Evidence review

School-based interventions to prevent the uptake of smoking among children and young people: cost-effectiveness model

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West Midlands Health Technology Assessment Collaboration

The West Midlands Health Technology Assessment Collaboration (WMHTAC) is an organisation involving several universities and academic groups who collaboratively undertake research synthesis to produce health technology assessments. Most of our members are based in the Public Health, Epidemiology & Biostatistics Unit, University of Birmingham, but other members are drawn from a wide field of expertise including economists and mathematical modellers from the Health Economics Unit, University of Birmingham.

WMHTAC produce systematic reviews, health technology assessments and economic evaluations for NHS R&D HTA programme (NCCHTA), the National Institute for Health and Clinical Excellence (NICE), and for the health service in the West Midlands. WMHTAC also undertakes methodological research on research synthesis, and provides training in systematic reviews and health technology assessment.

Name of other institution(s) involved

WMHTAC works in close collaboration with the Peninsula Technology Appraisal Group (PenTAG) with respect to providing support to the NICE Centre for Public Health Excellence (CPHE). PENTAG however was not involved in this particular project. Colleagues from the University of Bath undertook the qualitative review related to this project (described in a separate report).

Table of Contents

Table of Figures

Executive summary

The National Institute for Health and Clinical Excellence (NICE) has been asked by the Department of Health (DH) to develop guidance on public health interventions for the NHS and local authorities aimed at preventing the uptake of smoking among schoolchildren (National Institute for Health and Clinical Excellence 2008).

Two accompanying systematic reviews of the literature cover the effectiveness and cost-effectiveness evidence on school-based smoking prevention programmes. A further evidence review focuses on qualitative evidence related to such interventions. The review of the economic literature revealed no published economic evaluations of school-based smoking prevention programmes in the UK. Studies based in other countries are of limited relevance to the UK situation because of differences in both the populations being studied and the methodological framework used. A further limitation with the existing literature is that most published studies assume that school-based smoking prevention programmes can achieve a lasting reduction in smoking prevalence beyond school-age which is not supported by evidence in the effectiveness literature. Consequently, we conducted a *de novo* model to provide information in order to determine whether the implementation of a school-based smoking prevention initiative would be cost-effective.

Because of the lack of evidence for a lasting effect from school-based smoking prevention programmes, the modelling focused on exploring whether a delay in the age of smoking uptake may make smoking cessation later in life more likely. The modelling took place in two steps. Firstly, data from the General Household Survey were used to explore the association between the age at which someone initiates smoking and the probability that the person will quit in later life. This was called the "age of initiation model". We found a significant association between the age at which someone initiates regular smoking and the probability that the person will quit smoking later in life. The

association is reduced but is still significant when confounding variables (sex, ethnicity, socioeconomic class, education and geographical location) are taken into account.

Secondly, effect sizes (in terms of odds ratios of being a smoker in control and intervention arms) extracted from 26 randomised controlled trials identified during the systematic review of the effectiveness literature were used to determine the parameters for a second model, called the "effect model". Several forms of this model were fitted to the data, representing assumptions about whether a smoking intervention actually decreases smoking uptake in the long-term or simply delays the onset of smoking, and whether changes in the effect that the intervention has on participants over time are governed by the age of the participants or the time since the intervention began.

The outcomes from both the "age of initiation" and "effect" models were used in an economic analysis to extrapolate the lifetime health outcomes and cost-effectiveness of a school-based smoking prevention programme. Most of these analyses suggested that such a programme may be cost-effective at a willingness-to-pay threshold of £20,000 to £30,000 per QALY gained. The findings are fairly robust to changes in key model parameters governing the association between age of smoking initiation and probability of smoking in later life, mortality in smokers and non-smokers, health-related quality of life in smokers and lifetime medical costs of smokers.

The only analysis that predicted that an intervention would not be cost-effective was one using an effect model where an intervention simply delays smoking onset, and is dependent on time since start of intervention rather than age of participant. This suggests that further work needs to be done both on the long-term effect of interventions beyond adolescence, and also to determine whether the attenuation of the effects of such interventions over time is governed by the age of participants or the time since the intervention began.

Chapter 1. Introduction and background

Introduction

The National Institute for Health and Clinical Excellence (NICE) has been asked by the Department of Health (DH) to develop guidance on public health interventions for the NHS and local authorities aimed at preventing the uptake of smoking among schoolchildren (National Institute for Health and Clinical Excellence 2008).

Two accompanying systematic reviews of the literature cover the effectiveness and cost-effectiveness evidence on school-based smoking prevention programmes. A further evidence review focuses on qualitative evidence related to such interventions. This report outlines a *de novo* mathematical model on the cost-effectiveness of these programmes, and is designed to accompany the reviews.

As was discussed in the accompanying review of the economic literature, there are no published economic evaluations of school-based smoking prevention programmes in the UK. Studies based in other countries are of limited relevance to the UK situation because of differences in health care and education systems as well as demographic and socioeconomic characteristics of the relevant populations. They also make methodological choices about the type of evaluation to conduct, cost perspective to adopt and discount rate to use that are inconsistent with NICE recommendations. A further limitation with the existing literature is that most published studies assume that school-based smoking prevention programmes can achieve a lasting reduction in smoking prevalence beyond school-age. However, as we discuss in the accompanying review of the effectiveness literature, there is little evidence that an intervention can have an effect that lasts beyond school-age.

The aim of this economic modelling report is to provide information in order to determine whether the implementation of a school-based smoking prevention initiative is likely to be cost-effective. This has been done in two steps. Firstly, results from the General Household Survey are used to explore the association between the age at which a person initiates smoking and the probability that the person will quit later in life. This is called the "age of initiation model". Secondly, reported effect sizes of school-based interventions from the systematic review of the effectiveness literature for NICE were used to determine the parameters for a second model, called the "effect model". The outcomes from both these models are then used in an economic analysis to estimate the health outcomes and cost-effectiveness of a school-based smoking prevention programme.

Background

Smoking is responsible for about one fifth of deaths in the UK, including more than a third of deaths from respiratory causes and more than a quarter of deaths due to cancer (Peto et al. 2006). The cost of smoking to the NHS was recently estimated at £2.7 billion in 2006-7 (Callum 2008).

About two-thirds of respondents in the General Household Survey of Great Britain who were smokers or ex-smokers reported that they started smoking before the age of 18 (Robinson & Lader 2007). An early age of smoking initiation has been found to be associated with not quitting smoking later in life (Breslau & Peterson 1996;Khuder, Dayal, & Mutgi 1999), and to have a higher risk of smoking related morbidity (Muller 2007).

A 1998 Department of Health White Paper set a target to reduce smoking prevalence in children from 13% to 9% or less by the year 2010; with a decrease to 11% by the year 2005 (Department of Health 1998). This appears to have been successful, since among

secondary school pupils aged 11 to 15, the proportion who smoked regularly has decreased from 11% in 1982 to 6% in 2007 (Clemens et al. 2008). The decline of 3% points between 2006 and 2007 was substantially larger than the overall trend seen between 1982 and 2006. However, the prevalence of smoking in young people has declined much more gradually than prevalence of smoking in adults, which has declined steadily from 45% in 1974 to a little over 20% in 2007 (Robinson & Lader 2007).

One option for further decreasing the rate of smoking initiation during adolescence is through school-based smoking prevention programmes. Reviews of effectiveness studies of such programmes in the literature have shown that they can reduce the prevalence of smoking among adolescents in the short term, but have little or no effect in the long-term (Wiehe et al. 2005) (Thomas & Perera 2006). This was confirmed by the results of our own effectiveness review.

Chapter 2. The effect of age of smoking initiation on continuing to smoke in later life.

Background

Early smoking initiation has been linked to nicotine dependence in later life (Park et al. 2004). Because of this, several researchers have suggested that there is an association between the age of smoking initiation and the probability of smoking cessation later in life. However, the only published data exploring this association originate from studies in highly selected populations based in the United States.

A population sample survey of 1,700 males in Philadelphia found that age of smoking initiation was a significant predictor in a logistic regression model of smoking cessation, even after inclusion of confounding variables such as age at interview, race, marital status, educational level, number of cigarettes smoked per day and duration of smoking (Khuder, Dayal, & Mutgi 1999). The odds of a respondent who initiated smoking between age 16-19 years being a smoker at the time of the interview was 1.3 times that of a respondent who started smoking after the age of 20. For a respondent who started smoking before age 16 years, the odds were 2.1 times higher.

Another survey of smoking was conducted among a random sample of 1,007 young adults enrolled in a large health maintenance organisation in south-eastern Michigan (Breslau & Peterson 1996). Using a discrete Cox proportional hazards model, the authors found that age of smoking initiation was a significant predictor of smoking cessation, even after including sex, race and educational level as confounding variables. Smokers initiating when 14 to 16 years old were 1.6 times more likely to quit than those initiating by the age of 13 years, while smokers initiating after age 16 were 2.0 times more likely to quit.

Here we described a study examining the predictive power of age of smoking initiation on smoking in later life, using a large cross-sectional survey of households in Great Britain. To our knowledge this is the first study of this kind using a nationally representative sample, and the first to be conducted outside the United States.

Methods

Data extraction

The General Household Survey is an annual cross-sectional survey of individuals aged 16 years and over living in private households in Great Britain, with about 13,000 households sampled (National Statistics 2004). Data from 2004/5, 2005 and 2006 General Household Surveys were extracted, using the original survey weights. Information was extracted about respondents' current smoking status (in terms of being a current smoker, former regular smoker, former irregular smoker or never smoker), age of smoking initiation, current smoking frequency, age, ethnicity, social class and geographical region. Appendix 1 gives the algorithm used to determine a respondent's smoking status.

