The University of Nottingham

The Health and Economic Costs of Smoking in the Workforce: Premature Mortality, Sickness Absence and Workplace Interventions for Smoking Cessation

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Abstract

Background

The common argument used against the implementation of tobacco control policies is that revenue from tobacco duty is considerably higher than the health care costs smoking imposes on society. This point is true as revenue in the United Kingdom (UK) totalled £9.1 billion while recent costs estimates for the treatment of smoking-attributable disease totalled £5.2 billion to the UK National Health Service. However, this argument becomes unclear when indirect costs such as productivity loss or cost of absenteeism are incorporated. In the UK, there were 29.2 million employed adults in 2011 of which 20% were current smokers. This equates to approximately 5.84 million employed adult smokers. There are currently no studies which have quantified the economic impact of smoking-attributable indirect costs to both employers and the wider society in the UK. These costs are suspected to impose a large economic burden to society but the best practice methodology for estimating indirect costs and the magnitude of these costs are still unknown. Therefore, the aims of this thesis were to quantify the economic impact of smoking-attributable indirect costs due to productivity loss from premature mortality and absenteeism of workforce and to evaluate workplace interventions which could potentially decrease the burden of smoking in the workforce in the UK.

Methods

A number of methods were used along with a range of data sources which provided the information to quantify the economic impact of smoking in the workforce. Cost-of-illness methodology based on the human capital method was utilised to quantify the monetary burden of smoking in the workforce due to premature mortality in the UK. Systematic review and meta-analysis was used to examine the epidemiological association between smoking and absenteeism while also providing the necessary parameters to estimate costs of absence in the UK. Finally, decision analysis and Markov simulation modelling was used to conduct both cost-benefit analysis and cost-effectiveness analysis from the employer's perspective for evaluating workplace smoking cessation interventions of brief advice, individual counselling and nicotine replacement therapy with individual counselling.

Results

Cost-of-smoking modelling estimated that smoking was responsible for 96,105 deaths (58% male) in adults aged 35 years and over (17% of all deaths) in the UK annually, resulting in 1.2 million years of total life lost and 357,831 years of productive life lost valued at £4.93 billion in 2010. From the systematic review of 29 longitudinal studies, current smokers had a 33% increase in risk of absenteeism and were absent for an average of 2.74 more days per year compared with non-smokers. Compared with never smokers, ex-smokers had a 14% increase in risk of absenteeism; however, no increase in duration of absence could be detected. Indirect comparison meta-analysis showed that current smokers also had a 19% increase in risk of absenteeism compared with ex-smokers. Consequently, smoking was estimated to cost UK employers £1.46 billion in 2011 from absenteeism in the workplace.

Workplace interventions for smoking cessation provide a possible method for reducing the burden of smoking in the workforce. Cost-benefit analysis of workplace interventions resulted in brief advice being the optimal decision strategy for women while brief advice and individual counselling both were optimal decision strategies for men in terms of minimising total costs and maximising return on investment for the employer. If the employer valued maximising quitting instead, cost-effectiveness analysis showed that nicotine replacement therapy with individual counselling would be the optimal strategy given a maximised budget constraint.

Conclusion

This thesis has provided the first indirect cost-of-smoking study quantifying the productivity loss due to premature mortality and absenteeism in UK; the first systematic review and meta-analysis which has explored the association between smoking and absence from work; and the first cost-benefit and cost-effectiveness analyses of workplace interventions for smoking cessation in the UK. The implications of this research have particular relevance for UK policy makers and employers to justify stronger tobacco control policy which promotes smoking cessation. However, these findings are not unique to the UK. The thesis has provided the framework and methodology for studies that can strengthen the evidence-base around the economics of smoking in other countries as well. .

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List of Abbreviations

ASH: Action on Smoking and Health
ASHE: Annual Survey of Hours and Earnings
CDC: Centre for Disease Control
CHEC: Consensus on Health Economic Criteria
CHS: Continuous Household Survey
CI: confidence interval
COPD: chronic obstructive pulmonary disease
CPI: consumer price index
CVD: cardiovascular disease
ETS: environmental tobacco smoke
EU: European Union
FC: friction cost
FCTC: Framework Convention on Tobacco Control
GLS: General Lifestyle Survey
HSE: Health Survey for England
ICD: International Classification of Diseases
ICER: incremental cost-effectiveness ratio
IMF: International Monetary Fund
LCI: labour cost index
MOOSE: Meta-analysis of Observational Studies in Epidemiology
NHS: National Service
NICE: National Institute of Health and Care Excellence
NRT: nicotine replacement therapy
ONS: Office for National Statistics
OR: odds ratio
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses
PSA: probabilistic sensitivity analysis
PVFE: present value of future earnings
REML: restricted maximum likelihood
ROI: return on investment
RPI: retail price index
RR: risk ratio/relative risk
SAF: smoking attributable fraction
SAM: smoking attributable mortality
SAMMEC: Smoking-Attributable Mortality, Morbidity and Economic Costs
SHS: Scottish Health Survey
SHS: second hand smoke
TC: total cost
TPD: Tobacco Products Directive
UK: United Kingdom
US: United States
WHO: World Health Organisation
YPLL: years of productive life lost

PhD Thesis Publications

Weng SF, Ali S, Leonardi-Bee J. Smoking and absence from work: systematic review and meta-analysis of occupational studies. ***Addiction*** 2013, 108(2):307-319 [*In Press*]

Weng SF, Ali S, Leonardi-Bee J. Productivity cost of lost earnings due to smoking-attributable premature mortality in the United Kingdom. ***European Journal of Health Economics*** [*Submitted August 2013*]

Weng SF, Ali S, Leonardi-Bee J. What does the employer value for worksite smoking cessation intervention? Minimising costs or maximising quitting. ***Journal of Health Economics*** [*Manuscript in preparation*]

PhD Conferences and Seminars

Weng SF. Cost-benefit analysis of workplace smoking cessation interventions: Markov model from the employer's perspective. ***The Department of Health Sciences Spring Seminar Series.*** University of York. January 2013 [*Seminar*]

Weng SF. Indirect cost of productive life years lost due to smoking in England and Wales. ***Tackling Smoking in 21st Century Britain.*** UK Centre for Tobacco Control Conference. November 2012. York, UK [*Conference Presentation*]

