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Cessation to Screening
and Brief Intervention for
Alcohol in Distributional
Cost Effectiveness Analysis
to Explore the Sensitivity of
Results to Socioeconomic
Inequalities Characterised in
Model Inputs**

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CHE Research Paper 184

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September 2021

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What this study adds:

- A distribution of intervention impact across socioeconomic groups can be estimated from socioeconomic differences across a staircase using distributional cost effectiveness analysis (DCEA).

- The extent to which evidence on inequality at different steps of the staircase contributes to uncertainty in population level impact is not well understood.

- This study used two DCEAs to explore how socioeconomic inequality in model inputs impacts upon final conclusions about health inequality and value for money.

- There was no discernible pattern relating the extent and direction of socioeconomic variation in model inputs to socioeconomic variation in model outputs. Differences in deprivation structure of the local population and other factors would translate into different conclusions on the value for money of delivering the interventions locally compared to nationally.

- This study suggests there is limited scope for informally assessing the importance of lack of knowledge about socioeconomic variation in model inputs. The influence of socioeconomic variation differs between disease areas and settings.

Abstract

Introduction

A distribution of intervention impact across socioeconomic groups can be estimated from socioeconomic differences across a staircase from need (e.g. prevalence) up to intervention characteristics (e.g. effectiveness) using distributional cost effectiveness analysis (DCEA). The extent to which evidence on inequality at different steps of the staircase contributes to uncertainty in population level impact is not well understood. We used DCEAs in smoking cessation and alcohol interventions to explore how socioeconomic inequality in model inputs impacts upon final conclusions about health inequality and value for money.

Methods

Total population health and health inequality impacts were expressed using incremental net health benefit (NHB) and incremental 'equally distributed equivalent' (EDE) health, both measured in quality adjusted life years (QALYs). EDE reveals how the value of NHB is altered by inequality in its distribution. Scenario analyses explored: (i) the impact of ignoring socioeconomic differences in inputs; (ii) the value of eliminating differences; and (iii) how results differ between areas with different socioeconomic patterns.

Results

There was no discernible pattern relating the extent and direction of socioeconomic variation in model inputs to socioeconomic variation in model outputs. Differences in deprivation structure of the local population and other factors translate into different conclusions on the value for money of delivering the interventions locally compared to nationally.

Discussion

Our results suggest there is limited scope for informally assessing the importance of lack of knowledge about socioeconomic variation in model inputs. The influence of socioeconomic variation differs between disease areas and setting.

Executive Summary

Background/Introduction

Public health interventions can impact on total population health, and in doing so can alter the distribution of health within the population, which impacts on health inequalities. Inequality in health outcomes can be measured as an absolute difference between groups or individuals, as a relative difference, or in terms of the shortfall from some minimum standard. When health care decision makers are interested in improving health and reducing unfair health inequalities (i.e. reducing the perceived unfairness of the distribution of health across the population), they require tools that quantify changes in the distribution of health that result from the delivery of interventions. Where overall health improves but inequalities worsen, or vice versa, those tools should make explicit the trade-offs between them. Economic evaluations are routinely used to assess the impact of interventions on net health on average. This can be extended to characterise how net health benefits vary between groups in the population. For example, they may be used to determine the distribution of health outcomes across socioeconomic groups. When combined with information on the baseline distribution of health across these groups, impacts on absolute, relative and shortfall health inequality can be quantified. These extensions, known as distributional cost effectiveness analyses (DCEA), provide valuable information on the extent of any trade-offs between improvements in overall health versus reduction in measures of health inequality.

Uncertainty in the inputs to economic evaluation, including in the extent that variables differ between groups, translates into uncertainty over the results. For some inputs there may be a complete absence of evidence on the extent of socioeconomic variation. This uncertainty implies the possibility of an incorrect conclusion about intervention impacts, including impacts on total health, health inequality, and the overall value for money of an intervention. Sensitivity analysis can quantify how the uncertainty in inputs, including uncertainty in the extent of differences between groups, impacts on the uncertainty in the conclusions about an intervention's effect on overall health and health inequality. Using sensitivity analysis, we can explore how absence of evidence on socioeconomic differences in disease and intervention characteristics could impact on conclusions about value for money. The cost of uncertainty can be estimated in terms of the potential loss of health and/or greater avoidable health inequality from an incorrect decision. This can then be used to inform decisions about whether it would be worthwhile obtaining more information to reduce the uncertainty.

The between group differences in inputs may vary between settings, for example the prevalence of smoking by socioeconomic status may differ between areas with different ethnic composition. Evaluating the impact on the population distribution of health from national implementation of an intervention may, therefore, not be informative for the change in the distribution of health that would be expected at a local level. Therefore, it is relevant to local decision makers to understand how local level variation will impact on overall health and changes in health inequality, compared to the national level estimates.

Aims

This project aims to explore how models that characterise socioeconomic variation in the value of model inputs can be analysed to inform four broad questions:

(a) How influential is a lack of knowledge about socioeconomic differences on conclusions about the impact on overall health and health inequality?
(b) How valuable would it be to eliminate socioeconomic differences related to the intervention being considered?

(c) How generalisable are conclusions about impact on overall health and health inequality to contexts in which between group differences in the targeted populations differ?

(d) To what extent do the answers to these three questions differ between two models in different disease areas, and what conclusions can we draw about the generalisability of their results to other interventions or disease areas?

Methods

Two case study models, previously developed to assess i) smoking cessation interventions and ii) brief interventions for alcohol misuse, were adapted to incorporate local level socioeconomic patterned data and to perform a range of scenario analyses. For the smoking cessation model, probabilistic sensitivity and value of information analysis was also performed. Both models consider costs (pound sterling, 2018 price year) under an NHS and personal social services perspective and measure health outcomes in quality adjusted life years (QALYs).

Socioeconomic status is characterised by the Index of Multiple Deprivation (IMD). Outcomes considered are change in overall health, measured using incremental population net health benefit (i.e. health benefit of the intervention less health lost elsewhere as a result of resources not being available for other purposes) by assuming that £20,000 invested in other purposes produces one QALY. Change in health inequality is defined as the difference between the change in incremental health-related social welfare, measured using incremental equally distributed equivalent (EDE) health based on the Atkinson index, and change in incremental net health benefit. The Atkinson index describes the extent of welfare lost due to inequality in the population distribution of healthy life expectancy, based on UK population aversion to health inequality between rich and poor groups. The EDE is the amount of QALYs that, if equally distributed within the population, generate the same social welfare as the total QALYs in the distribution of health being evaluated.

For both case study models, we:

1. Describe socioeconomic 'gradients' in the model inputs, i.e. how the input values vary across the different socioeconomic groups. We distinguish between those gradients that are modifiable, and those that are exogenous (non-modifiable) and relate to the setting in which the intervention will be employed. The extent of socioeconomic differences in model inputs are summarised using concentration indices.
2. Perform scenario analyses in which we explore:
   a. The impact of ignoring the socioeconomic differences in inputs on the model results, i.e. setting each input in all groups to the average;
   b. The potential value of eliminating the differences by 'levelling up' the model inputs for modifiable socioeconomic differences, i.e. setting the input to the 'best' value across groups;
   c. How the results differ when using data from local settings (Local Authorities) with different characteristics.

The impact of each scenario is captured for pairwise comparisons by the change in incremental net benefit (iNHB), change in health-related social welfare (incremental EDE [iEDE] health) and change in inequality (iEDE-iNHB), compared to the base-case estimates. The pattern of socioeconomic differences in model inputs and the results of the scenario analyses are compared across the two case studies, to explore whether there are any patterns between the extent of inequality of model inputs and the estimated impact of the intervention on health inequality and other model outputs.

The smoking cessation model is a cohort Markov model that assesses the cost effectiveness of two active interventions (Varenicline and 7.2mg e-cigarette) to quit smoking and 'no intervention' in a

cohort of adult smokers (18-75 years) over a lifetime horizon. The model includes three discrete and mutually exclusive health states: i) smokers, ii) former smokers and iii) death. Smokers and former smokers are at risk of 6 smoking related comorbidities, which are modelled as events with impact on costs and QALYs. Health-related quality of life (HRQoL) in each state is age and smoking status dependent.

The Sheffield Alcohol Policy Model (SAPM) is a hybrid simulation/cohort modelling approach, incorporating two linked models that evaluates the cost effectiveness of screening and brief interventions (SBIs) to reduce alcohol misuse. Modelled strategies include delivery of SBIs to all patients when registering with a new primary care practice, or delivery to all patients as part of their next GP consultation. The first part of the model takes a baseline population of individual drinkers and simulates receipt of SBIs and the resulting age-adjusted trends in alcohol consumption over the 20-year modelled time horizon. The second part of the model aggregates these individuals into cohorts based on gender, age, IMD quintiles and baseline drinking level. The model simulates changes in the risk of 45 alcohol related health conditions, which are then linked to changes in associated rates of mortality and hospital admissions. The results of this second part of the model are equivalent to a 47-state Markov trace (45 health conditions, no disease and dead) for each model subgroup over a 20-year time horizon.

Both models consider socioeconomic gradients in baseline level of inequality (expressed in terms of the distribution of quality-adjusted life expectancy [QALE]), opportunity costs distribution, prevalence, mortality, comorbidities and intervention impact. However, there are differences in how the two models incorporate socioeconomic differences in prevalence and uptake.

The smoking cessation model was also modified to incorporate parameter uncertainty, to be able to perform probability sensitivity analysis. The contribution of uncertainty in groups of associated model inputs for determining uncertainty in model outputs was assessed using two methods: value of information (VOI) analysis and analysis of covariance (ANCOVA). VOI estimates the value of resolving all of the uncertainty in a decision problem (related to all parameters) which determines the expected value of perfect information (EVPI). Similarly, VOI can be used to estimate the value of resolving the uncertainty in a subset of parameters (expected value of partial perfect information [EVPPI]). The value is expressed in terms of the health outcomes that could be gained by avoiding the potential for incorrect decisions. The ANCOVA method fits a general linear regression model to estimate the relative contribution of variation in parameter sets to variation in the results. The ANCOVA does not provide information on how uncertainty in model parameters impacts decision uncertainty and the consequences of making the wrong decision. Nevertheless, it is expected that parameters that contribute most to decision uncertainty would also be the ones that explain most variation in model outputs. For VOI, the EVPPI for each subset of parameters is reported as a proportion of the overall EVPI, with a higher value indicating more importance for determining uncertainty in outputs. For ANCOVA, the proportion of sum of squares explained by uncertainty in input parameters is reported. Uncertainty in model outputs is considered with respect to positive overall health (iNHB), positive health-related social welfare (iEDE) and positive reduction in inequality (iEDE-iNHB).

Key findings and conclusions

The two models share some common gradients in the socioeconomic distribution of baseline health and health opportunity costs, but differ in others. Smoking is more prevalent (i.e. is concentrated) in disadvantaged groups, while intervention effects and uptake are greater (are concentrated) in advantaged groups. In contrast, alcohol misuse is more prevalent in advantaged groups but intervention use is greater in disadvantaged groups. The base-case analysis suggested that, compared to 'no intervention', smoking cessation interventions would increase population health

but also increase health inequality. For the alcohol model, both interventions appear to increase population health and reduce health inequality, although screening all individuals at their next GP consultation does both, to a much greater extent than screening at next registration.

(a) How influential is a lack of knowledge?
Ignoring all of the gradients has considerable impact on the estimates of how interventions affect health inequality compared to base-case. The impact of a lack of knowledge about socioeconomic gradients on estimates of how interventions influence overall health appears minor in the smoking cessation model (0.21% decrease), while the results suggest a small underestimate (5.83%) for the alcohol model. A complete absence of information about the model inputs which are expected to differ by socioeconomic status seem to produce reasonably reliable estimates on overall health, but may lead to biased estimates on health inequality impact.

Although a lack of knowledge of the gradient of individual parameters appears to affect overall health and health inequality in both models, there is no consistent pattern suggesting that any particular input is more influential across the two case studies. For the smoking cessation model, there is some suggestion of a positive correlation between the concentration index of inputs and the direction of impact on estimates of how interventions affect health inequality. In other words, ignoring the gradient in parameters that are more concentrated on the less deprived appears to diminish the extent by which the intervention alters the level of health inequality compared to base-case. Ignoring the gradient in parameters concentrated on the most deprived results increases the extent to which the intervention is estimated to impact on health inequality. However, this pattern is not observed for the alcohol model.

The probabilistic sensitivity analysis of the smoking cessation model revealed no decision uncertainty for the pairwise comparisons between each intervention and 'no intervention', for both impacts on overall health and health inequality. For these comparisons, uncertainty in overall health impact is mostly explained by uncertainty in the quit rate of the intervention and in intervention effectiveness, while uncertainty in uptake also explains uncertainty in the estimated health inequality impact. When comparing the two active interventions, there is decision uncertainty as to whether Varenicline increases overall health and reduces health inequality compared to e-cigarette. Value of information analysis suggests that the gradients that contribute the most to decision uncertainty, in terms of improvement in overall health, improvement in social welfare and reduction in health inequality, are the quit rates of the active interventions.

(b) How valuable are modifications to reduce socioeconomic differences?
Levelling up the model inputs related to the interventions across the whole population, to the highest level currently achieved in any socioeconomic subgroup, appears to result in greater gains in overall health and a reduction in health inequality (for the active interventions compared to 'no intervention') in both models. Given the potential to modify these inputs, decision makers may want to consider how delivery strategies for these health interventions can be improved so as to optimise the impact on both overall health and health inequality.

(c) How generalisable are conclusions about value for money between settings?
Results for specific local level settings are broadly consistent with those for England in terms of direction of change across scenarios and the influence of gradients in the results. This notwithstanding, local level differences in the socioeconomic gradients and population structure result in different conclusions on the value for money of interventions. Our findings suggest that Local Authority level decision making could be better supported by analysis incorporating data that reflects setting specific differences, as results cannot be inferred directly from national level data.

(d) How generalisable are these results between models and disease areas?
Both models were amenable to incorporate socioeconomic differences in parameters modifiable and relating to the intervention, as well as those that are exogenous and relate to the setting, despite the different model structures. There was no discernible consistent pattern to relate the extent and direction of socioeconomic variation in model inputs to the socioeconomic variation in model outputs. This suggests that there is limited scope for informally assessing the importance of lack of knowledge about socioeconomic variation in model inputs outside of a distributional cost effectiveness analysis.

The impact of reducing socioeconomic differences in the delivery and effects of interventions is positive for both improving overall health and reducing health inequality. Judgements on whether efforts to achieve this constitute value for money requires further study to estimate the additional costs associated with these efforts.

Adoption of national recommendations at Local Authority level should be done cautiously. Differences in deprivation structure of the local population and other disease- and intervention-related parameters, such as prevalence and uptake rate, may translate in different conclusions on the value for money of delivering the interventions locally compared to nationally.

Glossary

Atkinson index	An index that describes the extent by which the social welfare derived from a good is reduced by relative inequality in its distribution
Concentration index	An index that describes the level and direction of inequality in the distribution of a variable when the population is ranked by a second variable, ranging from -1 to 1 with negative/positive value indicating greater concentration in lower/higher ranked groups
Distributional cost effectiveness analysis (DCEA)	An economic evaluation that estimates who gains and who loses from an intervention and describes impacts on total health and health inequality
Economic evaluation	Comparison of alternative courses of action in terms of their costs and consequences
Equally distributed equivalent (EDE)	The level of an outcome that, if given to all individuals in a population, generates the same amount of social welfare as the current distribution of that outcome
Health inequality	Differences in health outcomes between individuals or groups
Index of Multiple Deprivation (IMD)	An index that ranks every small area of England by a measure of deprivation derived from measures of income, employment, health, education, housing, crime and living environment
Inequality aversion parameter	A measure that describes the extent of preference for an equal distribution in terms of the amount of social welfare that could be gained by redistributing an outcome such that everyone in a population receives an equal amount
Net health benefit (NHB)	A summary statistic that describes the value of an intervention in terms of health, where resources have been converted to health losses based on their opportunity cost
Opportunity costs	The value of resources expressed in terms of the outcomes forgone from alternative uses of those same resources
Quality adjusted life expectancy (QALE)	A measure of life expectancy that is weighted by the level of health-related quality of life in which it is lived
Quality adjusted life years (QALY)	A generic measure of health that includes both the quality and the quantity of life lived. One QALY equates to one year in perfect health
Socioeconomic characteristics	Factors that describe social and economic status, such as occupation, education, income, wealth, and place of residence
Socioeconomic distribution	How an outcome is distributed among members of a population according to their socioeconomic characteristics

1. Introduction/Background

When determining which public health interventions to implement, decision makers often consider the dual objectives of improving total population health and reducing unfair health inequality (1, 2). Information about how interventions impact on health inequality, as well as how they affect overall health, can therefore help to inform healthcare resource allocation decisions. Economic evaluations are routinely employed to assess the average impact of interventions on health outcomes and costs (3). Assessing value for money from these models entails comparing the health gain from an intervention to the health gain that would have been achieved with alternative investments. However, interventions that increase total population health may either increase or reduce health inequality at the same time. The intervention that provides the greatest increase in health may not be the intervention that provides the greatest reduction in health inequality. If decision makers determine value for money as a function of an intervention's impact on both overall health and health inequality, the distribution of the intervention's impact across the population is required to inform the decision. Where interventions increase health but increase health inequality, by favouring the most advantaged, the choice of intervention requires a value judgement about the trade-off between increases in overall health compared to reductions in health inequality. Similarly, where interventions reduce health inequality, by favouring the least advantaged, but do not increase overall health by more than alternative investments, the value judgement must be applied to the trade-off between improvements in health inequality compared to forgone population health.

Economic evaluations can be extended to look at how health benefits vary between groups in the population, such as groups with different socioeconomic characteristics. This requires defining the population groups of interest, and then searching for and incorporating evidence on how the value of model inputs varies between groups. Once the model employed for the economic evaluation describes a distribution of outcomes, assessment of value for money can be informed by information on how the intervention changes inequality in this distribution, as well as how it may impact on the average or total net health benefit. These types of models, described as distributional cost effectiveness analyses (DCEAs) (4), can be useful in answering a number of questions that policy makers may have about how interventions impact on health inequality, and the extent of any potential trade-offs between improvements in overall health versus reduction in health inequality. Additionally, a question frequently asked when evaluating intervention impact on health inequality is whether anything can be done to modify the intervention in order to alter its distributional impact. For example, if uptake is socially patterned, policy makers may be interested in whether it is worthwhile investing in actions that modify uptake. Investigating how changes in model inputs contribute to changes in outputs can inform the scope, by determining how far modifying intervention characteristics could alter final outcomes.

There are multiple sources of uncertainty in economic evaluation; when incorporating the differences between groups, the uncertainty in how the input values vary across groups will translate into uncertainty over the results. It is important to understand how lack of knowledge may impact on the uncertainty in the conclusions about an intervention's impact on overall health and health inequality. This includes the possibility of an incorrect conclusion about impacts on health inequality, and on the value for money of an intervention. When considering trade-offs, for example between increasing overall health and reducing health inequality, decision makers may be interested to know whether they are trading an uncertain gain for a certain loss. In general, the cost of uncertainty is determined by the potential loss of health from an incorrect decision. This can inform decisions about whether it would be worthwhile obtaining more information (thereby reducing uncertainty in the model inputs) to reduce the uncertainty of the model results. Distributional cost effectiveness analysis can extend this value of information analysis to look at the cost of uncertainty in terms of the extent of avoidable health inequality.

In addition, the extent and nature of the between group differences in model inputs can vary between settings. This may translate into variation in the set of interventions that provide value for money between settings. This is an important consideration when local decision makers seek to interpret public health recommendations, in terms of how they may increase local population health and reduce health inequality in the local population. Policy makers may wish to know how far conclusions about impact on overall health and change in health inequality generalise to their setting.

2. Project aims/Objective

This project aims to investigate how models that characterise socioeconomic variation in the value of model inputs can be analysed to inform a range of questions relating to the influence of socioeconomic variation in each input on conclusions about the impact on overall health and health inequality of different policies.

Two case study models (one assessing smoking cessation interventions and the other assessing brief interventions for alcohol misuse) were employed in the analysis to consider four broad questions:

(a) How influential is a lack of knowledge about socioeconomic differences on conclusions about the impact on overall health and health inequality?
(b) How valuable would it be to eliminate socioeconomic differences related to the intervention? In other words, what is the potential impact on population overall health and health inequality of interventions that eliminate differences, and for which inputs would it be most valuable to eliminate differences?
(c) How generalisable are conclusions about impact on overall health and health inequality to contexts in which the between group differences in the targeted population differ?
(d) To what extent do the answers to these three questions differ between the case study models, and what conclusions can we draw about the generalisability of their results to other interventions or disease areas?

2.1   How influential is a lack of knowledge?

One aim was to determine how an absence of information about socioeconomic variation in the model inputs would impact on conclusions about value for money. This represents the current situation, in which interventions are prioritised based on economic evaluations that describe only the average impact on population health. We aimed to explore the impact of using only the average value for inputs which are expected to differ by socioeconomic status, i.e. to use the same value across all socioeconomic groups instead of describing the between group variation.

Second, the model inputs incorporating socioeconomic variations differ in the extent of inequality and in the extent of their influence on the model results. Thus, it would be worth knowing how to determine the extent by which inequality in each of the model inputs affects the conclusion on overall health and health inequality. This can be explored by examining the changes in model outputs when ignoring the socioeconomic differences in one model input, i.e., comparing the results of setting the values of one model input in all groups to the average, with the results of incorporating the differences. This would help to identify which model input has the greatest influence on overall results, and allow us to determine whether there is any pattern or association between the most sensitive parameters and the most unequal parameters.

We also aimed to show how probabilistic sensitivity analysis and value of information analysis can be employed to answer questions about the value of obtaining more information on socioeconomic variation. Related to this, we show how value of information analysis indicates the relative contribution of each model input to decision uncertainty, and dichotomous conclusions about whether the interventions increase overall health or reduce health inequality. We also show how analysis of covariance can be used to explore the link between variation in a model input and variation in the magnitude of estimated intervention impact on overall health and health inequality.

2.2   How valuable are modifications to reduce socioeconomic differences?

We aimed to show how scenario analysis can be used to quantify potential improvements in health and reductions in health inequality, which could be achieved by changing potentially modifiable factors in intervention delivery. We explored this by estimating the potential increase in overall health and the change in health inequality from 'levelling up' these factors across the whole population to the highest level currently achieved in any socioeconomic subgroup. These results can help to inform efforts to design and improve delivery strategies for health interventions, informing questions such as: what are the likely health and inequality impacts of universal versus targeted delivery of an intervention, or what is the value of further research on interventions that might improve the effectiveness in more disadvantaged groups?

2.3   How generalisable are conclusions about value for money between settings?

The impact of a health intervention on health inequality depends on contextual factors such as the distribution of the targeted disease or risk factor varied by socioeconomic status. Even if the extent by which a model input varies between groups is the same across settings, the socioeconomic composition of the local population may differ, which can lead to different conclusions about how interventions impact on health inequality. We aimed to explore how the results would differ when incorporating Local Authority level data to reflect differences not only in the socioeconomic distribution in the population but also potentially in model inputs varied by socioeconomic status between Local Authorities. We considered what information and presentation of results from a distributional cost effectiveness analysis might be useful in allowing local decision makers to infer how results may differ in their setting without conducting a new analysis. We aimed to show whether knowledge of socioeconomic differences at Local Authority affects the value for money conclusion in the local setting, compared to other Local Authorities with different characteristics, or for the nation as a whole. These results will help to improve the extent to which local public health policies are tailored to the local context.

2.4   How generalisable are these results between models and disease areas?

By performing these analyses using two different models for different interventions and in different disease areas, we aimed to assess the extent to which our conclusions about how the lack of information on differences in model inputs affects the results, how modifying gradients can improve outcomes and how results change between settings, might vary. This could provide insight into the extent to which our findings are generalisable beyond the specific disease areas and interventions that we have examined in this project, and how they might inform both model and policy development in other areas.

3.   Design and Methods

As a starting point, we take that value for money is determined as a function of change in the distribution of health, reflecting both the change in the level of overall health and change in inequality in its distribution. Socioeconomic status is characterised based on the Index of Multiple Deprivation (IMD), which is a weighted composite index measure of deprivation by geographical area combining level of deprivation information from the inhabitants for small areas in England (5).

3.1   Metrics used for assessing outcomes

3.1.1   Net health benefit

In economic evaluation of health care interventions, a generic health outcome which captures both survival duration and health-related quality of life is typically used, such as the quality adjusted life year (QALY). In a public health system with a fixed budget, if an intervention is implemented which requires additional resources, there would be forgone health associated with not using that funding for other health-improving services. Therefore, the benefits of the intervention should be assessed relative to those displaced when resources are diverted from alternative activities, i.e. health opportunity costs. The National Institute for Health and Care Excellence (NICE) currently uses a cost-effectiveness threshold of £20,000 to £30,000 per QALY, implying that for every £20,000 to £30,000 additional funding required one QALY will be lost elsewhere in the NHS (6).

The change in overall health is defined here in terms of the incremental population net health benefit (NHB). An intervention with a positive NHB is considered to improve overall health because the health gains generated from its use will outweigh the health forgone (health losses) resulting from resources not being available for alternative health care investments. Health outcomes are expressed as QALYs and costs in pounds sterling (2018 price year). An annual discount rate of 3.5% is applied to both costs and benefits in accordance with NICE guidance (13). The costs are converted to health opportunity costs using the lower band of the NICE threshold, i.e. £20,000 per QALY, and then subtracted from the QALYs gains to estimate the population net health benefit.

The distribution in the direct health benefits from the intervention is informed by conditioning model inputs on socioeconomic status. The associated distribution of the healthcare costs must first be converted into a distribution of opportunity costs, before it can be used to calculate net health impacts. The opportunity costs may fall across different socioeconomic groups to those in which the healthcare resources are employed. As a change in the NHS budget is spent more on treating deprived groups, the distribution of the health opportunity cost falls more heavily on the more deprived. Therefore, these opportunity costs have a socioeconomic distribution. Taking money out of the budget to fund new interventions will disproportionately affect the care that disadvantaged groups are currently receiving. The additional costs of implementing a new intervention are converted to health opportunity costs, using the rate at which existing NHS activities produce health and then allocated to IMD quintile groups, following the distribution of health opportunity costs (7) (Table 1). For each group, the health opportunity costs are subtracted from the total QALYs benefits from the intervention in that group, to estimate the distribution of the incremental population NHB across socioeconomic groups in the population.

Table 1. Distribution of health opportunity costs by IMD quintile groups

Parameter	Value	Source
IMD1 (most deprived)	0.26	Love-Koh et al. (2016) (7)
IMD2	0.22	
IMD3	0.22	
IMD4	0.16	
IMD5 (least deprived)	0.14	

3.1.2   *Equally distributed equivalent health*

To assess the impact of the intervention on inequality in the level of health outcomes (as opposed to inequality in the change in health outcomes), the first step is to describe the baseline level of inequality. We express this in terms of the distribution of quality-adjusted life expectancy (QALE). QALE takes into account variation in both length and health-related quality of life (8). There is a social distribution of baseline QALE (before the intervention), as shown in Table 2. The distribution of incremental NHB due to intervention is then added to the distribution of baseline QALE to provide a picture of the distribution of QALE changes following the implementation of the intervention.

Table 2. The social distribution of health in England

	QALE at birth (years)	Source
IMD1 (most deprived)	64.7	Love-Koh et al. (2015) (8)
IMD2	68.5	
IMD3	70.6	
IMD4	73.6	
IMD5 (least deprived)	75.6	

To integrate the dual objectives of increasing total health and reducing health inequality, we use a single index measure of health-related social welfare, which formally combines both impacts using a health-related social welfare function. The welfare or value of a distribution of health can be characterised by defining an aggregation function that includes an inequality aversion parameter, which describes the amount of overall health that a decision maker would be willing to sacrifice to achieve a more equal distribution. A higher value assigned to the inequality aversion parameter reflects a greater concern for inequality at the lower end of the distribution. The existing empirical work has produced the estimates of level of inequality aversion in the UK, which provides us with an inequality aversion parameter based on elicited valuations from the general population (9).

We define the social welfare value of population health as 'equally distributed equivalent' (EDE) health (expressed in QALYs) based on the Atkinson index. The Atkinson index (10) is an index that describes the extent by which social welfare is reduced by relative inequality in the distribution of an outcome, and is the most popular welfare-based measure of inequality. It ranges from 0 to 1, where 0 represents no welfare loss from inequality and 1 represents complete welfare loss from inequality. 'Equally distributed equivalent' health is the level of population health that, if distributed completely equally, yields an equivalent amount of social welfare to the distribution being evaluated. The Atkinson inequality aversion parameter of 10.95, estimated from a survey in the general public in England (9), is used to calculate EDE health. The EDE health pre- and post-intervention is calculated based on the distribution of baseline QALE and the distribution of QALE with the intervention respectively, with the incremental EDE health indicating the change in social welfare.

The value of any change in health inequality expressed in terms of QALYs is defined as the difference between the change in incremental EDE health and change in incremental net health benefit. An intervention that reduces health inequality would have an incremental EDE health higher than its incremental NHB, with the difference showing the gain of health-related social welfare in terms of QALYs.

3.1.3   *Uncertainty analysis*

The uncertainty in the results is evaluated using the probability of incremental NHB (iNHB) being greater than zero (i.e., percentage of simulations with positive incremental NHB), the probability of incremental EDE (iEDE) being greater than zero (i.e., percentage of simulations with positive incremental EDE), and the probability of reducing inequality (i.e., percentage of simulations with

positive values in the difference between iEDE and iNHB). Results are also presented visually as scatter plots on the health equity impact plane.