Only respondents who gave complete answers about their smoking status, age of smoking initiation, current smoking frequency, age, ethnicity, social class and geographical region were included in the analysis. A total of 48,399 respondents out of a total sample size of 73,414 (65.9%) were included. The included respondents were more likely to be older (median age 49 compared to 39 in excluded respondents with age information) and female (53.2% compared to 51.6% in excluded respondents with sex information).

Statistical modelling

Three logistic regression models were developed to explore the relationship between current smoking status, current age and age of smoking initiation. In the first logistic regression model, only two explanatory variables (current age and age of smoking initiation) were included along with a constant. In order to avoid overlap between the age of smoking initiation and the age at which respondents were surveyed, the only respondents included in the analysis were those initiating smoking before age 19 years, and responding to the survey after age 19 years.

It is possible that individuals who initiate smoking at a young age have a greater predisposition towards smoking and are hence less likely to cease smoking later in life due to a mechanism independent of their age of smoking initiation. In order to account for this, a second model was constructed where demographic variables (sex, ethnicity, social class, education and geographical region) were included as possible confounders. Each confounding variable was coded as a binary variable except for social class which was coded as an ordinal variable with three levels (details in Appendix 2). The value of these variables was then fixed by the proportion of the sample population in different sex, ethnicity, social class, education and geographical region categories.

It is also possible that these demographic variables may alter not only an individual's overall predisposition towards smoking, but also the association between age of smoking initiation and current smoking status. For instance, the strength of the relationship between age of smoking initiation and likelihood of quitting may be different for men and women. In order to model this situation, a third model was considered, in which interaction terms between age of smoking initiation and each of the demographic variables were included. Both linear and interaction terms were then dropped using backward stepwise selection in order to obtain the most parsimonious model. A significance level of 0.10 was used in the variable selection for both removal and addition used.

Results

Smoking status by current age

Among respondents over 25 years old who initiated regular smoking at age 25 or younger, 39% began regular smoking before age 16 years, 41% at age 16-18 years and 19% at age 19-25 years. Figure 1 shows changes in the smoking status of respondents by age between 16 and 85 years old. The proportion of respondents who are never smokers and ex-irregular smokers is largely stable over this age range, varying in the range of 30 – 45% and 10 – 20% respectively. There is a slight decrease in the proportion of respondents who are never smokers after age 50 due to age-cohort effects. However, the proportion of respondents who are current smokers drops steadily from a peak of 40% at age 17 years to 5% at age 81 years, with a corresponding increase in the proportion of ex-regular smokers. This indicates that smoking initiation is rare after age 17, while smoking cessation happens at a steady rate after that age. In fact, age of respondent is a highly significant predictor ($p<0.001$) in a linear regression model of whether a respondent who has previously initiated smoking was still a smoker at the time of interview, as shown in Figure 2. The actual coefficients of this model and the others described in this report are presented in Appendix 2.

Figure 1. Smoking status of General Household Survey respondents by age between 16 and 85 years old.

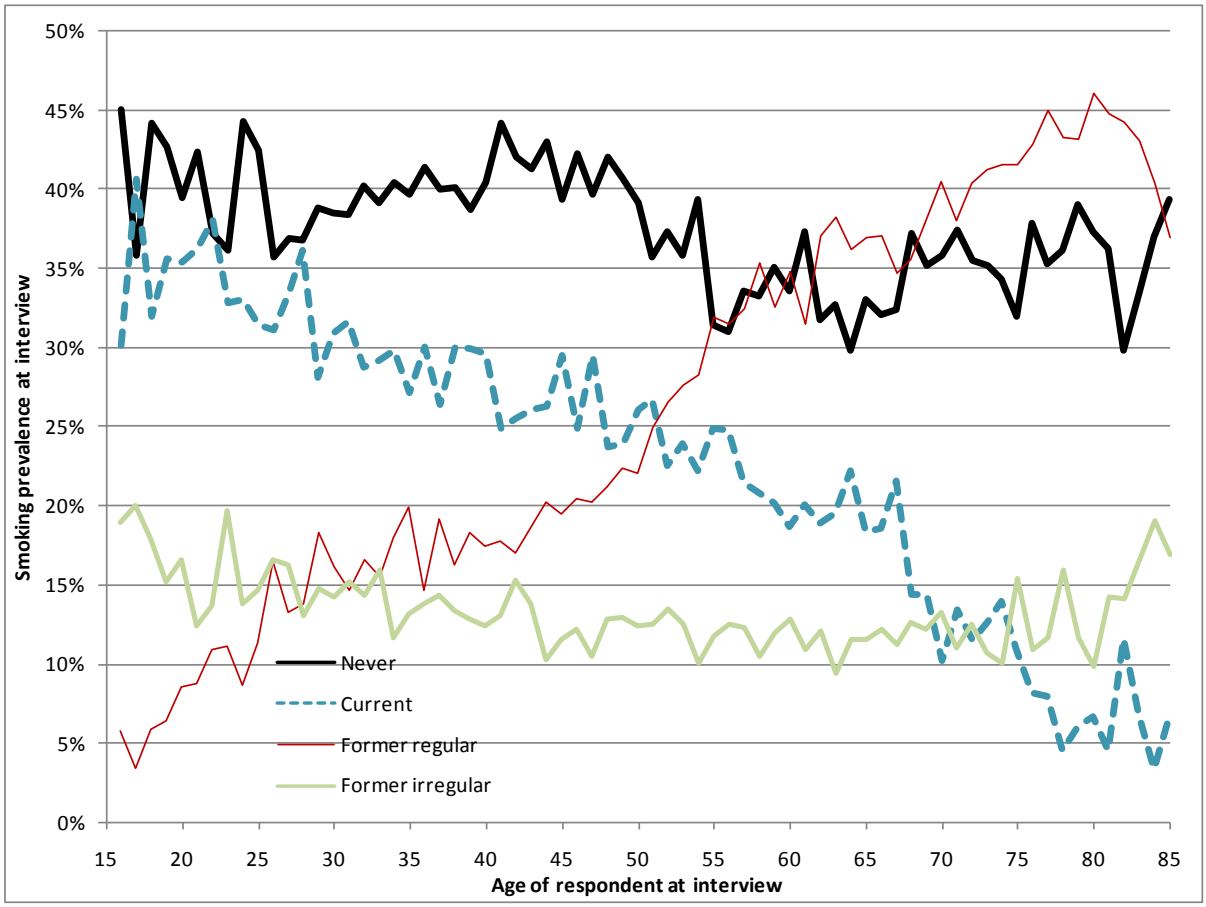
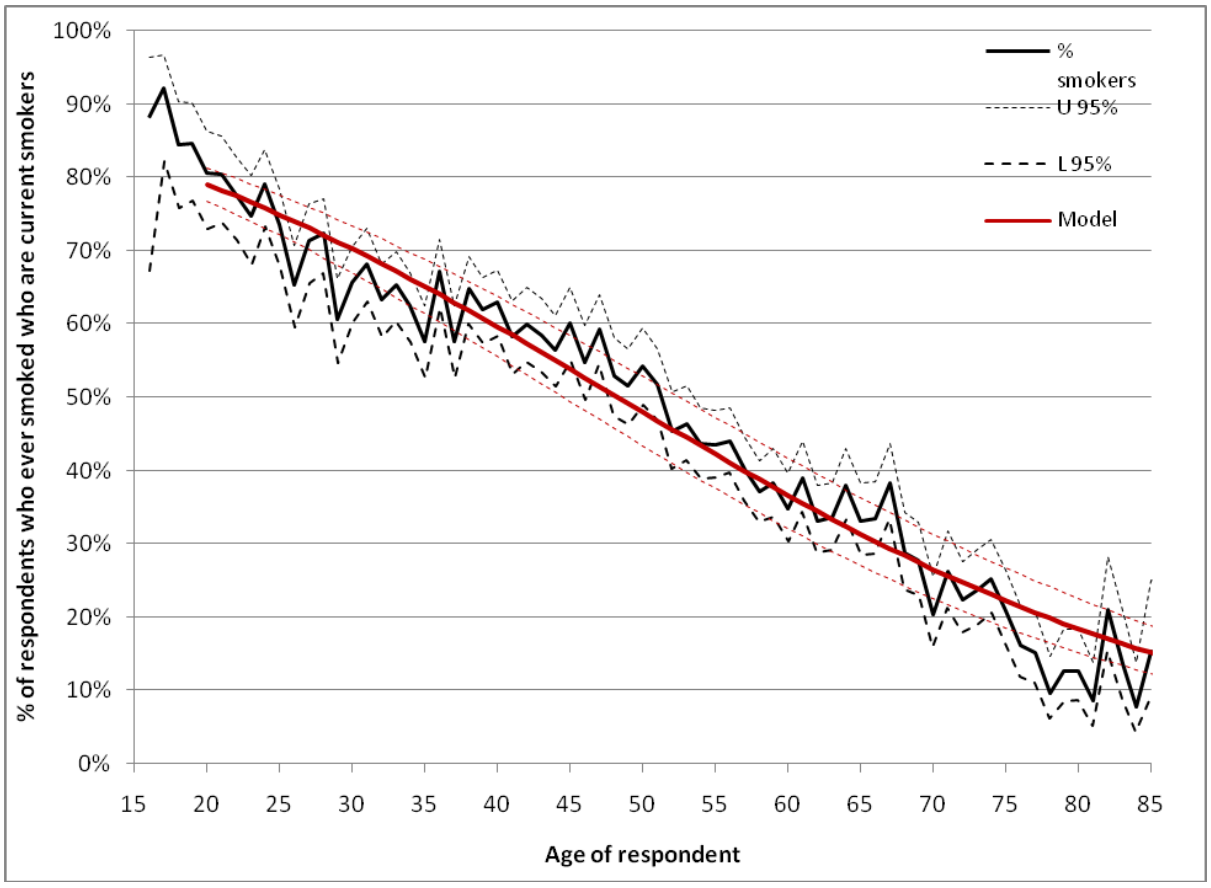


Figure 2. Proportion of respondents to the General Household Survey having initiated smoking, who are still smoking at different ages, as well as best fitting logistic regression model to survey data. Dashed lines show 95% confidence intervals for survey data and the model.



