven by emergency admissions. If emergency admissions were stripped out and this study were repeated using more recent data then the gradient would disappear entirely and indeed become slightly pro-rich. This is because the gradient in elective admissions reversed during the 2010s, from slightly pro-poor in the early 2010s to slightly pro-rich by the late 2010s, following a sustained period of slow economic growth and public sector austerity (NHS Digital 2024).

There is a steeper pro-poor gradient in emergency admissions than in elective inpatient admissions (Asaria et al. 2016) and outpatient visits (Stoye et al. 2020). This is because more deprived patients are sicker than less deprived patients of the same age, and their illnesses also tend to be diagnosed later and managed less successfully – leading to more acute episodes requiring emergency admission (Cookson et al. 2021). However, the gradient in health opportunity costs is not as steep as the gradient in emergency hospital admissions for two reasons. First, increases in secondary care funding tend to be used to increase elective and outpatient activity and reduce waiting times, rather than to improve the quality of emergency services, and the overall impact on emergency admissions could conceivably even be negative if some acute illnesses are prevented by improved non-emergency care. Second, more deprived populations tend to have worse long-term health outcomes from secondary care than less deprived populations, because they tend to be diagnosed later, to have greater co-morbidity, and to have fewer resources to co-invest in long-term recovery, rehabilitation and relapse prevention. This means that more deprived populations may gain less health benefit than less deprived populations from the same increase in secondary care utilization (Cookson et al. 2021).

A further complication is that health care utilization and outcomes for the least deprived groups may be less affected by changes in public health care expenditure than other groups, since they are more able to use privately funded care instead. This may tend to attenuate the health impacts of changes in public health care expenditure in the least deprived groups, resulting in smaller shares of health opportunity cost for the least deprived groups.

**What does the quasi-experimental evidence tell us?**

Rather than making indirect inferences from average health care utilization rates, a more direct approach is to conduct a “quasi-experimental” study that directly estimates the effects of changes in health care expenditure on the health of different social groups. Studies of this kind conducted using data from the 2000s to the early 2010s found monotonic gradients whereby more deprived groups gain larger health benefits from increased health expenditure (e.g. Currie et al. 2019, Martin et al. 2022). However, a study conducted using data from 2018/19 found the middle deprivation group gains the largest share of benefits, and no sign of a pro-poor pattern (Anaya-Montes et al. 2025). Indeed, if anything, the pattern tended to be slightly pro-rich in some model specifications though in most cases the null hypothesis of no linear gradient was not rejected. There are two plausible reasons for this discrepancy.

First, there may have been a structural change in the health opportunity cost gradient in England from moderate in the early 2010s to flat or pro-middle by the late 2010s, due to substantial and sustained deterioration in economic growth, health care and wider public services in England since 2010. Health and living conditions plausibly deteriorated more rapidly among deprived populations than other populations during the 2010s, resulting in even later diagnosis, even greater co-morbidity, and even less ability to co-invest in recovery, rehabilitation and relapse prevention. Supporting evidence for this hypothesis is that more deprived groups have tended to use disproportionately more emergency care and disproportionately less elective and outpatient care since the early 2010s (NHS Digital 2024, Stoye et al. 2020). If this structural change hypothesis is correct, there is little prospect of the gradient in health opportunity cost switching back again any time soon, since economic conditions and public services in England have deteriorated further since the Covid-19 pandemic, Ukraine war and cost-of-living crisis, and are unlikely to improve rapidly in the coming decade.

Second, this discrepancy might be due to more accurate measurement in the study by Anaya-Montes et al. (2025). The new study improved on previous studies by (1) using more precise data on mortality and deprivation based on small areas rather than large areas, (2) using a more robust instrumental variable study design, (3) looking directly at deprivation quantiles rather than mortality quantiles, and (4) using more precise data on health care expenditure based on NHS geographical boundaries rather than an indirect mapping to local government boundaries. Previous large area time series studies like Currie et al. (2019) may have been confounded by wider local government public expenditure trends beyond health care. And previous large area instrumental variable studies may have been biased by questionable instrument selection. For example, Martin et al. (2022) included other components of the funding formula (a need index and a price index) as additional instruments rather than as control variables. The latter is a more defensible approach, since these two components of the formula both have plausible causal links to the outcome (mortality) whereas valid instruments must be causally linked only to the variable being instrumented and not to the outcome as well.

**What would be reasonable base case and alternative scenarios for England?**

Given the conflicting evidence and substantial uncertainty in this area, it makes sense to conduct sensitivity analysis around alternative gradients. A sensible approach would therefore be to conduct sensitivity around three alternative gradients: (1) flat, (2) slight pro-poor, and (3) slight pro-rich. There is room for reasonable disagreement about which scenario to select as the base case. One might argue that scenario (2) should be the base case, since most studies have found that more deprived groups have larger health benefits than less deprived groups. On the other hand, one might argue that a flat gradient is the appropriate base case, on the grounds that the most recent study is more up-to-date and based on a more robust study design than previous studies, and that the burden of proof is on those who claim that opportunity costs are not simply shared equally among all groups.

A further issue is that the recent study finding a flat or higher HOC share in the middle deprivation group only examined secondary care data, so we might want to make an adjustment to allow for opportunity costs falling on primary care as well. Primary care may benefit the poor more than secondary care, because deprived patients have substantial unfulfilled potential for health benefit from earlier diagnosis and better management of long-term conditions in primary care. A slight gradient might therefore reflect the overall health care opportunity cost more accurately than a flat gradient. However, primary care expenditure is much lower than secondary care expenditure in England – around ten times lower – and so factoring this in is unlikely to change the overall health opportunity cost picture dramatically.

For the time being, therefore, one reasonable approach would be to select the flat gradient as the base case assumption but report sensitivity analysis around slight pro-rich and pro-poor gradients as well. Given all the uncertainty, however, this approach may need to change as further evidence accumulates.

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1. *GAP* can also be estimated as the OLS slope coefficient, ,from another linear regression,

   , where is group total health and is the group fractional rank rescaled such that the most and least disadvantaged groups get ranks of 0 and 1. With five equally sized groups, for example, these ranks are 0, 0.25, 0.5, 0.75 and 1, from most to least disadvantaged. [↑](#footnote-ref-1)
2. See SN2 and SN3 for reviews of basic concepts of cost-effectiveness analysis and DCEA. [↑](#footnote-ref-2)
3. The data are available at <https://github.com/bitowaqr/dcea> as part of this web tool <https://shiny.york.ac.uk/dceasimple>. [↑](#footnote-ref-3)