We further explore the importance of uncertainty in each group of associated parameters for determining uncertainty in model outputs using two methods: value of information (VOI) analysis via the SAVI (Sheffield Accelerated Value of Information) platform (27) and probabilistic analysis of covariance (ANCOVA) (28). VOI can be conducted including expected value of perfect information (EVPI) and expected value of partial perfect information (EVPPI). VOI characterises decision uncertainty by evaluating the health outcomes according to which intervention would be selected on the basis of a decision rule about value for money. It estimates the monetary value of resolving all of the uncertainty in a decision problem related to all parameters (EVPI) or a subset of parameters (EVPPI) (29) in terms of the health outcomes that could be gained by avoiding the potential error when selecting an intervention. In this case study, the VOI approach characterises uncertainty of parameters with respect to positive overall health (iNHB), positive health-related social welfare (iEDE) and positive reduction in inequality (iEDE-iNHB). ANCOVA method shows the relative effect of the variation in parameter sets to the variation in the results, by fitting a general linear regression model (28). This is distinct from VOI because it does not incorporate a decision rule, and unlike the VOI analysis does not analyses variation across a decision threshold. In some circumstances, an outcome might be highly variable, but all plausible values may be on one side of the decision threshold, and so it may be associated with no decision uncertainty. In other circumstances, there may be little variation in the outcomes, but if it is concentrated around the decision threshold this might translate into higher levels of decision uncertainty. However, in general we would expect that the parameters that contribute most to decision uncertainty would also be the ones that explain most variation in the model outputs. For VOI, the index to overall EVPI for the subset of parameters is reported, with a higher value indicating more importance for determining uncertainty in outputs. For ANCOVA, the proportion of sum of squares explained by uncertainty in input parameters is reported.

3.2 Approach for analysis

We start by describing how the socioeconomic differences are characterised in both case studies in detail, and perform the scenario analyses separately to investigate the impact of the model inputs on conclusions about value for money. If the model successfully measures the average health impact and the gradients are implemented correctly, we would expect ignoring the gradients to have little impact on overall health but a large impact on health inequality. If ignoring the gradients impacts on overall health substantially, this suggests that the base-case is not a good characterisation of the average overall health, or that we have altered things in how we have characterised the gradient. We also compare the two models in terms of how the model inputs are characterised, inequality of model inputs, and their impacts on the results. For brevity we present selected results in the main report to illustrate each analysis, with the remaining results detailed in Appendix.

First, the two case study models are described in terms of how they characterise differences between socioeconomic groups in the population. That is, the set of model inputs that take different values for different socioeconomic groups is described, along with the evidence to support these differences. The between group differences in each model input can be summarised broadly in terms of the 'gradient' (e.g. whether the input value is higher among the socioeconomically disadvantaged groups, whether it is higher among the socioeconomically advantaged groups, or whether there is no discernible pattern). The model inputs are characterised according to those that are modifiable and relate to the intervention, and those that are exogenous and relate to the setting in which the intervention will be employed. The level and direction of inequality in model inputs are summarised illustratively using the concentration index (11). This provides a summary measure of magnitude of socioeconomic-related inequality in a health variable of interest. It summarises the

distribution in one number, ranging from -1 to 1 with negative/positive value indicating greater concentration of health in more/less disadvantaged groups.

Second, scenario analyses are used to explore: (i) the impact of ignoring the socioeconomic differences in inputs on the model results, e.g. setting mortality in all groups to the average; (ii) the potential value of eliminating the differences by 'levelling up' the model inputs with modifiable socioeconomic differences, e.g. uptake, to that of the 'best' group; and (iii) how the results differ when applying to local (i.e., Local Authority) populations with different characteristics.

Each model describes how interventions change the level of overall health (population net health benefit) and inequality in its distribution. The health equity plane is used to jointly illustrate these changes. Interventions that improve overall health with a positive iNHB fall in the north of the plane (Figure 1 quadrant A and B). Interventions that reduce inequality with positive difference between iEDE and iNHB fall in the east of the plane (Figure 1 quadrant A and D).
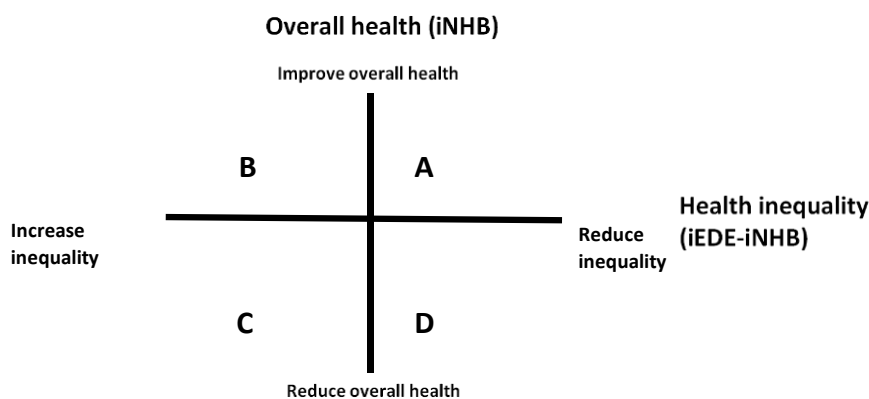

Figure 1. Health equity impact plane

Third, model inputs incorporating socioeconomic differences and results of the scenario analyses of the two case studies are compared, to explore the possible pattern between the extent of inequality of model inputs and the change in inequality of model output.

4. Case study one: smoking cessation model

An existing smoking cessation distributional cost effectiveness analysis (DCEA) was adapted to reflect uncertainty in the differences between socioeconomic groups. Uncertain model parameters were characterised as distributions with the uncertainty then propagated through the model using Monte Carlo simulation, i.e. probabilistic sensitivity analysis (PSA), to estimate uncertainty in model outputs, and determine the importance of uncertainty in each input for determining uncertainty in outputs.

4.1   Overview of the model

Details of the DCEA are reported elsewhere (12). In brief, the model evaluates the cost-effectiveness of smoking cessation strategies for adult smokers (18-75 years) from the NHS and personal social services perspective over the lifetime horizon. For simplicity, two active interventions from the 21 strategies assessed in the original model: i) Varenicline (14), and ii) 7.2mg e-cigarette (15), and the 'no intervention' strategy were included in this study. Varenicline is a prescription medication used to treat nicotine addiction which is expected to perform best in least deprived group; while e-cigarette is a battery-operated device that smokers use to quit smoking, reduce cigarette consumption, and relieve tobacco withdrawal symptoms, which could potentially perform better in more deprived groups. Nevertheless, the model did not consider the differences in uptake rate between the two interventions, as this is beyond the scope of this study.

The model is a cohort Markov model with the structure shown in Figure 2. The model includes three discrete and mutually exclusive health states: i) smokers, ii) former smokers and iii) death. The full cohort enters the model via the 'smokers' health state, and is exposed to the mortality and disease risks. Mortality differs by age and smoking status, with an age-specific relative risks (RRs) of death by smoking status applied to age specific all-cause mortality rates. The risk for developing smoking-related disease also differs by age and smoking status.

In each annual cycle, smokers have a probability of quitting smoking (and becoming 'former smokers'). Those who receive 'no intervention' have a 'background' quit rate of 2% (proportion of current smokers who naturally quit each year), while those who receive the interventions have higher quit rates, based on the original studies reporting the efficiency of the interventions (14, 15). Smokers are assumed to receive the intervention in the first year, and intervention costs are applied in the first cycle. Since the second cycle, smokers have the background quit rate and the model allows for relapse of former smokers (i.e. moving from former smoker to smoker), but the relapse rate is set to zero to simplify the analysis. Smokers and former smokers are at risk of six smoking related comorbidities (modelled as events): lung cancer (LC), coronary heart disease (CHD), chronic obstructive pulmonary disease (COPD), myocardial infarction (MI), stroke, and asthma exacerbation (asthma). Health-related quality of life (HRQoL) in each state is age and smoking status dependent. Each comorbidity has an associated cost and disutility. As these are modelled as events, rather than states in the model, when one or more comorbidities occur, the full event cost and disutility are applied in that cycle. The mortality risks of each co-morbidity are reflected in the overall mortality rate applied to smokers and non-smokers.
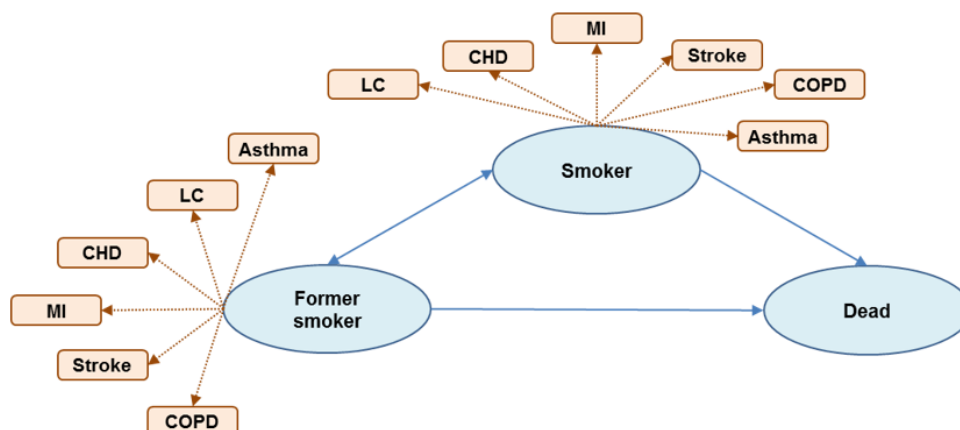
Figure 2. The NICE model structure for smoking cessation interventions

4.2   Socioeconomic variations in model inputs

The differences in model inputs across IMD quintiles characterised in the DCEA are described in the following sections. Uncertainty around each gradient, which was used for the PSA, is also summarised.

4.2.1   *Socioeconomic variation in the baseline health and behaviour*

Baseline health and behaviour correspond to the levels that would be observed with 'no intervention'. Baseline quality-adjusted life expectancy, health opportunity costs, smoking prevalence, mortality, prevalence of smoking-related comorbidities, and health-related quality of life are all known to differ according to IMD.

Gradients in baseline QALE and opportunity costs distribution
As described in section 3.1, the social distribution of QALE was taken from Love-Koh et al (2015) (8) (Table 2) and the socioeconomic gradient in the opportunity costs of additional healthcare expenditure was taken from Love-Koh et al. (2016) (Table 1). It is clear that the QALE is higher in less deprived areas, and more healthcare expenditure is allocated to residents in the more deprived areas. No uncertainty was assigned to these two gradients.

Gradient in smoking prevalence
The gradient in smoking prevalence by IMD quintiles was estimated using Public Health England Local Tobacco Control Profiles 2017 data. The smoking prevalence for each IMD quintile and 95% confidence intervals were available (Table 3). Smoking prevalence is higher in more disadvantaged areas. For smoking prevalence, we assigned independent Beta distributions to describe prevalence in each IMD quintile in order to reflect uncertainty in the PSA. Parameters that characterised the Beta distributions were estimated using the mean value and 95% confidence interval for smoking prevalence (Table 3).

Table 3. Smoking prevalence by IMD in England (2017)

Smoking prevalence	Mean	95% confidence interval
IMD1 (most deprived)	17.17%	16.55%, 17.79%
IMD2	15.96%	15.22%, 16.70%
IMD3	14.09%	13.24%, 14.95%
IMD4	12.68%	11.80%, 13.57%
IMD5 (least deprived)	11.38%	10.53%, 12.24%

Gradient in mortality
The annual mortality rates for smokers were estimated using the general population all-cause mortality by age and sex according to IMD quintiles, proportion of smokers, former smokers and non-smokers, and relative risk of death (smokers vs non-smokers by age group and smokers vs former smokers) (see equation 1 for details).

Equation 1:
Annual mortality rate for smokers

$$= \frac{\text{All cause annual mortality rate}}{\left(\text{proportion of smokers} + \dfrac{\text{proportion of former smokers}}{\text{relative risk of death (smokers vs former smokers)}} + \dfrac{\text{proportion of non smokers}}{\text{relative risk of death (smokers vs non smokers)}}\right)}$$

Data on all-cause mortality were extracted from the Office for National Statistics (ONS) data 2010-2015 (16). Data on proportion of smokers, former smokers and non-smokers were estimated in the previous version of the model (12) and used in this study. The relative risk of death for smokers vs non-smokers by age group (35-44, 45-54, 55-64, 65-74 and 75+ years) and associated 95% confidence intervals were estimated using mortality data reported in a previous UK observational study (17). The study also provided mortality rates for former smokers to enable estimates of relative risk of death for smokers vs non-smokers although this was not stratified by age. Therefore, it was assumed that the relative risk of death for smokers vs former smokers was constant across age groups.

Uncertainty in the estimates of all-cause mortality and proportions were not available, therefore no uncertainty is reflected regarding the underlying mortality rate conditioned on IMD. However, the use of relative risks of death (which are sampled from lognormal probability distributions) allows us to reflect some of the uncertainty in these estimates. Socioeconomic variation in annual mortality risk for smokers is presented in Figure 3, showing a higher death rate in more deprived areas.
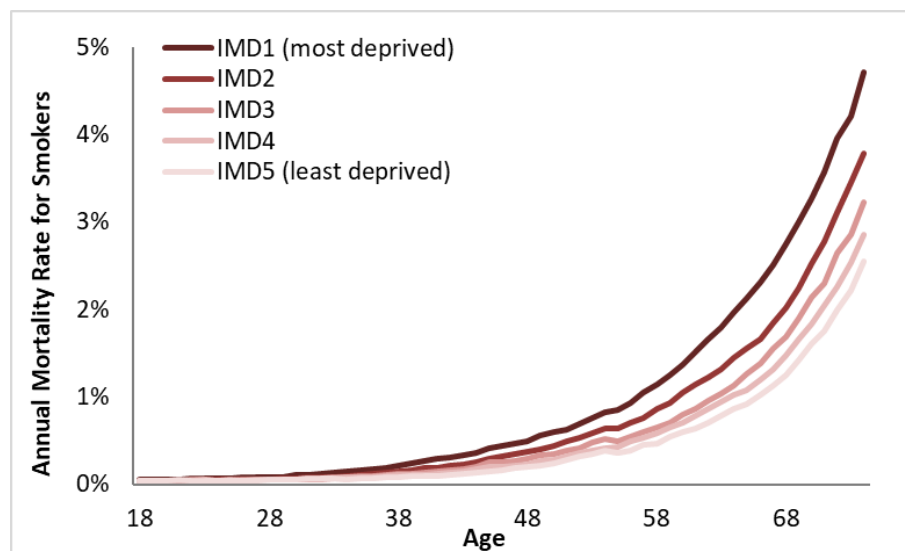

Figure 3. Socioeconomic variation in annual mortality risk for smokers

Gradient in smoking-related comorbidities
Incidence of smoking-related comorbidities was estimated in the previous version of the model (12), conditioned by age, sex and smoking status, but no information was available by socioeconomic status. A previous study in Scotland examined the relative risk of developing comorbidities by Scottish IMD (18), but similar information was not available for the English IMD. We assumed evidence on incidence of comorbidities was that in the middle IMD, i.e. IMD3 group, and then applied these relative risks to estimate the incidence by IMD.

Similar to the English IMD, the Scottish IMD provides a wealth of information on the small areas in Scotland and ranks all these areas from most deprived to least deprived (19). We assumed that the variation by SIMD was transferable to the English population. Relative risks and associated confidence intervals for each IMD (with IMD5 as the reference) were reported in that study and presented in Table 4, suggesting a higher probability of developing comorbidities for the less deprived areas. Since the study (18) did not run separate analysis for smokers and former smokers, we assumed the relative risk of developing comorbidities applied to both smokers and former smokers in each IMD quintile. The study did not report the variance-covariance matrix for the regression model, and so independent lognormal distributions were assigned to the log value of each of the relative risks. Thus, the independent distributions fail to control for the correlation between these parameters in the PSA.

Table 4. Relative risk of developing smoking-related comorbidity

Parameter	Value	95% confidence interval	Distribution	Source
IMD1 (most deprived)	1.15	1.06, 1.24	Lognormal[*]	Eberth et al. 2014 (18)
IMD2	1.12	1.03, 1.20	Lognormal[*]	
IMD3	1.12	1.04, 1.21	Lognormal[*]	
IMD4	1.08	1.00, 1.17	Lognormal[*]	
IMD5 (least deprived)	1	-	-	

[*]Estimates transformed to the log scale

Gradient in health-related quality of life (HRQoL)

The gradient in HRQoL was incorporated by estimating baseline HRQoL for smokers and former smokers without pre-existing circulatory and respiratory conditions by IMD quintiles. EQ-5D data in the Health Survey for England datasets (2012 and 2014) were used, comprising 4,960 observations with complete information on EQ-5D, age, IMD and smoking status. Ordinary least squares (OLS) regression was performed, with EQ-5D score as the dependent variable, and age group, smoking status (smoker/former smoker), and IMD quintile as explanatory variables. As previous work by Love-Koh et al (2018) (12) showed that the impact of smoking on HRQoL did not vary between IMD quintiles, we did not include interaction terms in the final model. The regression output used to predict the EQ-5D scores used in the economic model is reported in Table 5. The less deprived areas tend to have higher HRQoL. The variance-covariance matrix was extracted, and the corresponding Cholesky decomposition was used to obtain correlated draws from a multivariate normal distribution for use in the PSA. The regression coefficients were applied in the model to estimate EQ-5D values disaggregated by smoking status, age and IMD quintiles.

Table 5. Output from HRQoL regression model

Variable		Coefficient	Standard error
Constant		0.903[***]	0.0139
Age group	16-24	Ref	
	25-34	-0.0124[***]	0.0137
	35-44	-0.0544[***]	0.0133
	45-54	-0.0681[***]	0.0135
	55-64	-0.0986[***]	0.0138
	65-74	-0.107[***]	0.0145
	75+	-0.1630[***]	0.0165
Smoking status	Former smoker	Ref	
	Smoker	-0.0340[***]	0.0069
IMD	IMD1 (most deprived)	Ref	
	IMD2	0.0320[**]	0.0099
	IMD3	0.0281[**]	0.0101
	IMD4	0.0545[***]	0.0102
	IMD5 (least deprived)	0.0736[***]	0.0101
Adjusted R-squared		**0.0414**	

[*]p<0.05, [**]p<0.01, [***]p<0.001

4.2.2   Socioeconomic variation in intervention impact

Socioeconomic variations in intervention effectiveness, i.e. smoking quit rate, and the intervention uptake rate were incorporated

Gradient in intervention effectiveness
The 12-month quit rates of the interventions Varenicline and 7.2mg e-cigarette (e-cigarette) were extracted from the original studies (14, 15). The 12-month quit rate for 'no intervention' was 2% (20) and is the proportion of current smokers who spontaneously quit each year. As there was no information on socioeconomic status in the original studies reporting the quit rates of the interventions, it was assumed that the quit rates represent the IMD3 group. The relative risk of quit smoking by IMD was estimated using results of the Evaluating Long-term Outcomes of NHS Stop Smoking Services (ELONS) study (21). The ELONS study assessed all English stop smoking services and, therefore, the results are reflective of a mix of interventions. We assumed the same gradient in effectiveness in both interventions. We also assumed that the natural quit rate would follow the same socioeconomic pattern as the interventions. We then applied these to estimate the quit rate by IMD.

The ELONS study (21) reported the odds ratios of smoking cessation at 4 weeks by IMD quintiles, in relation to IMD1. It was assumed that the pattern observed at 4 weeks was reflective of that at 12 months as a result of a lack of similar data at 12 months. The method suggested by Grant (2014) (22) was used to convert the odds ratios and 95% confidence intervals, estimated in one multivariate regression model, to relative risks of quitting smoking (see Table 6 for details). As the variance-covariance matrix was not available for the regression model, independent lognormal distributions were assigned to the log value of each of the relative risks to reflect uncertainty for the PSA.

Uncertainty surrounding the quit rates of the two interventions were extracted from the original studies, and we assigned a Beta distribution to both to reflect uncertainty for the PSA. No uncertainty was assumed for the natural quit rate.

Table 6. Relative risk of quitting smoking

Parameter	Value	95% confidence interval	Distribution	Source
IMD1 (most deprived)	1	-		Dobbie et al. 2015 (21) Grant 2014 (22)
IMD2	1.35	0.94, 1.81	Lognormal[*]	
IMD3	1.22	0.79, 1.73	Lognormal[*]	
IMD4	1.27	0.91, 1.67	Lognormal[*]	
IMD5 (least deprived)	1.36	0.94, 1.82	Lognormal[*]	

[*]Estimates transformed to the log scale

Gradient in intervention uptake
The gradient in intervention uptake was estimated using the proportion of smokers supplied with an intervention from NHS Stop Smoking Services by IMD quintiles, estimated by Love-Koh et al. (2018) (12). The results are presented in Table 7, and suggest that a greater proportion of smokers in the less deprived groups (IMD4 and IMD5) are utilising the services compared to the more deprived quintiles. As there was no data on the uncertainty surrounding these estimates, we assumed a standard error of 10% of the uptake rate and Beta distributions in the PSA.

Table 7. Annual service uptake rate

Parameter	Value	Source
IMD1 (most deprived)	4.03%	Love-Koh et al. (2018) (12)
IMD2	6.48%	
IMD3	6.62%	
IMD4	10.14%	
IMD5 (least deprived)	9.92%	

4.2.3   Additional gradients not considered

Gradient in comorbidity costs

We assumed that a given smoking-related comorbidity event would incur the same costs regardless of IMD. To reflect uncertainty in comorbidity costs, we assumed the standard error was equal to 10% of mean value and assigned Gamma distributions.

Gradient in comorbidity disutility

The previous work by Love-Koh et al (2018) (12) did not identify any evidence to suggest variation in the overall health-related quality of life impact of smoking by socioeconomic status. Therefore, we applied the disutility due to each comorbidity event as absolute decrements to the baseline HRQoL estimates. Mean estimates and standard errors for the disutility were extracted from several studies (23-26) (see Table 8 for details), and a Gamma distribution was assigned to reflect the uncertainty in the PSA.

Table 8. Disutility due to co-morbidity

| Comorbidity	Mean	Standard error	Source
Stroke	0.4839	0.0461	(23)
Lung cancer	0.4233	0.1003	(23)
MI	0.1878	0.0334	(23)
CHD	0.2409	0.0122	(24)
COPD	0.2700	0.0416	(25)
Asthma exacerbation	0.3567	0.0694	(26)
CHD: coronary heart disease; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction.			

4.2.4   Summary of model inputs

The model inputs described above can be characterised into two broad categories: non-modifiable, which are related to the disease and the population groups of interest; and potentially modifiable, which are related to the interventions (Table 9). Concentration indices of model inputs are also summarised in Table 9 and presented in Figure 4. Among all the model inputs incorporating socioeconomic differences, baseline QALE, HRQoL, intervention effectiveness, and intervention uptake have positive concentration indices, showing higher values in less deprived groups, while the others have negative concentration indices, suggesting higher values in more deprived groups. The greatest dispersion is in intervention uptake, which favours the less deprived.

Table 9. Category and concentration index of model inputs incorporating socioeconomic variation

Category:	Gradient in:	Concentration index
Non-modifiable	Baseline QALE	0.03
	Health opportunity costs	-0.12
	Smoking prevalence	-0.08
	Mortality	-0.08
	Smoking-related comorbidities	-0.02
	HRQoL	0.01
Potentially modifiable	Intervention effectiveness	0.04
	Intervention uptake	0.17
QALE quality-adjusted life expectancy; HRQoL health-related quality of life		
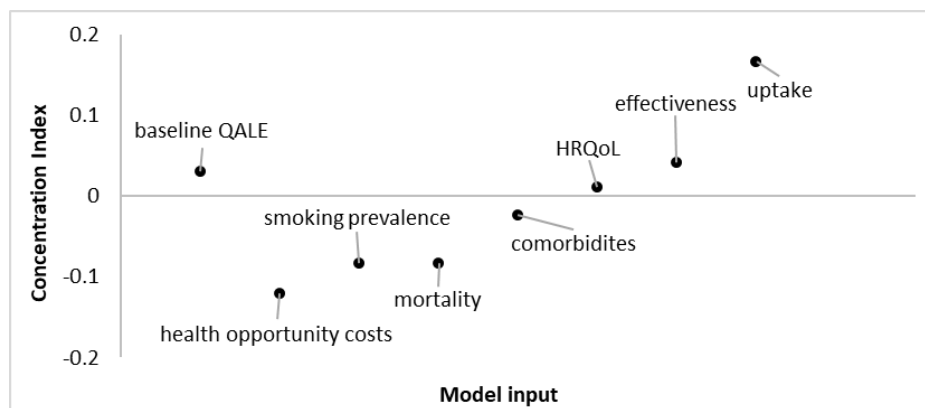
Figure 4. Concentration index of model inputs

4.2.5   Socioeconomic variation at Local Authority level

To explore the generalisability of results to different contexts, information reflecting socioeconomic variations between Local Authorities in England was obtained. Smoking prevalence could be defined at Local Authority level using data from the Public Health England Local Tobacco Control Profiles, with socioeconomic status reported according to the National Statistics Socio-Economic Classification (NS-SEC). Mapping between the NS-SEC and IMD quintiles was performed and then combined with the prevalence for each NS-SEC group, to estimate the smoking prevalence for IMD quintiles at local level. The distribution of NS-SEC groups by IMD quintiles is summarised in Appendix Table S1.

In this case study, we explore the results for **York** and **Sheffield**. The two Local Authorities were chosen to reflect the different pattern of population distribution by IMD (extracted from Public Health England Local Authority Health Profile 2017 and shown in Figure 5). There are more residents in York living in the least deprived area and more residents in Sheffield living in the most deprived area. In the absence of more detailed data at Local Authority levels, both Local Authorities are assumed to differ from the national model only on the basis of the deprivation structure of their respective populations and the smoking prevalence, i.e. the mortality risks, risks of comorbidities and HRQoL are the same for IMD quintiles in the national and both local models. The smoking prevalence in York and Sheffield is illustrated in Figure 6.
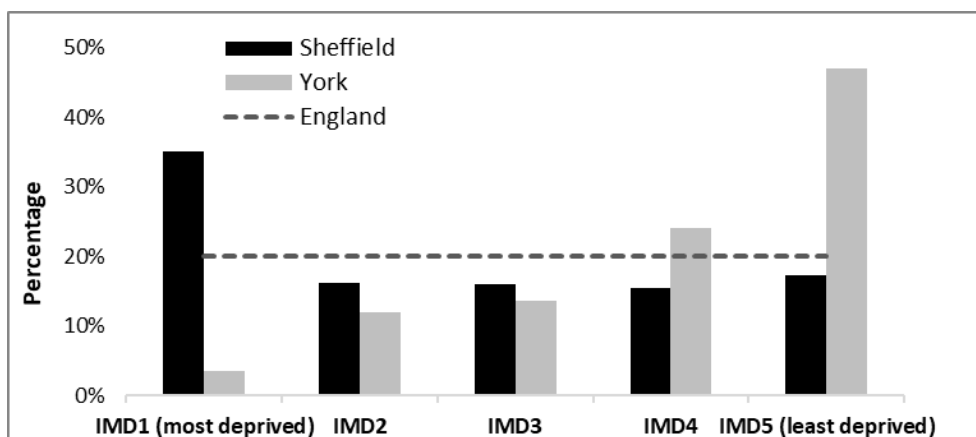
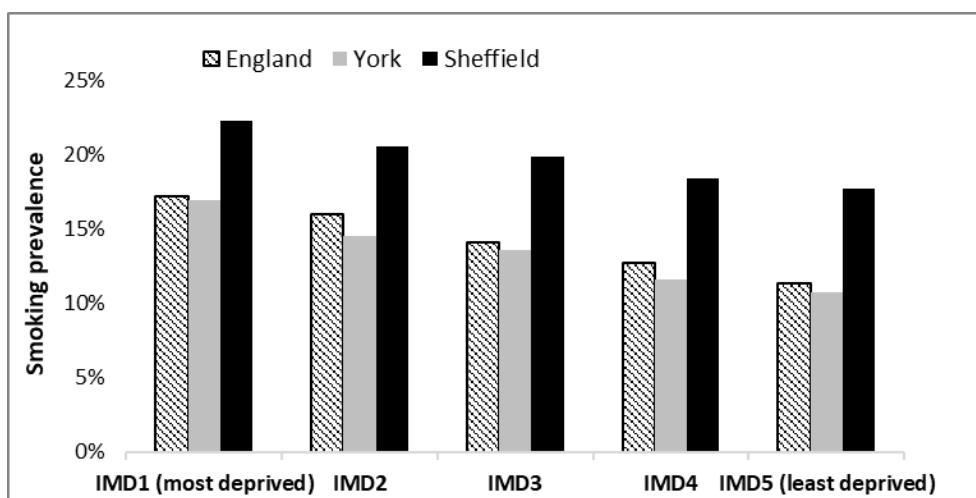**Figure 5. Population distribution according to IMD in York and Sheffield**

Figure 6. Variation in socioeconomic gradients in smoking prevalence for England, York and Sheffield

4.3   Analysis

4.3.1   Base-case analysis

The analysis is conducted for the two interventions and 'no intervention'. The incremental NHB, incremental EDE, and difference between incremental EDE and incremental NHB are estimated for all the pairwise comparisons (interventions vs 'no intervention'; Varenicline vs e-cigarette). The analysis is conducted based on adult smokers only and our baseline population size is 42,994,944 (all adults in England), distributed between IMD quintiles based on ONS mid-year population estimates for 2017 as shown in Table 10. For York and Sheffield, the total population size was extracted from Public Health England Local Authority Health Profile 2017 (York: 207,000 and Sheffield: 574,000).