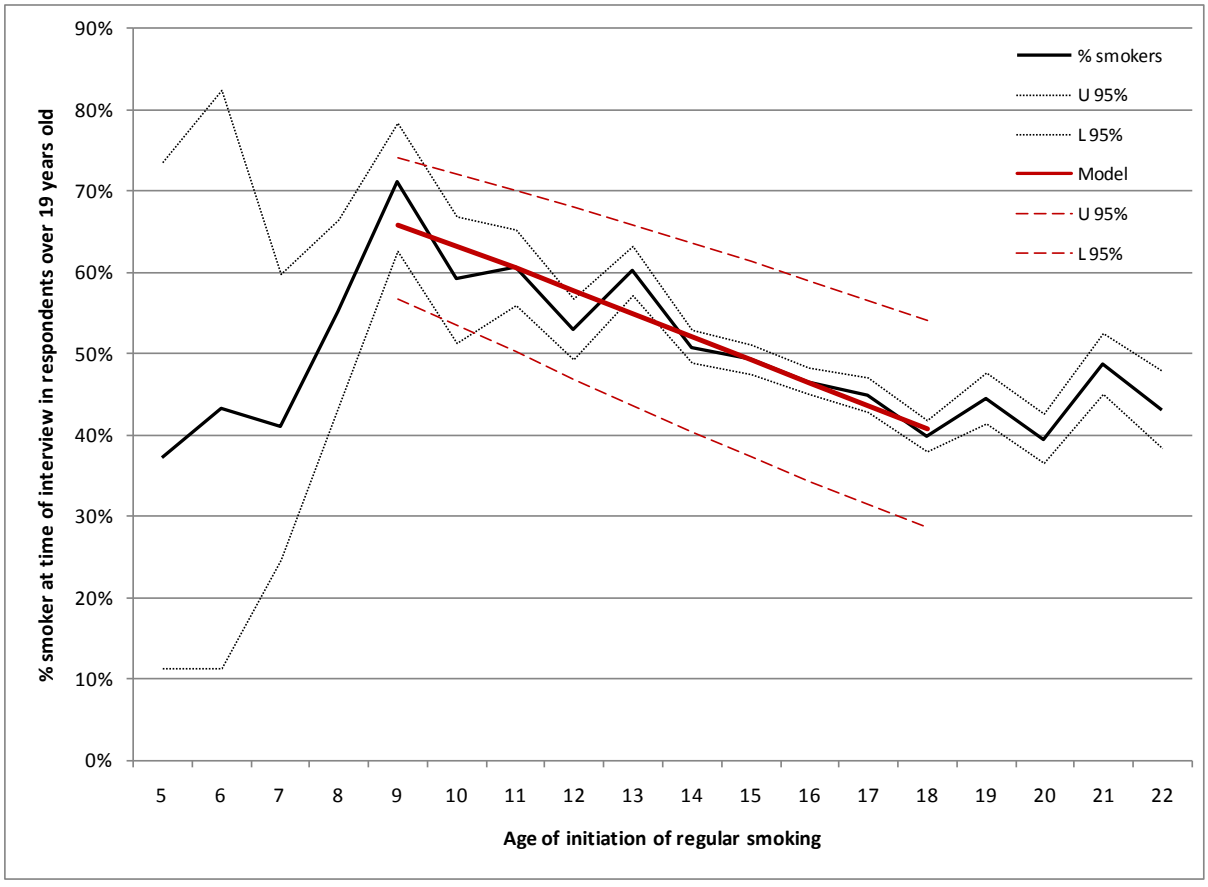
Age at regular smoking initiation

Figure 3 shows the proportions of all respondents over 19 years old who initiated regular smoking, who were still smokers at the time they were surveyed. For example, about 70% of children who started smoking at 9 years old were still smoking at the time of interview (when they could be any age over 19 years old). The figure shows that between age 8 and 18, the age of initiation of regular smoking is a highly significant predictor ($p<0.001$) in a model of whether a respondent over 19 years old who has previously initiated smoking was still a smoker at the time of interview. Data from respondents initiating outside the age range 9-19 years old were not included in the

model. The number of respondents initiating smoking below the age of 9 appears to be too small to make precise predictions, and may be particularly subject to bias due to the difficulty in recalling events in young childhood. Above the age of 19, there no longer appears to be a definite trend (either increasing or decreasing) in survey data.

When both current age and age at regular smoking initiation were included in the age of initiation model, both explanatory variables remained highly significant ($p<0.001$). Inclusion of current age decreases the magnitude of the coefficient of the variable for age at regular smoking initiation slightly (from -0.115 to -0.103). The reason for this is that older respondents are more likely to have started smoking later in life, and are also less likely to be current smokers (because they have had more time to quit smoking).

Figure 3. Proportions of respondents to the General Household Survey over 19 years old who initiated regular smoking, who were still smokers at the time they were surveyed, as well as best fitting logistic regression model to data for respondents who initiated smoking between ages 9 and 18 years old. Dashed lines show 95% confidence intervals for survey data and the model.



Including confounding variables

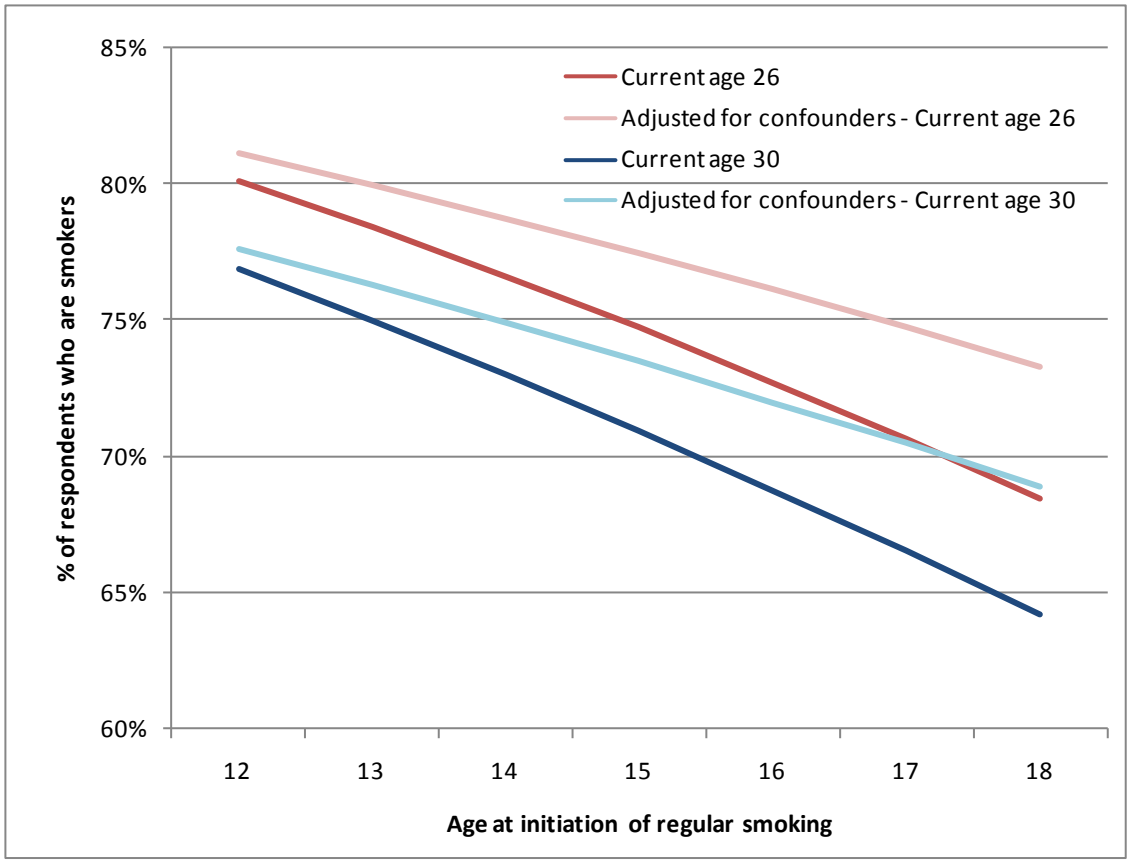
When confounding variables (sex, ethnicity, socioeconomic class, education and geographical region) were included in the model, all were significant ($p<0.05$). Inclusion of these confounders reduced the magnitude of the coefficient of the variable representing age at regular smoking initiation (from -0.103 to -0.075). This indicates, as suspected, that individuals at high risk of early regular smoking initiation were more likely to have independent risk factors (like being non-white British or from a low socioeconomic class) predisposing them to be less likely to quit smoking later. Hence the model with confounders is likely to be more accurate and was used for further analysis. (For example, it predicts that if you are now 35 years old, started smoking at age 14 and were also male, non-white British, from socioeconomic class II, left full-time education at age 18 and are from London then you have a 62% chance of being a smoker.)

The value of the confounding variables was fixed by the proportion of the sample population in different sex, ethnicity, social class, education and geographical region categories. This sample (representing respondents who initiated smoking before age 19 and responded to the survey after age 19) was 47% female, 3.2% non-white British, 47% from socioeconomic class IIIN or IIIM, 25% from socioeconomic class IV or V, 72% left full-time education at or before age 16, and 25% from Northern England or Scotland. Figure 4 shows model predictions of the proportion of respondents who remained smokers at age 26 and age 30 by their age of smoking initiation, before and after adjusting for confounders.