Weng SF. Smoking and absenteeism: Systematic review and meta-analysis of occupational studies. ***15th World Conference on Tobacco or Health.*** March 2012. Singapore [*Conference Presentation]*

Weng SF. Smoking and Absenteeism: Systematic review and meta-analysis of occupational studies. ***Epidemiology, Public Health and Primary Care Joint Seminar Series***. University of Nottingham. September 2011 [*Seminar*]

Yang M, Dhiman P, **Weng SF**. Developing risk prediction models: procedures, methods and issues. ***Epidemiologic Methods Discussion Group***. University of Nottingham. April 2013 [*Seminar*]

Research Associate Publications

Weng SF, Redsell SA, Swift JA, Yang M, Glazebrook C. Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. ***Archives of Disease in Childhood*** 2012, 97(12):1019-1026 [In Press]

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Weng SF, Redsell SA, Nathan D, Swift JA, Yang M, Glazebrook C. External validation of the Infant Risk of Obesity Checklist (IROC) to estimate overweight and obesity risk in childhood from predictors during infancy. ***The British Medical Journal*** [*Manuscript in preparation*]

Chapter 1

Introduction and Background

1.1 Health effects of smoking

1.1.1 Mortality

Tobacco use is the leading cause of preventable death and disease in the world.[1] In the 20th Century, tobacco use from smoking caused 100 million deaths.[2] Smoking-attributable diseases are currently responsible for one in ten[1] adult deaths worldwide resulting in the deaths of 6 million people per year.[3] On the basis of current consumption patterns, 450 million adults will be killed by smoking between 2000 and 2050 where over half of these deaths will occur prematurely between the ages of 30 and 69 years.[4] Latest estimates show that the overall number of deaths in the UK has declined from 106,000[5] per annum in 1998-2002 to 96,105[6] in 2010 due to a decrease in the adult smoking prevalence from 27%[5] from 1998-2001 to 20%[7] in 2010. Despite this decline, smoking is still responsible for one in six deaths[5] in the UK. In men, lifetime smokers are expected to die on average 10 years earlier than never smokers.[8] In women, lifetime smokers are expected to die on average 11 years earlier than never smokers.[9] The shortened life span is due to the causal link that has been established between smoking and a number of smoking-related diseases.[3] This section summarises the primary causes of mortality and morbidity from smoking.

1.1.2 Cancer

Since the 1950s, there has been evidence that tobacco smoking is associated with an increased risk of lung cancer (from case-control studies).[10] [11] In 1986, the International Agency for Research on Cancer (IARC) established a significant causal association between tobacco smoking and cancers of the lung, oral cavity, pharynx, larynx, oesophagus, pancreas, urinary bladder and renal pelvis from epidemiological studies.[12] Since then, new epidemiological evidence has established that smoking also causes cancer of many other organs including nasal cavities, paranasal sinuses, nasopharynx, liver, stomach, kidney, uterine cervix, adenocarcinoma of the oesophagus and myeloid leukaemia.[13] Compared to all other cancers, the risk of developing lung cancer is extremely high in smokers and increases with the number of cigarettes smoked.[14] Controversy exists as to whether women are more or less susceptible to the carcinogenic effects of cigarette smoke. Some biological studies have suggested women may be more predisposed than men to molecular aberrations resulting from the carcinogenic effects of tobacco smoke.[15] However, observational studies[16] [17] have not found a significant difference in lung cancer risk between men and women.

From 2010-2011 in England, a total of 160,300 primary diagnoses (11% of all diagnoses) of cancer were found to be attributable to smoking; of which lung cancer accounted for 66,200 diagnoses (41% of smoking-attributable cancers).[7] Smoking-attributable bladder cancer accounted for the second largest number of cancer diagnoses with 33,400 diagnoses (21% of smoking-attributable cancers).

1.1.3 Respiratory disease

There has been evidence since the 1960s that cigarette smoking was associated with a doubling of the risk of chronic bronchitis and chronic obstructive pulmonary disease (COPD) compared to non-smokers.[18 19] There also has been early evidence to show that patients with COPD have an increased risk of developing lung cancer.[20] A recent study[21] has suggested that long-term oxygen depletion stimulates signals that promote tumour growth. It has been estimated that 21% of smokers will develop moderate COPD and 4% of smokers will develop severe COPD.[22] However, evidence has also shown the majority of smokers will get COPD but it is routinely under-diagnosed due to smokers dying from co-morbidities.[23] Evidence from meta-analyses has shown that current smoking significantly increases the overall risks of COPD (RR 3.51, 95% CI 3.08 to 3.99, N = 129 studies), chronic bronchitis (RR 3.41, 95% CI 3.13 to 3.72, N = 114 studies) and emphysema (RR 4.87, 95% CI 2.83 to 8.41, N = 28 studies).[24] From 2010-2011 in England, a total of 126,200 diagnoses of respiratory disease were due to smoking; of which COPD accounted for 88,500 diagnoses (70% of smoking-attributable respiratory disease).[7]

1.1.4 Cardiovascular disease

There is strong evidence that supports the association between smoking and cardiovascular disease (CVD) including ischemic heart disease[25], cerebrovascular disease[26], atherosclerosis[25] and aortic aneurysms[27]. In addition, smoking is also associated with acute myocardial infarction[28] and stroke[26]. Smoking is associated with a two to four-fold increase in risk of ischemic heart disease, an increase in excess rate of death by 70% from ischemic heart disease and elevated risk of sudden death.[25] In a multicentre study in 52 countries, smoking was associated with an increased risk of myocardial infarction (Odds Ratio [OR] 2.95, 95% CI 2.77 to 3.14) compared with never smoking.[28] In a meta-analysis of 32 studies, the overall relative risk of stroke associated with cigarette smoking was 1.5 (95% CI 1.4 to 1.6).[26] In a

systematic review of 10 studies, the risk of aortic aneurysms was between three to six-fold greater in current smokers than in non-smokers.[27]

From 2010-2011 in England, a total of 135,400 diagnoses of cardiovascular diseases (15% of all CVD diagnoses) were found to be due to smoking; of which ischemic heart disease accounted for 64,700 diagnoses (48% of smoking-attributable CVD), other heart disease accounted for 37,600 diagnoses (28% of smoking-attributable CVD) and cerebrovascular disease accounted for 16,700 diagnoses (12% of smoking-attributable CVD).[7]

1.1.5 Passive smoking

In addition to the harmful effects smokers pose to their own health, tobacco smoke also generates considerable health threats to those who are exposed to second-hand smoke (SHS) or environmental tobacco smoke.[29] Passive smoking is the inhalation of SHS or ETS by persons other than the intended active smoker which occurs when tobacco smoke permeates any environment.