Table 10. Baseline distribution of the adult population of England

	Adult population
IMD1 (most deprived)	8,307,456
IMD2	8,863,275
IMD3	8,790,681
IMD4	8,657257
IMD5 (least deprived)	8,376,275

4.3.2   Scenario analysis

A series of scenario analyses are performed to explore the impacts of gradients on conclusions about overall health and health inequality:

(a) The impact of ignoring all gradients is explored, by setting the model inputs in all groups to the average value.
(b) For all the model inputs characterised with gradients, the impact of ignoring the differences in one model input on the results is explored, by setting the value of that model input to the average value.
(c) For the gradients that are potentially modifiable, the value of eliminating the differences is explored, by 'levelling up' to that of the 'best' group.

The impact is captured by the change in overall health (iNHB), change in health-related social welfare (iEDE), and change in inequality (iEDE-iNHB), compared to the base-case. Results are summarised and presented visually on the health equity impact plane.

4.3.3   Probabilistic sensitivity analysis

The uncertainty in model inputs has been described previously with parameters characterised as distributions (section 4.2). Uncertainty in these parameters is then propagated through the model using Monte Carlo simulation (1,000 simulations). For each simulation the iNHB, iEDE, and difference between iEDE and iNHB (iEDE-iNHB), are estimated for all the pairwise comparisons. The uncertainty in the results is evaluated using the probability of iNHB being greater than zero (i.e., percentage of simulations with positive incremental NHB), the probability of iEDE being greater than zero (i.e., percentage of simulations with positive incremental EDE), and the probability of reducing inequality (i.e., percentage of simulations with positive values in the difference between iEDE and iNHB). Results are also presented visually as scatter plots on the health equity impact plane. The 1,000 sets of input values and corresponding outcomes from the Monte Carlo simulations are recorded for input into SAVI to undertake the VOI, and to facilitate linear regression for ANCOVA.

5. Case study two: alcohol Brief Interventions model

The Sheffield Alcohol Policy Model (SAPM), an existing alcohol Screening and Brief Intervention (SBI) model used to inform NICE public health guidelines (30), has been adapted to quantify health equity impacts in subgroups defined according to socioeconomic status. In this study, we extended the model further to incorporate inequalities in health opportunity costs, in order to explore the key drivers of net inequality impacts in this area.

5.1 Overview of the model

Details of the model have been reported in full elsewhere (30). In brief, the model evaluates the delivery costs, downstream healthcare cost savings, and health impacts of alternative SBI delivery strategies from an NHS perspective. Modelled strategies include delivery of SBIs to all patients when registering with a new primary care practice, or delivery to all patients as part of their next GP consultation. Health outcomes are expressed as QALYs and costs in pounds sterling (2018 price year). Due to evidence that the effect of SBIs decays over time, with alcohol consumption estimated to return to age-adjusted pre-intervention levels after 7 years (31), and that there are delays between changes in alcohol consumption and changes in risk of harm, a 20 year time horizon is used (32). All costs and benefits are discounted at a rate of 3.5% in line with NICE guidance (13). For ease of exposition the present analysis focuses only on the comparison of 3 alternative scenarios: i) No SBI delivery, ii) All patients receiving an SBI when they register with a new GP practice and (Next Reg), iii) All patients receiving an SBI when they next visit their GP (Next Con).

The basic structure of SAPM is a hybrid simulation/cohort modelling approach incorporating two linked models. The first model takes a baseline population of individual drinkers and simulates receipt of SBIs under each scenario and the resulting age-adjusted trends in alcohol consumption over the 20 year modelled time horizon. SBI delivery costs for each scenario are calculated in this model, accounting for the number of patients screened and the number of interventions delivered, using published estimates of practitioner time required for each stage (33). The second model aggregates these individuals into cohorts based on gender, age (4 groups: 18-24, 25-34, 35-54, 55+), IMD quintiles and baseline drinking level (3 groups: drinking within current UK guidelines of 14 units/week (moderate); exceeding current guidelines but drinking no more than 50 units/week for men and 35 units/week for women (increasing risk); and drinking above these levels (high risk). Within these cohorts, within each year following baseline, the Potential Impact Fraction approach of Gunning-Schepers is used to estimate changes in rates of mortality and hospital admissions for 45 different alcohol-related health conditions based on changes in alcohol consumption. The approach used to model changes in the risk of each health condition varies depending on whether the condition is associated with long-term chronic drinking or short-term acute intoxication, and whether the condition is exclusively caused by alcohol, or if alcohol is just a risk factor. The results of this model are equivalent to a 47-state Markov trace (45 health conditions, no disease and dead) for each model subgroup. HRQoL is calculated by assigning subgroup and condition-specific health state utilities within each model year. From this, the total number of QALYs accrued within each population subgroup in each year is calculated. Healthcare costs are calculated similarly using published health state-specific costs (33). The net cost of each intervention scenario is calculated by combining the intervention costs and downstream healthcare costs over the 20-year time horizon, after discounting. The total QALY gains are calculated similarly, divided by the initial population size and combined with the baseline QALE estimates from Table 2, to give estimates of the revised QALE under the intervention scenario being modelled.

5.2   Socioeconomic variation in model inputs

As for the smoking cessation model, socioeconomic status is characterised throughout the model using IMD. Socioeconomic gradients in key model inputs are described below, followed by a brief discussion of several key areas where potential gradients are not directly accounted for in the model.

5.2.1   Socioeconomic variation in baseline health and behaviour

Baseline levels of health and behaviour correspond to the levels that would be observed with 'no intervention'. Prevalence of drinking, average consumption levels among drinkers, and patterns of drinking are all known to vary between IMD quintiles. There are also important gradients in baseline levels of mortality and disease prevalence for conditions which are related to alcohol consumption.

Gradient in baseline QALE and opportunity costs distribution
As for the smoking model, the social distribution of QALE was taken from Love-Koh et al (2015) (8) (Table 2) and the socioeconomic gradient in the opportunity costs of additional healthcare expenditure was taken from Love-Koh et al. (2016) (Table 1).

Gradient in baseline drinking
Alcohol consumption data comes from self-reported alcohol consumption of adults (aged 18+) in England taken from the pooled Health Surveys for England 2015 and 2016 (N=12,157). Three dimensions of consumption are used in SAPM: 1) whether an individual drinks alcohol at all, 2) the average weekly consumption of individuals who drink, 3) the consumption on the day of the previous week that the survey respondent drank the most, used as a proxy measure for binge drinking. Whilst SAPM's individual-level nature accounts for age, gender and deprivation-level variation in drinking behaviours, the aggregated IMD quintile-level figures are summarised in Table 11. In contrast to gradients in baseline smoking prevalence, those in more deprived groups are less likely to drink, drink less on average if they do drink, and 'binge' drink at lower levels.

Table 11. Socioeconomic gradients in drinking

Deprivation quintile	Abstention rate	Mean consumption (units/drinker/week)	Peak day consumption (units/drinker)
IMD1 (most deprived)	28.2%	13.00	4.44
IMD2	32.0%	12.01	3.96
IMD3	14.1%	12.54	4.33
IMD4	12.3%	13.63	5.11
IMD5 (least deprived)	7.1%	14.95	5.71

Gradient in mortality
Unlike the smoking cessation model, SAPM models outcomes separately by health condition, including 45 separate health conditions which are causally linked to alcohol, as well as mortality from all other causes combined. For each of these conditions, gradients in mortality were extracted from mortality records held by the ONS for the period from 2012-2016. Separate gradients were included in the model for each age-sex group for each condition. The implied population-level gradients are illustrated in Figure 7.
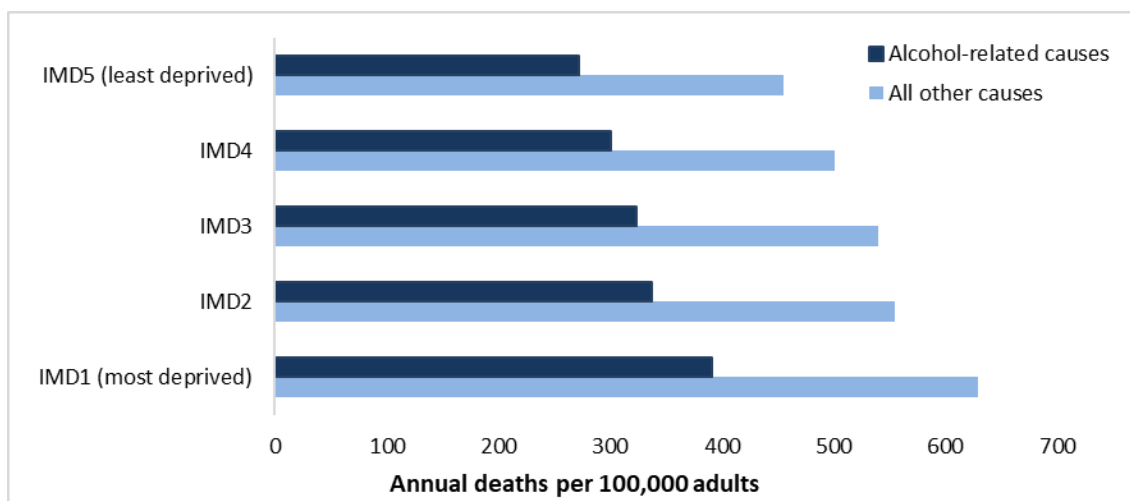
Figure 7. Socioeconomic variation in annual mortality rates

Gradient in alcohol-related comorbidities

Data on disease prevalence was obtained at the condition-specific level from analysis of Hospital Episode Statistics data for England for the period from 2012/13 to 2016/17. As individual admissions can have multiple diagnostic codes, each admission is coded to a single health condition using the 'broad measure' approach, which is recommended by Public Health England as the most appropriate measure of 'the total burden that alcohol has on community and health services' (34). In order to prevent double-counting within the model, admissions within a year for the same individual are linked and where there are multiple admissions coded to different alcohol-related conditions within the same year, only the admissions for one condition are retained (see Jones et al. for a full description of this process (35)). Morbidity rates are calculated at the individual level (i.e. after removing repeat admissions for each individual). Population-level prevalence gradients are summarised in Figure 8.
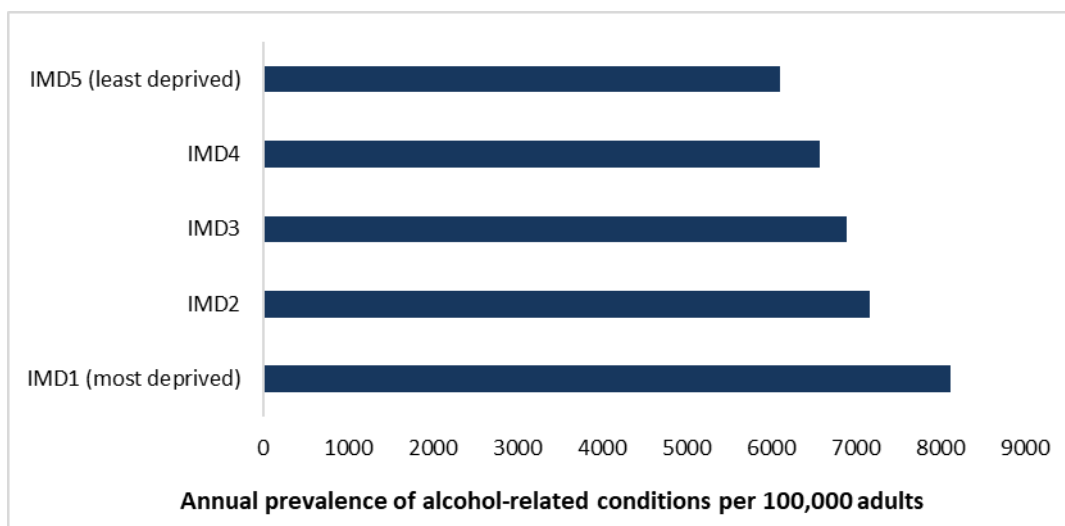
Figure 8. Socioeconomic variation in prevalence of alcohol-related disease

5.2.2 Socioeconomic variation in intervention impact

The intervention consists of two distinct steps – an initial 'Screening' step to identify individuals who are drinking at risky levels, and a secondary 'Brief Intervention' step. The overall gradient in receipt of the intervention is, therefore, the product of two distinct gradients:

1. A gradient in who is screened
2. A gradient in the rate at which screened patients are identified as risky drinkers

Gradient in screening rates

The rates at which different subgroups in the population are screened for risky alcohol consumption, using a validated tool such as the Alcohol Use Disorders Identification Tool (AUDIT) (36) depends on the scenario to be modelled. For the 'next registration' scenario, it is the rate at which individuals in each subgroup register with new GP practices. For the 'next consultation' scenario, it is the proportion of the population who attend primary care for any reason over the course of a year. Data on the rate of new GP registrations by socioeconomic status is derived from The Health Improvement Network (THIN), a database of computerised primary care patient records covering approximately 6% of the UK population (37). For each age-gender-deprivation subgroup included in SAPM, rates of new registrations were calculated from 2015-16 THIN data. The aggregated IMD quintile rates are shown in Table 12. Data on GP consultation frequencies are taken from the Health Survey for England, which included questions on whether a patient had seen a primary care practitioner in the preceding 12 months (Table 12).

Table 12. Socioeconomic gradients in screening rates

Deprivation quintile	Next registration scenario	Next consultation scenario
IMD1 (most deprived)	9.4%	76.4%
IMD2	12.6%	74.1%
IMD3	12.8%	74.7%
IMD4	11.2%	72.4%
IMD5 (least deprived)	11.1%	72.9%

Gradient in screen positive rates

Screening tools such as AUDIT typically include a series of questions asking about drinking levels, as well as questions about whether the individual has suffered negative consequences from their drinking. Whilst gradients in drinking levels are already captured in the model as described above, there may be additional gradients in the likelihood of screening positive, arising from additional gradients in experiencing negative consequences. We, therefore, fitted a logistic regression to estimate the likelihood of screening positive for an individual, conditional on their mean consumption, age, sex and IMD quintile using data from the Alcohol Toolkit Study (38). The coefficients from this regression are shown in Table 13.

Table 13. Output from screening outcome regression model

Variable		Odds Ratio	Standard Error
Constant		0.1226***	0.0055
Age group	16-24	Ref	
	25-34	0.4944***	0.0216
	35-54	0.2655***	0.0105
	55+	0.0750***	0.0035
Sex	Male	Ref	
	Female	0.7267***	0.0215
Mean consumption (units/week)		1.2463***	0.0029
IMD	IMD5 (least deprived)	Ref	
	IMD4	1.1851***	0.0436
	IMD3	1.2540***	0.0556
	IMD2	1.2730***	0.0668
	IMD1 (most deprived)	1.7310***	0.1120
*p<0.05, **p<0.01, ***p<0.001			

5.2.3 Additional gradients not considered

Several important gradients which are incorporated into the smoking cessation model are not considered explicitly within this application of SAPM.

Gradient in intervention effectiveness

Unlike many other public health interventions, several studies have found no evidence of a socioeconomic gradient in the effectiveness of alcohol Brief Interventions (39, 40), although this is largely due to a lack of primary studies exploring this area. In the absence of clear evidence of such a gradient, we therefore assume an equal relative effect for all individuals receiving a brief intervention of an 8.2% reduction in mean alcohol consumption, in line with the findings of the latest Cochrane review.

Gradient in health-related quality of life

As described previously, health outcomes in SAPM are essentially modelled as a 47-state Markov model, with separate states for each of the 45 alcohol-related health conditions included in the model, death, and the remainder of the population. For each of these states, health state utilities are taken from previously published research using the Health Outcomes Data Repository (41). Separate utilities for each condition have been estimated for each age-sex subgroup in the model, giving a total of 47x8=376 different utility values. It was not possible to further stratify these values by socioeconomic status, although population-level gradients in HRQoL are incorporated into the model, to some extent, through differing prevalences of the various health conditions across socioeconomic groups.

Gradient in healthcare costs

Similarly to utility values, healthcare costs are taken from previously published estimates and are calculated separated for each health condition and by age (41). It was not possible to disaggregate these costs further, although an overall socioeconomic gradient in costs is incorporated in the model through variations in disease prevalence across socioeconomic groups.

5.2.4 Summary of model inputs

As for the smoking model, the model inputs described above can be characterised as either exogenous or endogenous to the intervention (Table 14). Concentration indices of model inputs are also summarised in Table 14 and presented in Figure 9. Baseline QALE, drinking prevalence and

mean and peak consumption among drinkers have positive concentration indices, showing higher values in the less deprived groups, while the others have negative concentration indices, suggesting higher values in the more deprived ones. The greatest dispersion is in health opportunity costs, which are greater among the more deprived. In the potentially modifiable inputs, the screening rate has a low level of concentration in both scenarios, while the likelihood of an individual screening positive is more concentrated in more deprived groups.

Table 14. Category and concentration index of model inputs incorporating socioeconomic variation

Category:	Gradient in:		Concentration index
Non-modifiable	Baseline QALE		0.03
	Health opportunity costs		-0.12
	Drinking prevalence		0.06
	Mean consumption		0.03
	Peak day consumption		0.06
	Alcohol-attributable mortality		-0.07
	Alcohol-attributable morbidity		-0.05
	Probability of screening positive		-0.01
Potentially modifiable	Population screened	Next Registration	-0.01
		Next Consultation	-0.10
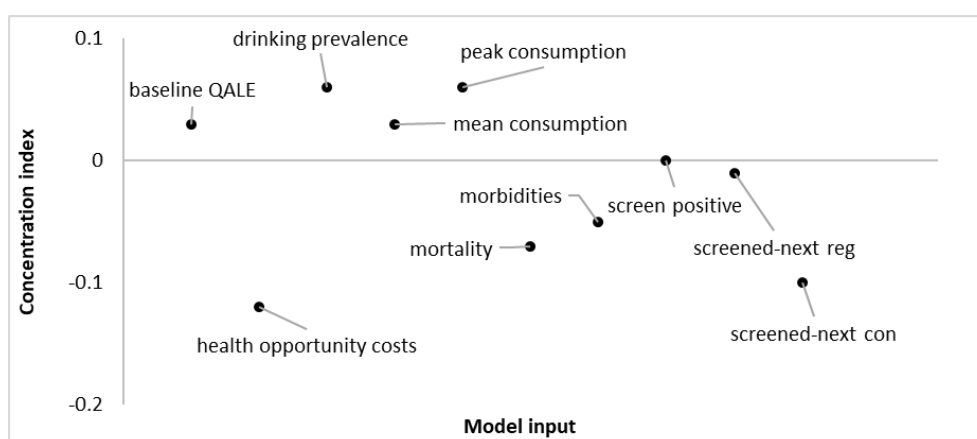
Figure 9. Concentration index of model inputs

5.2.5   *Socioeconomic variation at Local Authority level*

We explore the generalisability of our results across contexts, by utilising specific Local Authority-level adaptations of SAPM which have been developed as part of an NIHR-funded project (42). In order to maximise the potential variation in results, we have selected two Local Authorities, **Liverpool** and **Trafford**, which have very different population structures, as illustrated in Figure 10.
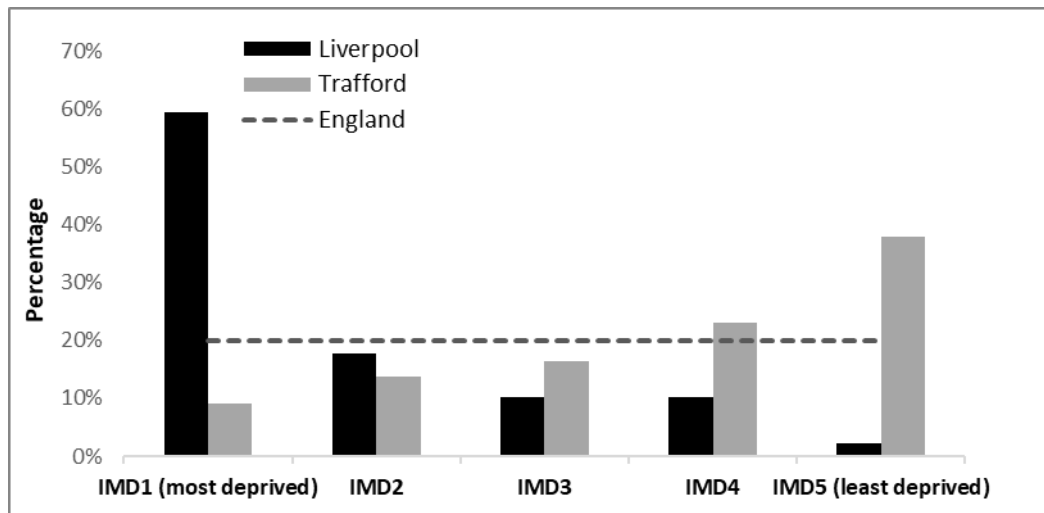
Figure 10. Population structure for modelled Local Authorities

These Local Authority-level models include detailed estimates of the local levels and patterns of alcohol consumption and how this is distributed across the population, as well as data on local prevalence of and mortality from alcohol-related disease. Unlike the smoking model, this variation in baseline harm rates are based on data taken directly from each of the Local Authorities and, therefore, the baseline mortality and prevalence rates are able to vary from the national rates within each IMD quintile. The differences in these gradients are illustrated in Figure 11 below.
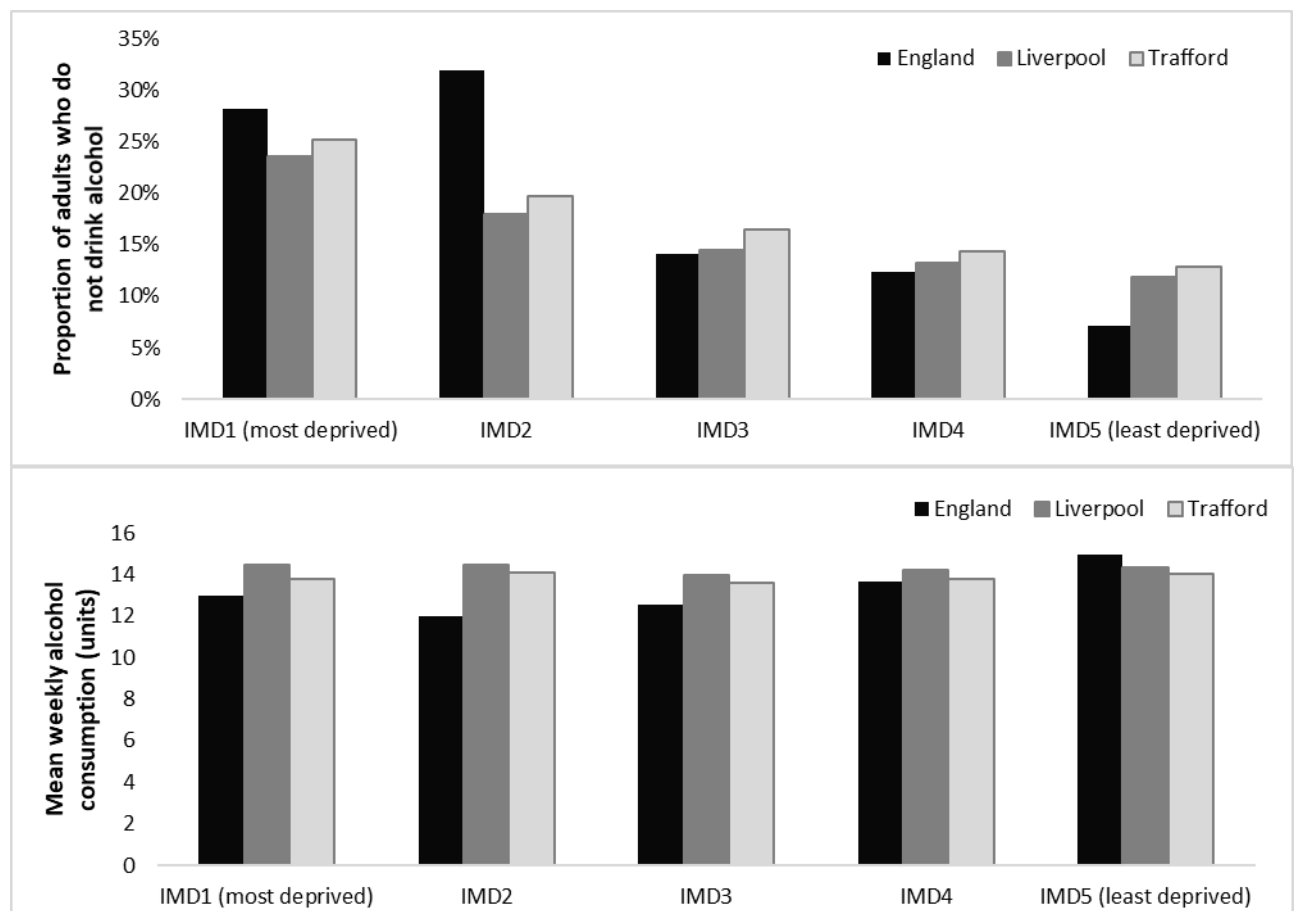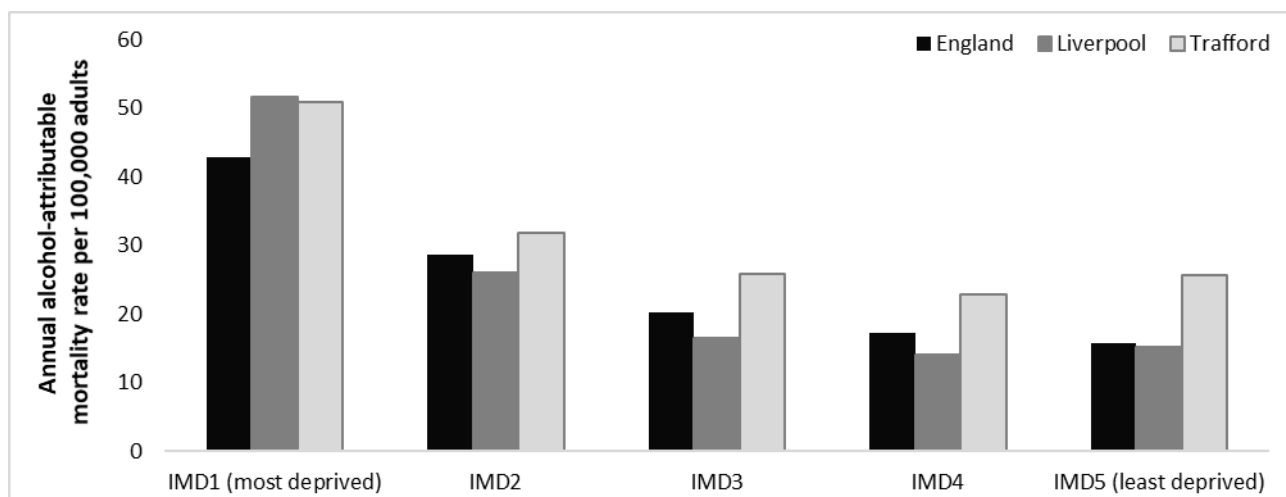
Figure 11. Variation in socioeconomic gradients in model inputs for England, Liverpool and Trafford

5.3   Analysis

5.3.1   Base-case analysis

As with the smoking model, we only model intervention delivery among adults (aged 18+) and, therefore, the population size shown in Table 10 is used. The model estimates the costs of intervention delivery and the cumulative discounted incremental NHS cost savings, as well as QALYs over a 20-year period after one year of intervention delivery. The incremental NHB, incremental EDE, and difference between incremental EDE and incremental NHB are then calculated for all the pairwise comparisons.

5.3.2   Scenario analysis

Scenario analyses are performed to explore the impact of the various socioeconomic gradients described in Section 5.2 on model results.
(a) The impact of ignoring all these gradients is explored by setting the model inputs in all groups to the average value within each age-sex group.
(b) The impact of ignoring each of the following gradients within the model is examined in turn:
- Abstention
- Mean consumption
- Peak day consumption
- Whether individuals are screened
- The likelihood of screening positive
- Baseline disease prevalence rates
- Baseline mortality rates
- Health opportunity cost

For each of these analyses, the levels of the input are set at the average within each age-sex group, except for the health opportunity cost, which is assumed to be equal across all IMD quintiles.
(c) An additional analysis, in which we take the potentially modifiable gradient in who within the population is screened and 'level this up', firstly to the maximum delivery level within each age-sex group, and secondly to the population maximum delivery level.

6.   Comparison of models

Both models consider the gradients in baseline QALE, opportunity costs distribution, prevalence, mortality, comorbidities and intervention impact. Due to the different behaviours affected by the intervention (i.e. smoking and drinking), the set of comorbid health conditions included varies substantially between models. There are also major differences in the structure of the models. The smoking model uses a Markov structure to model adult smokers (18-75 years) through their life, with the model stratified by smoking status (smoker/non-smoker/former smoker) and IMD quintiles. In contrast, the alcohol model uses a hybrid individual-level simulation/cohort Markov model to model post-intervention levels of alcohol consumption and harm, with the model stratified throughout by age, sex, drinking level and IMD quintile. This additional complexity in the alcohol model means that there is substantially more scope for non-linearity between model inputs and outcomes, particularly since the relationships between alcohol consumption, which is modelled as a continuous variable, and harm outcomes are predominantly non-linear in nature.

There are also important differences in the way the models incorporate socioeconomic differences which warrant further discussion. First, the gradient in prevalence is defined using proportion of smokers across IMD quintiles in the smoking model, while the alcohol model incorporates gradients in drinking rate, mean consumption, and peak day drinking. Second, the gradient in intervention impact is incorporated using the odds of successful quit attempt and intervention uptake rates in the smoking model, while in the alcohol model, access to the intervention consists of two steps. The model comprises an initial step where individuals attending primary care are selected to be screened, and a second step where those individuals are screened with only those identified as drinking at potentially risky levels receiving an intervention, so gradients in both steps are incorporated. The summary of concentration indices for the model inputs incorporating socioeconomic differences in both models is presented in Figure 12. Negative concentration indices demonstrate higher levels of the input in more deprived groups, while positive indices demonstrate higher levels in less deprived groups. This illustrates that the smoking prevalence is higher in more deprived groups, while all three dimensions of alcohol consumption are higher in less deprived groups. The concentration indices for the smoking cessation intervention impact (effectiveness and uptake) show higher levels in less deprived groups, while those for alcohol interventions show the opposite. In this comparison between two models, we focus on the concentration index of the model input, but note that the actual gradient can vary in shape, even when the concentration indices are similar in magnitude, as the gradients for the majority of inputs in both models are non-linear.