When interaction terms are included, many variables (both linear and interaction) become non-significant. When variables are selected to obtain the most parsimonious model, linear terms for current age, age at smoking initiation, sex and education are retained, as well as interaction terms between age at smoking initiation and ethnicity, socioeconomic class and region. When the proportion of the sample population in different demographic groups is applied to the model, the coefficient of the variable

representing age at regular smoking initiation drops by a very small amount (from -0.07482 to -0.07453). There does not seem to be any obvious sociological or epidemiological explanation for why particular variables appeared in linear or interaction terms. Hence it would appear that the model without interaction terms is preferred on the grounds that it is more transparent and gives almost identical results when applied on a population-level.

Figure 4. Model predictions of the proportion of respondents who remained smokers at age 26 and age 30 by their age of smoking initiation, before and after adjusting for confounders.



Discussion

Our statistical analysis confirms earlier findings from smaller selective samples based in the United States that an early age of smoking initiation is positively correlated with the risk of continuing to be a smoker in later life. The association is still significant when confounding variables such as sex, ethnicity, social class, education and geographical location are taken into account. While there may be additional variables (such as income or alcohol consumption) that are associated with both smoking early in life and continuing to be a smoker in later life, these are likely to be collinear with the existing variables in the model. Indeed, we may even have overcompensated for confounding variables, since it is not clear that the behavioural confounders (socioeconomic and educational status) are causal. For instance, initiating smoking early in life may cause poor educational attainment and consequently low income in later life rather than the other way round. Hence our analysis suggests that smoking prevention initiatives among children and teenagers could have substantial benefit even if their effect is simply to delay the onset of smoking without achieving an overall reduction in the number of participants initiating smoking.

Two types of models have been used in the published literature to investigate the association between age of smoking initiation and smoking cessation: logistic regression and Cox proportional hazards regression. A Cox model, while mechanistically easier to interpret in terms of a constant hazard of smoking cessation, is less easy to apply to cross-sectional survey data of the kind that was available to us as it requires accurate determination of the age of cessation. Consequently, a logistic regression model was considered to be more appropriate for modelling data from the General Household Survey, and so this has been used here.

Our model was parameterised using the three most recent datasets of the General Household Survey. There are a number of issues in the use of these data for this purpose. The first concerns the use of cross-sectional survey data to represent

longitudinal effects. This is not as serious a problem as it seems, because we were able to use retrospectively recalled information on the previous smoking history of respondents (that is, their age of regular smoking initiation). The main existing limitation is that there have been changes over time in the age of smoking initiation and overall smoking prevalence that have a different effect on each age cohort. However, the use of retrospective data about age of smoking initiation may introduce recall bias. It is not certain in which direction any bias may occur - that is, whether older respondents are more likely to overestimate or underestimate their age of smoking initiation. A further issue concerns the different mortality rate among smokers and non-smokers. Since smokers have a higher mortality rate than non-smokers, they are more likely to leave the denominator, and hence their rate of smoking cessation is overestimated unless the results are interpreted as representing a cohort who have survived up to their age of interview. This is implicitly what we do in the next chapter, since a different mortality rate is applied to smokers and non-smokers in a cohort model.

These three shortcomings are outweighed by the advantages of having individual-level data, which allows for more precise estimation of the association between age of smoking initiation and smoking cessation in later life.

Chapter 3. The cost-effectiveness of school-based smoking prevention programmes

Background

A systematic review we conducted concluded that the evidence from randomised studies of school-based smoking prevention suggests that such interventions may reduce smoking prevalence in the short-term, but that there is no robust evidence of any effects lasting beyond adolescence. Only a few studies followed participants beyond school-leaving age and these indicate that any beneficial effect diminishes in the long-term (Klepp et al. 1994;Lynam et al. 1999;Peterson et al. 2000;Shean et al. 1994). The studies did find that at final follow-up there was slightly decreased smoking prevalence in the intervention group compared to controls, but the difference was not statistically significant. A further issue that was unclear is whether the attenuation of the effect of such interventions over time was governed by the age of student participants or by the time since the intervention started. Due to the paucity of evidence, models were developed to represent two alternative possibilities about the long-term outcomes of school-based smoking prevention programmes: (i) "decrease models" representing a decrease in smoking prevalence persisting beyond adolescence, and (ii) "delay models" representing a delay in smoking uptake without any change in prevalence beyond adolescence.

There are two possible causal explanations for the attenuation of intervention effect over time. Firstly, this may be caused by students growing older, with attendant changes in their physiology, personality and social environment. Secondly, the impact of an intervention at any given age may simply attenuate as time passes, due to decreasing cognitive recall of the intervention and contamination between control and intervention groups in studies. It is of course possible that both mechanisms contribute towards the

attenuation of effect size over time. In order to incorporate both possibilities, we constructed two types of models: (i) "age of participant-dependent models" fitted to outcomes of randomised clinical trials stratified by age of participant, and (ii) "time-dependent models" fitted to outcomes stratified by time elapsed since the start of the intervention. Hence a total of four models were fitted to data: (i) decrease/age of participant-dependent, (ii) decrease/time-dependent, (iii) delay/age of participant-dependent, (iv) delay/time-dependent. Results from these models were then extrapolated to estimate lifetime smoking outcomes and health economic indicators for an economic evaluation of school-based smoking prevention programmes.

Methods

Intervention effect

A generic school-based smoking prevention programme was modelled based on a composite of information extracted from the systematic review of relevant randomised studies. The odds ratio of being a smoker in the control and intervention arms (adjusted for baseline smoking prevalence) was extracted from the 26 high-quality randomised studies identified during the systematic review of relevant literature which had usable data for meta-analysis (see accompanying systematic review of effectiveness literature).

The effect of the intervention on the uptake of smoking between age 9 and 23 was estimated based on these data. The relationship between effect size and age (or time since start of intervention) was represented using an exponential decay model, with functional form $y(x) = 1 + a - e^{-\lambda(x-b)}$, where λ, a, b are parameters to be fitted, x is age (or time since start of intervention) and y is effect size. Two alternative models were fitted to data: (i) an exponential function without a fitted constant term (a=0) and (ii) an

exponential function with a fitted constant term (a>0). The former function (the "delay model") represents a situation where there is no persistent effect from an intervention on smoking prevalence beyond adolescence, while the latter function (the "decrease model") represents a persistent effect throughout the lifetime of the intervention cohort. Hence both "delay" and "decrease" models assume that effect size diminishes with increasing age (or time since start of intervention), but for "delay" models effect size can decrease to almost zero, while for "decrease models" effect size always remains substantially greater than zero. Models were fitted to data extracted from the systematic review using maximum likelihood estimation with binomial likelihood functions in order to capture the uncertainty around each study's estimate of the odds ratio.

The baseline risk of regular smoking initiation in school-age children under 16 years old was obtained from the most recent (2007) round of an annual survey carried out among 7,831 secondary school children aged 11 to 15 in England (Clemens, Jotangia, Lynch, Nicholson, & Pigott 2008). The proportion of smokers among children below age 11 years was assumed to be negligible, as was the proportion of regular smokers who quit before age 16. After age 15 years, the proportion of regular smokers was assumed to increase by 1.5% a year until age 23 years, based on previously described data from the General Household Survey fitted to a linear model to smoothen out stochastic variation (National Statistics 2004). Beyond age 23 years, smoking uptake as reported by the General Household Survey appears to be negligible.

When using the effect models based on time since start of intervention, the intervention was assumed to occur at age 11. Individuals who initiate smoking are assumed to have a probability of still being a smoker based on their current age and age of smoking initiation, as described in the previous chapter (see Figure 4). This analysis was based on respondents initiating smoking between ages 9 and 19 years. Below this age range, data was not required since the intervention would have yet to have occurred. Smokers who initiate smoking above age 18 years are assumed to have the same age-dependent probability of quitting as smokers who initiate at 18 years, because data from the

General Household Survey no longer show a definite trend (either increasing or decreasing) above that age (see Figure 3).

Health-related outcomes of smoking

A population cohort model was used to estimate the health-related quality of life and mortality implications of changing the prevalence of smoking as a result of a school-based intervention. The model assumes that smokers over 25 years old have an increased risk of death and a decreased quality of life while alive compared to non-smokers. Ex-smokers are assumed to have the same risk of death and quality of life as individuals who have never smoked before, as are smokers 25 years old and younger (due to lack of available data for these groups).

Age-dependent mortality rates for non-smokers were assumed to be the same as those for the general population, obtained from standard sources (Office for National Statistics 2006). The increase in mortality in smokers was estimated from the 50-year follow-up of the British Doctors Study, a cohort study of British male doctors (Doll et al. 2004). However, the sample of smokers in the study is unlikely to be representative of the current UK population due to the peculiar demographics of the cohort in terms of socioeconomic class (doctors, i.e. class I), sex (male) and year of birth (between 1900 and 1930). Hence, instead of imputing mortality figures directly, the ratio of the mortality rate in smokers and non-smokers (stratified by year of age) was applied to the mortality rate in the overall UK population to obtain an adjusted mortality rate for smokers.

For instance, in the British Doctors Study, a smoker aged 55 – 64 years old has an annual mortality rate of 0.84% while a non-smoker in the same age group has an equivalent rate of 2.14%. The risk ratio is therefore 2.55. However, the latest figures from the Office for National Statistics indicate that the mortality rate in a 60-year old is 0.73%. Hence we assume that 60-year old non-smokers currently have a mortality rate of 0.73%, while 60-

year old smokers have a rate of 0.73% × 2.55 or 1.86%. This assumes that differences in mortality between people of different socioeconomic classes, sexes and years of birth affect smokers and non-smokers in equal proportion- an assumption we have to make since there are no equivalent data to the British Doctors Study for other groups in the population.

