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Communication of personalised disease risk by general practitioners to motivate smoking cessation in England: A cost-effectiveness and research prioritisation study

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Abstract

Background and Aims

Communication of personalised disease risk can motivate smoking cessation. We assessed whether routine implementation of this intervention by general practitioners (GPs) in England is cost-effective or whether we need further research to better establish its effectiveness.

Design

Cost-effectiveness analysis (CEA) with value of information (VoI) analysis from the UK National Health Service perspective, using GP communication of personalised disease risk on smoking cessation versus usual care.

Setting

GP practices in England.

Study population

Healthy smokers aged 35-60 attending the GP practice.

Measurements

Effectiveness of GP communication of personalised disease risk on smoking cessation was estimated through systematic review and meta-analysis. A Bayesian CEA was then performed using a lifetime Markov model on smokers aged 35-60 that measured lifetime costs and quality-adjusted life-years (QALYs) assigned to the four diseases contributing the most to smoking-related morbidity, mortality and costs: chronic obstructive pulmonary disease, lung cancer, myocardial infarction, and stroke. Costs and QALYs for each disease state were obtained from the literature. VoI analysis identified sources of uncertainty in the CEA and assessed how much would be worth investing in further research to reduce this uncertainty.

Findings

The meta-analysis odds ratio for the effectiveness estimate of GP communication of personalised disease risk was 1.48 (95% credibility interval (CrI): 0.91-2.26), an absolute increase in smoking cessation rates of 3.84%. The probability of cost-effectiveness ranged from 89-94% depending on sex and age. VoI analysis indicated that: 1) uncertainty in the effectiveness of the intervention was the driver of the overall uncertainty in the CEA and 2) a research investment to reduce this uncertainty is justified if lower than £27.6million (£7 per smoker).

Conclusions.

Evidence to date shows that, in England, incorporating disease risk communication into general practitioners' practices to motivate smoking cessation is likely to be cost-effective compared with usual care.

Introduction

Despite the well-known adverse effects of smoking on health, smoking cessation remains a challenge for smokers and healthcare providers alike, with some evidence suggesting it takes an average of 30 attempts to quit smoking successfully for one year(1). Smoking cessation can be encouraged in many ways, ranging from societal level interventions such as increasing taxes on tobacco(2), to the use of motivational text messages addressing/targeting smokers(3). One method of encouraging smoking cessation is through doctor advice, and the National Institute for Health and Care Excellence (NICE) in the UK recommends that general practitioners (GPs) advise all smokers to quit(4). A meta-analysis on the effect of stop-smoking advice delivered by physicians found that even brief general information on the health effects of smoking along with a message to quit smoking resulted in a relative risk of smoking cessation of 1.66 (95% CI 1.42 to 1.94)(5) compared to receiving no advice. Because GPs are in a unique position to access the general population of smokers, including those who are not motivated to quit, identifying means to further increase smoking cessation at that level can result in a large impact.

One possible avenue to improve on brief GP advice is to use disease risk prediction tools to provide information to smokers on their own personal risk of disease and how this could be reduced by quitting smoking. A qualitative study by Usher-Smith et al. found that GPs consider that a cancer risk prediction tool could be useful in encouraging smoking cessation(6). There is evidence suggesting the effectiveness of communication of personalised disease risk by GPs to motivate smoking cessation (for example, informing patients of their risk of cardiovascular disease, or 'lung age' based upon lung function measurements) has been shown to increase quitting rates(7,8). Providing personalised feedback on genetic susceptibility to smoking-related disease has also been explored in the context of smoking cessation(9,10), although there does not seem to be evidence that it is effective(11,12) and it would not be possible to apply opportunistically in a GP setting where genotype information is generally not available.

In 2009, the British National Health Service (NHS) introduced the NHS health checks programme, a population-level intervention that aims to reduce the rates of cardiovascular disease by offering all citizens aged 40-75 an appointment at their GP surgery during which they receive an estimate of their cardiovascular risk along with advice on how this risk could be reduced(13). Participants at higher cardiovascular risk are then offered interventions to lower modifiable risk factors, including use of smoking cessation aids and stop smoking services for smokers. While NHS health checks appear to be effective in motivating smoking cessation(14), this service has had lower than expected uptake(15), with 75% of the eligible population invited but only 36% receiving it(16). The low uptake of the NHS health checks has negatively affected its cost-effectiveness(17), which leads to discussion of whether it should be offered only to those most at risk. A more cost-effective approach might be to apply this sort of intervention opportunistically to all smokers attending the GP surgery. Applying this intervention during an appointment scheduled for a separate reason means that patients do not need to set additional time aside to attend, which was a commonly reported reason for non-attendance at NHS health checks(18,19).