In terms of modelling the Local Authority level results, both models consider local information on prevalence and population distribution, while most of the remaining gradients are still based on those for England, and therefore the heterogeneity may not be well reflected. For example, socioeconomic pattern in utilisation of the interventions may vary between Local Authorities. The alcohol model also considers the degree of alcohol consumption and mortality from alcohol-related disease at Local Authorities level, which may provide more information on the difference in intervention impact at local level.
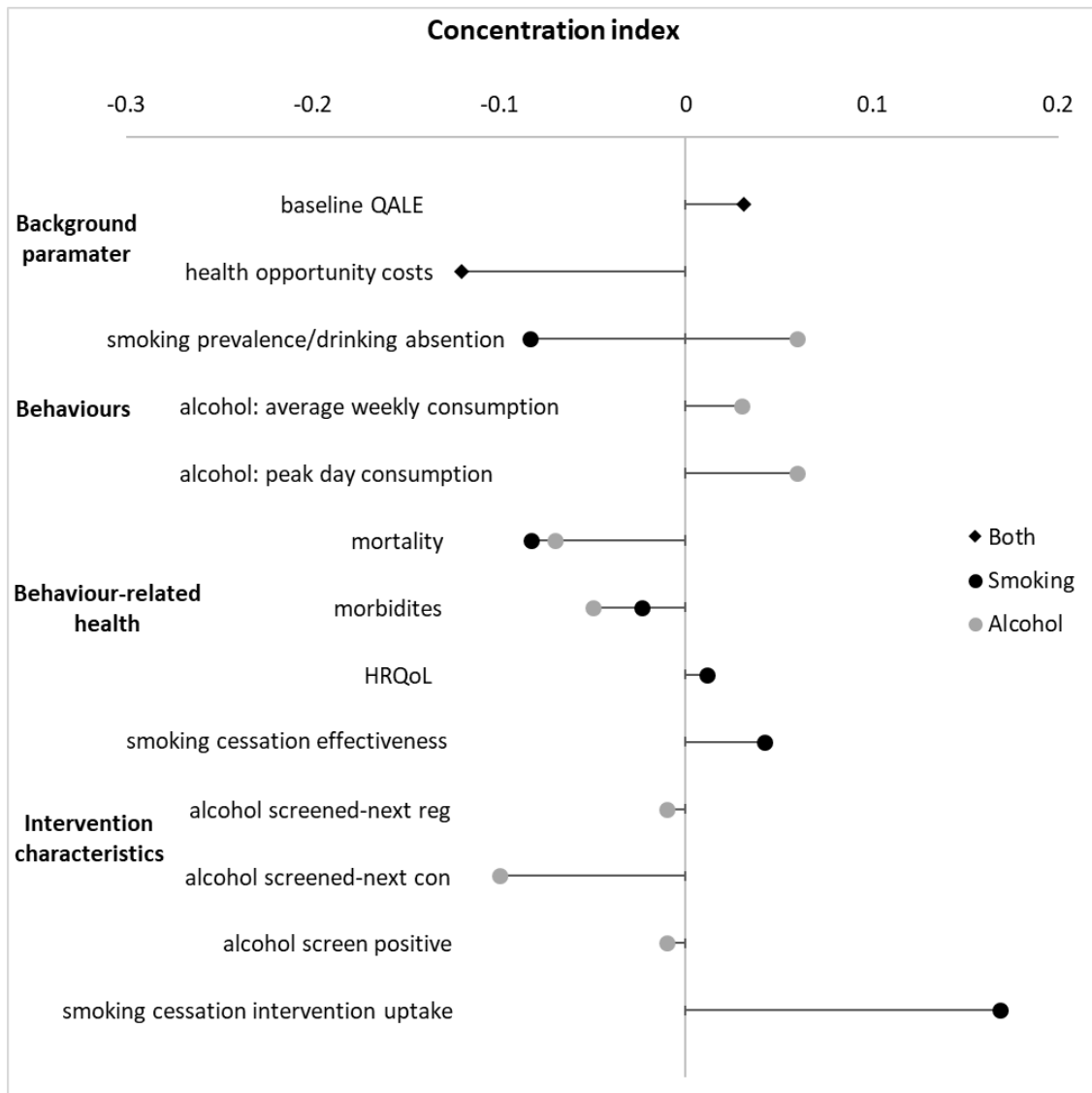
Figure 12. Concentration index of model inputs in both models

7. Findings: smoking cessation model

7.1 Base-case analysis

The base-case results are presented in Table 15. Compared to 'no intervention', both interventions improve NHB (Varenicline: 123,749 QALYs; e-cigarette: 80,782 QALYs) and EDE (Varenicline: 106,553 QALYs; e-cigarette: 70,002 QALYs), but increase health inequality (negative difference between incremental EDE and incremental NHB). The impact on overall health and health inequality impact are plotted in Figure 13. Compared to 'no intervention', both interventions lie in the north-west quadrant of the plane, indicating that they increase population health but increase inequality. Compared to e-cigarette, Varenicline improves NHB and EDE, but increases inequality (Table 15) and results are plotted in Figure S1.

Table 15. Estimates of incremental NHB and incremental EDE in base-case analysis

	iNHB	iEDE	Inequality (iEDE-iNHB)
Varenicline vs 'no intervention'	123,749	106,553	-17,196
e-cigarette vs 'no intervention'	80,782	70,002	-10,780
Varenicline vs e-cigarette	42,968	36,551	-6,417
NHB net health benefit; EDE equally distributed equivalent health			
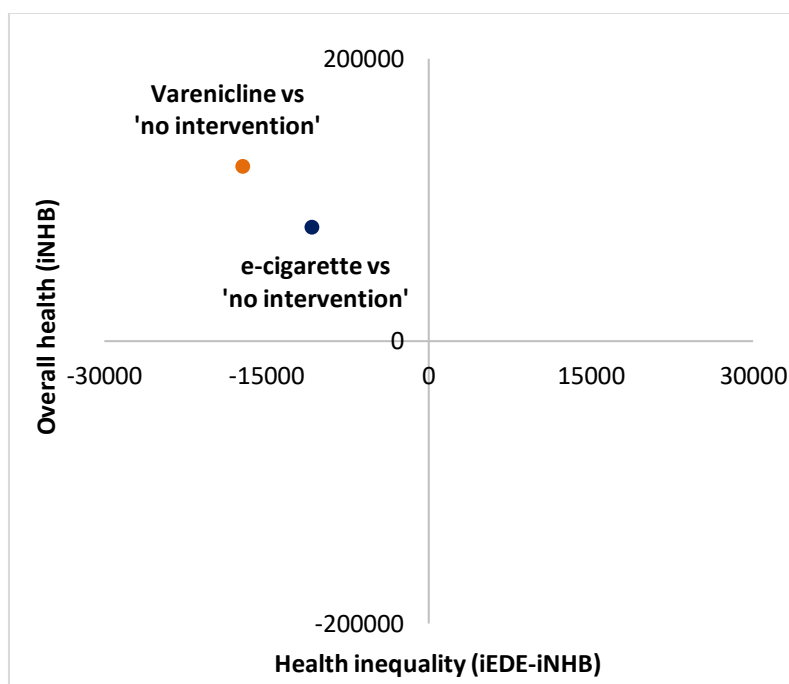
Figure 13. Equity impact plane showing the overall health and health inequality

7.2 Scenario analysis

The results of scenario analyses for Varenicline compared to 'no intervention' are summarised in Table 16 and plotted in Figure 14 and Figure 15. Results for the other two comparisons are presented in Table S2-S3 and Figure S2-S3.

Ignoring all gradients
Ignoring all gradients has little impact on the overall health (-0.21%) but increases EDE health by 15.89%. There is no effect on inequality when all gradients are ignored.

Ignoring one gradient

Ignoring the gradients (separately or jointly) does not appear to have a great impact on overall health (Figure 14). Ignoring gradients in baseline QALE and opportunity costs has little effect on estimated impact on overall health (Table 16). Ignoring gradients in smoking prevalence and comorbidities slightly increases the estimated intervention impact on overall health by 7,506 QALYs (6.07%) and 2,563 QALYs (2.07%), while ignoring gradients in effectiveness, mortality, uptake and HRQoL results in modest reductions in estimated overall health impact by 5,280 QALYs (-4.27%), 1,929 QALYs (-1.56%), 492 QALYs (-0.40%) and 239 QALYs (-0.19%) (Table 16).

Ignoring one individual gradient appears to affect the estimated impact on health inequality (Figure 14). Ignoring the gradient in opportunity costs increases the amount by which the interventions are estimated to increase inequality, as does ignoring gradients in smoking prevalence and risk of comorbidities. Ignoring gradients in baseline QALE, mortality risks, HRQoL, effectiveness and uptake reduces the amount by which the interventions are estimated to increase inequality, with removal of the gradient in uptake making Varenicline inequality reducing, compared to 'no intervention'.

The same pattern is observed for the comparisons between e-cigarette and 'no intervention' and between the two interventions (Figure S2). Ignoring the gradient in uptake suggests Varenicline reduces health inequality more than e-cigarette (Table S3 & Figure S2).

Levelling up to the best

Levelling up the effectiveness to that of the group with the maximum effect increases the estimated gain in overall health and EDE health (Table 16); it reduces the amount by which the intervention is estimated to increase health inequality (Figure 15). Similarly, levelling up the uptake rate increases the estimated gain in overall health and EDE health (Table 16); it alters the health inequality impact substantially to make Varenicline inequality reducing compared to 'no intervention' (Figure 15).

Similar results were obtained for the comparisons between e-cigarette and 'no intervention' and between the two interventions (Figure S3).

Table 16. Estimates of incremental NHB and incremental EDE in base-case and scenario analysis

|	iNHB	Change in iNHB from base-case	iEDE	Change in iEDE from base-case	Inequality (iEDE-iNHB)	Change in the impact on inequality compared to base-case
Varenicline vs 'no intervention'						
Base-case	123,749	-	106,553	-	-17,196	Increase inequality
(a) Ignoring all gradients	123,489	-260 (-0.21%)	123,489	16,936 (+15.89%)	0	No effect
(b) Ignoring gradient in:						
Baseline QALE	123,749	0 (0%)	123,747	17,194 (+16.14%)	-2	Smaller increase
Health opportunity costs	123,749	0 (0%)	105,432	-1,121 (-1.05%)	-18,318	Larger increase
Smoking prevalence	131,255	7,506 (+6.07%)	105,444	-1,109 (-1.04%)	-25,811	Larger increase
Mortality	121,820	-1,929 (-1.56%)	106,991	438 (+0.41%)	-14,829	Smaller increase
Comorbidities	126,312	2,563 (+2.07%)	107,883	1,330 (+1.25%)	-18,429	Larger increase
HRQoL	123,511	-239 (-0.19%)	106,637	84 (+0.08%)	-16,874	Smaller increase
Effectiveness	118,470	-5,280 (-4.27%)	106,463	-89 (-0.08%)	-12,006	Smaller increase
Uptake	123,258	-492 (-0.40%)	124,781	18,228 (+17.11%)	1,523	Inequality-reducing
(c) Levelling up to the best in:						
Effectiveness	134,837	11,088 (+8.96%)	121,333	14,780 (+13.87%)	-13,504	Smaller increase
Uptake	168,033	44,284 (+35.79%)	170,110	63,557 (+59.65%)	2,076	Inequality-reducing
NHB net health benefit; EDE equally distributed equivalent health						
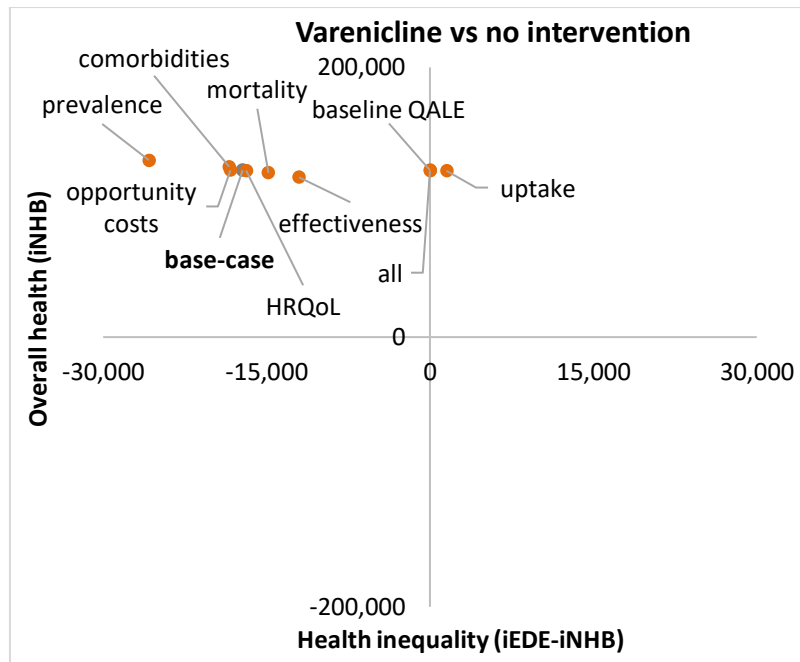
Figure 14. Equity impact plane showing scenario analysis results where gradients are ignored
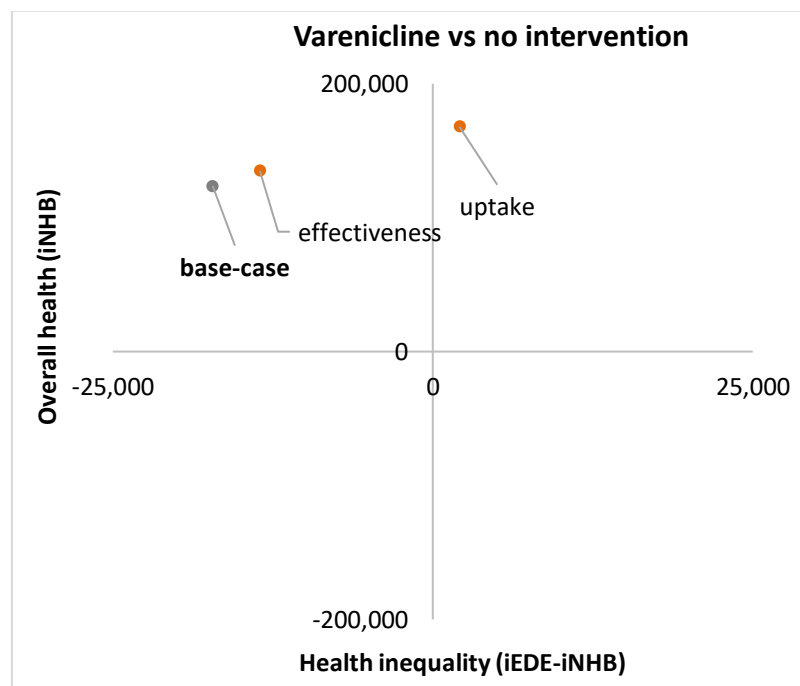

Figure 15. Equity impact plane showing scenario analysis results where levelling up to the best

7.3   Probabilistic sensitivity analysis

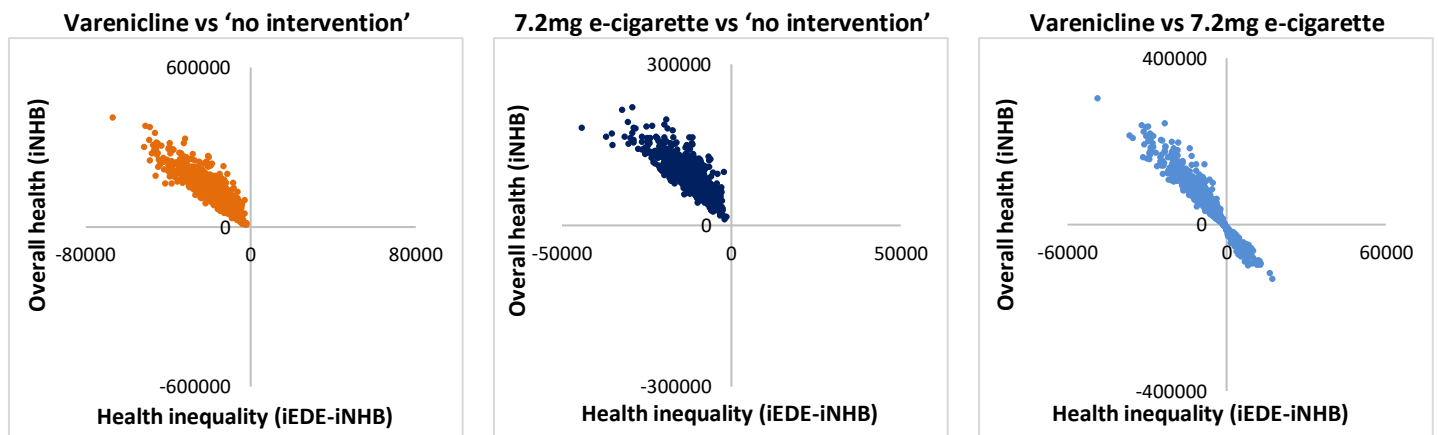The scatter plots on the equity plan are shown in Figure 16.

Figure 16. Scatter plots on equity impact plane

For both interventions compared to 'no intervention', the probability of positive iNHB and the probability of positive iEDE are both 100%, while the probability of iEDE greater than i NHB is 0%. This suggests that there is no uncertainty around the result that both interventions improve population health and increase inequality, relative to 'no intervention'. When comparing the two active interventions (Varenicline vs e-cigarette), the probability of Varenicline having greater NHB than e-cigarette is 74.90%, and the probability of Varenicline having greater EDE compared to e-cigarette is 74.20%, and the probability that Varenicline reduces health inequality compared to e-cigarette is 19.80% (Table 17).

Table 17. Probability of improving overall health and reducing health inequality

	Probability of:		
	iNHB>0	iEDE>0	iEDE>iNHB
Varenicline vs 'no intervention'	100.00%	100.00%	0.00%
e-cigarette vs 'no intervention'	100.00%	100.00%	0.00%
Varenicline vs e-cigarette	74.90%	74.20%	19.80%

The results of the value of information analysis for the comparison between Varenicline and e-cigarette are presented in Figure 17. The EVPI per person is estimated to be £142,617,861 for the decision about improvement in overall health, and £94,657,996 for the decision about reduction in health inequality (Table S4). Results show that, for the decision about improvement in overall health, improvement in social welfare and reduction in health inequality, the uncertainty is mostly determined by uncertainty in the quit rate of Varenicline, followed by uncertainty in the quit rate of e-cigarette. None of the other uncertain gradients appear to contribute to the decision uncertainty for the comparison between the two active interventions. The value of further research into each input is shown by the EVPPI estimates in Table S4.

The results from the ANCOVA are similar to those from the VOI analysis, with quit rates contributing the most to the variation in the incremental difference in outcomes between the two interventions (Figure 17). For the pairwise comparisons between each intervention and 'no intervention', the variation in iNHB and iEDE is mainly explained by the variation in the quit rate of the intervention and its effectiveness; the variation in health inequality is also explained by these, and by variation in uptake (Figure S4).

Varenicline vs e-cigarette
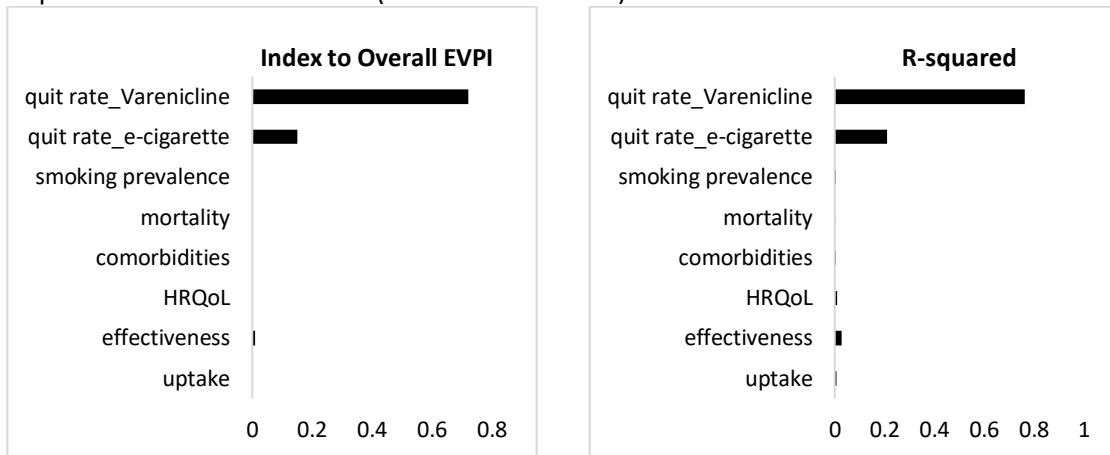
Improvement in overall health (incremental NHB>0)

Improvement in social welfare (incremental EDE>0)
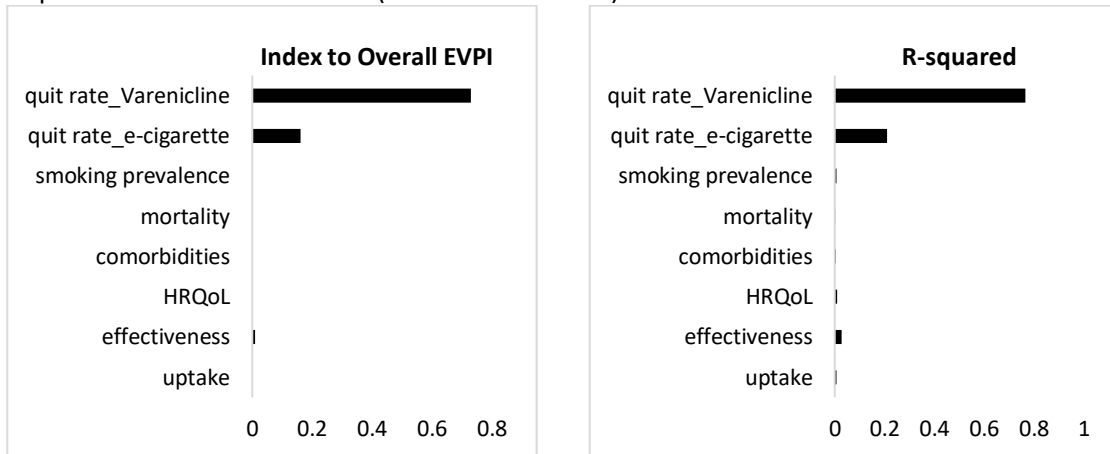
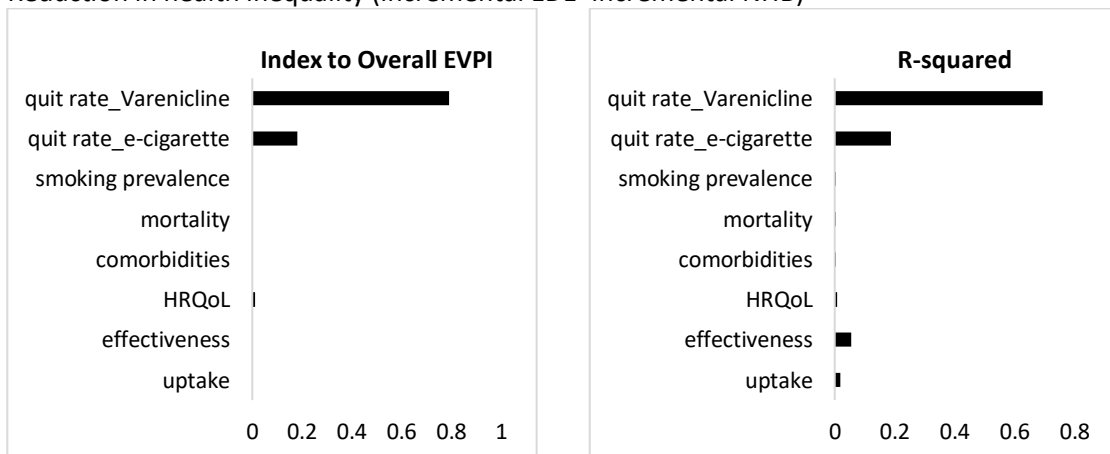Reduction in health inequality (incremental EDE>incremental NHB)

Figure 17. Value of information analysis results using SAVI and ANCOVA

7.4   Local Authority level results

The base-case results for York and Sheffield are presented in Table 18, Figure 18 (intervention vs 'no intervention') and Figure S5 (Varenicline vs e-cigarette). Sheffield has a much larger population than York (547,000 versus 207,000), but the relative difference in the intervention impacts by local area exceeds the relative difference in population size. Compared to 'no intervention', both interventions are estimated to increase overall health and EDE health. However, the estimated impact on health inequality differs by area, with smaller impacts in York, and e-cigarette estimated to reduce health inequality for York but not for Sheffield.

Table 18. Estimates of incremental NHB and incremental EDE in base-case analysis

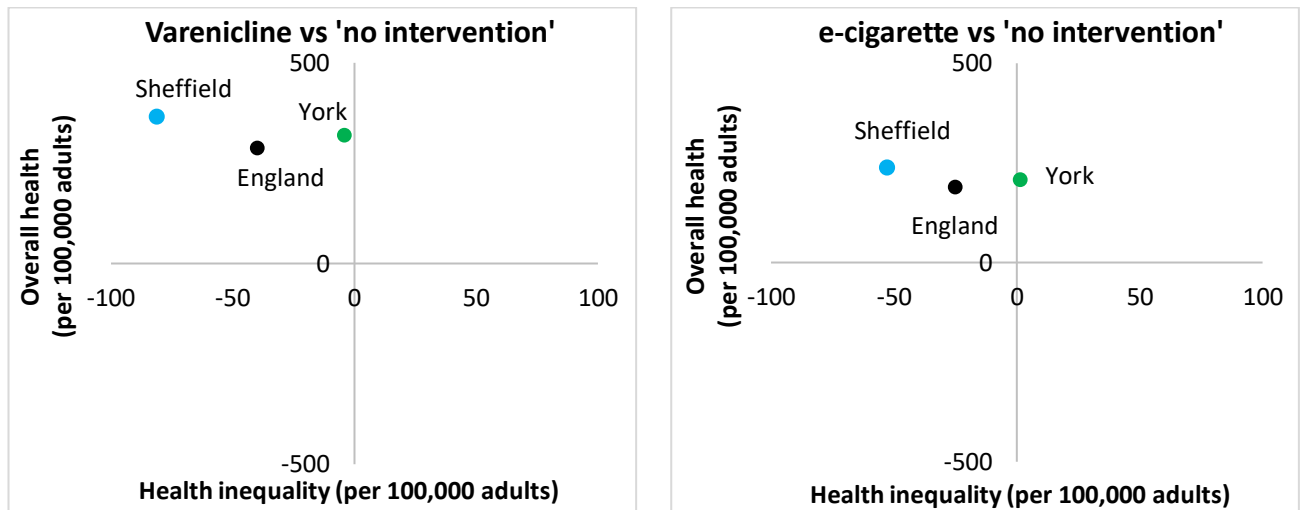|	York			Sheffield		
	iNHB (QALYs)	iEDE (QALYs)	Inequality (iEDE-iNHB)	iNHB (QALYs)	iEDE (QALYs)	Inequality (iEDE-iNHB)
Varenicline vs 'no intervention'	659	651	-9	2,092	1,625	-467
e-cigarette vs 'no intervention'	431	433	3	1,365	1,062	-303
Varenicline vs e-cigarette	229	217	-11	727	563	-164
NHB net health benefit; EDE equally distributed equivalent health						
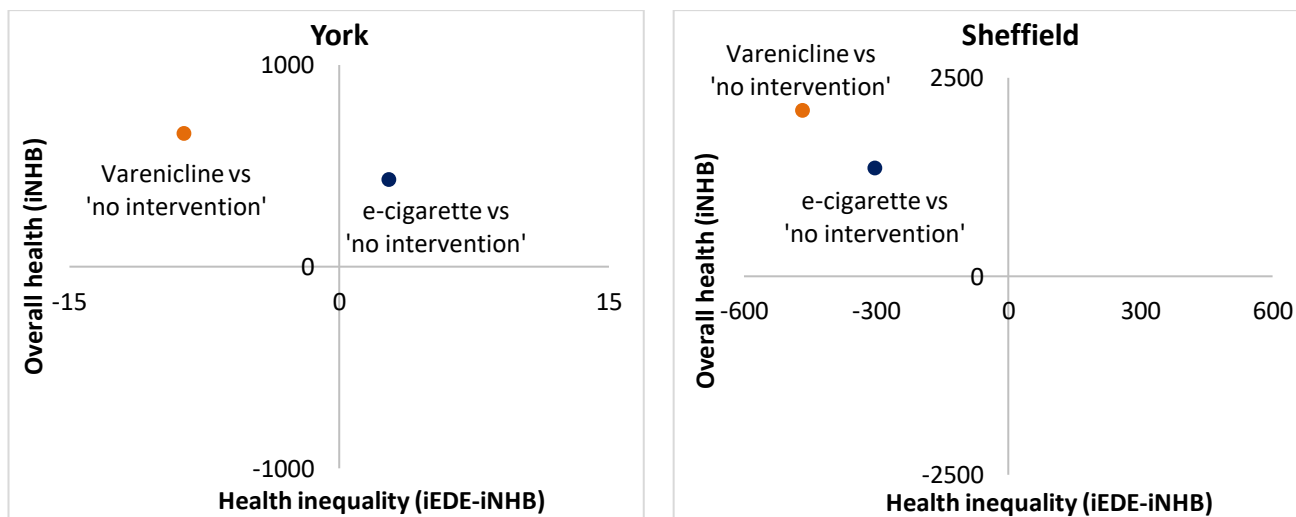
Figure 18. Equity impact plane showing the overall health and health inequality for Local Authority analysis

To present comparable results for England, York and Sheffield, we estimate the impacts on overall health and health inequality per 100,000 adults. The qualitative results for Varenicline are the same in all settings: in both York and Sheffield, Varenicline is estimated to increase overall health and increase inequality. The amount by which Varenicline is estimated to increase inequality is greatest in Sheffield, followed by England, and then York (Figure 19). The same pattern between local areas and England is observed for iNHB and iEDE health is observed for e-cigarette compared to 'no intervention', but the results suggest that the intervention could reduce inequality in York (Figure 19).