Systematic review evidence has shown that exposure to second-hand smoke significantly increases the overall risk of lung cancer (RR 1.29, 95% CI 1.17 to 1.43, N = 43 studies)[30], heart disease (RR 1.25, 95% CI 1.17 to 1.32, N = 18 studies)[31] and stroke (RR 1.25, 95% CI 1.12 to 1.38, N = 20 studies)[32] in lifelong non-smokers. There is also some evidence to suggest that exposure to as little as an hour of second-hand smoke in adults is linked to an acute decline in lung function while longer term exposure can induce asthma and COPD.[33] While the health risks of passive smoking are small in comparison with the effects of active smoking, the overall health impact is large due to the outcomes being common.[34] In the UK, passive smoking at work is estimated to be responsible for 617 deaths per year while the burden is even greater in domestic settings.[35] Each year passive smoking in the home is estimated to account for another 2,700 deaths in persons aged 20-64 years and 8,000 deaths among people aged $\geq$ 65 years.[35]

Since a large proportion of passive smoking occurs in the home, children are particularly vulnerable. Systematic review evidence has shown that second-hand smoke exposure in non-smoking pregnant women is associated with an increased risk of low birth weight (OR 1.32, 95% CI 1.07 to 1.63, N = 23 studies).[36] Additionally, second-hand smoke exposure to

children in the home increases the risks of sudden infant death syndrome[37] (OR 2.08, 95% CI 1.83 to 2.38, N = 19 studies), asthma in childhood[38] (OR 1.37, 95% CI 1.15 to 1.64, N = 14 studies) and bacterial meningococcal disease[39] (OR 2.02, 95% CI 1.52 to 2.69, N = 16 studies). Each year in the UK, second-hand smoke exposure leads to 20,000 cases of respiratory infections; 120,000 cases of middle-ear disease; 22,000 cases of wheezing and asthma; 200 cases of bacterial meningitis and 40 sudden infant deaths.[40]

1.1.6 Smoking in pregnancy

Second-hand smoke exposure is not the only means in which smoking can harm others. Smoking in pregnancy can cause harm to the unborn child. Maternal smoking in pregnancy is known to be associated with an increased risk of low birth weight[41 42], pre-term delivery[43 44], certain congenital malformations[45-47], spontaneous miscarriage[48] and placenta abruption[49]. Recent review evidence has also shown that maternal smoking in pregnancy has also been linked to an increased risk of being overweight in childhood (OR 1.47, 95% CI 1.26 to 1.73, N = 7 studies).[50] Even though maternal smoking in pregnancy may result in growth restriction *in utero* resulting in low birth weight infants, some studies have found that affected infants exhibit extremely high rapid postnatal weight gain.[51 52] It is also likely that maternal smoking in pregnancy is a proxy for other social and lifestyle characteristics. In a US study of low income children and their parents, children of smokers were found to have poor diet quality with high levels of saturated fat, high levels of cholesterol intake and low levels of fibre intake.[53]

1.1.7 Other diseases

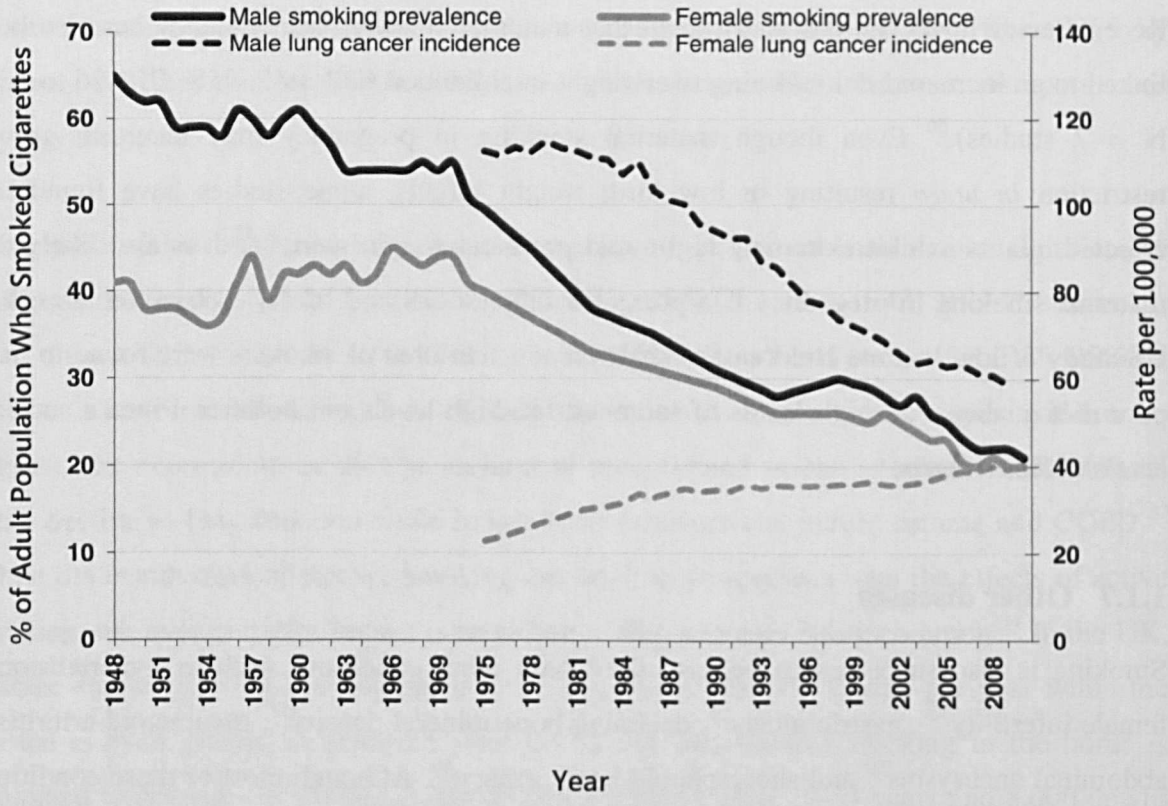
Smoking is also suspected to be associated with other conditions such as hypertension[54], female infertility[55] , gastric ulcers[56], declining bone-mineral density[57], rheumatoid arthritis[58], abdominal aneurysms[59] and subarachnoid haemorrhage[60]. Although most of these conditions are established as being associated with smoking through observational evidence, the exact casual mechanisms are not entirely known compared to other more well-established casual relationships (e.g. lung cancer, CVD, COPD).