The present study aimed to assess whether communication of personalised disease risk by GPs to smokers attending their practice is cost-effective for smoking cessation, through a cost-effectiveness analysis (CEA). We then evaluated if the currently available evidence is sufficient to recommend for this intervention to be routinely implemented by GPs in their clinical practice,

or if more research is required before we can make an informed decision. We used a value of information (VoI) analysis to identify parameters in the CEA model where uncertainty in the evidence most impacts the findings, therefore informing on whether and where further research is necessary(20).

Methods

Systematic review and meta-analysis on effectiveness of the intervention

Personalised disease risk communication by GPs to motivate smoking cessation involves smokers receiving an estimate of their risk of developing a certain disease, and an explanation of how much this risk could be lowered through quitting smoking. There are a number of tools available that provide estimates in the form of 10-year or life-time risk(21,22), or presented in forms such as 'lung age' or 'heart age'(21,23). We conducted a systematic review of published literature with meta-analysis on the effectiveness of communication of personalised disease risk by GPs on smoking cessation. An electronic search was performed on 29th February 2020 using Medline, Embase, and the Cochrane library, and it was limited to articles published in English (the full search strategy for each database is reported in Supplementary Tables 1-3). We included both observational and interventional studies if they had measured smoking cessation as an outcome after a minimum of 12 weeks, and if they contained an appropriate comparative group not receiving the intervention. We considered only peer-reviewed studies, and a risk-of-bias analysis was not performed. A meta-analysis to obtain a pooled odds ratio (OR) was performed using a Bayesian random-effects model, with 95% credible interval (95%CrI) being used as the Bayesian analogue of the frequentist 95% confidence interval (95%CI). Credible intervals directly reflect our degree of belief in where an estimate lies, rather than the more abstract concept of confidence intervals based on the idea of hypothetical repeated sampling. Between-study heterogeneity was assessed using the I^2 statistic(24), which estimates the proportion of variability in effect estimates explained by differences between studies rather than by sampling error. We used the estimate of effectiveness obtained from this meta-analysis in the CEA. A Bayesian analysis was carried out here and throughout the analysis. The Bayesian approach has a number of advantages. The flexibility of the Bayesian framework allows parameter uncertainty to be easily propagated through the analysis. Additionally, the Bayesian analysis allows the incorporation of prior information. In meta-analyses that contain few studies, such as in our case, the between-trial heterogeneity can be difficult to estimate accurately, and we have therefore incorporated prior beliefs on between-study heterogeneity to stabilise its estimate, as previously suggested(25).

CEA

Long-term health outcomes can be modelled through the use of Markov models, which can be used to describe the progression of individuals across a finite set of clinical states that describe a simplified version of the natural history of disease. We applied a life-time Markov model on a simulated cohort of 10,000 smokers who start in the 'healthy' state and move through model disease states according to pre-defined transition probabilities until entering the 'death' state.

For the target population, we considered healthy adult smokers aged 35-60 from the general population. The reason for not considering younger ages is that the disease outcomes evaluated are rare before the age of 35, and quitting smoking before this age brings the risk of mortality back to the level in never-smokers(26). Additionally, because this intervention revolves around communication of disease risk, and the risk of disease in young smokers is low, we only considered the use of personalised disease communication in those for whom changes in risk are likely to be apparent. At the other end of the spectrum, it is for this reason that only smokers free of disease are modelled, as it is not possible to give an estimate of risk to those who already have been diagnosed with disease.

The model uses yearly cycles, and at each cycle the population in each state in the model can change state or remain in the same state according to the transition probabilities associated with that state and population. Each state was associated with a given cost and quality-adjusted life-year (QALY) value. The total costs and QALYs at the end of the model are calculated from the total time spent in each model state, and the cost of the intervention, which was calculated by multiplying GP time cost by the length of time taken to use a tool to calculate personalised disease risk (10 minutes). The tool was assumed to have no direct effect on a patients' quality of life. We used QALYs from the perspective of the individual and direct costs from the perspective of the health service, a willingness-to-pay threshold of £30,000 per QALY(27), and a yearly discount rate of 3.5%(27) that gives less weight to costs and QALYs further in the future. More details on the model are reported in the Supplemental methods section 2.