Figure 19. Equity impact plane showing the overall health and health inequality for Local Authority analysis

The detailed results of the scenario analysis are presented in Table S5 (York) and Table S6 (Sheffield). Compared to the results in England, ignoring all gradients affects both overall health and health inequality to a greater extent for Sheffield than for York (Table S5-S6).

Scenario analyses of ignoring the gradients (Varenicline vs 'no intervention') are plotted in Figure 20 (York) and Figure 21 (Sheffield). The direction of change in the estimated results of ignoring one gradient on overall health and health inequality is the same as that observed for England, but due to the different base-case results, the removal of a gradient in uptake or effectiveness makes the intervention inequality reducing, compared to 'no intervention' for York (Figure 20) but not so for Sheffield (Figure 21).
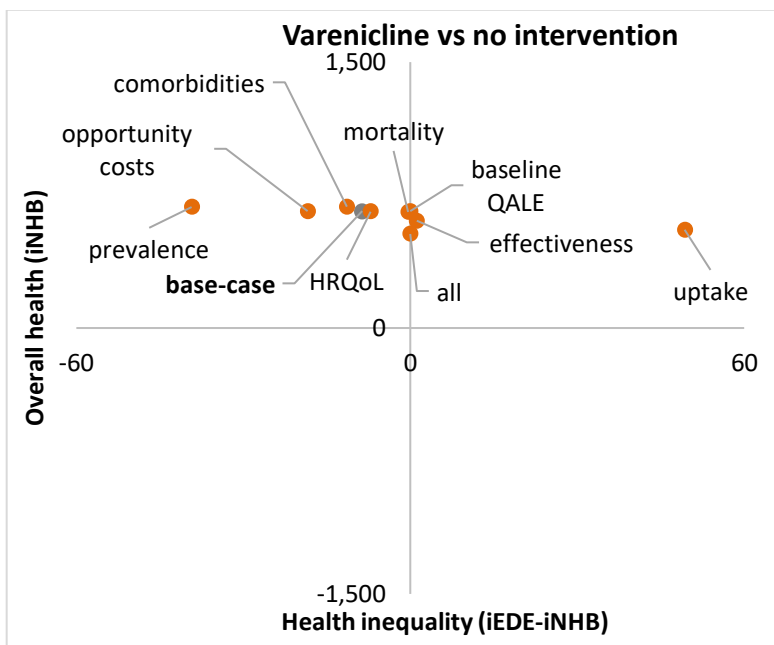
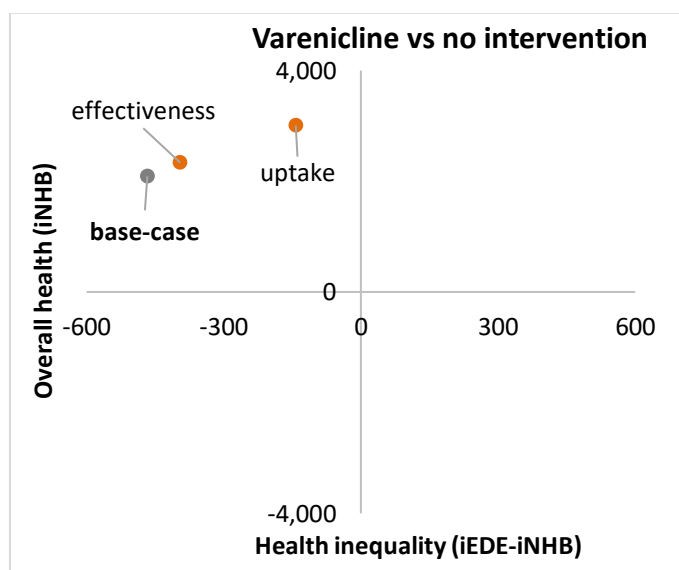**Figure 20. Equity impact plane showing scenario analysis results for York where gradients are ignored**
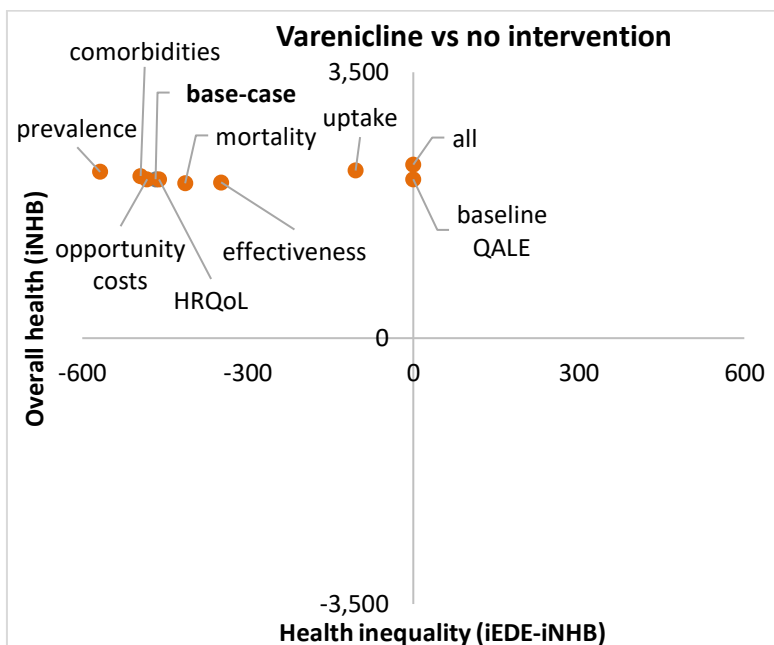
Figure 21. Equity impact plane showing scenario analysis results for Sheffield where gradients are ignored

The direction of change in the results from levelling up modifiable gradients compared to base-case follows the same direction in York and Sheffield as for England. However, due to the different base-case results, levelling up either effectiveness or uptake makes the intervention inequality reducing for York (Figure 22), but not for Sheffield (Figure 23).
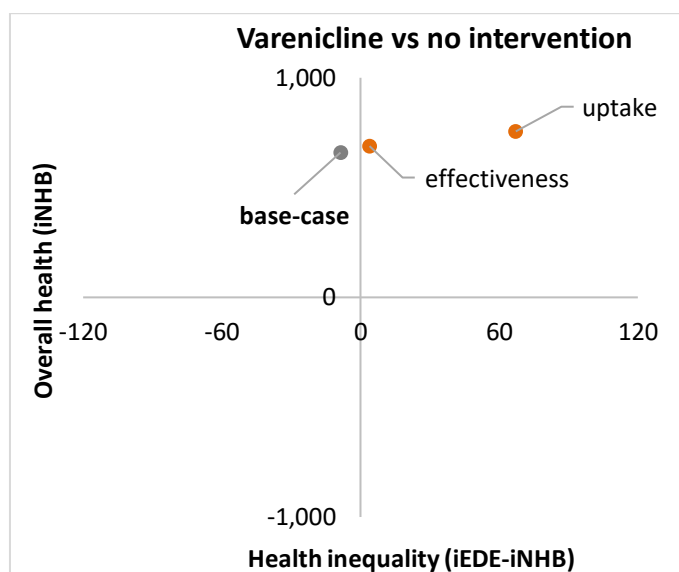
Figure 22. Equity impact plane showing scenario analysis results for York where levelling up to the best

Figure 23. Equity impact plane showing scenario analysis results for Sheffield where levelling up to the best

The same pattern of the change in the results of ignoring gradients and levelling up gradients is observed for York and Sheffield as for England in the comparisons between e-cigarette and 'no intervention' and between the two interventions (Table S5-S6 & Figure S6-S9).

Probabilistic sensitivity analysis results are shown in Table 19. In contrast with those for England, there is some uncertainty around the results the intervention increases health inequality compared to 'no intervention' (Varenicline: 37.2% and e-cigarette: 55.4%) for York, but not so for Sheffield. Similarly, there is uncertainty around the comparison between the two active interventions at Local Authority level (Table 19). The scatter plots on the equity plan are shown in Figure 24 (York) and Figure 25 (Sheffield).

Table 19. Probability of improving overall health and reducing health inequality at Local Authorities

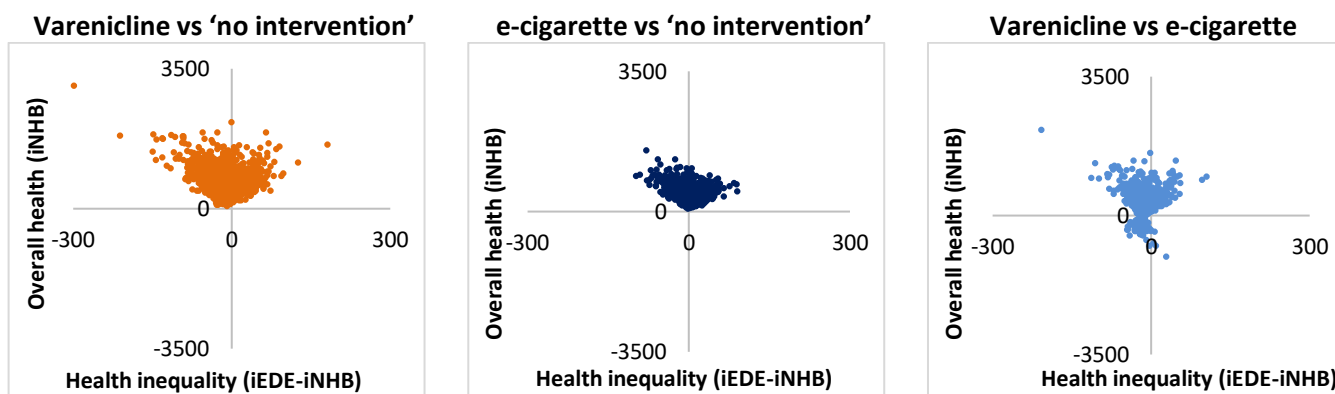|	York			Sheffield		
	Probability of:			Probability of:		
	iNHB>0	iEDE>0	iEDE>iNHB	iNHB>0	iEDE>0	iEDE>iNHB
Varenicline vs 'no intervention'	100.00%	100.00%	37.20%	100.00%	100.00%	0.00%
e-cigarette vs 'no intervention'	100.00%	100.00%	55.40%	100.00%	100.00%	0.00%
Varenicline vs e-cigarette	76.50%	74.80%	18.00%	75.20%	74.70%	22.60%
NHB net health benefit; EDE equally distributed equivalent health						

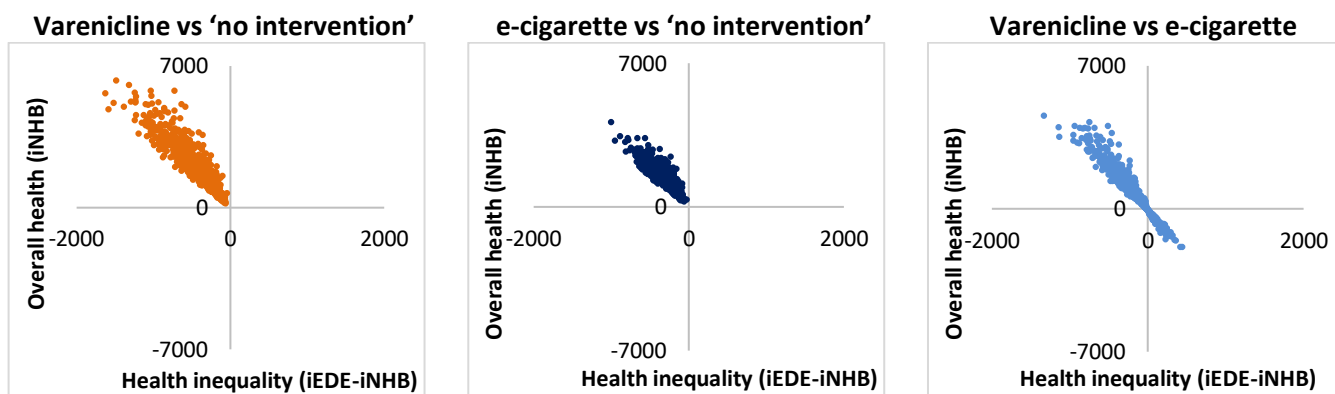**Figure 24.** Scatter plots on equity impact plane for York

**Figure 25.** Scatter plots on equity impact plane for Sheffield

Results of the value of information analysis are presented in Figure 26 (York) and Figure 27 (Sheffield). At Local Authority level, the results of the comparison between Varenicline and e-cigarette are consistent with that observed for England, with the exception that the decision uncertainty about reduction in health inequality is mainly driven by smoking prevalence and effectiveness for York (Figure 26). For York, VOI analysis is also conducted for the uncertainty around the results of reducing inequality when comparing the intervention (Varenicline or e-cigarette) and 'no intervention'. It is mostly determined by uncertainty in smoking prevalence, effectiveness and uptake. Overall EVPI and EVPPI estimates for uncertainty in iNHB and iEDE are available in Table S7 (York) and Table S8 (Sheffield). ANCOVA shows similar results to the VOI analysis.

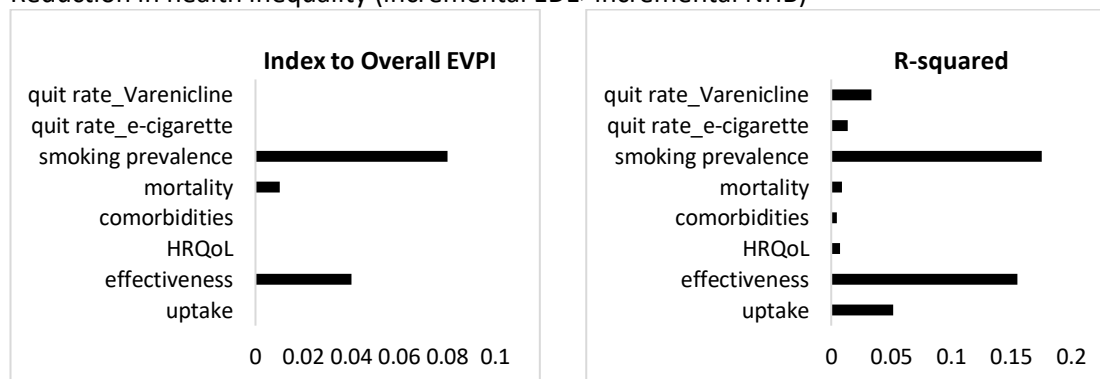**Varenicline vs e-cigarette**
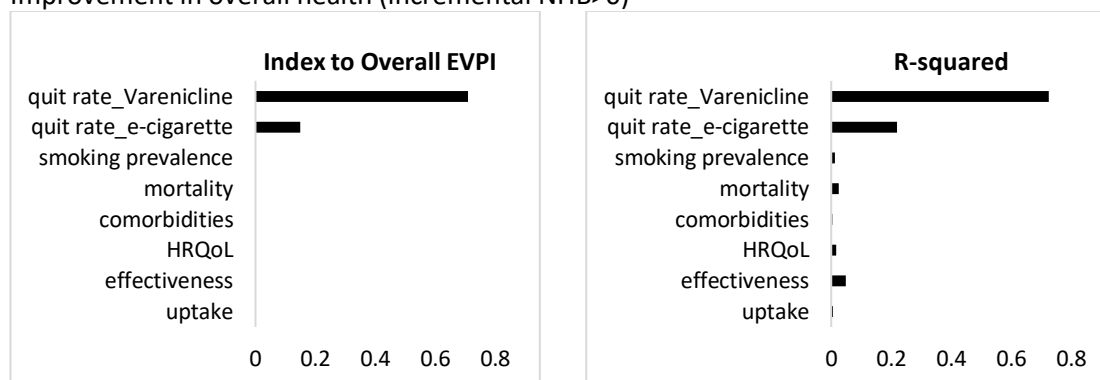
Improvement in overall health (incremental NHB>0)

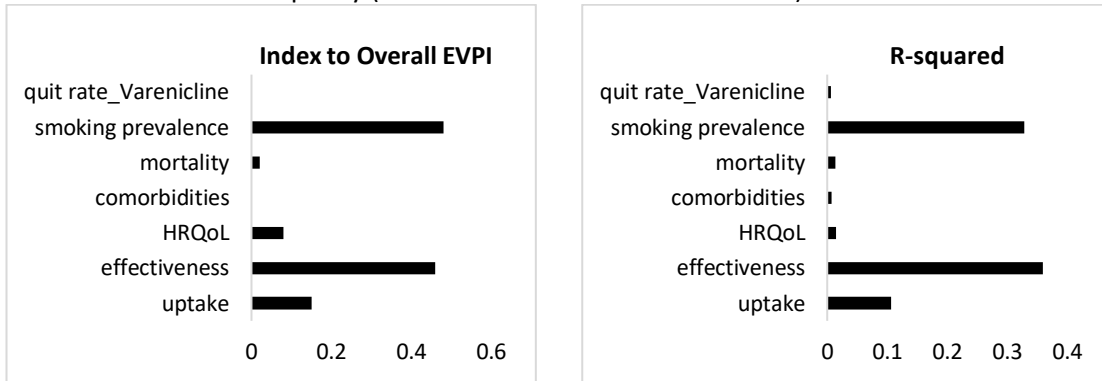Improvement in social welfare (incremental EDE>0)
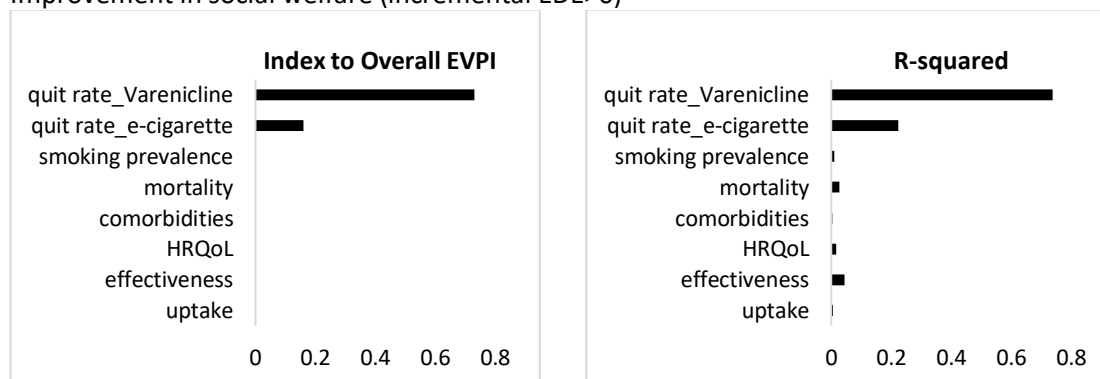
Reduction in health inequality (incremental EDE>incremental NHB)

Varenicline vs 'no intervention'

Reduction in health inequality (incremental EDE>incremental NHB)

e-cigarette vs 'no intervention'

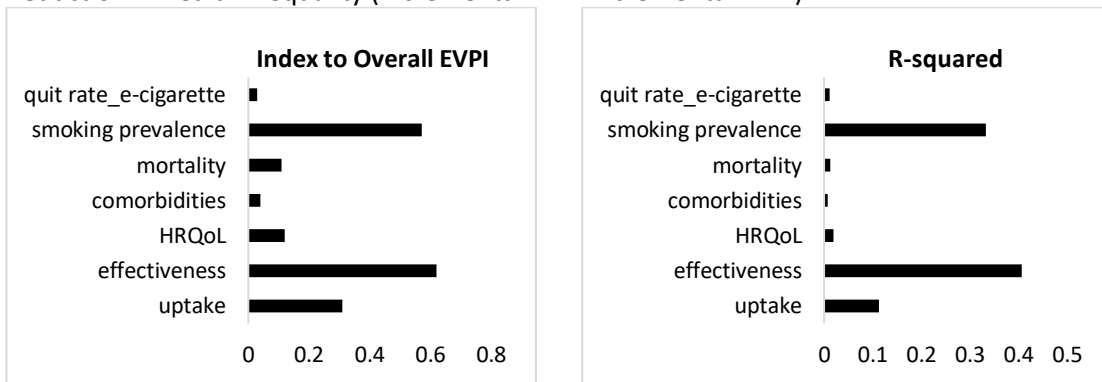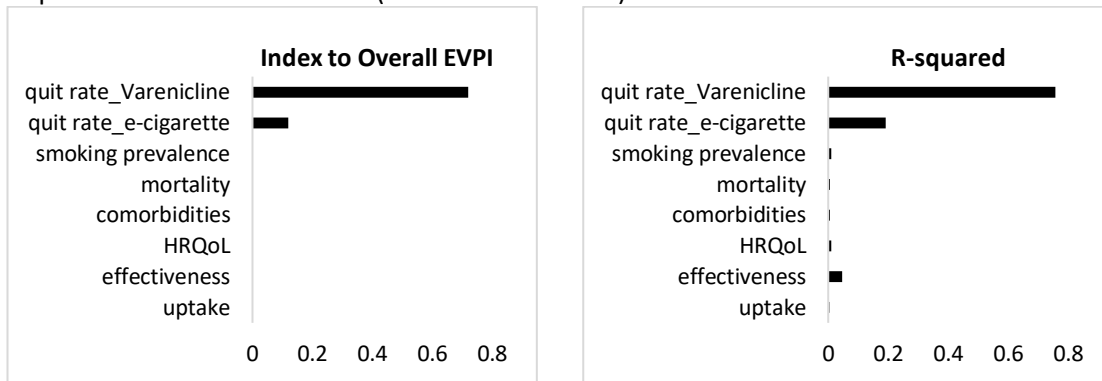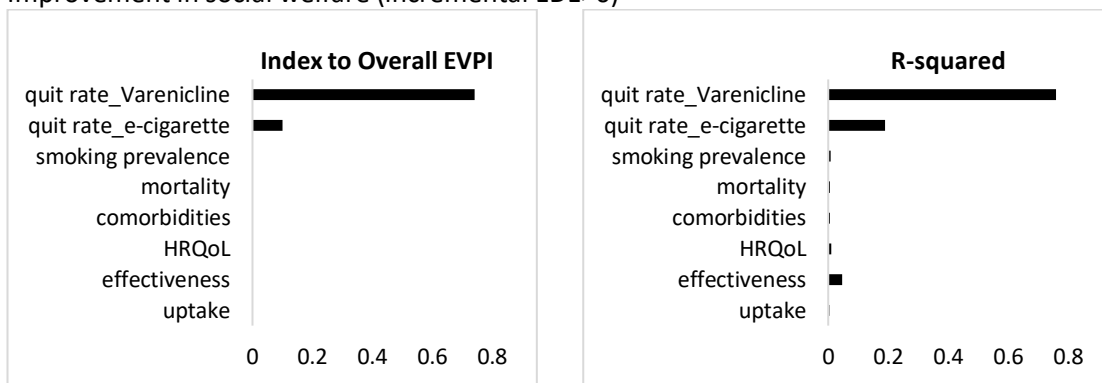Reduction in health inequality (incremental EDE>incremental NHB)

Figure 26. Value of information analysis results using SAVI and ANCOVA for York

Varenicline vs e-cigarette

Improvement in overall health (incremental NHB>0)

Improvement in social welfare (incremental EDE>0)

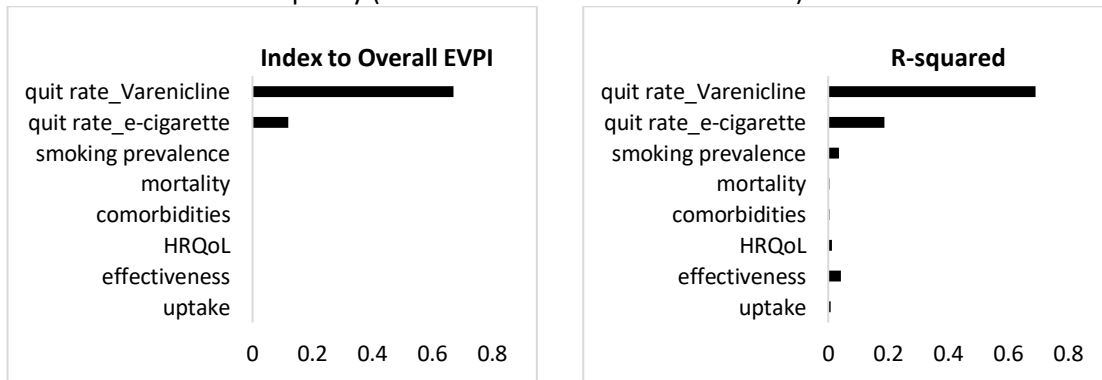Reduction in health inequality (incremental EDE>incremental NHB)

Figure 27. Value of information analysis results using SAVI and ANCOVA for Sheffield

8. Findings: alcohol brief interventions model

8.1   Base-case analysis

The main base-case results are presented in Table 20. For England, both interventions improve NHB (Next Reg: 4,336 QALYs, Next Con: 43,016 QALYs) and EDE (Next Reg: 4,780 QALYs, Next Con: 50,594 QALYs). The incremental NHB and EDE compared to 'no intervention' are plotted in Figure 28. Both interventions lie in the north-east quadrant of the plane, indicating that they increase population health and reduce inequality, although screening all individuals at their next GP consultation does both to a much greater extent.

Table 20. Estimates of NHB and EDE in base-case analysis

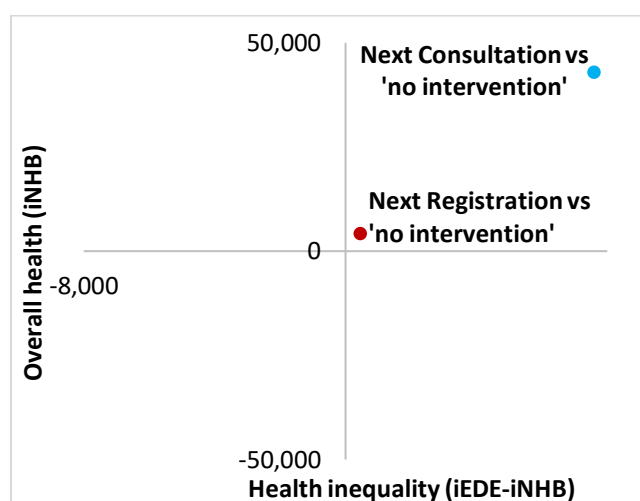|	iNHB	iEDE	Inequality (iEDE-iNHB)
Next Registration vs. 'no intervention'	4,336	4,780	444
Next Consultation vs. 'no intervention'	43,016	50,594	7,578
Next Consultation vs. Next Registration	38,680	45,814	7,134

Figure 28. Equity impact plane showing base-case impacts on health and health inequality

8.2   Scenario analysis

Results of the scenario analyses for the Next Registration and Next Consultation scenarios compared to 'no intervention' are summarised in Table 21-22 and plotted in Figure 29-30. Results for the incremental comparison between the two scenarios are shown in Table S9 and Figure S13-S14.

Ignoring all gradients

For the Next Registration scenario, ignoring all gradients in the model leads to a modest 6% reduction in the estimated NHB, but a substantial fall of 25% in the estimated EDE arising from the policy (Table 21). As a result, in this scenario the intervention is estimated to *increase* inequality overall, in contrast to the base-case finding of reduced inequality. Results for the Next Consultation scenario are broadly similar, with the inequality impact of the policy falling by 13% and the intervention estimated to increase rather than reduce inequality. The impact on the estimated NHB, however, runs in the opposite direction, seeing a 6% increase when all gradients are removed from the model (Table 21).

Ignoring one gradient

Under a Next Registration approach, ignoring gradients in mean consumption, peak consumption, screening coverage, likelihood of screening positive, and the health opportunity cost increases the estimated reduction in inequality arising from the intervention, while ignoring gradients in abstention, disease prevalence and mortality rates, reduces the impact on inequalities, with removal of the gradient in morbidity estimated to make the programme inequality-increasing overall compared to 'no intervention' (Figure 29). Removal of most gradients increases the estimated NHB, by up to 17.4% in the case of the gradient in mean consumption, although ignoring gradients in abstention gradients reduces the NHB by 9.0%.

For the Next Consultation scenario, the picture is broadly similar, with the exception that excluding the gradient on abstention increases the estimated reduction in inequality, rather than reducing it (Figure 29). Also, ignoring all gradients except (by definition) opportunity costs, increases the estimated NHB by up to 10.4% in the case of the gradient in peak consumption. Unlike the scenario where all gradients are ignored, the removal of any single gradient is not sufficient to change the overall conclusion that the intervention is health-improving and inequality-reducing.