1.2 Smoking trends in the UK

1.2.1 Gender

Cigarette smoking had become extremely common in the UK in the first half of the 20th Century in which an estimated 80% of men and 40% of women smoked.[61] The Office for National Statistics (ONS) started collecting official smoking prevalence data from 1948 in the General Lifestyle Survey (GLS). The trends in smoking prevalence and lung cancer incidence are shown from 1948 to 2010 in **Figure 1**.

Figure 1. Cigarette smoking prevalence and lung cancer incidence in the UK 1948-2010



*Source: Cancer Research UK[62] (Original data from ONS General Lifestyle Survey)

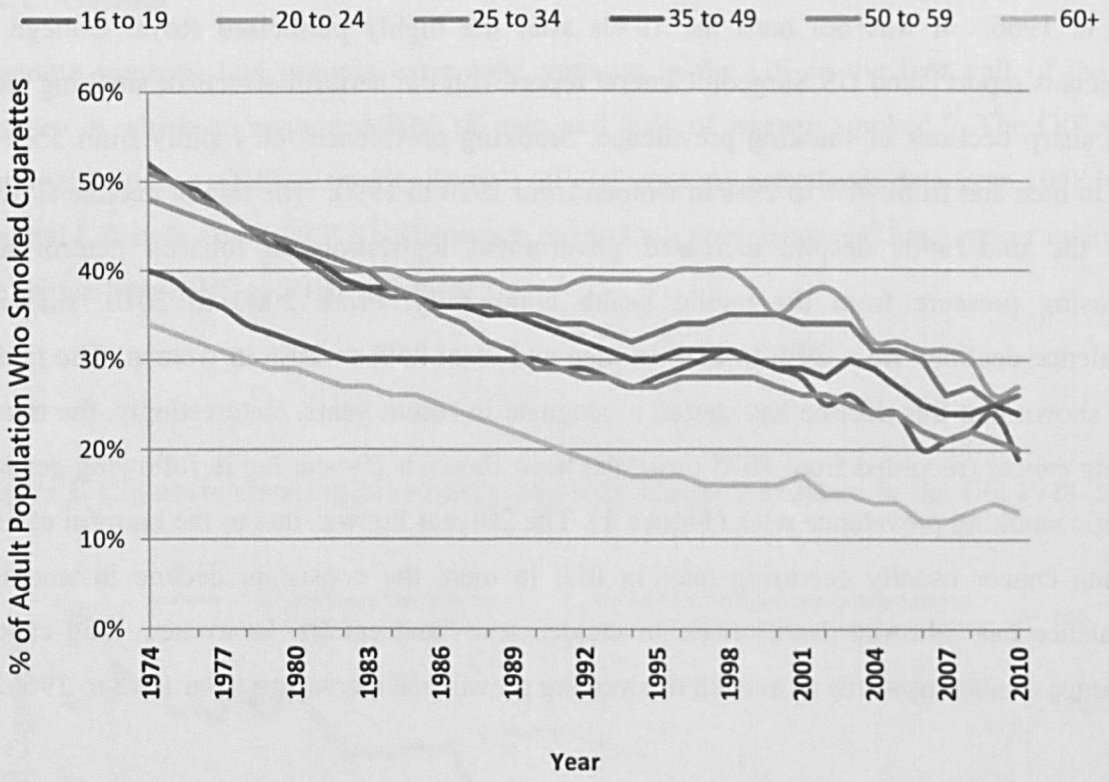
Since the start of data collection, smoking prevalence in men was already declining from 65% in 1948 to 54% in 1966. In women, smoking prevalence increased from 41% in 1948 to 45% in 1966. It was not until the 1970s after the highly publicised Royal College of Physicians report[63] and US Surgeon General report[64] on the harmful effects of smoking were there sharp declines in smoking prevalence. Smoking prevalence fell rapidly from 55% to 31% in men and from 44% to 29% in women from 1970 to 1990. The rate of decline slowed from the mid-1990s despite increased government legislation on tobacco control and increasing pressure from the public health community. From 2000 to 2010, smoking prevalence declined from 29% to 21% in men and from 25% to 20% in women. The trends have shown that this decline has started to stagnate in recent years. Interestingly, the trends in lung cancer (recorded from 1975 onwards) have shown a 20-year lag in following gender-specific smoking prevalence rates (**Figure 1**). The 20-year lag was due to the harmful effects of lung cancer usually occurring later in life. In men, the consistent decline in smoking prevalence has followed the decrease in incidence of lung cancer. In women, lung cancer incidence trended upwards as a result of smoking prevalence increasing from 1948 to 1966.

1.2.2 Age-groups

Smoking prevalence historically has been high in all age-groups. In 1974, smoking prevalence was highest in the middle-age-groups (25-59 years) with relatively low levels of youth smoking (16-19 years) and older adult smoking (60+ years) (**Figure 2**). Since then, the largest declines in smoking prevalence have occurred in the middle-age-groups. In 1974, more than half of adults aged 35-49 years smoked cigarettes. In 2010, the prevalence declined to 24% in adults aged 35-49 years. Smoking prevalence in 2010 was lowest in individuals 60 years or older (13%) and youths aged 16-19 years (19%). Smoking prevalence was relatively higher in 2010 for adults aged 20-24 years (27%) and 25-29 years (26%).