Both the baseline and intervention models were run with the population varied according to age (35, 40, 45, 50, 55, 60) and sex (male, female), resulting in 24 different scenarios. We included a background smoking cessation rate in both models, reflecting that the intervention (personalised disease risk communication) would be used in addition to, rather than instead of, current smoking cessation interventions in England. We use the expected difference in costs and QALYs from implementation of the intervention to calculate the incremental cost-effectiveness ratio (ICER), which is the expected monetary cost of the intervention per QALY gained. The ICER can be compared to the willingness-to-pay threshold to determine whether an intervention is likely to be considered cost-effective. It is not possible to calculate meaningful confidence intervals for an ICER when there is a chance of obtaining negative ratios(28), so instead we calculated the probability of cost-effectiveness by running the model multiple times (N=15,000 iterations) under parameter uncertainty and assessing the proportion of times in which the intervention is cost-effective at the willingness-to-pay of interest. The CEA was carried out following the reporting guidelines outlined in the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Statement.

VoI

VoI analysis is a tool for research prioritisation that assesses whether we have enough evidence at present to make the decision now, or whether it is worth investing in further research to lower the uncertainty surrounding the decision(20,29). We calculated the expected value of perfect information (EVPI) per smoker and the expected value of partially perfect information (EVPPI) for each parameter in the model.

The CEA will tell us whether the intervention is cost-effective given the current information and the resulting uncertainty in the model inputs; if the intervention is cost-effective then it is the best treatment under current parameter uncertainty. If the intervention is not cost-effective then the baseline treatment is the best decision. The EVPI calculates the expected cost of making the wrong decision due to uncertainties in all parameters, i.e. the maximum amount that a decision-maker should be willing to pay to obtain "perfect" information on all parameters to inform their decision. To calculate the EVPI, we require the net monetary benefit (NMB) for both the baseline and the intervention arms. The NMB converts QALYs into costs so that both costs and effectiveness can be assessed using the same unit (£). The NMB is calculated for each iteration in both treatment arms by multiplying QALYs by the willingness-to-pay and subtracting the costs. The higher of the two NMBs is the best decision under the parameter values of the given iteration, representing the decision made under complete certainty for all parameter values. When calculating the EVPI, the NMB of the best treatment decided by the CEA is subtracted from the higher of the two NMBs for each iteration. This difference represents the expected benefits from further research that are lost when making the decision under current evidence, and so if the higher NMB in the iteration is that of the best treatment decided by the CEA, the difference is £0 indicating no benefit from further research. The average difference across all iterations is the EVPI.

Whilst the EVPI is helpful in quantifying the overall value of information, it is ultimately a theoretical threshold, because we will never be in a position of completely eliminating the uncertainty in all the model parameters. For this reason, we also calculated the EVPPI for each parameter in the model, which shows how uncertainty in each parameter affects the decision, and how much a decision-maker should be willing to pay to obtain perfect information on each separate parameter. It is calculated by assessing the difference between the expected NMB of a decision made with perfect information on the parameter(s) of interest and the expected NMB with the current information on this parameter. EVPPI proves more helpful than the EVPI, because it can be used to determine which of the many model inputs are responsible for the uncertainty driving the current decision-making process, as well as to place an upper limit on the amount of resources that we should be willing to invest to reduce that uncertainty.

The EVPI and EVPPI were calculated by the BCEA R package(30) using the multivariate distribution of parameter uncertainties and the estimated costs and QALYs of each CEA scenario. The per-smoker EVPI and EVPPI estimates were then multiplied by the total number of smokers in England, obtained from the Office of National Statistics (ONS)(31), to assess the maximum costs of further research that would be justified to improve decision-making.

Data sources

The effectiveness of communication of personalised disease risk by GPs on smoking cessation was obtained through systematic review and meta-analysis. The model includes four explicitly modelled disease pathways: COPD, lung cancer, myocardial infarction, and stroke, which account for 75% of smoking-related deaths(32). Costs, QALYs, and transition probabilities for each disease pathway and smoking cessation were obtained from the literature and using governmental data. Data values, sources and assumptions for key parameters can be found in

Tables 1-3, with a detailed description in the Supplemental methods section 2. Costs were adjusted for inflation by multiplying costs as provided in
Godfrey et al(33) and Punekar et al(34) by the hospital and community health services (HCHS) yearly inflation indices presented in section 15.3 of Unit Costs of Health and Social Care guidelines(35) up to year 2017-18 (Table 3).

Pre-registration

The analyses reported in this paper were not pre-registered.