Table 21. Estimates of NHB and EDE for scenario analyses

|	iNHB	Change in iNHB from base-case	iEDE	Change in iEDE from base-case	Inequality (iEDE-iNHB)	Change in the impact on inequality compared to base-case
Next Registration vs. 'no intervention'						
Base-case	4,336	-	4,780	-	444	**Reduces inequality**
(a) Ignoring all gradients	4,083	-253 (-5.83%)	3,580	-1199 (-25.08%)	-503	Increases inequality
(b) Ignoring gradient in:						
Baseline QALE	4,336	0 (0%)	4,336	-444 (-9.29%)	0	No effect
Health opportunity costs	4,336	0 (0%)	4,989	209 (+4.37%)	652	Larger reduction
Drinking prevalence	3,947	-389 (-8.97%)	4,125	-655 (-13.7%)	178	Smaller reduction
Mean consumption	5,092	756 (+17.44%)	6,253	1474 (+30.84%)	1,162	Larger reduction
Peak consumption	4,724	388 (+8.95%)	5,421	642 (+13.43%)	698	Larger reduction
Morbidity	4,856	519 (+11.97%)	4,645	-135 (-2.82%)	-211	Increases inequality
Mortality	4,530	194 (+4.47%)	4,565	-215 (-4.5%)	35	Smaller reduction
Screening coverage	4,493	157 (+3.62%)	5,492	713 (+14.92%)	999	Larger reduction
Screening positive	4,803	466 (+10.75%)	5,512	732 (+15.31%)	709	Larger reduction
Next Consultation vs. 'no intervention'						
Base-case	43,016	-	50,594	-	7,578	**Reduces inequality**
(a) Ignoring all gradients	45,730	2715 (+6.31%)	44,045	-6548 (-12.94%)	-1,685	Increases inequality
(b) Ignoring gradient in:						
Baseline QALE	43,016	0 (0%)	43,016	-7578 (-14.98%)	0	No effect
Health opportunity costs	43,016	0 (0%)	51,185	591 (+1.17%)	8,169	Larger reduction
Drinking prevalence	45,518	2502 (+5.82%)	56,586	5993 (+11.85%)	11,068	Larger reduction
Mean consumption	44,710	1694 (+3.94%)	54,590	3996 (+7.9%)	9,880	Larger reduction
Peak consumption	47,494	4478 (+10.41%)	58,383	7789 (+15.4%)	10,888	Larger reduction
Morbidity	45,172	2157 (+5.01%)	46,760	-3834 (-7.58%)	1,588	Smaller reduction
Mortality	44,169	1153 (+2.68%)	47,828	-2766 (-5.47%)	3,659	Smaller reduction
Screening coverage	45,824	2809 (+6.53%)	55,070	4476 (+8.85%)	9,245	Larger reduction
Screening positive	45,061	2045 (+4.75%)	55,537	4944 (+9.77%)	10,476	Larger reduction
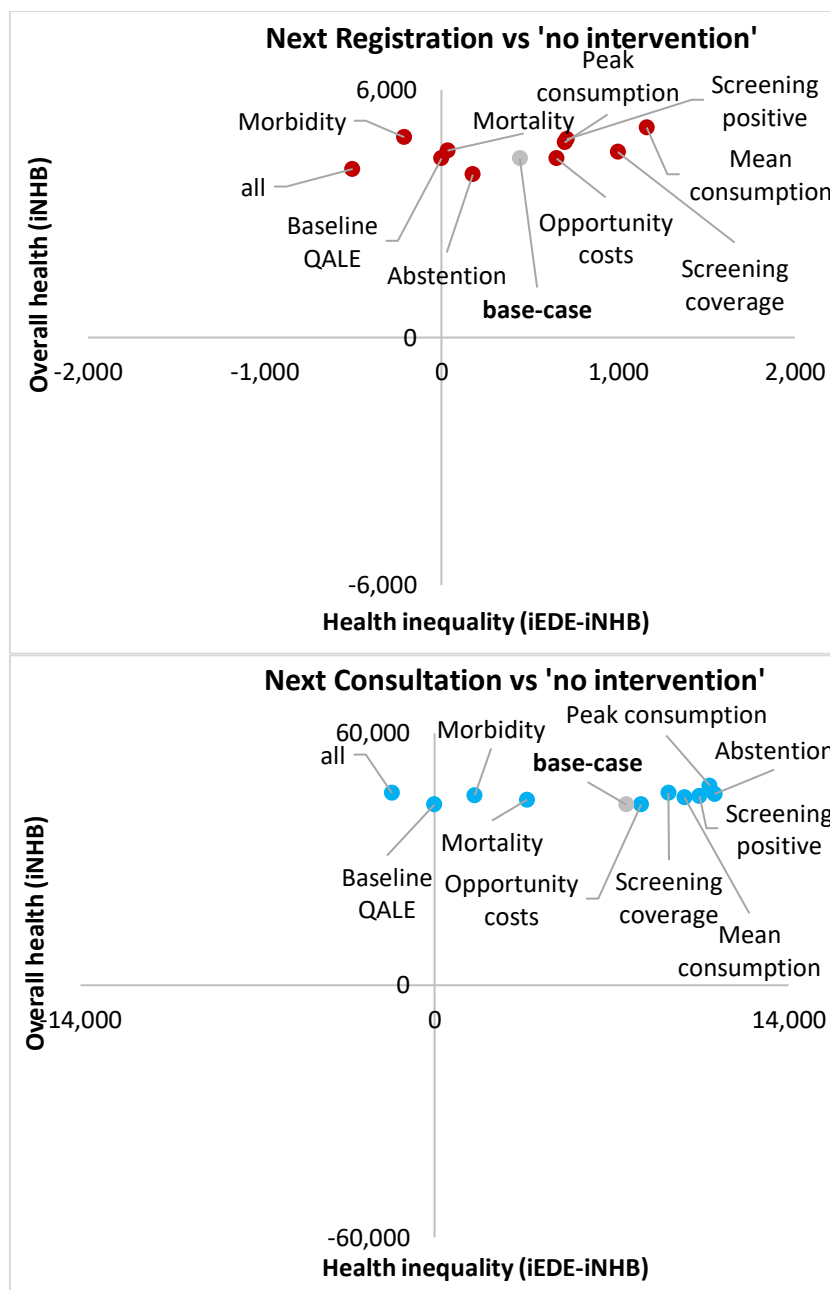
Figure 29. Equity impact planes showing results in the scenario analysis where gradients are ignored

Levelling up to the best

Table 22 presents the estimated impacts of increasing coverage of each intervention to both the age-sex specific and population maximum level. These results are illustrated in Figure 30. The incremental comparison of Next Consultation vs. Next Registration scenarios is shown in Table S9 and Figure S14. For both interventions, increasing coverage increased NHB and further reduced inequalities than the base-case. For the Next Registration scenario, the marginal increases in both NHB and EDE was substantially greater between the age-sex and global maxima, compared to between the base-case and the age-sex optimum. The converse was true for the Next Consultation scenario.

Table 22. Estimates of the NHB and EDE in the base-case and 'levelled-up' analysis

	iNHB	Change in iNHB from base-case	iEDE	Change in iEDE from base-case	Inequality (iEDE-iNHB)	Change in the impact on inequality compared to base-case
Next Registration vs 'no intervention'						
Base-case	4,336	-	4,780	-	444	**Reduces inequality**
Levelling up to the best in:						
Screening rates (age-sex optimum)	4,817	480 (+11.07%)	6,213	1433 (+29.98%)	1,397	Larger reduction
Screening rates (global optimum)	17,893	13556 (+312.64%)	22,141	17361 (+363.2%)	4,248	Larger reduction
Next Consultation vs 'no intervention'						
Base-case	43,016		50,594		7,578	**Reduces inequality**
Levelling up to the best in:						
Screening rates (age-sex optimum)	55,436	12420 (+28.87%)	67,802	17208 (+34.01%)	12,366	Larger reduction
Screening rates (global optimum)	61,716	18700 (+43.47%)	75,673	25079 (+49.57%)	13,956	Larger reduction
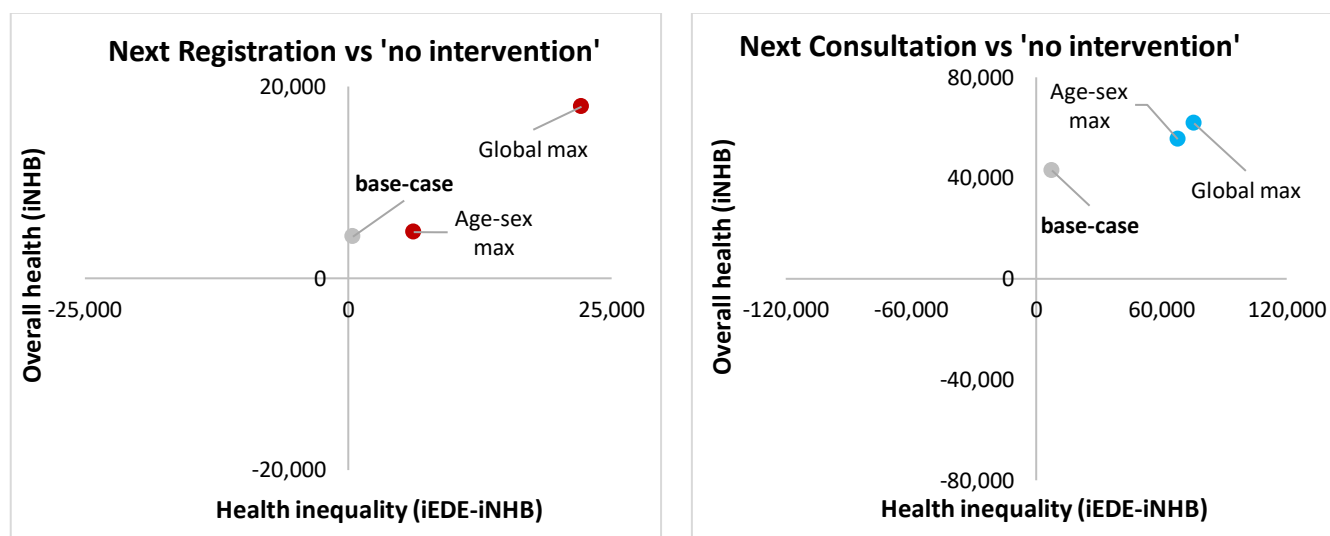
Figure 30. Equity impact plane for increased intervention coverage scenarios

8.3 Local Authority level results

The differences in modelled impacts of both policies in Liverpool and Trafford are shown in Table 23. In spite of the radically different population structures, the results are very similar, although differences in the baseline population sizes (England = 43m, Liverpool = 376k, Trafford = 174k) mean that the absolute magnitudes of effect are quite different. We, therefore, also present effects per 100,000 population. In both areas, the Next Registration scenario is estimated to increase NHB and reduce inequality, while the Next Consultation scenario does both to a much greater extent after adjusting for the differences in population. This is illustrated in Figure 31. For both modelled policies, the estimated impact per 100,000 people on overall health is greater in Liverpool and Trafford sees a larger effect on health inequality, likely driven by the very different deprivation structures of the population (see Figure 10).

Table 23. Estimated impacts of SBI programmes in Liverpool and Trafford

|		iNHB	iEDE	Inequality (iEDE-iNHB)
Next Registration vs. 'no intervention'				
England	Total	4,336	4,780	444
	Per 100,000	10	11	1
Liverpool	Total	79	88	9
	Per 100,000	21	23	2
Trafford	Total	31	37	6
	Per 100,000	18	21	3
Next Consultation vs. 'no intervention'				
England	Total	43,016	50,594	7,578
	Per 100,000	100	118	18
Liverpool	Total	829	898	69
	Per 100,000	220	239	18
Trafford	Total	285	361	75
	Per 100,000	164	207	43
Next Consultation vs. Next Registration				
England	Total	38,680	45,814	7,134
	Per 100,000	90	107	17
Liverpool	Total	750	810	60
	Per 100,000	199	215	16
Trafford	Total	254	324	70
	Per 100,000	146	186	40
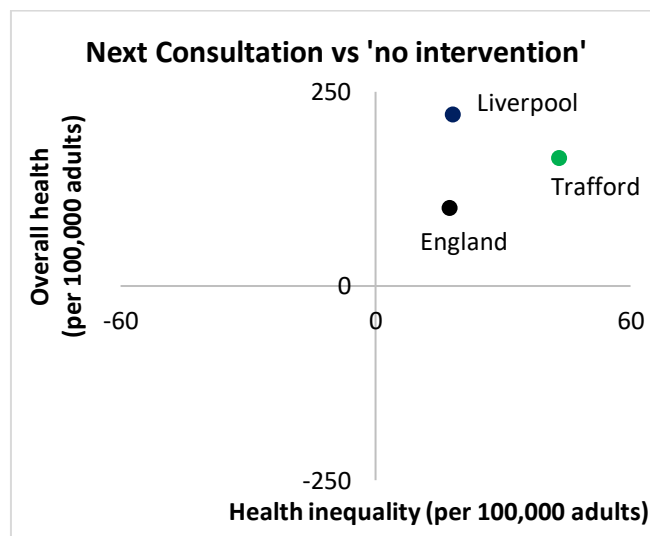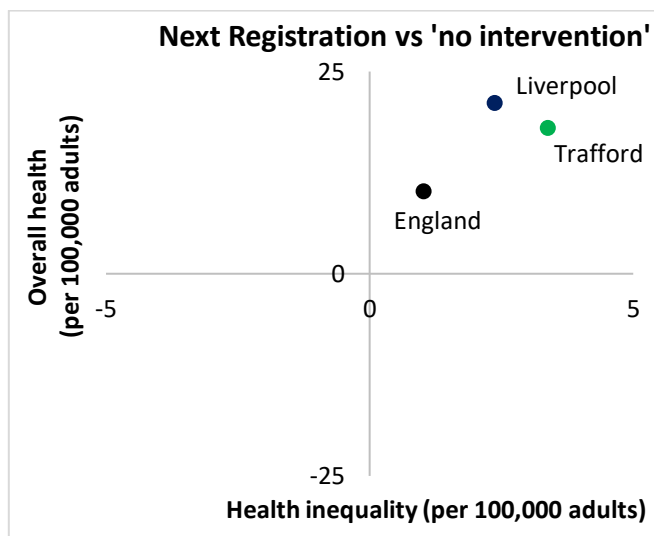
Figure 31. Equity impact places for Local Authority analysis

9.   Main Findings

9.1   How influential is a lack of knowledge?

Failing to incorporate any gradients would make a significant impact on the estimated health inequality impact (smoking model: +15.89%; alcohol model: -25.08%), which is in line with our expectation as detailed in section 3.2. In terms of impact on overall health, ignoring all gradients has little impact in the smoking model (-0.21%) and affects to a greater extent the alcohol model (-5.83%). These results suggest that a complete absence of information about the model inputs which are expected to differ by socioeconomic status could still produce reliable estimates of how interventions change overall health, but lead to biased estimates on health inequality impact.

Ignoring socioeconomic variation in individual model inputs would affect the estimates on overall health and health inequality, and may even change the conclusions about whether the intervention reduces/increases health inequality, but there is no clear pattern about which gradient has the greatest influence. The extent of inequality in the model input which is ignored (measured using concentration index) and the impacts on the amount the intervention is estimated to change overall health and health inequality is plotted in Figures 32 and 33. In the smoking model (Figure 32 and Figure S15), there is no clear correlation between the concentration index of model input and how ignoring inequality in the input affects the estimated results on overall health, but there is a weak suggestion of a positive correlation between the concentration index of input and the impact of ignoring socioeconomic variation on the estimated intervention impact on health inequality. However, such a pattern is not observed in the alcohol model (Figure 33 and Figure S16).
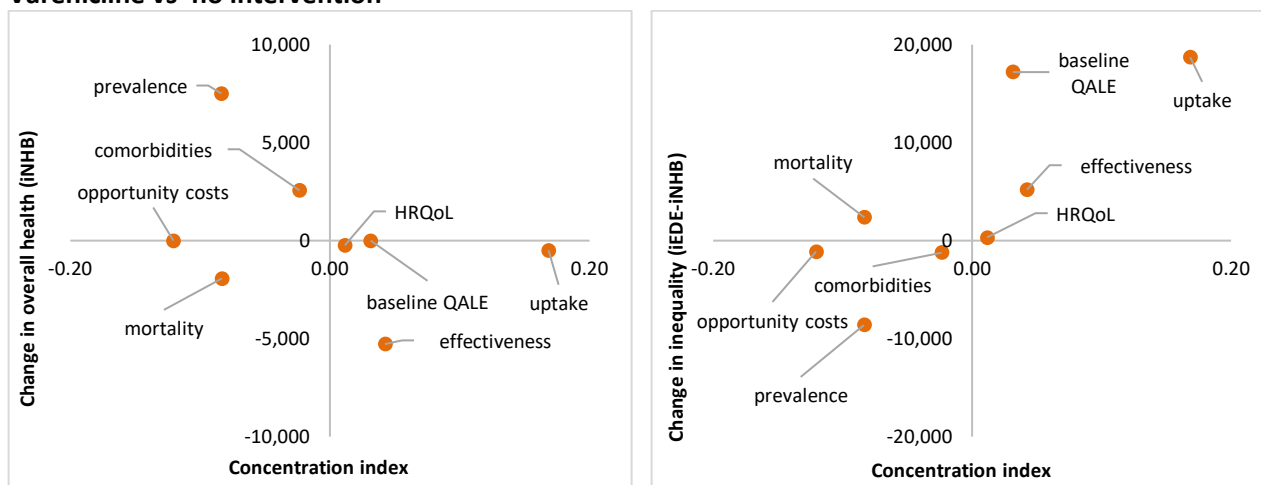
Varenicline vs 'no intervention'

Figure 32.   Impact of ignoring gradients vs. concentration indices in those gradients in smoking model
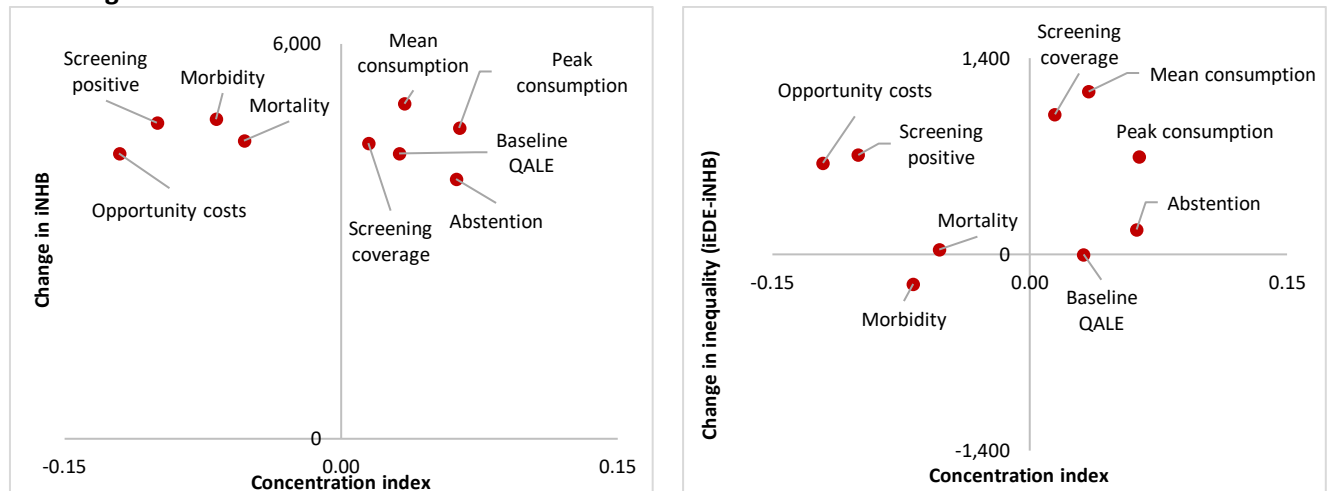
Next Registration vs 'no intervention'

Figure 33. Impact of ignoring gradients vs. concentration indices in those gradients in alcohol model

Probabilistic sensitivity analysis in the smoking model shows that for the pairwise comparisons between each intervention and 'no intervention', the variation in overall health impact is mostly explained by the quit rate of the intervention and effectiveness, while the variation in uptake also explains the variation in health inequality impact. For the comparison between the two interventions, which share the same gradients, there is little impact of uncertainty in the gradients on uncertainty in estimates of incremental overall health and health inequality. This suggests that the lack of information on socioeconomic differences in intervention characteristics would affect the decision uncertainty about value for money more than the differences in background parameters, behaviour, or behaviour-related health (Figure 17).

9.2   How valuable are modifications to reduce socioeconomic differences?

Levelling up each model input to the highest level currently achieved in any socioeconomic subgroup would drive the impact on health inequality to the direction that favours the intervention, by either making the intervention inequality reducing or reducing the extent of inequality, as we would expect. It also increases the impact on overall health, so it would not impose a trade-off between overall health and inequality, unless the cost of achieving the improvement exceed the benefits. As these inputs are potentially modifiable, these results would help to guide the efforts to improve the delivery strategies for the health interventions to achieve the optimal impacts on both overall health and health inequality.

9.3   How generalisable are conclusions about value for money between settings?

Generally, the influence of ignoring gradients shows a similar pattern of change across different settings. Similarly, the direction of change is the same for levelling up the potentially modifiable gradients to the best, which would increase overall health and reduce inequality.

However, there are differences in some of the conclusions between settings. In the smoking cessation model, the intervention e-cigarette increases overall health and marginally reduces inequality for York, but exacerbates health inequality for England as a whole and in Sheffield. In the alcohol model, the magnitude of effects is different when assuming the same population size: Trafford is estimated to see a reduction in inequality that is over 2 times greater than the national figure, while Liverpool is estimated to see an improvement in overall health that is over 2 times greater. Also, in the smoking model, ignoring all gradients would affect the estimated intervention impact on overall health to a greater extent at the Local Authority level than at the national level (England: -0.21%, York: -19.56% and Sheffield: +9.19%). For individual gradients, the impact of

ignoring socioeconomic variation can lead to different qualitative conclusions in different settings, e.g., ignoring the gradient in uptake would result in Varenicline being estimated to reduce inequality compared to 'no intervention' for England and York, but not so for Sheffield. These differences are likely driven by the very different deprivation structure of the population (Figure 5 for smoking cessation model and Figure 10 for alcohol model).

Furthermore, probabilistic sensitivity analysis in the smoking model shows the different levels of uncertainty in the conclusions on overall health and health inequality between settings. For England and Sheffield, the intervention increases overall health and reduces inequality with no uncertainty, but for York the probability of the intervention being inequality reducing is 37.20% and 55.40%. VOI and ANCOVA results demonstrate that the uncertainty/variation in health inequality at the Local Authority level is partly explained by the variation in smoking prevalence, while this is not the case at the national level. As there is more uncertainty associated with socioeconomic gradients in smoking prevalence at Local Authority level than that at the national level, this translates into more variation in model outputs.

Although the impact of ignoring socioeconomic differences on the estimates of overall health and health inequality is in the same direction between settings, the conclusion about value for money of the intervention at one Local Authority would be different compared to other Local Authorities or the nation as a whole. Therefore, when making decisions at Local Authority levels, it would be ideal to incorporate Local Authority level data to reflect the differences rather than use the data at the national level.

9.4   How generalisable are these results between models and disease areas?

Socioeconomic differences in background parameters, behaviours, behaviour-related health, and intervention characteristics are considered in both models. However, the models differ in model structure and in the pattern of the socioeconomic gradient assigned to the same input, e.g. the opposing gradients in prevalence shown in Figure 12.

Failing to consider gradients entirely, or specific individual gradients, would affect estimates of how interventions impact on health inequality and could fundamentally change the conclusions about value for money of the interventions. However, there are no clear patterns between models about what gradients have what effect and to what extent, which is very context-specific. This may mean there is limited scope to triage public health interventions for distributional cost effectiveness analysis, as information on inequality in the model inputs does not appear to reliably predict overall changes in health inequality.

It is clearly observed that reducing socioeconomic differences in the delivery and effects of interventions is unequivocally a good thing, by increasing overall health and reducing health inequality, although this might attract additional costs, and further analysis might be needed to explore whether the additional costs are worth it. The cost of modifying interventions might vary between disease areas even if the benefits of doing so are similar.

10. Conclusions

Policy makers require information on the distributional impact of potential public health interventions, but may lack the resources and time to conduct bespoke distributional cost effectiveness analysis in all circumstances. Developing greater understanding of how socioeconomic gradients in prevalence, uptake, efficacy, and benefit from treatment interact and translate into differential net health inequality impact will be valuable in demonstrating the potential for distributional cost effectiveness analysis to add value.

By conducting two case studies, one assessing smoking cessation interventions and the other assessing alcohol brief intervention, we found that there is a strong need to consider socioeconomic differences in decision models to assess the impact on health inequality of public health interventions, otherwise, the conclusions about value for money would be greatly affected. Among all the socioeconomic differences defined in both models, the intervention-related differences seem to affect the estimates of health inequality most and, therefore, should be considered in future evaluations. Furthermore, reducing socioeconomic differences in the delivery and effects of interventions has been found to significantly affect the estimates of value for money, by increasing overall health and reducing health inequality, although this might attract additional costs and further analysis might be needed to explore whether the additional costs are worth it. Finally, the conclusions seem different between settings and, therefore, caution should be taken when generalising results from national level to Local Authorities, and between Local Authorities differing in deprivation structure of the population and other disease- and intervention-related parameters, such as prevalence and uptake rate.

References

1. Marmot M, Friel S, Bell R, Houweling TA, Taylor S, Commission on Social Determinants of H. Closing the gap in a generation: health equity through action on the social determinants of health. *Lancet*. 2008;372(9650):1661-9.

2. Marmot M, Allen J, Bell R, Bloomer E, Goldblatt P, Consortium for the European Review of Social Determinants of H, et al. WHO European review of social determinants of health and the health divide. *Lancet*. 2012;380(9846):1011-29.

3. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed. Oxford, UK: Oxford University Press; 2005.

4. Asaria M, Griffin S, Cookson R. Distributional Cost-Effectiveness Analysis: A Tutorial. *Med Decis Making*. 2016;36(1):8-19.

5. Department for Communities and Local Government. The English Indices of Deprivation 2015 Statistical Release 72015.

6. Earnshaw J, Lewis G. *NICE Guide to the Methods of Technology Appraisal*. Springer; 2008.

7. Love-Koh JC, R. Claxton, K. Griffin, S. Does public healthcare spending reduce inequality? Estimating the socioeconomic distribution of health gains and losses from marginal changes to NHS expenditure in England. Winter 2016 Health Economists' Study Group Meeting.

8. Love-Koh J, Asaria M, Cookson R, Griffin S. The Social Distribution of Health: Estimating Quality-Adjusted Life Expectancy in England. *Value Health*. 2015;18(5):655-62.

9. Robson M, Asaria M, Cookson R, Tsuchiya A, Ali S. Eliciting the Level of Health Inequality Aversion in England. *Health Econ*. 2017;26(10):1328-34.

10. Atkinson AB. On the measurement of inequality. *Journal of Economic Theory*. 1970;2(3):244-63.

11. O'donnell O, Van Doorslaer E, Wagstaff A, Lindelow M. Analyzing health equity using household survey data: a guide to techniques and their implementation: The World Bank; 2007.

12. Love-Koh J, Pennington R, Owen L, Griffin S. Frameworks for considering health inequalities and their suitability for use within NICE public health guidelines. 2018.

13. National Institute for Health and Care Excellence. Guide to the methods of technology appraisal 2013. NICE; 2013.

14. Chengappa KN, Perkins KA, Brar JS, Schlicht PJ, Turkin SR, Hetrick ML, et al. Varenicline for smoking cessation in bipolar disorder: a randomized, double-blind, placebo-controlled study. *J Clin Psychiatry*. 2014;75(7):765-72.

15. Caponnetto P, Campagna D, Cibella F, Morjaria JB, Caruso M, Russo C, et al. EffiCiency and Safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study. *PLoS ONE*. 2013;8(6):e66317.

16. Number of deaths by sex, single year of age and IMD decile, England, deaths registered 2001-2015 [press release]. 2017.

17. Doll R, Peto R. Mortality in relation to smoking: 20 years' observations on male British doctors. *Br Med J*. 1976;2(6051):1525-36.

18. Eberth B, Olajide D, Craig P, Ludbrook A. Smoking-related disease risk, area deprivation and health behaviours. *J Public Health (Oxf).* 2014;36(1):72-80.

19. Office of the Chief Statistician, Scottish Executive. Scottish index of multiple deprivation 2006 technical report. 2006.

20. West R. Background smoking cessation rates in England 2006 [Available from: www.smokinginengland.info/Ref/paper2.pdf.

21. Dobbie F, Hiscock R, Leonardi-Bee J, Murray S, Shahab L, Aveyard P, et al. Evaluating Long-term Outcomes of NHS Stop Smoking Services (ELONS): a prospective cohort study. *Health Technol Assess*. 2015;19(95):1-156.

22. Grant RL. Converting an odds ratio to a range of plausible relative risks for better communication of research findings. *BMJ*. 2014;348:f7450.

23. Tengs TO, Wallace A. One thousand health-related quality-of-life estimates. *Med Care*. 2000;38(6):583-637.

24. Stevanovic J, Pechlivanoglou P, Kampinga MA, Krabbe PF, Postma MJ. Multivariate Meta-Analysis of Preference-Based Quality of Life Values in Coronary Heart Disease. *PLoS ONE*. 2016;11(3):e0152030.

25. Rutten-van Molken MP, Oostenbrink JB, Tashkin DP, Burkhart D, Monz BU. Does quality of life of COPD patients as measured by the generic EuroQol five-dimension questionnaire differentiate between COPD severity stages? *Chest*. 2006;130(4):1117-28.

26. Szende A, Svensson K, Stahl E, Meszaros A, Berta GY. Psychometric and utility-based measures of health status of asthmatic patients with different disease control level. *Pharmacoeconomics*. 2004;22(8):537-47.

27. Strong M, Oakley JE, Brennan A. Estimating multiparameter partial expected value of perfect information from a probabilistic sensitivity analysis sample: a nonparametric regression approach. *Med Decis Making*. 2014;34(3):311-26.