One group that **Figure 2** does not show is the prevalence in children under the age of 16 years. The majority of UK smokers begin smoking before the age of 16 years.[65] In 2011, approximately 25% of pupils aged 11-15 years had tried smoking at least once and about 5% were regular smokers (smoking at least one cigarette per week).[7] Evidence has also shown that an earlier age of initiation leads to a decrease in success for smoking cessation later in life.[66 67]

Figure 2. Cigarette smoking prevalence by age in the UK 1974-2010

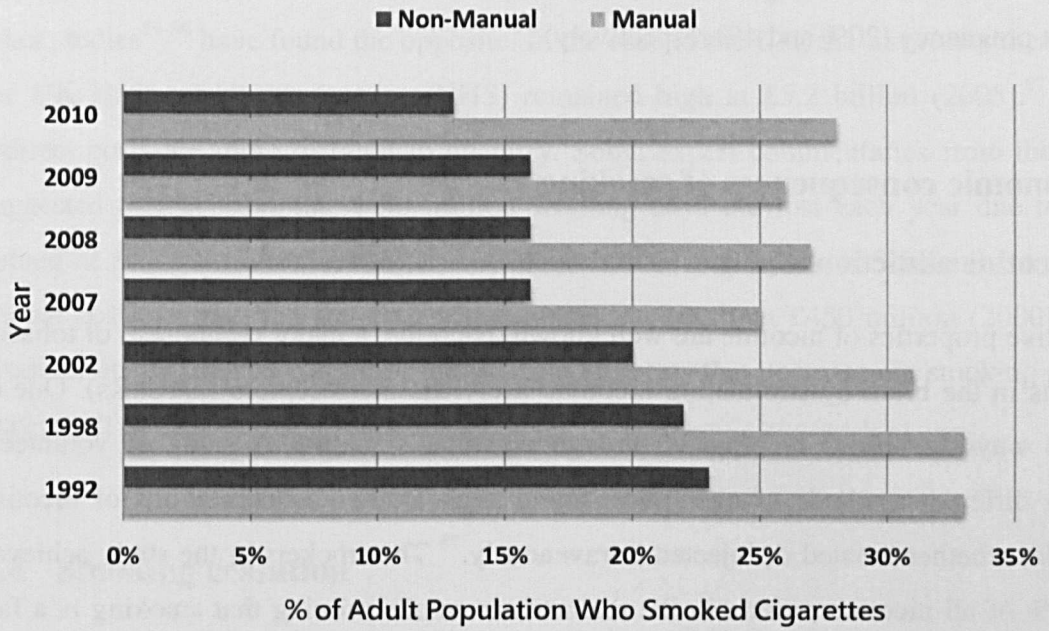


*Source: Cancer Research UK[68] (Original data from ONS General Lifestyle Survey)

1.2.3 Socio-economic groups

Smoking has been established as having the single largest impact on health inequalities.[69] Before the associations between smoking and lung cancer were first reported in the 1950s, there was little difference in smoking prevalence between socioeconomic groups. The rate of decline in smoking prevalence from the 1970s onwards is now known to differ by socio-economic status.[70] **Figure 3** illustrates the differential decline of adult smoking prevalence in manual and non-manual occupational groups from 1992 to 2010. In 1992, the prevalence of smoking in manual workers was 33% while the prevalence of smoking in non-manual workers was 23%. After 18 years, the prevalence of smoking in manual workers declined by only 5% to 28% in 2010 while the prevalence of smoking in non-manual workers declined by 10% to 13% in 2010. The discrepancies in smoking prevalence by socio-economic status are likely due to higher uptakes rates and less successful quit attempts in more disadvantaged groups.[71]

Figure 3. Prevalence of cigarettes smoking by occupational group, adults aged 16 and over, UK 1992-2010



*Source: Cancer Research UK[72]

Studies have also suggested that disadvantaged groups have reduced social support for quitting, low motivation to quit, stronger addiction to tobacco, lack of self-efficacy and increased likelihood of not completing smoking cessation interventions.[71] As a result, large survey studies[73] [74] in the UK have shown that smoking rates are significantly higher in deprived groups than in more affluent groups.

1.2.4 Maternal smoking in pregnancy

In 2005, nearly 33% of mothers in the UK smoked at some point in the 12 months immediately before or during their pregnancy while 17% of mothers continued to smoke throughout their pregnancy.[75] The latest figures from the Infant Feeding Survey[76] showed a decrease in smoking in pregnancy. In 2010, around 26% of mothers in the UK smoked directly before or during their pregnancy while 12% of mothers continued to smoke throughout their pregnancy.[76] The Department of Health has identified a national target to reduce smoking during pregnancy to 11% or less by 2015 measured at the time of delivery.[77] The target is likely to be achieved as 54% of smoking mothers in the UK currently give up smoking at some stage before birth.[76] However, there is a strong association between

smoking levels and socio-economic status. Mothers in routine and manual occupations were five times more likely than those in managerial and professional occupations to have smoked throughout pregnancy (20% and 4% respectively).[76]

1.3 Economic consequences of smoking

1.3.1 Nicotine addiction and individual costs

The addictive properties of nicotine are well known. Nicotine, a major component of tobacco smoke, acts in the brain by stimulating nicotinic acetylcholine receptors (nAChRs). One of the fastest ways to absorb nicotine is through cigarette smoking. A study of volunteers comparing different methods of absorption found peak arterial concentrations of nicotine were similar whether inhaled or injected intravenously.[78] The smokers in the study achieved almost 90% of all nicotine present in the mainstream smoke proving that smoking is a fast and efficient way to absorb nicotine.[78] However, nicotine is not the only addictive property of cigarettes. Smokers rely on many non-nicotine components (i.e. the 'act' of smoking, 'scratchy' throat) that reinforce smoking behaviour. A more recent literature review of smoking cessation interventions found that smokers also relied on the non-nicotine components of the smoking to provide many of the rewarding effects, often surpassing the direct effects of nicotine itself.[79] As a result of the physical and psychological dependency on smoking, an individual who smokes 20 cigarettes a day will spend about £2,600 a year (2011) on cigarettes.[80] The total household expenditure on tobacco has decreased since 1980 to 2.0% of total household expenditure in 2011.[7] Despite this decline, the total amount spent on tobacco in the UK remains substantial ranging from estimates of £15.3 billion to £18.3 billion in 2011.[80]

1.3.2 Societal costs of smoking

The costs of smoking to society can come in the form of direct healthcare costs and indirect costs. Globally, net economic loss amounts to $200 billion (1998) USD (£132 billion) per year attributable to health care costs and lost productivity.[1] The health consequences of addiction and smoking-related morbidity and mortality can be directly attributed to between 6% and 15% of total healthcare expenditures in high-income countries.[1] To date, most economic studies evaluating the cost of smoking have focused only on healthcare costs.