Sensitivity analyses

We performed several sensitivity analyses in the meta-analysis and CEA. In our Bayesian meta-analysis, we repeated the analysis under a variety of vague priors (Supplementary Table S4) to assess whether our choice of vague prior could have affected our results. We also performed sensitivity analyses to investigate heterogeneity in the meta-analysis, by considering: exclusion of studies of smokers with a mean age greater than 60; exclusion of studies that did not objectively assess smoking cessation; and exclusion of studies that did not apply ITT or did not include smokers lost-to-follow-up as continuing to smoke (i.e. worst-case scenario). Finally, we performed a sensitivity analysis in the CEA whereby 10% of ex-smokers in their first year of quitting reverted back to smokers, to assess the robustness of our model and results to relapse.

Results

Systematic review and meta-analysis on effectiveness of the intervention

After removal of duplicates, the search returned a total of 3,554 studies, of which 7 studies were eligible to be included in the meta-analysis (Benner et al (2008)(36), Foraker et al (2016)(37), Lowensteyn et al (1998)(38), Mills et al (2010)(39), Parkes et al (2008)(8), Segnan et al (1991)(40), Stol et al (2020)(41)). All identified studies were randomised controlled trials carried out across Europe and North America. The studies used lung age(8,40) and cardiovascular disease risk scores(36–39,41) to communicate personalised disease risk, and measured smoking cessation between 3-12 months after the intervention. Further details on the included studies can be found in Supplementary Table 5.

We found evidence that communication of personalised disease risk from a GP increases rates of smoking cessation, with smokers provided with their personalised disease risk being about 50% more likely to quit smoking (OR=1.48, 95%CrI:0.91-2.26). This corresponds to an absolute increase in smoking cessation rates of 3.84% when applied to 2021 smoking cessation prevalence estimates for England(42). There was some evidence of heterogeneity between the studies (I^2=21%, 95%CrI: 0-64). Due to the low number of studies included in the meta-analysis, a sensitivity analysis found that our results were sensitive to the choice of prior for the between-study variance (Supplementary Table 4), with the choice of prior distribution used for the analysis affecting the 95%CrI of the calculated effect size. Given that it was not possible to choose a vague prior that would not affect the results of the meta-analysis, we used a weakly informative prior for between-study variance as proposed by Turner et al(25), based on empirical assessment of the between-study variance in 14,886 published meta-analyses. In

particular we used the prior suggested for meta-analyses of non-pharmacological interventions studies with subjective outcomes.

We performed several sensitivity analyses to explore heterogeneity in the trials included in the meta-analysis and their applicability to our hypothetical study population. When excluding studies of smokers with a mean age greater than 60, we found similar results (OR=1.58, 95%CrI:0.93-2.56) from four studies. A sensitivity analysis that excluded studies that did not objectively assess smoking cessation found an effectiveness of 1.73 (95% CrI 0.67 to 4.22) from three studies. Finally, when excluding studies that did not apply ITT or did not include smokers lost-to-follow-up as continuing to smoke (i.e. worst-case scenario), we found an effectiveness of 1.96 (95% CrI 0.88 to 5.30) from two studies. While the findings of all these sensitivity analyses were consistent with the original estimate, the low number of studies remaining in some sensitivity analyses resulted in a reduced precision of the estimate with larger credible intervals.

CEA

We found that communication of personalised risk prediction in GP practices to motivate smoking cessation is cost-effective at a willingness-to-pay threshold of £30,000 per year at all modelled ages of healthy smokers. Table 4 shows the difference in costs and QALYs, and the incremental cost-effectiveness ratio for scenarios in which the personalised risk score is used at ages 35, 40, 45, 50, 55, and 60 for males and females. Calculated ICERs for all scenarios were below this threshold, so they are deemed cost-effective. The intervention was more effective but more expensive in 4 out of the 12 scenarios, with the rest of the scenarios showing the intervention as both more effective and less expensive. The probability of cost-effectiveness tended to increase with age, from 89-91% when given at age 35 up to 94% when given at age 60, and tended to be higher for males than for females. For illustration, Figure 2 shows the cost-effectiveness plane for the intervention when given to males aged 35. A sensitivity analysis in which we assumed that ex-smokers in their first year of quitting have a 10% probability of relapsing did not substantially alter the results (supplementary tables S16 and S17), with ICERs at all age groups still indicating cost-effectiveness.

VoI

The value of information at the willingness-to-pay threshold of £30,000 per QALY ranged from £5-10 per smoker in all scenarios (Table 5), with a population-weighted average of £7 per smoker. Combining the EVPI with the population of smokers in England, we found that further research to reduce uncertainty is justified at the population level, but only if the investment is lower than £27.6 million (obtained by multiplying the number of smokers in each age/sex group by the EVPI cost per smoker for that group).