28. Campbell JD, McQueen RB, Libby AM, Spackman DE, Carlson JJ, Briggs A. Cost-Effectiveness Uncertainty Analysis Methods: A Comparison of One-Way Sensitivity, Analysis of Covariance, and Expected Value of Partial Perfect Information. *Med Decis Making*. 2015;35(5):596-607.

29. Claxton K. The irrelevance of inference: a decision-making approach to the stochastic evaluation of health care technologies. *J Health Econ*. 1999;18(3):341-64.

30.   Purshouse RC, Brennan A, Rafia R, Latimer NR, Archer RJ, Angus CR, et al. Modelling the cost-effectiveness of alcohol screening and brief interventions in primary care in England. *Alcohol Alcohol.* 2013;48(2):180-8.

31.   Fleming MF, Mundt MP, French MT, Manwell LB, Stauffacher EA, Barry KL. Brief physician advice for problem drinkers: long-term efficacy and benefit-cost analysis. *Alcohol Clin Exp Res*. 2002;26(1):36-43.

32.   Holmes J, Meier PS, Booth A, Guo Y, Brennan A. The temporal relationship between per capita alcohol consumption and harm: a systematic review of time lag specifications in aggregate time series analyses. *Drug Alcohol Depend*. 2012;123(1-3):7-14.

33.   Angus C, Li J, Romero-Rodriguez E, Anderson P, Parrott S, Brennan A. Cost-effectiveness of strategies to improve delivery of brief interventions for heavy drinking in primary care: results from the ODHIN trial. *Eur J Public Health*. 2018.

34.   Perkins C, Hennessey M. Understanding alcohol-related hospital admissions 2014 Available from: https://publichealthmatters.blog.gov.uk/2014/01/15/understanding-alcohol-related-hospital-admissions/

35.   Jones L, Bellis M, Dedman D, H S, Tocque K. Alcohol-Attributable Fractions for England: Alcohol-Attributable Mortality and Hospital Admissions 2008.

36.   World Health Organisation. AUDIT: The alcohol use disorders identification test: Guidelines for use in primary health care. Geneva: World Health Organization; 2001.

37.   Weir S, Juhasz A, Puelles J, Tierney TS. Relationship between initial therapy and blood pressure control for high-risk hypertension patients in the UK: a retrospective cohort study from the THIN general practice database. *BMJ Open*. 2017;7(7):e015527.

38.   Beard E, Brown J, West R, Acton C, Brennan A, Drummond C, et al. Protocol for a national monthly survey of alcohol use in England with 6-month follow-up: 'the Alcohol Toolkit Study'. *BMC Public Health*. 2015;15:230.

39.   Littlejohn C. Does socio-economic status influence the acceptability of, attendance for, and outcome of, screening and brief interventions for alcohol misuse: a review. *Alcohol Alcohol*. 2006;41(5):540-5.

40.   Kaner EF, Beyer FR, Muirhead C, Campbell F, Pienaar ED, Bertholet N, et al. Effectiveness of brief alcohol interventions in primary care populations. *Cochrane Database Syst Rev*. 2018;2:CD004148.

41.   Purshouse R, Brennan A, Latimer N, Meng Y, Rafia R, Jackson R, et al. Modelling to assess the effectiveness and cost-effectiveness of public health related strategies and intervention to reduce alcohol attributable harm in England using the Sheffield Alcohol Policy Model version 2.0. 2009.

42.   Brennan A, Angus C, Pryce R, Buykx P, Henney M, Gillespie D, et al. The effectiveness of 'MUPLocal' – Modelling the potential impact of implementing a Local Minimum Unit Price for Alcohol at Local Authority and Regional level in England. 2019.

Appendix

Table S1. Distribution of NS-SEC groups by IMD quintiles based on HSE datasets

	IMD1 (most deprived)	IMD2	IMD3	IMD4	IMD5 (least deprived)
Managerial and professional	18.30%	27.26%	32.24%	40.40%	46.31%
Intermediate	18.16%	23.48%	25.83%	27.38%	25.21%
Routine and manual	55.71%	43.46%	38.82%	28.76%	24.75%
Never worked and long term unemployed	7.83%	5.80%	3.11%	3.46%	3.73%
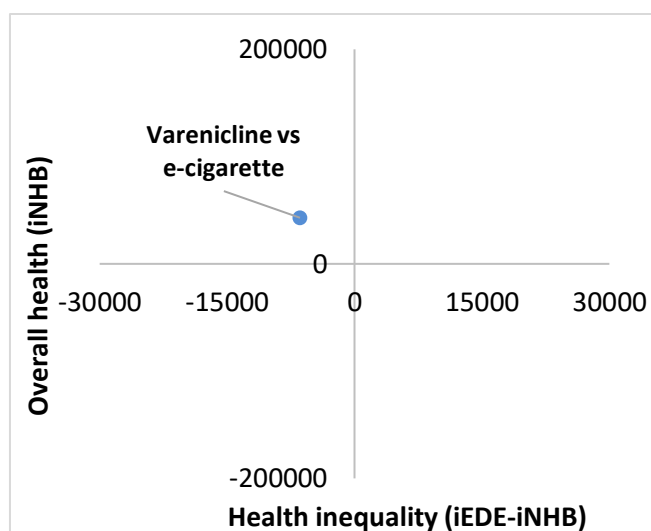
Figure S1. Equity impact plane showing the overall health and health inequality

Table S2. Estimates of incremental NHB and incremental EDE in base-case and scenario analysis

	iNHB	Change in iNHB from Base-case	iEDE	Change in iEDE from Base-case	Inequality (iEDE-iNHB)	Change in the impact on inequality compared to base-case
e-cigarette vs 'no intervention'						
Base-case	80,782	-	70,002		-10,780	**Increases inequality**
(a) Ignoring all gradients	80,510	-272 (-0.34%)	80,510	10,508 (15.01%)	0	No effect
(b) Ignoring gradient in:						
Baseline QALE	80,782	0 (0%)	80,781	10,779 (15.40%)	-1	Smaller increase
Health opportunity costs	80,782	0 (0%)	69,019	-983 (-1.40%)	-11,763	Larger increase
Smoking prevalence	85,683	4,902 (6.07%)	69,454	-548 (-0.78%)	-16,229	Larger increase
Mortality	79,543	-1,239 (-1.53%)	70,261	259 (0.37%)	-9,282	Smaller increase
Comorbidities	82,418	1,636 (2.03%)	70,853	851 (1.22%)	-11,564	Larger increase
HRQoL	80,628	-153 (-0.19%)	70,053	51 (0.07%)	-10,575	Smaller increase
Effectiveness	77,236	-3,546 (-4.39%)	69,942	-60 (-0.09%)	-7,294	Smaller increase
Uptake	80,436	-345 (-0.43%)	81,463	11,461 (16.37%)	1,027	Inequality-reducing
(c) Levelling up to the best in:						
Effectiveness	88,229	7,448 (9.22%)	79,929	9,927 (14.18%)	-8,300	Reduce
Uptake	109,656	28,875 (35.745)	111,057	41,055 (58.65%)	1,400	Inequality-reducing

Table S3. Estimates of incremental NHB and incremental EDE in base-case and scenario analysis

	iNHB	Change in iNHB from Base-case	iEDE	Change in iEDE from Base-case	Inequality (iEDE-iNHB)	Change in the impact on inequality compared to base-case
Varenicline vs e-cigarette						
Base-case	42,968	-	36,551	-	-6,417	**Increases inequality**
(a) Ignoring all gradients	42,979	11 (0.03%)	42,979	6,428 (17.59%)	0	No effect
(b) Ignoring gradient in:						
Baseline QALE	42,968	0 (0%)	42,966	6,415 (17.55%)	-1	Smaller increase
Health opportunity costs	42,968	0 (0%)	36,413	-138 (-0.38%)	-6,555	Larger increase
Smoking prevalence	45,572	2,604 (6.06%)	35,990	-561 (-1.53%)	-9,581	Larger increase
Mortality	42,277	-690 (-1.61%)	36,730	179 (0.49%)	-5,548	Smaller increase
Comorbidities	43,895	927 (2.16%)	37,029	478 (1.31%)	-6,865	Larger increase
HRQoL	42,882	-85 (-0.20%)	36,584	33 (0.09%)	-6,298	Smaller increase
Effectiveness	41,234	-1,734 (-4.03%)	36,522	-29 (-0.08%)	-4,712	Smaller increase
Uptake	42,821	-146 (-0.34%)	43,317	6,766 (18.51%)	496	Inequality-reducing
(c) Levelling up to the best in:						
Effectiveness	46,608	3,641 (8.47%)	41,404	4,853 (13.28%)	-5,204	Reduce
Uptake	58,377	15,409 (35.86%)	591,053	22,502 (61.56%)	676	Inequality-reducing

e-cigarette vs 'no intervention'

200,000

comorbidities

all

baseline QALE

prevalence

mortality

opportunity
costs

uptake

effectiveness

base-case

HRQoL

0

Overall health (iNHB)

-30,000

30,000

-200,000

Health inequality (iEDE-iNHB)

Varenicline vs e-cigarette

100,000

HRQoL

mortality

baseline QALE

comorbidities

effectiveness

all

prevalence

uptake

opportunity
costs

base-case

0

Overall health (iNHB)

-15,000

0

15,000

-100,000

Health inequality (iEDE-iNHB)

Figure S2. Equity impact plane showing scenario analysis results where gradients are ignored

e-cigarette vs 'no intervention'

Varenicline vs e-cigarette
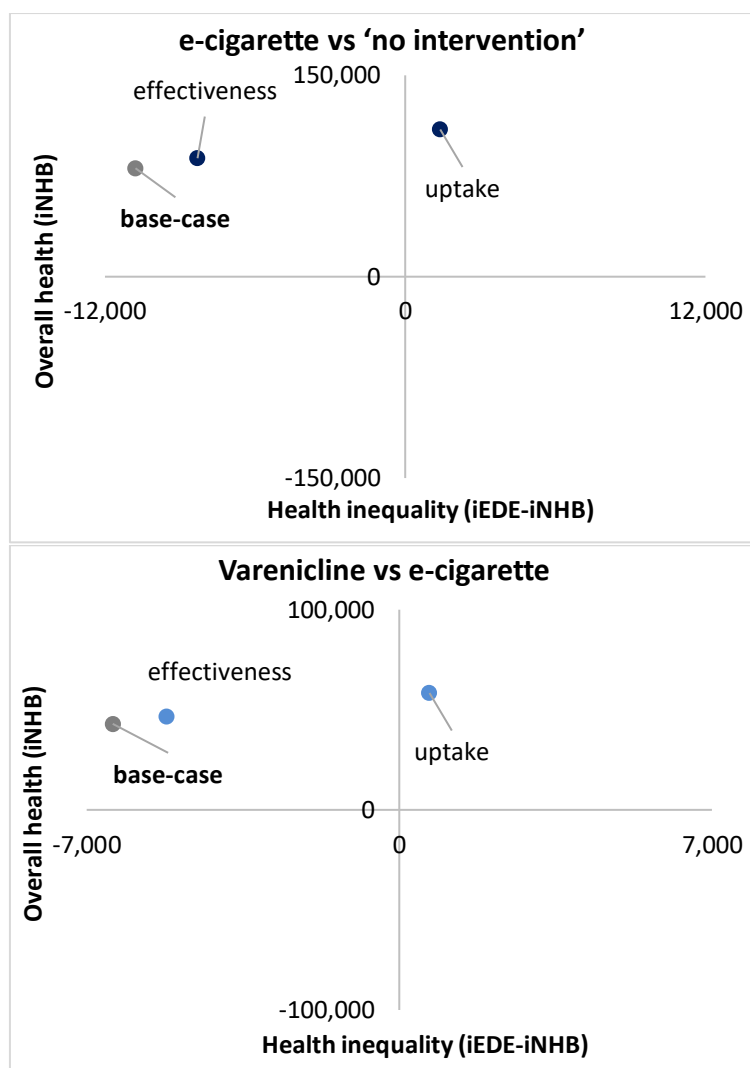
Figure S3. Equity impact plane showing scenario analysis results where levelling up to the best

Table S4. Overall EVPI and EVPPI of Varenicline vs e-cigarette for England

	Improvement in overall health (incremental NHB>0)	Improvement in social welfare (incremental EDE>0)
Overall EVPI per person	£142,617,861	£94,657,996
quit rate_Varenicline	£116,647,056	£77,425,155
quit rate_e-cigarette	£24,472,449	£17,188,784
smoking prevalence	0	£7,344
mortality	0	0
comorbidities	0	0
HRQoL	£429,714	£390,824
effectiveness	£1,750,667	£1,394,317
uptake	0	0

Overall health (incremental NHB)
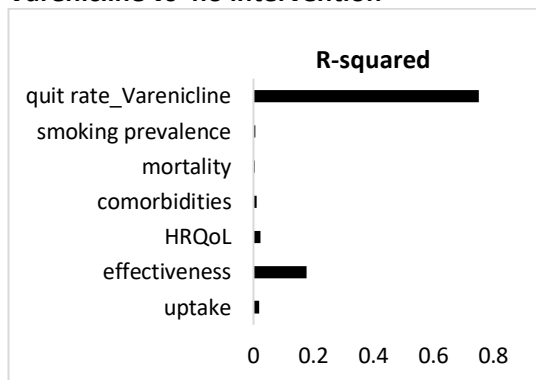
Varenicline vs 'no intervention'

e-cigarette vs 'no intervention'
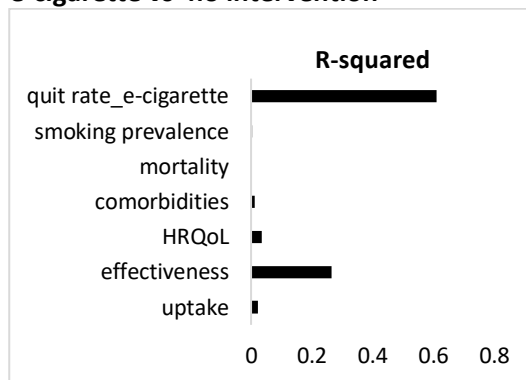
Health-related social welfare (incremental EDE)

Varenicline vs 'no intervention'
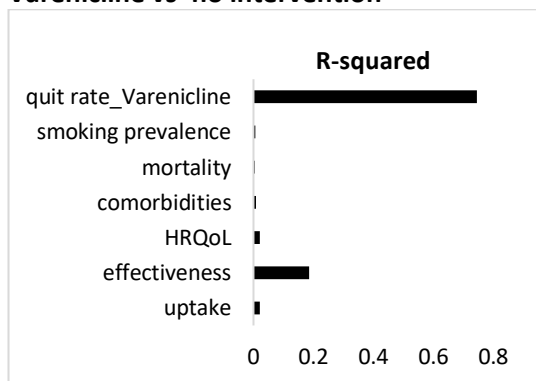
e-cigarette vs 'no intervention'
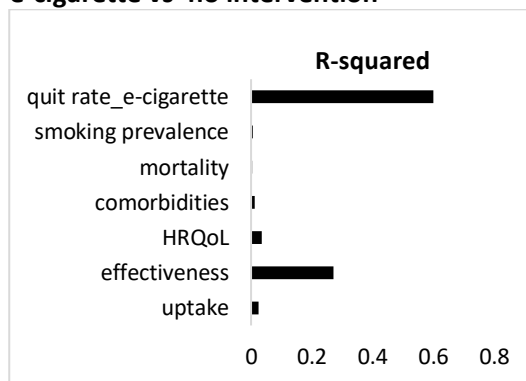
Reduction in health inequality (incremental EDE - incremental NHB)

Varenicline vs 'no intervention'
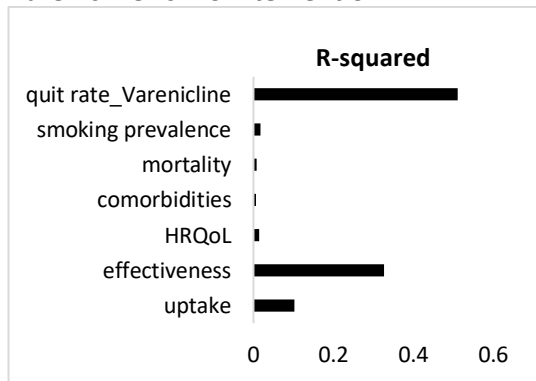
e-cigarette vs 'no intervention'
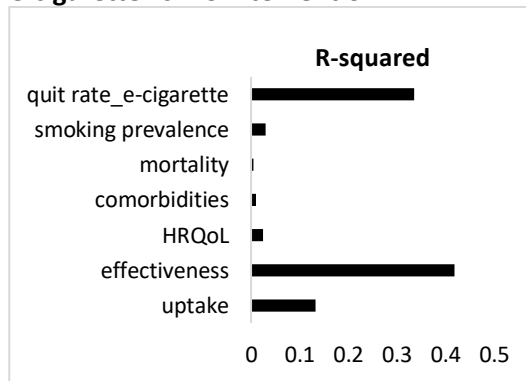
Figure S4. ANCOVA results for England
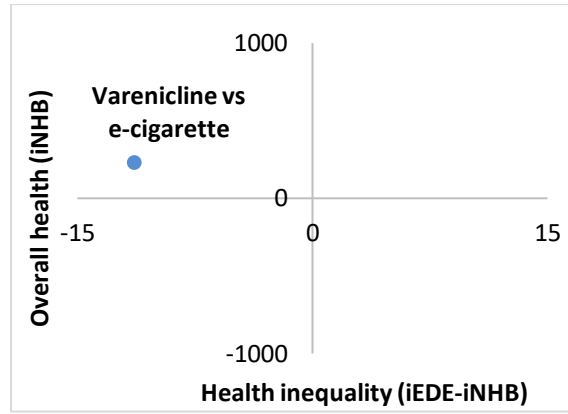
Figure S5. Equity impact plane showing the overall health and health inequality for York

Table S5. Results of base-case and scenario analysis for York

	iNHB	Change in iNHB from base-case	iEDE	Change in iEDE from base-case	Inequality (iEDE-iNHB)	Change in the impact on inequality compared to base-case
Varenicline vs 'no intervention'						
Base-case	659	-	651	-	-9	**Increases inequality**
(a) Ignoring all gradients	531	-129 (-19.56%)	531	-120 (-18.49%)	0	No effect
(b) Ignoring gradient in:						
Baseline QALE	659	0 (0%)	659	9 (1.33%)	0	Smaller increase
Health opportunity costs	659	0 (0%)	641	-10 (-1.51%)	-18	Larger increase
Smoking prevalence	682	23 (3.47%)	643	-8 (-1.19%)	-39	Larger increase
Mortality	655	-5 (-0.72%)	654	4 (0.54%)	0	Smaller increase
Comorbidities	685	25 (3.82%)	673	22 (3.45%)	-11	Larger increase
HRQoL	656	-3 (-0.51%)	649	-2 (-0.29%)	-7	Smaller increase
Effectiveness	605	-54 (-8.21%)	607	-44 (-6.81%)	1	Inequality-reducing
Uptake	554	-105 (-15.93%)	604	-47 (-7.24%)	49	Inequality-reducing
(c) Levelling up to the best in:						
Effectiveness	689	29 (4.45%)	693	42 (6.44%)	4	Inequality-reducing
Uptake	756	96 (14.61%)	823	172 (26.46%)	67	Inequality-reducing
e-cigarette vs 'no intervention'						
Base-case	431	-	433	-	3	**Reduces inequality**
(a) Ignoring all gradients	345	-85 (-19.81%)	345	-88 (-20.32%)	0	No effect
(b) Ignoring gradient in:						
Baseline QALE	431	0 (0%)	431	-3 (-0.64%)	0	Inequality-increasing
Health opportunity costs	431	0 (0%)	425	-8 (-1.93%)	-6	Inequality-increasing
Smoking prevalence	446	15 (3.47%)	429	-4 (-0.99%)	-16	Inequality-increasing
Mortality	428	-3 (-0.70%)	436	2 (0.51%)	8	Larger reduce
Comorbidities	447	16 (3.74%)	448	14 (3.31%)	1	Smaller reduce
HRQoL	429	-2 (-0.50%)	432	-1 (-0.28%)	4	Larger reduce
Effectiveness	394	-36 (-8.45%)	404	-30 (-6.87%)	9	Larger reduce
Uptake	362	-69 (-15.93%)	400	-33 (-7.65%)	38	Larger reduce
(c) Levelling up to the best in:						
Effectiveness	450	20 (4.58%)	462	28 (6.50%)	11	Larger reduce
Uptake	494	63 (14.61%)	546	112 (25.90%)	52	Larger reduce
Varenicline vs e-cigarette						
Base-case	229	-	217	-	-11	**Increases inequality**
(a) Ignoring all gradients	185	-44 (-19.08%)	185	-32 (-14.83%)	0	No effect
(b) Ignoring gradient in:						
Baseline QALE	229	0 (0%)	229	11 (5.25%)	0	Smaller increase
Health opportunity costs	229	0 (0%)	216	-1 (-0.66%)	-13	Larger increase
Smoking prevalence	237	8 (3.47%)	214	-3 (-1.60%)	-23	Larger increase
Mortality	227	-2 (-0.74%)	219	1 (0.61%)	-8	Smaller increase
Comorbidities	238	9 (3.99%)	226	8 (3.74%)	-12	Larger increase
HRQoL	228	-1 (-0.54%)	217	-1 (-0.31%)	-11	Smaller increase
Effectiveness	211	-18 (-7.77%)	203	-15 (-6.70%)	-8	Smaller increase
Uptake	192	-36 (-15.93%)	203	-14 (-6.42%)	11	Inequality-reducing
(c) Levelling up to the best in:						
Effectiveness	238	10 (4.21%)	231	14 (6.33%)	-7	Smaller increase
Uptake	262	33 (14.62%)	277	60 (27.58%)	15	Inequality-reducing

Table S6. Results of base-case and scenario analysis for Sheffield

	iNHB	Change in iNHB from base-case	iEDE	Change in iEDE from base-case	Inequality (iEDE-iNHB)	Change in the impact on inequality compared to base-case
Varenicline vs 'no intervention'						
Base-case	2,092	-	1,625	-	-467	**Increases inequality**
(a) Ignoring all gradients	2,284	192 (9.19%)	2,284	659 (40.58%)	0	No effect
(b) Ignoring gradient in:						
Baseline QALE	2,092	0 (0%)	2,092	467 (28.74%)	0	Smaller increase
Health opportunity costs	2,092	0 (0%)	1,610	-15 (-0.94%)	-482	Larger increase
Smoking prevalence	2,188	96 (4.60%)	1,621	-4 (-0.26%)	-568	Larger increase
Mortality	2,039	-53 (-2.54%)	1,625	0 (0.02%)	-414	Smaller increase
Comorbidities	2,135	43 (2.04%)	1,640	16 (0.96%)	-494	Larger increase
HRQoL	2,089	-3 (-0.15%)	1,628	3 (0.20%)	-461	Smaller increase
Effectiveness	2,052	-40 (-1.92%)	1,703	79 (4.84%)	-348	Smaller increase
Uptake	2,207	115 (5.49%)	2,102	477 (29.39%)	-105	Smaller increase
(c) Levelling up to the best in:						
Effectiveness	2,335	243 (11.64%)	1,940	315 (19.40%)	-395	Smaller increase
Uptake	3,008	917 (43.82%)	2,866	1,241 (76.39%)	-143	Smaller increase
7.2mg e-cigarette vs 'no intervention'						
Base-case	1,365	-	1,062	-	-303	**Increases inequality**
(a) Ignoring all gradients	1,490	125 (9.17%)	1,490	428 (40.28%)	0	No effect
(b) Ignoring gradient in:						
Baseline QALE	1,365	0 (0%)	1,365	303 (28.49%)	0	Smaller increase
Health opportunity costs	1,365	0 (0%)	1,049	-14 (-1.27%)	-316	Larger increase
Smoking prevalence	1,428	63 (4.61%)	1,061	-1 (-0.08%)	-367	Larger increase
Mortality	1,331	-34 (-2.50%)	1,062	0 (-0.02%)	-269	Smaller increase
Comorbidities	1,392	27 (2.00%)	1,072	10 (0.95%)	-320	Larger increase
HRQoL	1,363	-2 (-0.15%)	1,064	2 (0.18%)	-299	Smaller increase
Effectiveness	1,338	-27 (-1.98%)	1,115	53 (4.97%)	-223	Smaller increase
Uptake	1,439	74 (5.43%)	1,364	302 (28.44%)	-75	Smaller increase
(c) Levelling up to the best in:						
Effectiveness	1,528	163 (11.98%)	1,274	212 (19.94%)	-254	Smaller increase
Uptake	1,962	597 (43.73%)	1,860	798 (75.09%)	-102	Smaller increase
Varenicline vs 7.2mg e-cigarette						
Base-case	727	-	563	-	-164	**Increases inequality**
(a) Ignoring all gradients	794	67 (9.23%)	794	232 (41.15%)	0	No effect
(b) Ignoring gradient in:						
Baseline QALE	727	0 (0%)	727	164 (29.21%)	0	Smaller increase
Health opportunity costs	727	0 (0%)	561	-2 (-0.30%)	-166	Larger increase
Smoking prevalence	760	33 (4.58%)	559	-3 (-0.60%)	-201	Larger increase
Mortality	708	-19 (-2.62%)	563	1 (0.10%)	-145	Smaller increase
Comorbidities	742	15 (2.12%)	568	6 (0.99%)	-174	Larger increase
HRQoL	726	-1 (-0.15%)	564	1 (0.22%)	-162	Smaller increase
Effectiveness	714	-13 (-1.81%)	588	26 (4.59%)	-125	Smaller increase
Uptake	768	41 (5.61%)	738	175 (31.18%)	-30	Smaller increase
(c) Levelling up to the best in:						
Effectiveness	807	80 (10.99%)	666	104 (18.40%)	-141	Smaller increase
Uptake	1,047	320 (43.98%)	1,006	443 (78.83%)	-41	Smaller increase
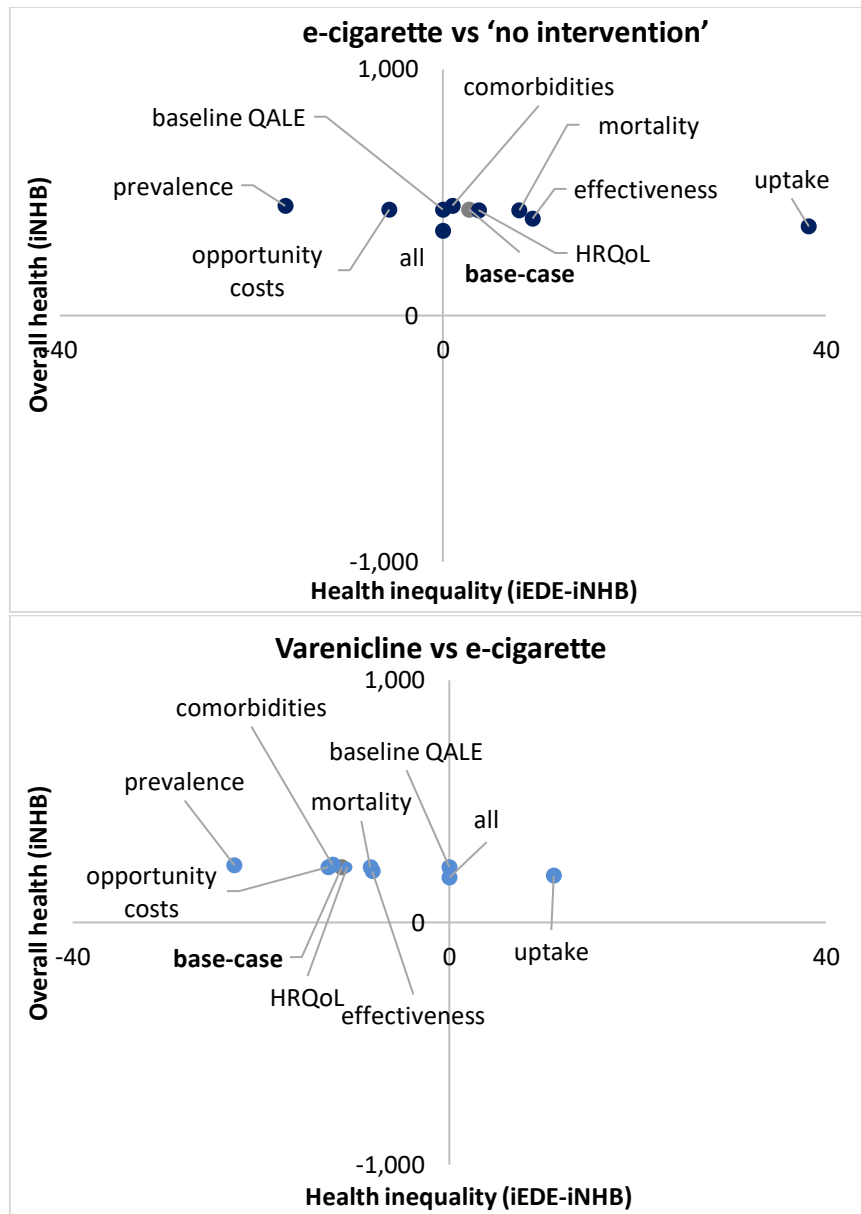
Figure S6. Equity impact plane showing scenario analysis results for York where gradients are ignored
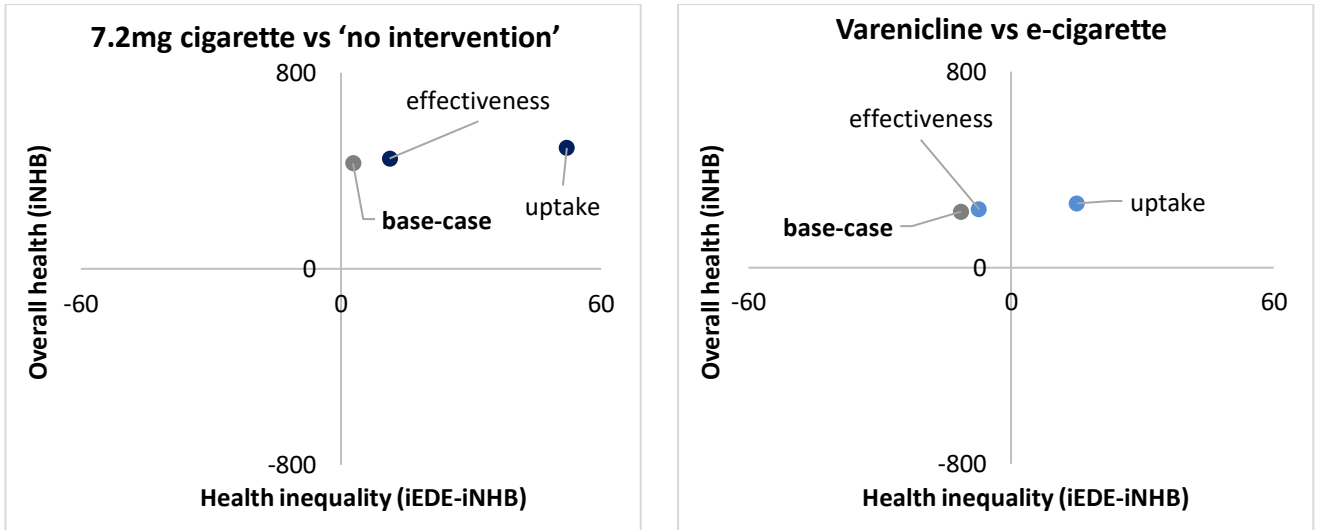
7.2mg cigarette vs 'no intervention'