Similarly, quality of life weights for non-smokers were obtained from a UK-wide population health survey using the EuroQol EQ-5D questionnaire (Kind et al. 1998). Although the EQ-5D is the measure preferred by NICE, there were no reliable population-wide estimates of health-related quality of life in smokers using the EQ-5D. Instead, quality of life in smokers was estimated from an analysis of the years of healthy life (YHL) in smokers and non-smokers reported in the National Health Interview Survey in the United States (Fiscella & Franks 1996). Here non-smokers represented ex-smokers who had quit for at least 15 years. This analysis assessed health state values linked to the Health Utilities Index. Once again, the ratio of quality of life weights for smokers and non-smokers was applied to weights for the overall UK population to obtain estimates of quality of life of smokers.

Economic costs

In line with the requirements of the NICE reference case for evaluating public health interventions, a public sector costing perspective was adopted. Future costs and outcomes were discounted at an annual rate of 3.5% to the time of the intervention.

Smokers may impose a greater cost on the health service compared to non-smokers of the same age because they have higher risks of morbidity due to a range of conditions such as cardiovascular disease, stroke and cancer. On the other hand, smokers have a lower life expectancy so it is not clear that the lifetime cost of providing health care to a smoker is greater. As there were no reliable UK-based studies that looked at both costs

and cost savings to the health service due to smoking prevention, we used results from a simulation model of medical costs in the Netherlands (van Baal et al. 2008). This compared the annual medical costs of never-smoking and lifetime smoking individuals of normal weight by year of age. We assumed that annual medical costs associated with ex-smokers were the same as those for non-smokers. Results were given in 2003 euro prices, which we converted to 2003 sterling prices using average rates for 2003 from HM Revenue & Customs (available at http://www.hmrc.gov.uk/exrate).

The intervention was assumed to cost £45 per student participant. This was based on a literature review of economic evaluations we conducted, in which the range of costs reported for school-based smoking prevention programmes ranged from £30 to £60, excluding two studies which were outliers. In addition, threshold analysis was conducted to estimate the cost per student at which the intervention would have to be delivered in order to elicit health benefits at less than £20,000 per QALY gained. The entire cost was assumed to be incurred at the start of the intervention (age 11).

Sensitivity analysis

An extreme value approach was taken to sensitivity analysis. Sensitivity analysis was conducted by varying four key sets of parameters: (i) the association between age of smoking initiation and the chance of being a smoker later in life, (ii) the increased mortality rate in smokers compared to non-smokers, (iii) the reduced health-related quality of life in smokers compared to non-smokers, and (iv) the additional annual medical costs associated with being a smoker compared to a non-smoker. For (i), we varied the coefficient for age of regular smoking initiation to the limits of its 95% confidence interval obtained from the fit to data by logistic regression. For (ii), (iii) and (iv), we were unable to obtain evidence-based estimates of uncertainty as the source literature (Doll, Peto, Boreham, & Sutherland 2004;Fiscella & Franks 1996(van Baal,

Polder, De Wit, Hoogenveen, Feenstra, Boshuizen, Engelfriet, & Brouwer 2008)) did not report confidence intervals around their point estimates. However, we explored the effect on cost-effectiveness of increasing or decreasing by 50% the difference in outcomes between smokers and non-smokers (eg. assuming that the difference in the mortality rate between smokers and non-smokers is 50% greater than what was reported by Doll and co-workers).

Mass media interventions

At the request of the NICE Technical Team, our model was also applied to estimate the cost-effectiveness of a mass media campaign to prevent smoking uptake in young people. A previous economic evaluation conducted for NICE estimated that such an intervention would cost £15 per person over 5 years, and reduce the prevalence of smoking by 5% by age 18 (Raikou & McGuire 2007). We assumed that the intervention would begin at age 11 years and that the reduction in prevalence is equally spread out between ages 11 and 18 years (i.e. 0.63% reduction per year of age).

Results

Intervention effect

Figure 5 shows the delay and decrease effect models that best fit effect sizes reported in randomised controlled trials (in terms of odds ratios), stratified by the age of students at follow-up. As expected, the delay model indicates that the odds ratio is almost 1 by age 18 (point A on the graph) and continues at this level to age 23 years, while the decrease

model suggests that at age 18 and even up to age 23, the odds ratio is still well below 1 (point B on the graph). The same models when the odds ratios are stratified by time since start of intervention are shown in Figure 6, and these show similar results, but with a more rapid attenuation in the effect of interventions over time in the delay model. Actual values of best fitting model parameters are shown in Appendix 3.

These odds ratios were used to estimate the prevalence of being a regular smoker. The delay models (stratified by either age or time since start of intervention) indicate that there is little difference in smoking prevalence between control and intervention arms by age 18, while the decrease models suggest that a small difference still persists at age 23. For the models fitted to odds ratios based on age of participant, the difference in smoking prevalence at age 23 between intervention and baseline populations is 0.01% (for the delay model) and 2.5% (for the decrease model). For the models fitted to odds ratios based on time since start of intervention, the differences in smoking prevalence at age 23 between the two populations are 0% (for the delay model) and 3.6% (for the decrease model).

Figure 5 Best fitting delay and decrease exponential models to study odds ratios stratified by age of students.

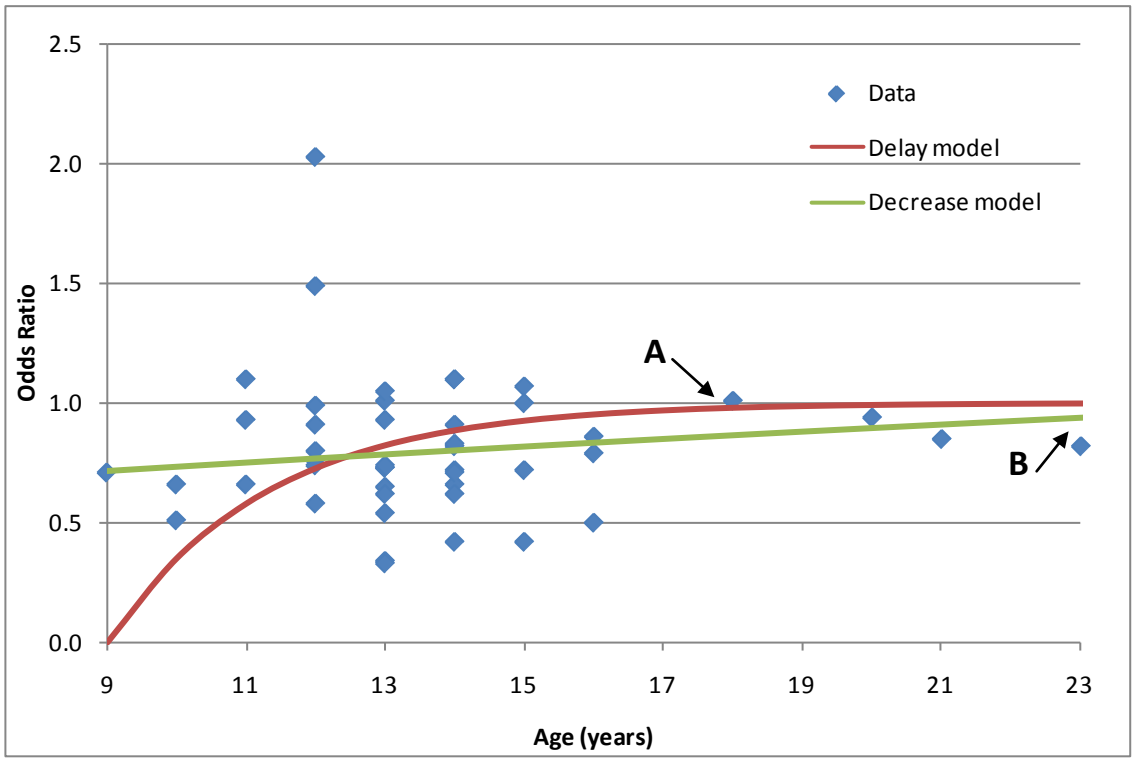
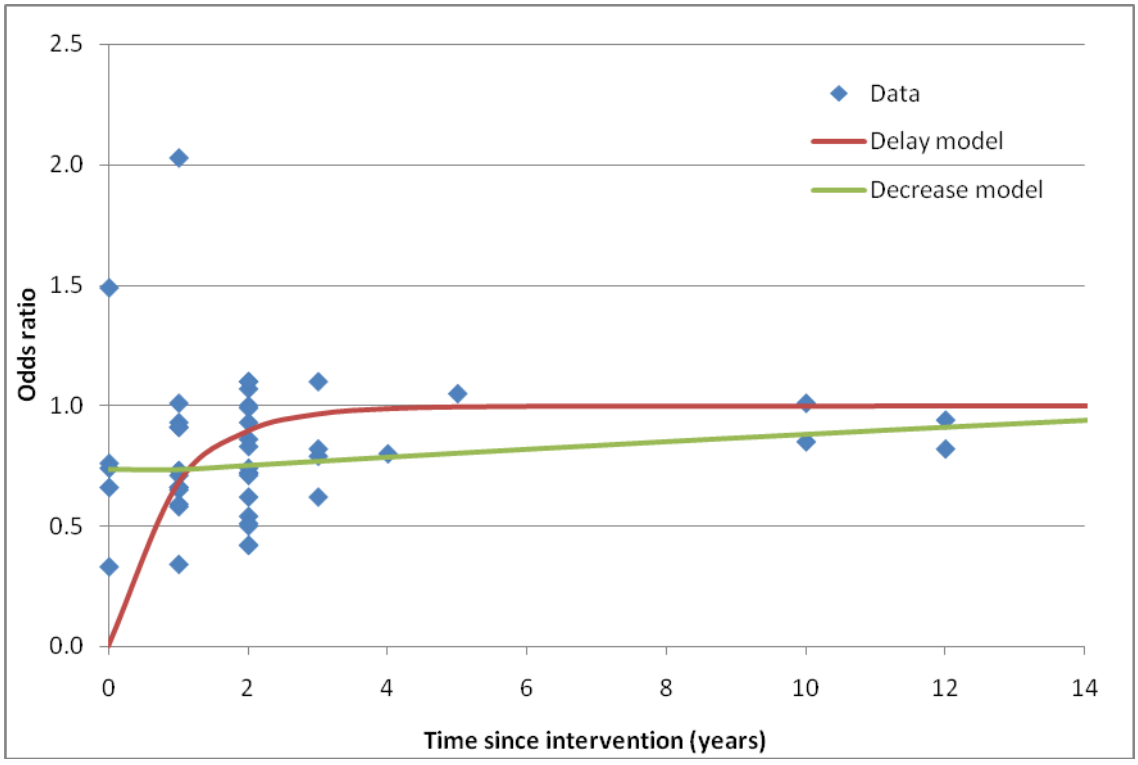