Based on the computed EVPPI for each variable in the model, the effectiveness of the intervention was the only parameter for which further research was justified, with an EVPPI almost equal to EVPI in all scenarios. Uncertainties in disease costs, QALYs, and smoking cessation rates each gave an EVPPI of £0.

Discussion

We found that communicating personalised disease risk through use of a prediction tool is likely to be cost-effective if used by GPs in England to motivate smoking cessation, with a probability of cost-effectiveness of 89-94%. However, there is some uncertainty in this result and our VoI analysis suggests that further research to reduce this uncertainty would be justified, but only at a cost lower than £27.6 million (£7 per smoker on average). VoI accounts for both the probability of cost-effectiveness and the impact of making a wrong decision(43). Given the high prevalence of smokers, the health and economic consequences of implementing an ineffective intervention on a population level justifies collecting further information rather than carrying out the intervention based on current evidence.

The effectiveness of GP communication of personalised disease risk for smoking cessation was the only parameter with an EVPPI greater than £0 and therefore the only driver of uncertainty in our cost-effectiveness analysis, suggesting that this is where future research should focus on. Methods for personal risk communication differ for the disease considered or for the way the risk is communicated. For example, Berry et al(44) found that Canadian women perceive breast cancer to be more serious than heart disease, which could affect their response to receiving an estimate of their risk of these diseases. A large number of participants attending NHS health checks are confused by or misunderstand their cardiovascular risk score(45), and other methods of presenting risk, such as through the use of concepts such as “heart age”(21), may be a more effective way in presenting risk information(46). The methods of risk presentation in our systematic review were cardiovascular risk and ‘lung age’. Whilst ‘lung age’ calculation uses spirometry and may be outside the scope of routine GP practice, the calculation of cardiovascular risk is simple and is currently used in NHS health checks, where it is presented as ‘heart age’.

VoI sensitivity analyses showed a high probability of cost-effectiveness, mainly due to the low cost of the implementation of the intervention compared with the high cost of smoking-related diseases and the large health benefits of smoking cessation. However, this intervention had a low effectiveness overall, evidenced by the low difference in QALYs gained. The meta-analysis for the use of personalised disease risk communication to motivate smoking cessation suggests that the intervention is likely to be nearly 50% more effective in motivating smoking cessation over the baseline cessation rate, although the wide 95%CrI of the pooled odds ratio shows uncertainty around this estimate of effectiveness.

Our CEA, which considered communication of personalised disease risk prediction in healthy smokers aged 35-60, found that the intervention was cost-effective at all ages for both men and women, but it was more cost-effective at higher ages. This result may seem counter-intuitive when considering that quitting smoking at earlier ages is more beneficial for health, but a possible explanation is that discounting was used, whereby present-day health and costs are valued higher than health and costs in the future. Smoking-related diseases tend to occur later in life, and so in scenarios when the intervention is given at younger ages, the negligible immediate health benefits of smoking cessation in younger smokers are given a greater weight than the much larger benefits in older smokers, resulting in a lower cost-effectiveness.

We did not model ages younger than 35, which raises the question over how cost-effective this intervention may be in younger ages. The studies that were included in the meta-analysis for the effectiveness of the intervention have an average age of 46-67, with young adults only eligible for inclusion in 2 out of the 7 studies, so it is difficult to predict how effective this intervention may be in younger ages given different attitudes towards risky behaviours and the length of time in which smoking-related disease is likely to occur. Prokhorov et al (47) assessed a smoking cessation intervention that included provision of personalised disease risk communication in college students (mean age = 23); they found higher cessation rates in students who received the intervention but this result was not statistically significant, indicating that further research in young adults is needed.

The model takes 'smokers' as a homogenous group and does not account for pack-years smoked due to a lack of disease incidence data stratified by pack-years in addition to stratification by age and sex. As smokers will be heterogeneous with regards to their pack-years smoked when given the intervention, use of values that apply to smokers as a whole was deemed acceptable. Moreover, we did incorporate the reduction in disease risk according to the length of time since quitting smoking.