While many of these studies[81-83] have found that the lifetime healthcare costs of smokers (taking account of shorter life expectancy in smokers) are higher than those of non-smokers, other studies[84-86] have found the opposite. In the case of the UK, the direct healthcare costs to the UK National Health Service (NHS) remained high at £5.2 billion (2005).[87] However, indirect costs are more difficult to quantify. Some expert commentaries from the UK have suggested that approximately 50 million working days are lost each year due to smoking valued at £1,710 million (1998).[88] Another study of employers in Scotland found that the annual cost of employee smoking was estimated to be about £450 million (2000) from lost productivity.[89] The sheer scale of the finances suggests that decreases in smoking prevalence may result in huge gains in productivity.

1.4 Smoking cessation

1.4.1 Health benefits

The most obvious benefits of smoking cessation are the improvements in life expectancy and prevention of disease. Smoking cessation at any age has been shown to result in a gain of life years; those who stop at the age of 60, 50, 40, 30 years gain on average 3, 6, 9, 10 years respectively.[8] The gain in life years is due to the overwhelming health benefits of quitting smoking. When an individual quits smoking, the benefits are seen immediately.[90 91] These immediate benefits will lead to longer term benefits from sustained quitting. Evidence has shown that heart rate and blood pressure drop approximately 20 minutes after quitting[91] and blood carbon monoxide levels drop to normal after about 8 hours.[90] Smoking cessation also leads to significant medium term health benefits in the first year.[92 93] From 2 to 3 months after quitting, circulation improves and lung function increases.[92] From 1 to 9 months after quitting, coughing and shortness of breath decrease and individuals start to regain normal function of the lungs which increases their ability to handle mucus, clean the lungs and reduce the risk of infection.[92] From one year after quitting, the excess risk of coronary heart disease is reduced by 50% compared to the risk in continuing smoking.[93]

The major decrease in the risk of smoking-attributable disease is seen in the long-term.[93 94] From about 5 years after quitting, the risk of cancers of the mouth, throat, oesophagus and bladder are decreased by 50% while the risk of cervical cancer and stroke decrease to the level of a non-smoker.[93] From about 10 years after quitting, the risk of death from lung

cancer is about half that of continuing smokers.[93] The risk of cancers of the larynx and pancreas decrease by slightly less.[93] The evidence on the decrease in risk of other types of cancers are inconclusive.[94] After about 15 years since quitting, the risk of coronary heart disease drops to the level of risk in a non-smoker.[94] As a result of the short, medium and long-term health benefits, cessation can improve an individual's quality of life as smokers tend to have lower self-reported health status than non-smokers.[95]

1.4.2 Interventions

There is substantial evidence that self-help materials such as books and brochures (RR 1.21, 95% CI 1.05 to 1.39, N = 12 studies)[96], brief advice (RR 1.66, 95% CI 1.42 to 1.94, N = 17 studies)[97], individual behaviour counselling (RR 1.39, 95% CI 1.24 to 1.57, N = 22 studies)[98] and group behaviour therapy (RR 1.98, 95% CI 1.60 to 2.46, N = 13 studies)[99] can improve the chances of quitting. In addition, pharmacological interventions can be used to complement self-help or counselling therapies. Pharmacotherapy for smoking cessation can increase the chance of successful quitting more than self-help, brief advice or behavioural therapy alone.[101] The three forms of pharmacotherapy that are licensed to be used in smoking cessation in the UK are nicotine replacement therapy (NRT), bupropion (Zyban) and varenicline (Champix/Chantix).

Nicotine replacement therapy (NRT) is licensed to be the only nicotine-based medication in the UK. Several forms of NRT are available: gum, tablet, inhalators, nasal spray and lozenges. NRT aims to reduce the motivation to smoke and withdrawal symptoms during a quit attempt and therefore increase the likelihood of quitting.[100] Meta-analytic studies[101] have shown that nicotine gum increases the likelihood of quitting by 43% (95% CI 1.33 to 1.53, N = 53 studies); nicotine patch increases the likelihood of quitting by 66% (95% CI 1.53 to 1.81, N = 41 studies); nicotine inhaler increases the likelihood of quitting by 90% (95% CI 1.63 to 2.45, N = 4 studies); oral tablets or lozenges increase the likelihood of quitting by 100% (95% CI 1.53 to 2.45, N = 6 studies); and nicotine nasal spray increase the likelihood of quitting by 102% (95% CI 1.49 to 3.73, N = 4 studies). The recommended length of usage of NRT is around 8 to 12 weeks with gradual reductions in dosage through the latter part of the course. NRT can be obtained over-the-counter (OTC) or by prescription through the NHS. Common side-effects of NRT include heart palpitations, chest pains, nausea, vomiting, gastrointestinal complaints and insomnia.[102]

Unlike NRT, bupropion and varenicline are prescription medications that do not contain any nicotine. Bupropion is an antidepressant medication licensed for smoking cessation usage by prescription only. Review evidence has found that bupropion increased the odds of quitting by 97% (95% CI 1.67 to 2.34, N = 16 studies) compared to placebo.[103] Studies have observed that depression is more frequently found in smokers than non-smokers, smoking cessation may precipitate depression and nicotine is suspected to have antidepressant effects.[104 105] Serious side-effects from bupropion use are rare. The major adverse effect is the risk of seizures (estimated 0.1%) and therefore it is not recommended for patients with current seizure disorders or a history of seizures.[106] Other less serious side-effects include allergic reactions, dry mouth, headaches and insomnia.[106]

Varenicline is the latest prescription medication used to aid smoking cessation. Varenicline is a nicotine receptor partial antagonist which works by maintaining moderate levels of dopamine to counteract withdrawal symptoms (acting as an agonist) while simultaneously reducing smoking satisfaction (acting as an antagonist). Evidence has shown that varenicline increases the likelihood of sustaining smoking abstinence for six months compared to placebo (RR 2.33, 95% CI 1.95 to 2.80, N = 6 studies).[107] Furthermore, varenicline has also been shown be more effective in maintaining long-term abstinence for one year compared to bupropion (RR 1.52, 95% CI 1.22 to 1.88, N = 3 studies) and NRT (RR 1.31, 95% CI 1.01 to 1.71, N = 1 study).[107] Post-marketing safety data suggests that varenicline may be associated with depression, agitation, suicidal behaviour or ideation.[107] More recent analysis of clinical trials found no evidence that varenicline was associated with psychiatric disorders other than sleep disturbances.[108] However, previous trials may not have been powered to detect a significant relationship. Ongoing research is currently being conducted to evaluate this relationship.