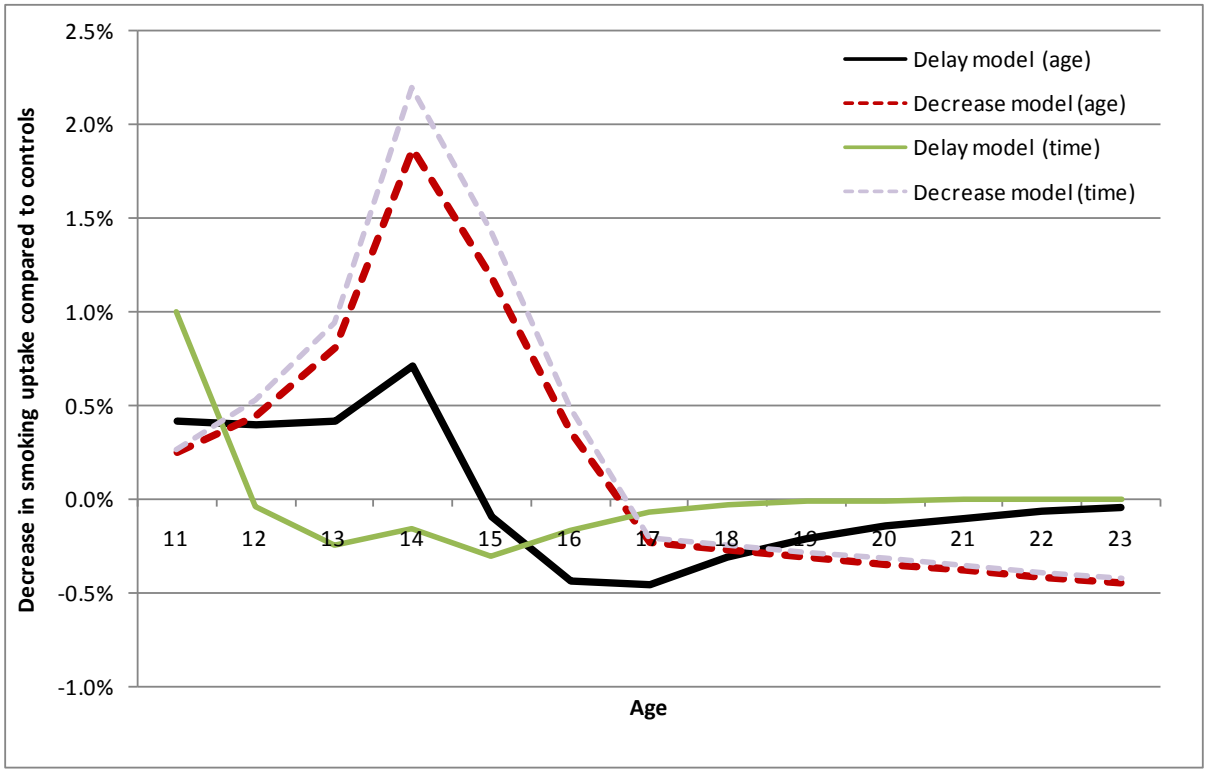
Figure 6 Best fitting delay and decrease exponential models to study odds ratios stratified by time since start of intervention.



The rate of smoking uptake in the baseline population was obtained from the two previously described surveys (Clemens, Jotangia, Lynch, Nicholson, & Pigott 2008) (National Statistics 2004). The corresponding rate in the population receiving the intervention was estimated from the different effect models described above. The difference between the two rates of uptake for populations up to 23 years old, for each of the effect models, is shown in Figure 7.

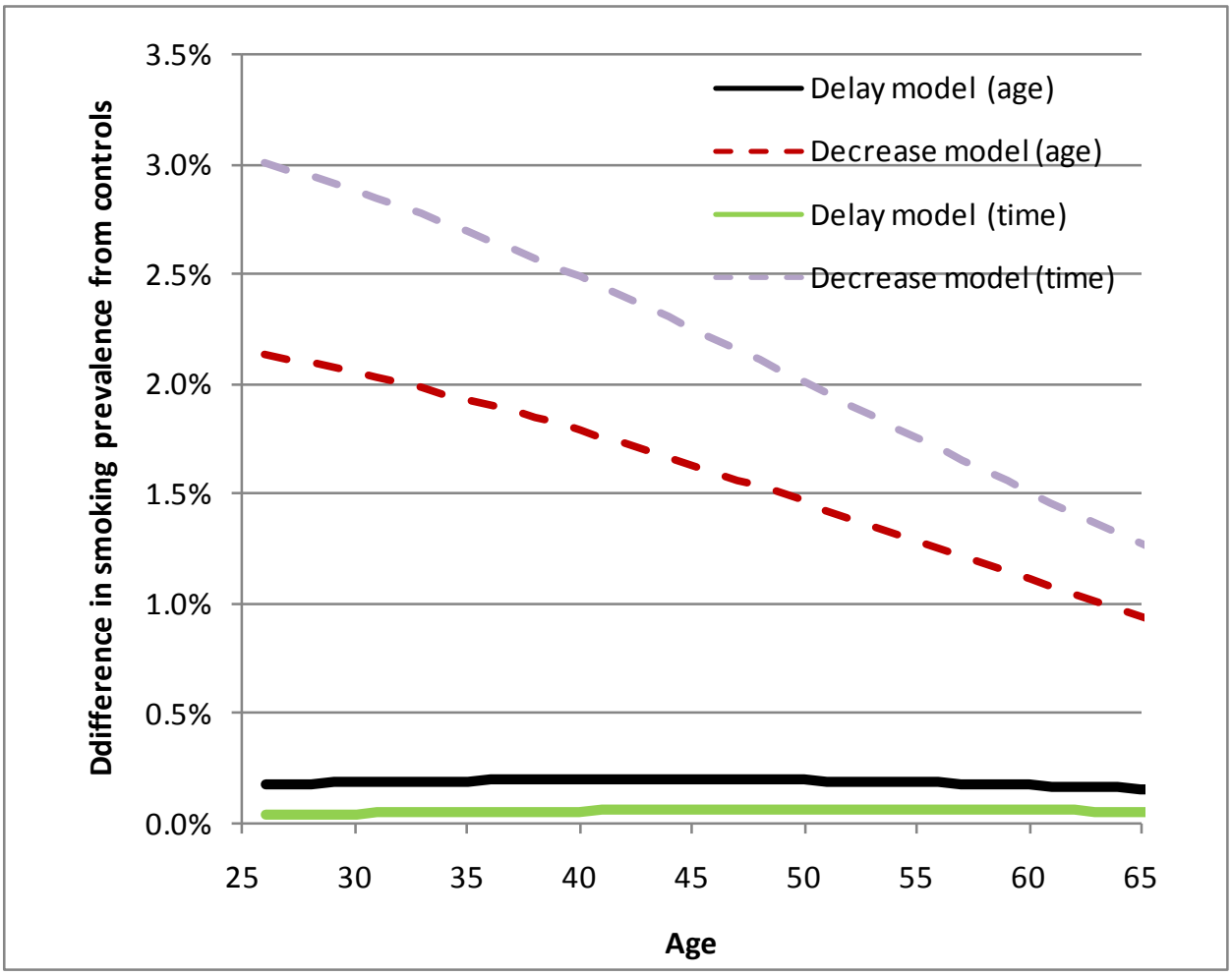
The two decrease models predict an initial decrease in smoking uptake in the intervention population up to about age 17 compared to the baseline population, after which the intervention population has a slightly higher rate of uptake. The delay model based on age of student predicts a smaller decrease in smoking uptake up to age 15 compared to baseline, followed by an increase after that age. The delay model based on time since start of intervention predicts a decrease in uptake compared to baseline only for 11 year olds, after which there is an increase in uptake.

Figure 7 Decrease in smoking uptake between intervention and baseline populations until age 23 years predicted by different models.



When the change in smoking initiation due to the intervention is extrapolated through the lifetime of the model cohort, the effect on smoking prevalence at different ages is shown in Figure 8. Using the decrease model based on time since start of intervention as an example (purple dashed line), there is a 3% decrease in smoking prevalence due to the intervention at age 26. This occurs for two reasons. Firstly, the intervention has caused an overall net decrease in smoking uptake because the decrease in smoking uptake between age 11 and 17 years old outweighs the increase in uptake after age 17 years (see Figure 7). Secondly, the intervention has caused a general increase in the age at which students initiate smoking, causing them to have been more likely to give up smoking by age 26. As can be seen in Figure 8, the decrease models predict a change in smoking prevalence of an order of magnitude greater than the delay models.