Overall health (iNHB)

800

effectiveness

base-case

uptake

0

-60   0   60

Health inequality (iEDE-iNHB)

-800

Varenicline vs e-cigarette

Overall health (iNHB)

800

effectiveness

base-case

uptake

0

-60   0   60

Health inequality (iEDE-iNHB)

-800

Figure S7. Equity impact plane showing scenario analysis results for York where levelling up to the best
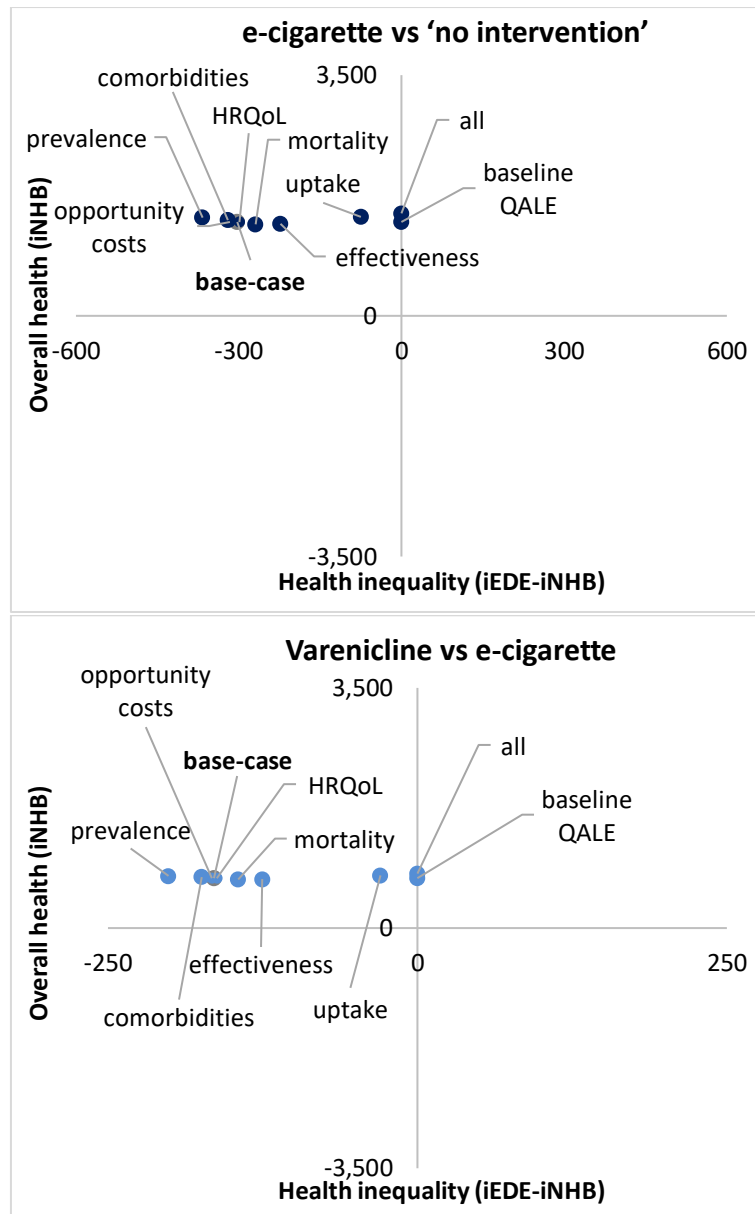
Figure S8. Equity impact plane showing scenario analysis results for Sheffield where gradients are ignored
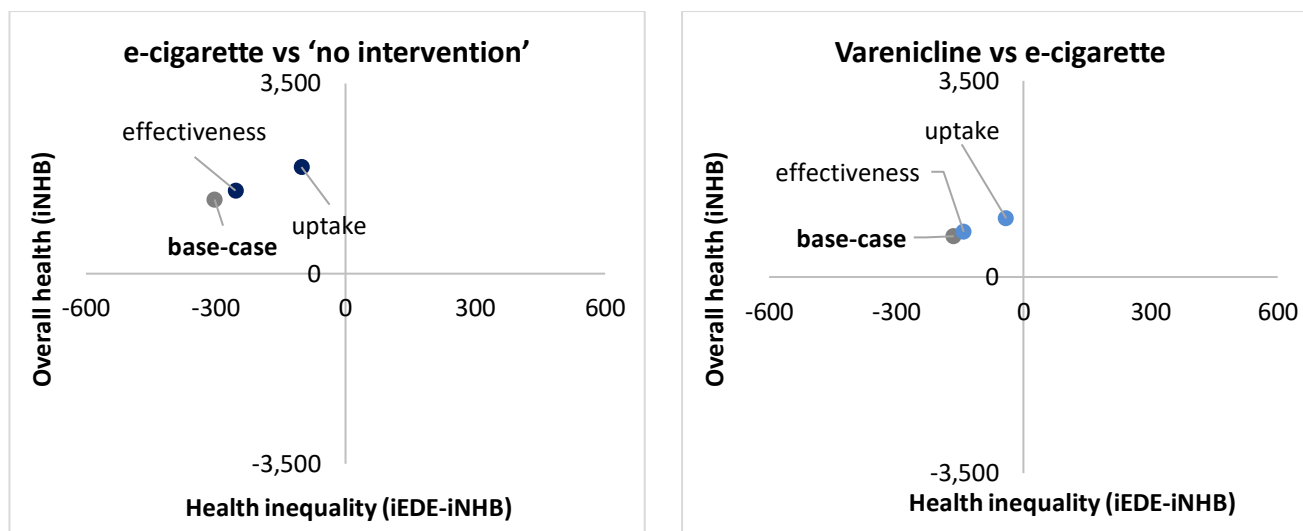
Figure S9. Equity impact plane showing scenario analysis results for Sheffield where levelling up to the best

Table S7. Overall EVPI and EVPPI of Varenicline vs e-cigarette for York

	Improvement in overall health (incremental NHB>0)	Improvement in social welfare (incremental EDE>0)
Overall EVPI	£750,593	£461,779
quit rate_Varenicline	£535,369	£338,400
quit rate_e-cigarette	£114,783	£75,836
smoking prevalence	0	0
mortality	0	£299
comorbidities	0	00
HRQoL	0	£215
effectiveness	£1,222	£892
uptake	0	0

Table S8. Overall EVPI and EVPPI of Varenicline vs e-cigarette for Sheffield

	Improvement in overall health (incremental NHB>0)	Improvement in social welfare (incremental EDE>0)
Overall EVPI	£2,206,030	£1,249,991
quit rate_Varenicline	£1,583,066	£913,999
quit rate_e-cigarette	£259,060	£172,692
smoking prevalence	0	0
mortality	0	0
comorbidities	0	0
HRQoL	0	£131
effectiveness	0	0
uptake	0	0

Overall health (incremental NHB)
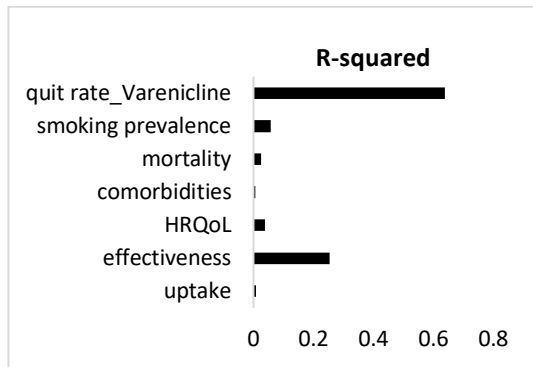
Varenicline vs 'no intervention'   **e-cigarette vs 'no intervention'**
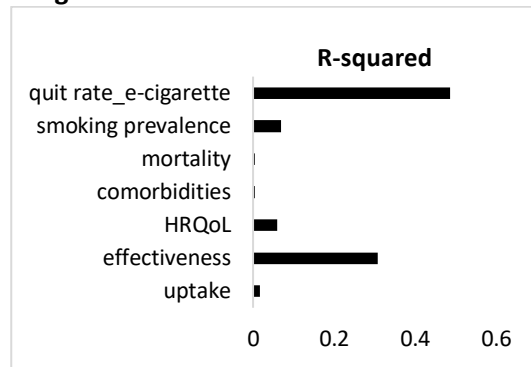
Health-related social welfare (incremental EDE)
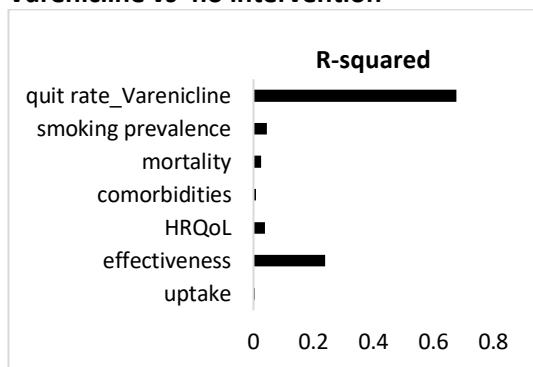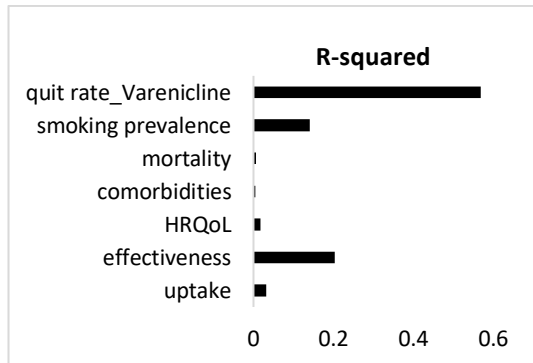
Varenicline vs 'no intervention'   **e-cigarette vs 'no intervention'**
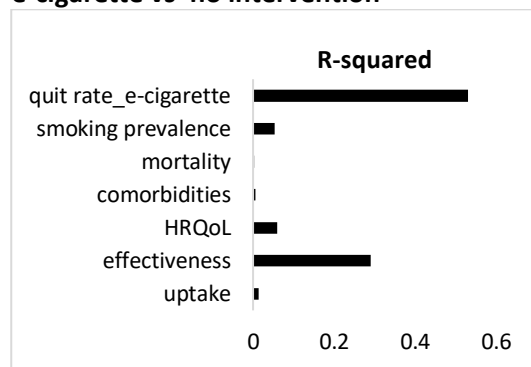
Figure S10. ANCOVA results for York
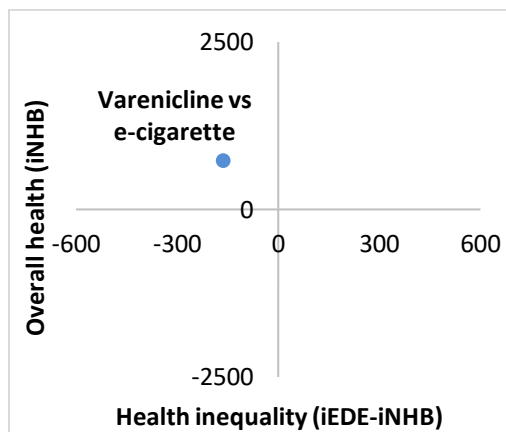
Figure S11. Equity impact plane showing the overall health and health inequality for *Sheffield*

Overall health (incremental NHB)
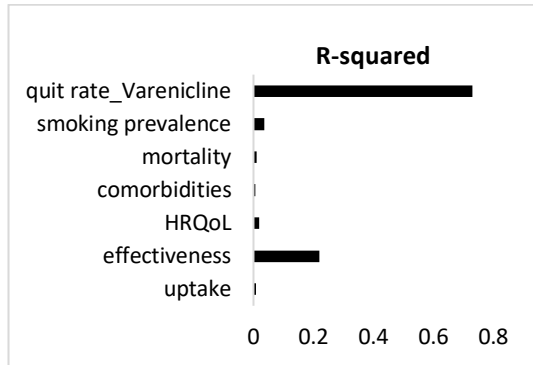
Varenicline vs 'no intervention'　　　　　**e-cigarette vs 'no intervention'**
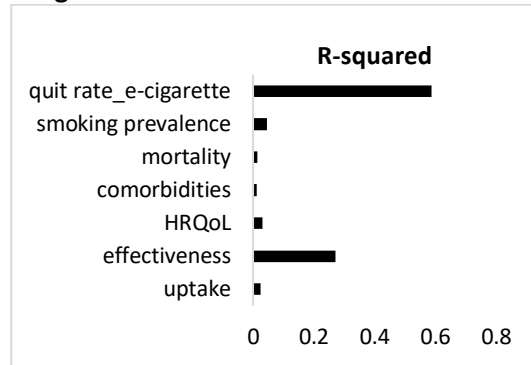
Health-related social welfare (incremental EDE)

Varenicline vs 'no intervention'　　　　　**e-cigarette vs 'no intervention'**
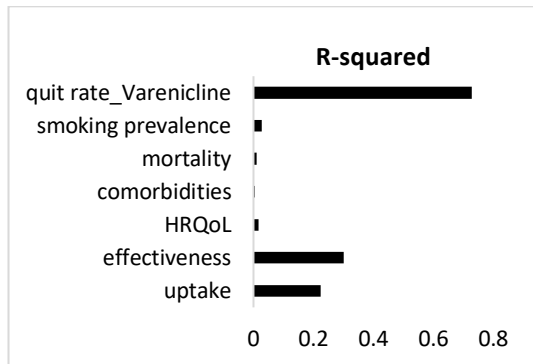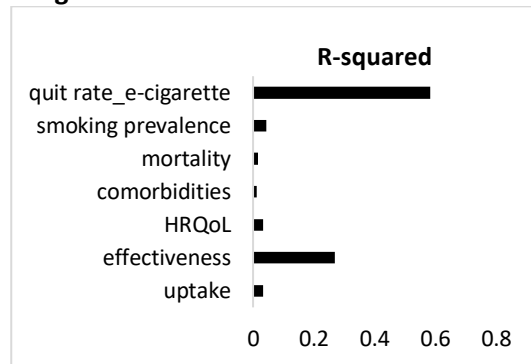
Reduction in health inequality (incremental EDE - incremental NHB)

Varenicline vs 'no intervention'　　　　　**e-cigarette vs 'no intervention'**
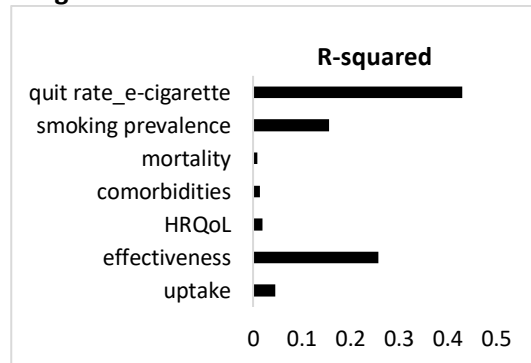
Figure S12. ANCOVA results for Sheffield

Table S9. Incremental results for scenario analyses for alcohol model

|	iNHB	Change in iNHB from base-case	iEDE	Change in iEDE from base-case	Inequality (iEDE-iNHB)	Change in the impact on inequality compared to base-case
Next Consultation vs. Next Registration						
Base-case	38,680		45,814		7,134	**Reduces inequality**
(a) Ignoring all gradients	41,647	2968 (+7.67%)	40,465	-5349 (-11.68%)	-1,182	Increases inequality
(b) Ignoring gradient in:						
Baseline QALE	38,680	0 (0%)	38,680	-7134 (-15.57%)	0	Increases inequality
Health opportunity costs	38,680	0 (0%)	46,196	382 (+0.83%)	7,517	Larger reduction
Drinking prevalence	41,571	2891 (+7.47%)	52,462	6648 (+14.51%)	10,891	Larger reduction
Mean consumption	39,618	938 (+2.43%)	48,336	2522 (+5.5%)	8,718	Larger reduction
Peak consumption	42,770	4091 (+10.58%)	52,961	7147 (+15.6%)	10,191	Larger reduction
Morbidity	40,317	1637 (+4.23%)	42,115	-3699 (-8.07%)	1,799	Smaller reduction
Mortality	39,639	959 (+2.48%)	43,263	-2551 (-5.57%)	3,624	Smaller reduction
Screening coverage	41,331	2652 (+6.86%)	49,577	3764 (+8.22%)	8,246	Larger reduction
Screening positive	40,259	1579 (+4.08%)	50,026	4212 (+9.19%)	9,767	Larger reduction
(c) Levelling up to the best in:						
Screening rates (age-sex optimum)	50,619	11940 (+30.87%)	61,589	15775 (+34.43%)	10,969	Larger reduction
Screening rates (global optimum)	43,824	5144 (+13.3%)	53,532	7718 (+16.85%)	9,708	Larger reduction
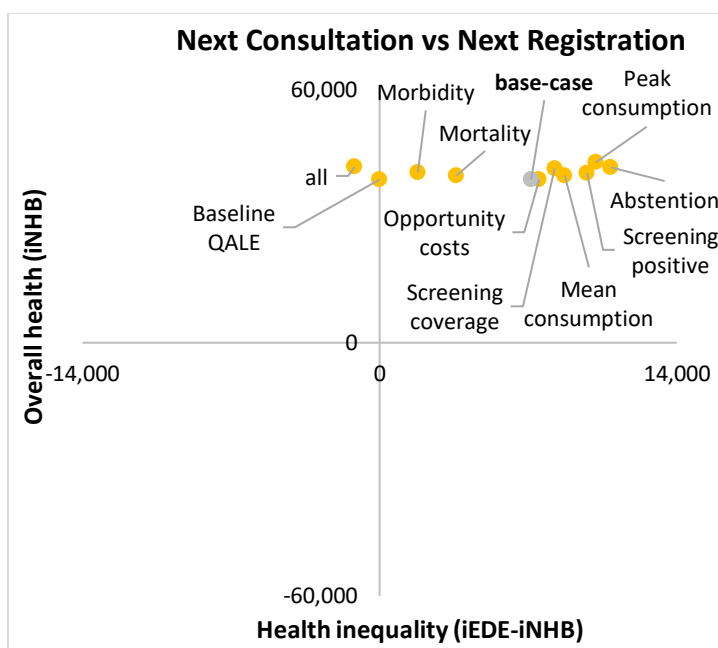
Figure S13. Equity impact plane showing scenario analysis results where gradients are ignored
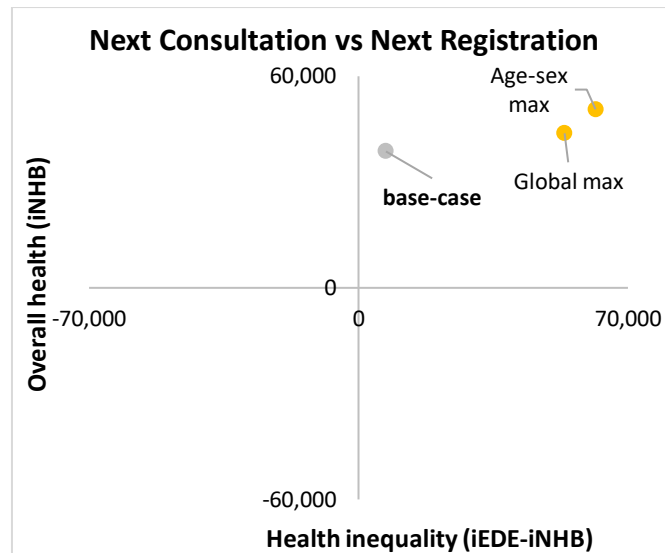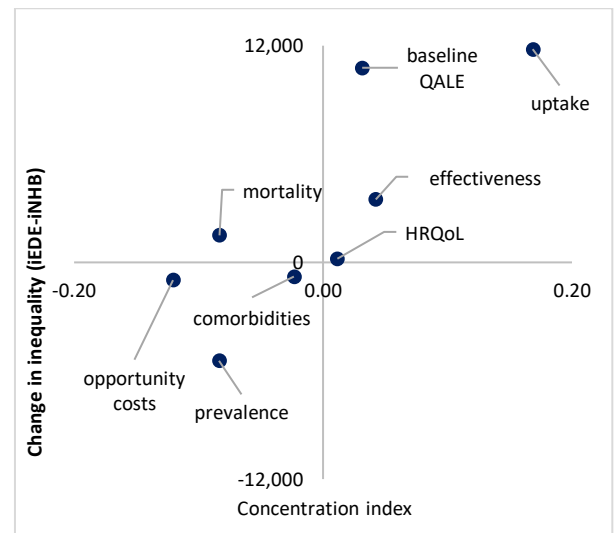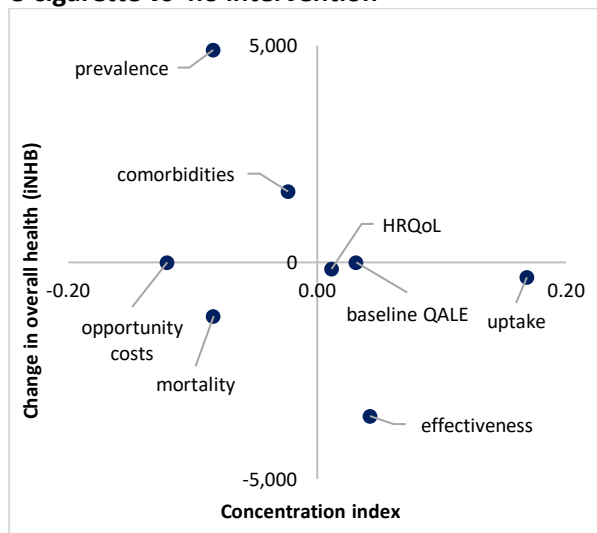
Figure S14. Equity impact plane showing scenario analysis results where levelling up to the best

e-cigarette vs 'no intervention'
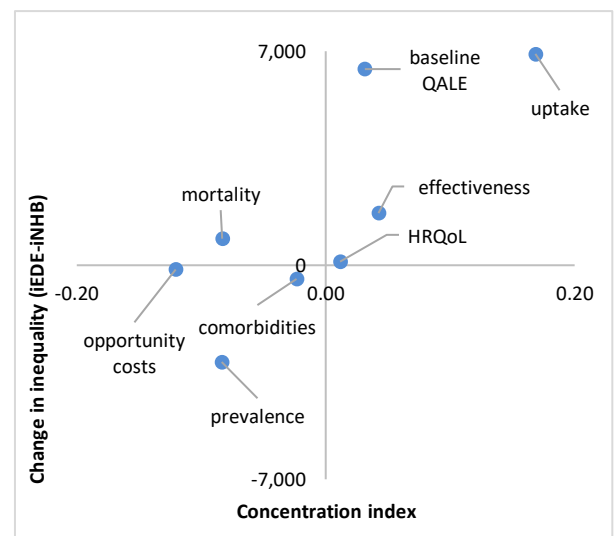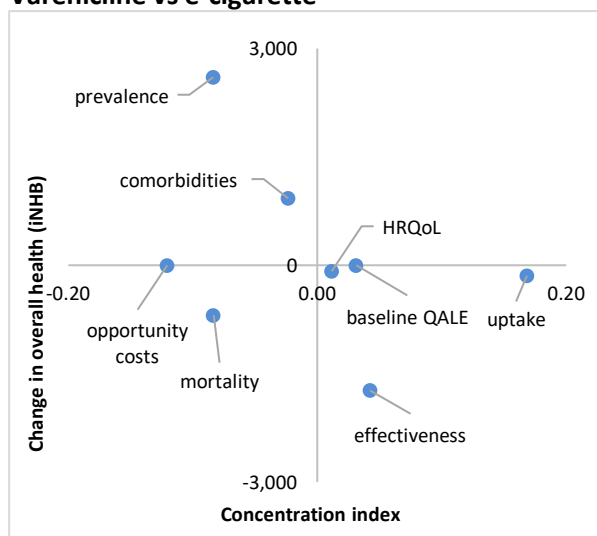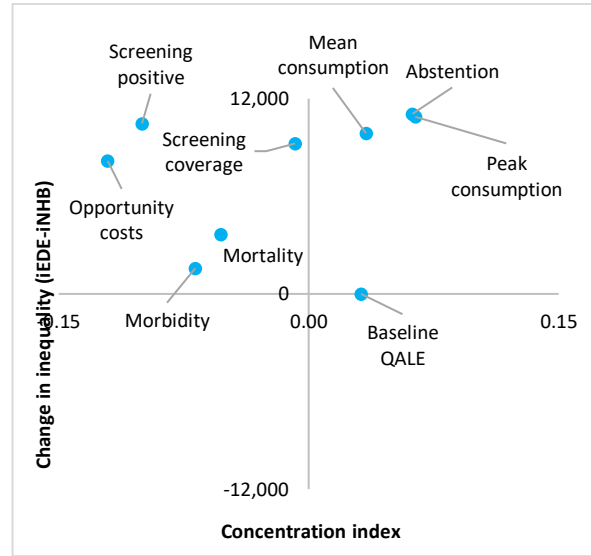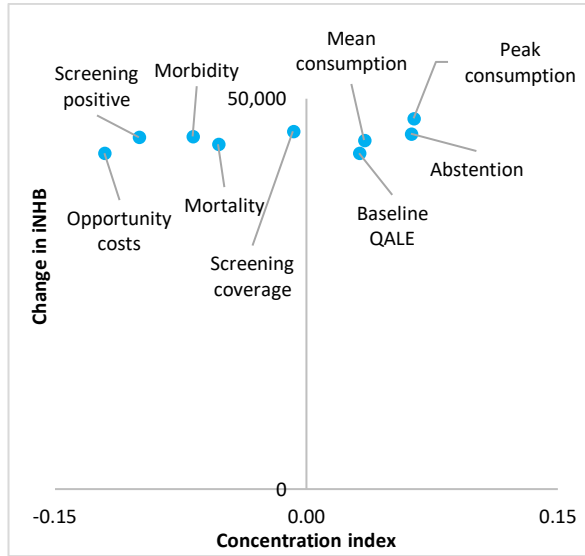

Varenicline vs e-cigarette

Figure S15. Impact of ignoring gradients vs. concentration indices in those gradients in smoking model

Next Consultation vs 'no intervention'
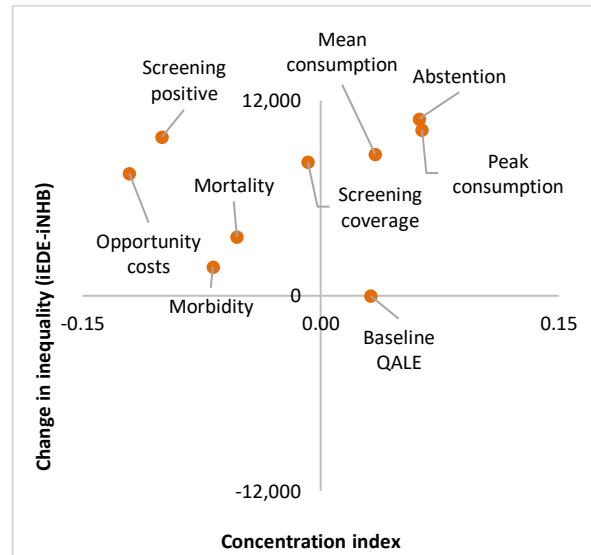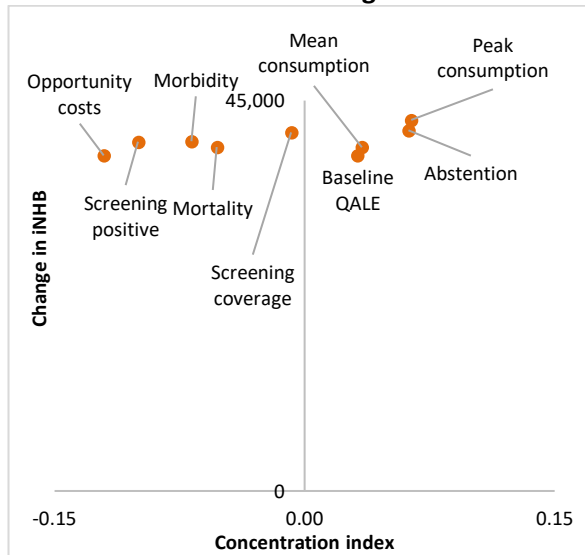

Next Consultation vs Next Registration

Figure S16. Impact of ignoring gradients vs. concentration indices in those gradients in alcohol model