1.4.3 Economic benefits

The health consequences of addiction and smoking-related morbidity and mortality can be directly attributed to between 6% and 15% of total healthcare expenditures in high-income countries.[1] For instance, latest figures show that the cost of smoking to the UK NHS was £5.2 billion.[87] Therefore, there are potential economic benefits to individuals and society from smoking cessation such as reducing the effects of passive smoking and decreasing expenditures of the health service and employers.[95] These benefits can be short-term or long-

term benefits as seen in several studies. A study in California estimated that a 1% decrease in smoking prevalence resulted in 924 fewer hospitalisations for acute myocardial infarction and 538 fewer hospitalisations for stroke resulting in an immediate savings of $44 million (1995) USD (£28 million).[109] A 7-year program that reduced smoking prevalence by 1% per year would result in $3.2 billion (1995) USD (£2.1 billion) in cost savings preventing approximately 13,100 deaths resulting from acute myocardial infarction.[109] A study in Denmark found that the total lifetime cost-savings (1999 costs) associated with smokers who quit before 35 was €24,800 (£21,085) per male smoker and €34,100 (£28,940) per female smoker in terms of health care costs and lost productivity.[110] Another US modelling study had found that an annual 1% drop in maternal smoking prevalence would prevent 1,300 cases of low birth weight and save $21 million (1995) USD (£14 million) in direct medical costs in the first year of the programme; the programme would prevent 57,200 cases of low birth weight and save $572 million (1995) USD (£375 million) in direct medical costs in 7 years.[111]

It must also be acknowledged, however, that tobacco provides a large source of revenue for the government from taxation of sales and imports. In the UK, the revenue generated from tobacco duties totalled £9.1 billion in 2010-2011.[112] Controversially, some studies[84-86] have suggested that a decline in population smoking prevalence may actually result in cost savings in health care costs in old-age due to smokers dying prematurely. Despite revenue from taxation and potential old-age cost-savings due to premature mortality, the human cost (loss of life, quality of life, impact on family and friends) due to smoking from mortality and morbidity has no true measurable value. When the human costs are considered with direct health care costs and indirect costs, smoking cessation increases the overall health, social and economic welfare of society.[88]

1.5 Tobacco control policy

1.5.1 International influence

The previous sections have highlighted the harmful health effects of smoking, smoking trends in the UK, the economic costs of smoking and the clear benefits of individually targeted smoking cessation. The evidence favours strong tobacco control policies which encourages smokers to quit and prevent new smokers from starting. In the UK, tobacco control policy is

determined by the government. However, wider international influences of European legislation and the WHO Framework Convention on Tobacco Control (FCTC)[113] have also influenced UK tobacco control.

While health policy, management, financing and legislation are the responsibilities of individual member states, EU policy does in fact exert some influence over tobacco control policy in the UK. Most notable is Article 168 of the Lisbon Treaty[114] which highlights the importance of cooperation between Member States in coordinating health policy. Tobacco is specifically mentioned in Section 5 of Article 168[114] stating that the European Council may 'adopt incentive measures designed to protect and improve human health and in particular to combat the major cross-border health scourges, measures concerning monitoring, early warning of and combating serious cross-border threats to health, and measures which have as their direct objective the protection of public health regarding tobacco and the abuse of alcohol, including any harmonisation of the laws and regulations of the Member States'.[114] These are non-binding agreements between Member States but the direct effects of the treaty can be seen in the implementation of the Tobacco Products Directive (TPD)[115] across the EU which bans tobacco advertising of products, covers the use of health warnings on packets, prohibits the use of 'mild' or 'light' descriptions on cigarette packets and prohibits the sale of tobacco for oral use (except for Sweden). Legislation such as the TPD is extremely important as it harmonises prohibitions around the sale of tobacco products within a single EU market giving the UK and other EU countries the legal justification to implement these policies. In 2012, there has been a proposal to review (ongoing) the TPD to include regulations on plain packaging, smokeless tobacco, hand-rolled tobacco, cross-border internet sales, oral tobacco, electronic cigarettes, herbal products, pictorial health warnings and illicit trade.[116]

UK tobacco control policy is also influenced by the WHO global guidelines due to the UK government's signing, ratification and enforcement of the Framework Convention on Tobacco Control (FCTC).[113] The FCTC is an evidence-based public health treaty developed as a response to the global tobacco epidemic. All signatories to the convention are responsible for the implementation of several provisions[113]:

- Price and tax measures to reduce the demand for tobacco
- Protection from exposure to tobacco smoke

- Regulation of the contents of tobacco products
- Implement health warning labels on tobacco products
- Regulation of tobacco product disclosures
- Packaging and labelling of tobacco products
- Education, communication, training and public awareness
- Prohibition of tobacco advertising, promotion and sponsorship
- Demand reduction measures concerning tobacco dependence and cessation
- Combat illicit trade and sales to minors
- Provision for support of economically viable alternatives

These FCTC and EU policies have largely influenced UK government policy on tobacco control in recent years.

1.5.2 UK tobacco control policy

The comprehensive framework on tobacco control which the UK has developed has been consistent with EU and FCTC priorities. In 1998, the government published its first White Paper[117] 'Smoking Kills' detailing comprehensive tobacco control strategies. The objectives of the strategy were to reduce smoking in children and young people, help smokers give up smoking, reduce smoking-related inequalities and reduce smoking in pregnancy. In order to achieve these objectives, a variety of policy measures were enacted:

- Ban on tobacco advertising and sponsorship and reduction of point-of-sales advertising
- Increase taxation on tobacco products
- Enforcement of under-age sales
- Restrictions on cigarette vending machines
- Introduce NHS smoking cessation services
- Facilitate easy access to pharmacotherapy
- Combat illicit trade

Many of these measures are still in place today while others have evolved. The 1998 'Smoking Kills' White Paper[117] had noted the harmful effects of passive smoking, however

concluded that a ban on smoking in public places was not possible to implement. This view changed when the government released another White Paper[118] in 2004 with a proposal to ban smoking in cafes, restaurants, pubs, workplaces and factories. After many government consultations, the smoking ban came into force 1 July 2007.