Figure 8. Decrease in smoking prevalence in intervention population compared to baseline population after age 25 years predicted by different models.



Cost-effectiveness

The estimated cost-effectiveness of a generic school-based smoking prevention programme delivered to 11-year old students is presented in Table 1, assuming an intervention cost of £45 per student. At a threshold willingness-to-pay of £20,000 per QALY gained, all of the models suggest that an intervention will be cost-effective, except for the delay model based on time since start of intervention. The decrease models are far more optimistic than the delay models in their predictions about the cost-effectiveness of an intervention. Table 1 also shows the threshold cost of the intervention per student at which it will be cost-effective using the same willingness-to-pay threshold (£20,000 per QALY gained).

Preventing smoking appears to impose net costs to the health service, although these costs are much smaller than the cost of the intervention itself. Delay models predict that the additional costs are smaller compared to decrease models. This is for two reasons. Firstly, delay models predict that the overall effect of the intervention on smoking prevalence at any age is smaller, so the corresponding mortality reduction is similarly lower. Secondly, decrease models predict that the greatest difference in prevalence between the intervention and non-intervention cohorts is in early adulthood, when the difference in annual medical costs between smokers and non-smokers is small.

Table 1. Results of the cost-effectiveness evaluation of school-based smoking prevention programmes using different effect models.

	Delay model (age)	Decrease model (age)	Delay model (time)	Decrease model (time)
Intervention cost	£45.00	£45.00	£45.00	£45.00
Extra medical cost	£0.66	£5.20	£0.21	£7.21
Discounted QALYs gained per student	0.00287	0.0212	0.000989	0.0293
Cost per QALY gained	£15,900	£2,370	£45,700	£1,780
Threshold cost per student	£57	£419	£20	£578

The model also estimates that a mass media campaign to prevent smoking uptake in young people would gain 0.036 discounted QALYs per participant, impose £8.94 in additional lifetime medical costs per participant, cost £2,160 per QALY gained and have a threshold cost of £711 per student.

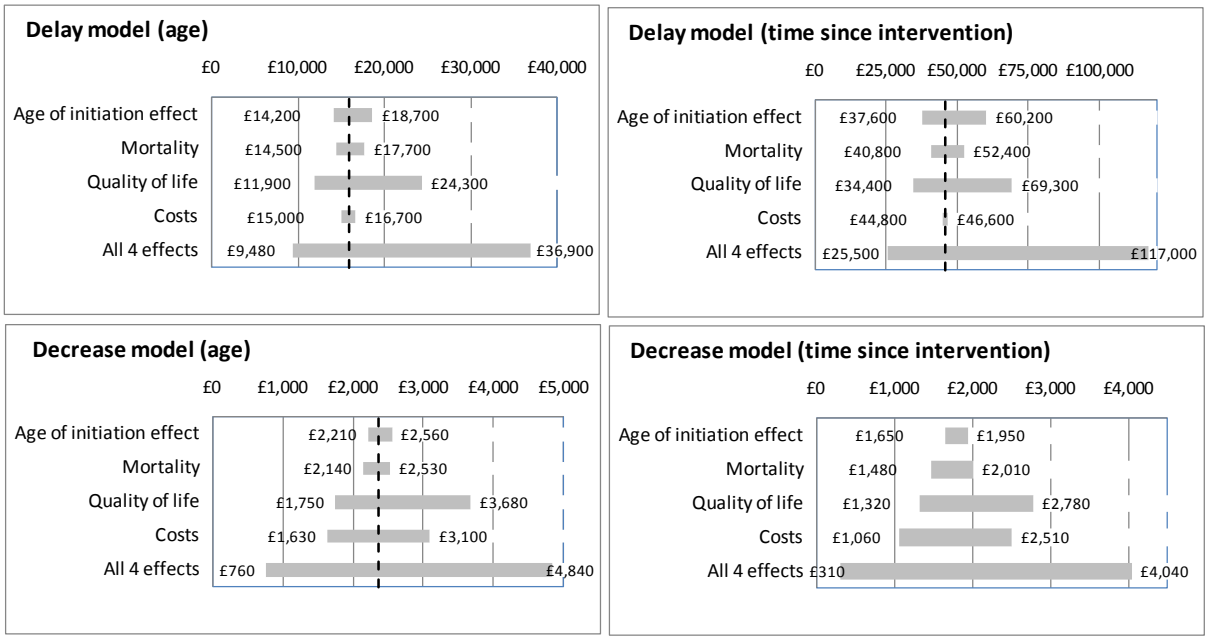
Sensitivity analysis

Figure 9 shows the results of varying key parameters on the incremental cost-effectiveness ratio (ICER). The decrease models suggest ratios that are still well below a willingness-to-pay threshold of £20,000 per QALY gained even when all parameters take their most unfavourable values. Results are mixed for the delay model, although the delay model based on age of student generally predicts a ratio below £30,000 per QALY gained unless all parameters take their most unfavourable values.

Note that strengthening the association between age of initiation and being a smoker later in life actually decreases the cost-effectiveness of the decrease models. This is

because these models obtain most of their health benefits from an absolute decrease in the number of new smokers. If the effect of age of initiation is strengthened, there is less benefit to be obtained from averting new smokers, since they are more likely to quit smoking later.

Figure 9. Graphs showing the effects of varying key parameters on the ICER. Values of the endpoints of the ICER range are also shown. Dashed vertical lines indicate base case ICERs.



Discussion

General findings

A cohort model used to extrapolate lifetime health outcomes of students initiating smoking suggests that under most assumptions, a school-based smoking prevention programme may be cost-effective at a willingness-to-pay threshold of £20,000 to £30,000 per QALY gained commonly used by NICE. This result appears to hold even if the programme is unable to actually decrease smoking uptake, and only succeeds in delaying the uptake of smoking, as long as the rebound effect causing participants to take up smoking at a higher rate when older is estimated from randomised controlled trial data based on age of participant rather than time since start of intervention. The findings are robust to changes in key model parameters governing the association between age of smoking initiation and probability of smoking in later life, smoking-related mortality and health-related quality of life in smokers.

Our estimate of the cost-effectiveness of a mass media campaign to prevent smoking uptake in young people is substantially higher than the estimate in a previous report (Raikou & McGuire 2007), which estimated that such a campaign would only cost £49 per QALY gained. However, the model by Raikou and McGuire did not consider medical costs due to diseases not related to smoking, which will increase if smoking prevalence decreases as a result of increased life expectancy. Consequently, the model by Raikou and McGuire predicts that a mass media campaign would have a net discounted cost of only £5 per cohort of 1,000 students. In contrast, our model suggests that a mass media campaign would actually increase the average lifetime medical costs of each participant by about £9. Our findings concur with an economic studies based in the Netherlands (van Baal, Polder, De Wit, Hoogenveen, Feenstra, Boshuizen, Engelfriet, & Brouwer 2008) which suggests that once the additional medical cost in non-smokers due to their higher life expectancy is taken into account, the net cost of preventing

smoking to the health service is positive (that is, the additional cost outweighs the cost savings).

Limitations of the analysis

Several assumptions were made during the construction of these models due to lack of complete data. The proportion of smokers among children below age 11 years was assumed to be negligible, as was the proportion of regular smokers who quit before age 16. Data from the General Household Survey suggests that these assumptions may not be unrealistic, although it is difficult to draw firm conclusions due to potential biases from cohort effects and retrospective recall. Furthermore, it was assumed that ex-smokers have the same quality of life and mortality rate as non-smokers immediately after ceasing to smoke. While this is clearly unrealistic in terms of how quickly ex-smokers obtain health benefits, the British Doctors Study suggests that smokers who quit rapidly gain years of life expectancy to attain the same life expectancy as a non-smoker (Doll, Peto, Boreham, & Sutherland 2004).