One of the limitations of the model is that it assumes that those who entered a disease pathway remain on that pathway and cannot switch to a different one or be part of multiple pathways simultaneously. This will underestimate the costs and (loss of) QALYs associated with smoking, because the costs and QALYs of living with comorbidities will not be accounted for. However, the model does consider all-cause mortality, which includes mortality from diseases other than the disease pathway the subject has been "assigned" to, thus partly addressing this issue in an implicit way. The model assumes that disease progression and risk of death after lung cancer diagnosis, acute myocardial infarction and acute stroke is unaffected by smoking status and previous history of the disease, which will produce more conservative estimates of the impact of smoking cessation as smokers have more myocardial events than quitters(48). The model also assumes stable risk in the second year onwards after myocardial infarction and stroke, which is lower than the risk in the first year but higher than the risk in the general population with no history of myocardial infarction or stroke(49). Healthcare costs and QALYs attached to a disease state are assumed to be the same for both smokers and ex-smokers. Disease management does not differ according to smoking status, however, smokers tend to have a worse prognosis than ex-smokers(50) and may utilise more healthcare resources, with increased costs(51). Therefore, assuming that disease progression, costs and QALYs are the same in smokers and ex-smokers will produce more conservative estimates for the benefits of quitting smoking.

The model incorporates the four diseases that contribute to 75% of smoking-related deaths(32), which will produce conservative estimates for the benefits of smoking cessation, as the mortality rate for diseases not included in the model was assumed to be the same for both smokers and ex-smokers and used the mortality rate of the general population.

The model assumes that those who quit smoking do not relapse, when in fact the relapse rates after a quit attempt are extremely high(52). However, smoking cessation was calculated with ex-smokers who had quit in the last 5 years, suggesting that the smoking cessation data used in the model reflects long-term quitters at low risk of relapse, and so it is not necessary to

additionally include relapse in the model. Moreover, a sensitivity analysis in which relapse was included did not substantially alter our results.

In summary, we found that provision of personalised disease risk communication to motivate smoking cessation in GP surgeries in England is likely to be cost effective; however, further research would be beneficial in reducing the uncertainty in the effectiveness of this intervention before its implementation, but only if it can be successfully carried out for less than £27.6 million.

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Table 1: Parameters in the Markov model

Parameter	Smokers	Ex-smokers	Assumptions
Disease transition parameters			• *Smokers were treated as a homogenous group ignoring the amount of pack-years smoked, (no available data linking pack-years to disease incidence by age and sex)* • *Once an individual enters a particular disease pathway, they remain in that pathway for life and cannot return to the healthy state or enter another disease pathway.* • *Unlike for COPD, disease progression and risk of death after disease diagnosis for lung cancer, acute myocardial infarction and acute stroke, are unaffected by smoking status (no available data split by age and sex)* • *Disease progression and risk of death is unaffected by previous disease history, due to lack of available data*
Healthy to COPD GOLD stage 1	0.0003 to 0.0083	0.0002 to 0.0047	
Healthy to COPD GOLD stage 2	0.0003 to 0.0074	0.0001 to 0.0041	
Healthy to 1st year lung cancer	0.0001 to 0.0178	0.0000 to 0.0111	
Healthy to 1st year MI	0.0002 to 0.0322	0.0001 to 0.0237	
Healthy to 1st year stroke	0.0002 to 0.0111	0.0002 to 0.0081	
COPD GOLD stage 1 → 2	0.0276 to 0.0486	0.0173 to 0.0306	
COPD GOLD stage 2 → 3	0.0623 to 0.1076	0.0387 to 0.0668	
COPD GOLD stage 3 → 4	0.0522 to 0.0901	0.0341 to 0.0590	
Mortality rates			
Healthy to MI death	0.0000 to 0.0061	0.0000 to 0.0045	
Healthy to stroke death	0.0001 to 0.0057	0.0000 to 0.0042	
Healthy to all-cause mortality	0.0005 to 0.0437	0.0005 to 0.0437	
COPD GOLD stage 1 to COPD death	0.0019 to 0.0532	0.0012 to 0.0221	
COPD GOLD stage 2 to COPD death	0.0032 to 0.1123	0.0021 to 0.0639	
COPD GOLD stage 3 to COPD death	0.0059 to 0.2266	0.0040 to 0.1444	
COPD GOLD stage 4 to COPD death	0.0070 to 0.2779	0.0048 to 0.1806	
1st year lung cancer to lung cancer death	0.3760 to 0.7110	0.3760 to 0.7110	
2nd year+ lung cancer to lung cancer death	0.1273 to 0.2702	0.1273 to 0.2702	
1st year MI to MI death	0.0013 to 0.0393	0.0013 to 0.0393	
2nd year+ MI to MI death	0.0017 to 0.0233	0.0017 to 0.0233	
1st year stroke to stroke death	0.0226 to 0.0338	0.0226 to 0.0338	

2nd year+ stroke to stroke death	0.0113 to 0.0169	0.0113 to 0.0169
Baseline proportion of smoking cessation	0.06 to 0.19	-

Disease transition parameter and mortality rate ranges for smokers given for females aged 35 to males aged 80

Disease transition parameter and mortality rate ranges for ex-smokers given for females aged 35 who have been ex-smokers for 20 years to males aged 80 who have been ex-smokers for 1 year

Baseline proportion of smoking cessation given for those with the lowest proportion (males aged 50-54) to the highest proportion (females aged 35-39). Proportions calculated using Health Survey for England data.