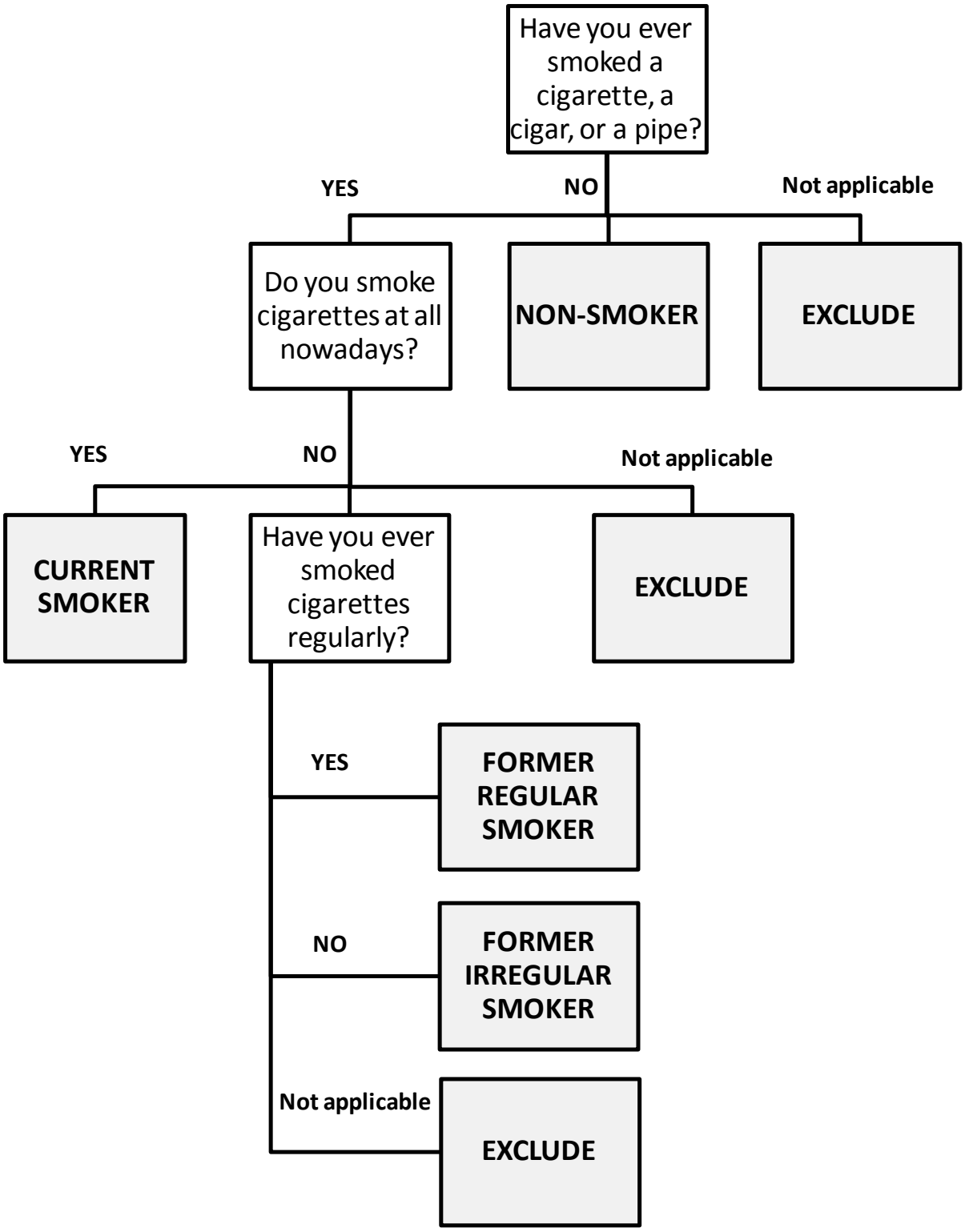
Also, the model does not take into account the causal effect that the age of smoking initiation may have on the intensity of smoking (such as the number of cigarettes smoked each day). This is because the direction of this causal effect is uncertain. While an earlier age of smoking could result in a longer period of time to develop cigarette addiction and hence greater smoking intensity, it is also plausible that genetic risk factors that predispose individuals to early smoking uptake are also associated with high smoking intensity.

Recommendations for future research

We found differences in model predictions depending on whether the attenuation of intervention effect size was related to age of participant or time since start of intervention. Indeed, the only analysis that predicted that an intervention would not be cost-effective was one using an effect model where an intervention simply delays smoking onset, and is dependent on time since start of intervention rather than age of participant. There is little discussion in the literature about whether the attenuation of effect size is related to age of participant or time since start of intervention, and it is difficult to disentangle both possible causal mechanisms from published results. Furthermore, both types of models appear to fit published results almost equally well, while yielding quite different results. This suggests that further work needs to be done both on the long-term effect of interventions beyond adolescence, and also to determine whether the attenuation of the effects of such interventions is due to the age of participants or the time since the intervention began.

If the time since the intervention began is the determining factor, then the use of booster sessions may be able to prolong the effect of the intervention in order to achieve cost-effective outcomes. Indeed, the effectiveness systematic review found clear evidence that the addition of booster sessions enhanced the effectiveness of main programmes.

Appendix 1. Algorithm used to determine an individual's smoking status from the General Household Survey.



Appendix 2. Coefficients of the logistic regression models used to fit data from the General Household Survey.

All models have as the outcome variable whether or not a respondent who has initiated smoking, is a smoker at the time of interview..

Model 1. Current age of respondent as explanatory variable.

	Coefficient	Standard Error	t	P>|t|	L 95%	U 95%
Current age	-0.0468	0.000932	-50.23	0	-0.04863	-0.04498
Constant	2.260747	0.04981	45.39	0	2.163116	2.358378

Model 2. Age of smoking initiation of respondent as explanatory variable.

	Coefficient	Standard Error	t	P>|t|	L 95%	U 95%
Age of smoking initiation	-0.11467	0.0082	-13.98	0	-0.13074	-0.0986
Constant	1.690692	0.127038	13.31	0	1.441686	1.939698

Model 3. Current age and age of smoking initiation of respondent as explanatory variables.

	Coefficient	Standard Error	t	P>|t|	L 95%	U 95%
Current age	-0.04781	0.001084	-44.1	0	-0.04994	-0.04569
Age of smoking initiation	-0.1028	0.008757	-11.74	0	-0.11996	-0.08563
Constant	3.86844	0.146211	26.46	0	3.581853	4.155027

Model 4. Current age, age of smoking initiation, sex, ethnicity, socioeconomic class, education and geographical region of respondent as explanatory variables.

	Coefficient	Standard Error	t	P>|t|	L 95%	U 95%
Current age	-0.0499	0.001241	-40.22	0	-0.05234	-0.04747
Age of smoking initiation	-0.09234	0.009183	-10.06	0	-0.11034	-0.07434
Sex [1]	0.087272	0.036303	2.4	0.016	0.016114	0.158431
Ethnicity [1]	0.38645	0.114285	3.38	0.001	0.162439	0.610461
Socioeconomic [1]	0.450791	0.042202	10.68	0	0.36807	0.533512
Socioeconomic [2]	0.932033	0.050387	18.5	0	0.83327	1.030796
Region [1]	0.298917	0.04031	7.42	0	0.219906	0.377929
Constant	3.254103	0.157474	20.66	0	2.945438	3.562769

Variable coding for Model 4:

- Sex: 0 male 1 female
- Ethnicity: 0 white British 1 other
- Socioeconomic: 0 I and II 1 IIIN and IIIM 2 IV and V
- Education: 0 left full-time education after age 16 1 left full-time education before or during age 16
- Region: 0 Wales and Southern England (East and West Midlands, London, South-East and South-West) 1 Scotland and Northern England (Yorkshire and the Humber, North-East, North-West)

Model 5. Same as model 4, but with confounders taking values equal to the proportion of the sample population in each relevant category.

	Coefficient	L 95%	U 95%
Current age	-0.05414	-0.05672	-0.05156
Age of smoking initiation	-0.07482	-0.09315	-0.0565
Constant	3.764977	3.574096	3.955857

Model 6. Same as model 4, but with interaction terms between demographic variables and age of smoking initiation (ASI).

	Coefficient	Standard Error	t	P>|t|	L 95%	U 95%
Current age	-0.05412	0.00132	-40.99	0	-0.05671	-0.05153
ASI	-0.09578	0.023937	-4	0	-0.1427	-0.04886
Sex [1]	0.182169	0.293411	0.62	0.535	-0.39295	0.757285
Ethnicity [1]	0.198986	0.940958	0.21	0.833	-1.64539	2.043364
Socioeconomic [1]	-0.42391	0.354009	-1.2	0.231	-1.11781	0.269985
Socioeconomic [2]	-0.09831	0.412242	-0.24	0.812	-0.90635	0.709724
Education [1]	0.922979	0.360033	2.56	0.01	0.217275	1.628682
Region [1]	-0.11549	0.324967	-0.36	0.722	-0.75246	0.521478
ASI × Sex [1]	-0.0054	0.018878	-0.29	0.775	-0.0424	0.031603
ASI × Ethnicity [1]	0.019427	0.059288	0.33	0.743	-0.09678	0.135638
ASI × Socioeconomic [1]	0.048911	0.022714	2.15	0.031	0.004389	0.093432
ASI × Socioeconomic [2]	0.056797	0.026664	2.13	0.033	0.004533	0.109061
ASI × Education [1]	-0.02792	0.022821	-1.22	0.221	-0.07265	0.016814
ASI × Region [1]	0.025705	0.021011	1.22	0.221	-0.01548	0.066889
Constant	3.253433	0.384386	8.46	0	2.499996	4.00687

Model 7. Same as model 6, but with terms removed using backward stepwise variable selection to obtain the most parsimonious model.

	Coefficient	Standard Error	t	P>|t|	L 95%	U 95%
Current age	-0.05417	0.001318	-41.1	0	-0.05676	-0.05159
ASI	-0.1029	0.009445	-10.89	0	-0.12142	-0.08439
Sex [1]	0.097695	0.036521	2.68	0.007	0.026109	0.169281
Education [1]	0.484163	0.046198	10.48	0	0.393611	0.574715
ASI × Ethnicity [1]	0.031871	0.007387	4.31	0	0.017392	0.046349
ASI × Socioeconomic [1]	0.021805	0.002796	7.8	0	0.016326	0.027285
ASI × Socioeconomic [2]	0.050633	0.003371	15.02	0	0.044025	0.05724
ASI × Region [1]	0.018209	0.002614	6.97	0	0.013085	0.023333
Constant	3.371651	0.157858	21.36	0	3.062233	3.681069

Appendix 3. Best fitting values for the exponential decay models relating effect size to age or time since start of intervention.

All models have the functional form $y(x) = 1 + a - e^{-\lambda(x-b)}$, where λ, a, b are parameters to be fitted, x is age (or time since start of intervention) and y is effect size. For delay models, we fix a=0, while for decrease models, we allow any a>0. Also, for age-based models x represents age, while for time of intervention-based models, x represents time since start of intervention.

	a	b	λ
Delay, age-based model	0	9.00	-0.434
Decrease, age-based model	1.716	9.00	-0.017
Delay, time of intervention-based model	0	0	-1.131
Decrease, time of intervention-based model	1.735	0	-0.027

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