COPD = Chronic Obstructive Pulmonary Disease, GOLD = Global Initiative for Chronic Obstructive Lung Disease, MI = myocardial infarction

Table 2: Quality-adjusted life-years associated with each state in the model

Model state	Mean QALY (SE)	Reference	Assumptions
COPD pathway			*QALYs do not differ according to age, sex or smoking status.*
Gold 1	0.828 (0.062)	Einarson et al(53)	
Gold 2	0.765 (0.09)	Einarson et al(53)	
Gold 3	0.711 (0.12)	Einarson et al(53)	
Gold 4	0.607 (0.12)	Einarson et al(53)	
Lung cancer pathway			
Lung cancer	0.665 (0.102)	Sturza(54)	
MI pathway			
First year after MI	0.8136 (0.0091)	Nikolic et al(55)	
Second year+ after MI	0.8763 (0.0028)	Nikolik et al(55)	
Stroke pathway			
First year after stroke	0.7 (0.013)	Luengo-Fernandez et al(56)	
Second+ year after stroke	0.66 (0.018)	Luengo-Fernandez et al(56)	

Table 3: Cost values for health states and interventions. Costs presented are adjusted for inflation. All costs associated with health states were artificially given uncertainty using a normal distribution about the mean cost with a standard error of 10% of the mean.

Model state	Cost (£)	Reference from which we obtained cost estimates, with year to which costs were adjusted	Original paper in which costs were estimated, with year of cost assessment	Assumptions
COPD pathway				*Costs do not differ according to age, sex, or smoking status.*
Gold 1	2,165	Punekar et al(34), 2010-11	-	
Gold 2	2,278	Punekar et al(34), 2010-11	-	
Gold 3	2,499	Punekar et al(34), 2010-11	-	
Gold 4	2,880	Punekar et al(34), 2010-11	-	
Death from COPD	2,020	Godfrey et al(33), 2009	Britton et al(57), 2000-01	
Lung cancer pathway				
Lung cancer	6,345	Godfrey et al(33), 2009	Allender et al(58), 2005-06	
Lung cancer death	16,870	Godfrey et al(33), 2009	US Environmental Protection agency(59), 2005-06	
MI pathway				
First year after MI	10,127	Godfrey et al(33), 2009	Hartwell et al(60) and Vergel et al(61), 2002-04**	
Second year+ after MI	1,103	Godfrey et al(33), 2009	Briggs et al(49), 2004	
Death from MI	4,074	Godfrey et al(33), 2009	Briggs et al(49), 2004	
Stroke pathway				
First year after stroke	15,611	Godfrey et al(33), 2009	Kalra et al(62), 1997-98	
Second+ year after stroke	2,714	Godfrey et al(33), 2009	Kalra et al (62), 1997-98	
Death from stroke	9,513	Godfrey et al(33), 2009	Youman et al(63), 2004	
All pathways				
Death from any other cause	11,630	Godfrey et al(33), 2009	Briggs et al(49), 2004	
Intervention costs				

GP time cost	263.00 (per hour)	Curtis & Netten(35), 2018	-	

*Godfrey et al(33) amalgamated the various costs in their model and adjusted them for inflation to 2009 levels. Costs were extracted after inflation adjustment and further adjusted to 2017-18 levels.

**Combination of Initial treatment (2002-03) from (60) and MI state year 1 (2003-04) from (61)

Table 4: Results from the cost-effectiveness analysis, broken down according to sex and age. All scenarios compare use of a personalised risk score at a designated age to the baseline smoking cessation scenario. Results based on a cohort size of 10,000.

Scenario	Age at which intervention is given	Mean difference in costs (95%CrI) (£)*	Mean difference in QALYs (95%CrI)**	ICER (£ per QALY)	Probability of cost-effectiveness***
Males	35	90,600 (-242,700 to 398,600)	48 (1 to 99)	1,884	0.91
	40	-22,000 (-489,700 to 396,000)	70 (1 to 146)	-316	0.92
	45	-223,600 (-914,500 to 390,600)	115 (3 to 241)	-1,952	0.94
	50	-36,300 (-593,600 to 396,600)	89 (2 to 202)	-407	0.92
	55	-211,900 (-888,200 to 391,600)	162 (4 to 340)	-1,306	0.94
	60	-191,700 (-895,800 to 393,300)	172 (3 to 374)	-1,116	0.94
Females	35	223,200 (30,300 to 401,200)	44 (1 to 92)	5,030	0.89
	40	126,400 (-181,000 to 399,200)	70 (1 to 147)	1,805	0.92
	45	-34,100 (-514,200 to 395,100)	114 (3 to 240)	-298	0.94
	50	58,700 (-381,600 to 398,400)	91 (2 to 207)	642	0.92
	55	-230,900 (-930,900 to 391,000)	181 (4 to 377)	-1,279	0.94
	60	-156,200 (-819,400 to 393,900)	172 (4 to 374)	-906	0.94

*Positive cost differences indicate that the intervention is more costly than the baseline scenario
**Positive QALY differences indicate that the intervention results in greater total QALYs than the baseline scenario
***Proportion of times that the intervention was cost-effective across all model runs

Table 5: The expected value of perfect information, estimates of smoker population, and total research costs justified according to sex and age group for smokers in England.

Age	Male EVPI (£ per smoker)	Male smoker population	Research costs justified for male smokers according to age (£)	Female EVPI (£ per smoker)	Female smoker population	Research costs justified for female smokers according to age (£)
35-39	5	431,000	2,155,000	5	349,000	1,745,000
40-44	6	408,000	2,448,000	6	330,000	1,980,000
45-49	8	455,000	3,640,000	7	373,000	2,611,000
50-54	6	388,000	2,328,000	6	312,000	1,872,000
55-59	10	347,000	3,470,000	10	278,000	2,780,000
60-65	10	132,000	1,320,000	10	125,000	1,250,000

Figure 1: Forest plot on the effect of personalised disease risk communication on the odds of quitting smoking. Analysis uses an informed prior for between-trial variance for a subjective non-pharmacological intervention as specified by Turner et al(25) of a log-normal distribution with mean=-2.01 and variance=1.64^2:

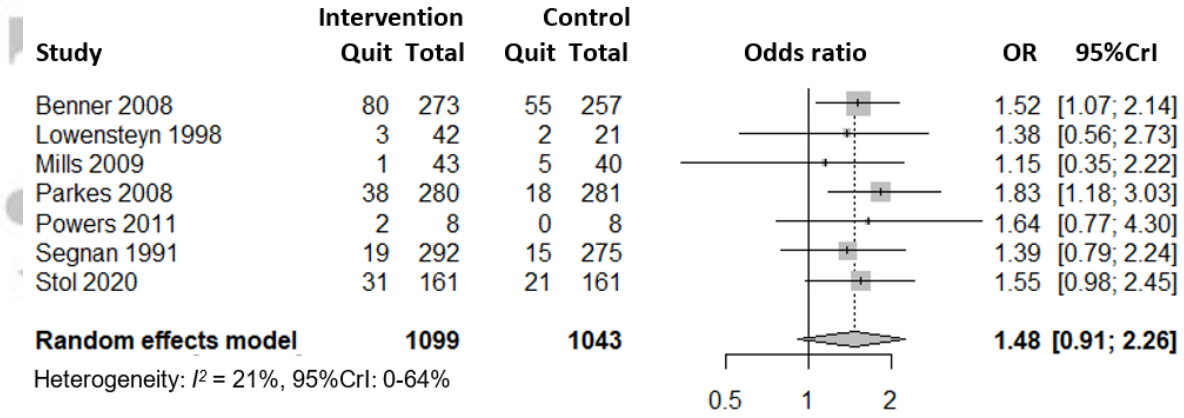

Figure 2: Cost-effectiveness plane for the use of personalised risk communication by GPs to motivate smoking cessation in males aged 35 (discounted analysis). Results are presented per 100 people. The plot displays the difference in costs and QALYs due to use of the intervention compared with the baseline scenario. Each grey dot represents the output from one of the 15,000 iterations, which are used to assess uncertainty in the analysis. The x-axis represents difference in QALYs, with positive values representing greater beneficial effects of the intervention. The y-axis represents difference in costs, with negative values indicating that the intervention is less expensive than not using it. Points that lie in the shaded area on the right of the line are deemed to be cost-effective. The mean incremental cost-effectiveness ratio (ICER) is plotted as a red point. The cost effectiveness gradient is the black line running through the origin of the graph.