The most recent tobacco control strategy was detailed in 2011 in the White Paper[119] 'Healthy lives, healthy people'. The report detailed that in addition to continuing the enforcement of existing tobacco control legislation; there were several objectives to implement over the next few years:

- Legislation to end point-of-sales displays in shops
- Evaluate the possibility of plain packaging as an effective means to reduce uptake of smoking by young people and to support adult smokers in trying to give up
- Maintain the high price of tobacco products through taxation
- Encourage smokers to quit using the most effective forms of smoking cessation through local stop smoking services
- Effective enforcement of tobacco control policies at the local level

These objectives can be achieved through regulation, service provision, legislation and enforcement. The specific strategies of tobacco control policy in the UK are described in this section. In addition, evidence is provided on the effectiveness of each measure.

1.5.3 Age restrictions and availability

Age restrictions are common measures used to reduce the availability of tobacco products to youths. In October 2007, the minimum age for the legal purchasing of tobacco products was raised from 16 years to 18 years in England, Wales and Scotland (the minimum of possession remains 16 years). In Northern Ireland, the minimum age for the legal purchasing of tobacco products was raised from 16 years to 18 years in 2008.

There is evidence showing that age restrictions decrease the ability of tobacco purchases by youths from legal vendors.[120-122] Review studies[120 122] have found that age restrictions can significantly reduce the rate of illegal tobacco sales to youth. However, both studies concluded that lack of enforcement and the ability of youths to acquire cigarettes from social

sources can undermine the effectiveness of age restrictions. This fact is supported by a community intervention study in the US which found that communities with strict enforcement had reduced illegal sales to minors compared to communities without strict enforcement.[121]

1.5.4 Smoke free legislation

Due to harmful effects of passive smoking and the large number of individuals exposed as described in **Section 1.1.5**, there is strong rationale for legislation imposing smoke-free public places. In July 2007, smoking was banned in cafes, restaurants, pubs, workplaces and factories in England. Smoke-free legislation was imposed in Scotland in March 2006 while Wales and Northern Ireland imposed a smoking ban in April 2007.

There has been substantial evidence attributing the decline of passive smoking exposure to the decrease in negative health effects as a result of the smoking ban. In a sample of bar staff in Ireland, salivary cotinine concentrations dropped by 80% after the smoke-free laws were imposed while respiratory symptoms declined.[123] In another study, air nicotine concentrations were tested at city centre bars and the results showed that concentrations were reduced by 83%.[124] A study in Scotland found that the percentage of bar workers with respiratory and sensory symptoms declined by 32.5% approximately 2 months after the ban while lung function increased.[125] In addition, the smoking ban was also found to be associated with significantly reducing the number of emergency admissions for myocardial infarction after the implementation of smoke-free legislation.[126] Time-series analyses conducted in the US have also found significant reductions in number of hospital admissions and incidence of myocardial infarction after smoking bans were imposed.[127 128]

A potential unintended consequence of the smoking ban was the displacement of smoking into homes. A cross-sectional survey in Hong Kong found a significant increase in passive smoking exposure in young children at home.[129] This led to a large EU-wide study of five countries (Ireland, France, Germany, Netherlands, UK) which found that smoke-free legislation did not result in more smoking in homes and in fact encouraged many parents to enforce their own smoking ban inside the home.[130]

1.5.5 Health warnings

The requirement for all tobacco products sold in the UK to display health warnings is due to the EU Tobacco Products Directive (TPD).[115] The TPD requires all tobacco products to display general health warnings covering at least 30% of the front of the pack and health warnings covering at least 40% of the back of the pack.[115] This requirement has since been enforced in the UK from 2002. There is a good body of evidence to suggest that health warning labels are an effective means of communicating the health risks of smoking and influencing quitting behaviour.[131-133] The studies also found that larger and clear health warnings labels across packs of cigarettes tended to be more effective than smaller warning labels.[131-133] In addition, there is a growing body of research on the effectiveness of pictorial or graphic warning labels on cigarette packs. Studies on graphic or pictorial warning labels have shown that picture warnings improve smokers' recall of health risks and are more effective than text-only warnings to influence quitting behaviour.[134-136] As a result of the growing evidence, more than 60 countries now require pictorial health warnings on cigarette packets. Canada was the first country to implement pictorial health warning labels in 2001 while Belgium became the first EU country to implement pictorial health warnings in 2007. In 2008, the UK was the third EU country (behind Romania and Belgium) to implement pictorial health warning labels. Due to the number of EU countries adopting pictorial health warnings, there is a planned proposal for the mandatory use of picture warnings on all tobacco products for sale in the EU.[116]

1.5.6 Tobacco promotion, advertising and sponsorship

Cigarettes are one of the most heavily advertised and promoted products in history.[137] From 1975 to 1983, the amount of money spent to promote cigarettes increased 288% from $490 million USD (£324 million) to $1.9 billion USD (£1.3 billion) in the United States alone.[137] The primary purpose of tobacco promotion, advertising and sponsorship is to encourage uptake of smoking by young people and discourage current smokers from quitting as specified directly in tobacco industry documents.[138-140] Evidence has shown that adolescents with high exposure to cigarette advertising are significantly more likely to be smokers than those with low exposure to cigarette advertising.[141 142] Time-series analysis has shown that advertising bans may have some impact of reducing consumption; however this effect is marginal in countries without comprehensive tobacco control policies.[143 144] In other words,

advertising bans in one area may lead to the tobacco industry diverting resources to other areas or media outlets, thus undermining the initial advertising ban.[145]

Advertising of tobacco products on television was banned in the UK in 1965 under the Television Act of 1964. Other forms of advertising in the press, billboards and films were governed by a self-regulatory agreement with the UK government. After the release of the White Paper[117] 'Smoking Kills', the government proposed and passed the Tobacco Advertising and Promotion Act of 2002 which banned tobacco advertising in the press and billboards along with direct marketing of tobacco products. Subsequently, all tobacco sponsorship was prohibited in Member States under the EU Tobacco Products Directive (TPD)[115] which was enforced from 2005 onwards in the UK.

One of the media outlets where tobacco imagery still occurs is in films. Although tobacco imagery in films has declined substantially in the past 20 years in the UK, older yet popular films with tobacco imagery are easily accessible to children. A study on the most popular films viewed in the UK from 1989 to 2008 found that tobacco imagery occurred in 70% of all films, with over half of those containing tobacco imagery being rated by the British Board of Film Classification (BBFC) as being suitable for children.[146] Observational evidence from the US has suggested that increased exposure to smoking in movies is independently associated with teenage smoking uptake.[147-149] The current government tobacco control plan has a proposal to work with media regulators and the entertainment industry around the portrayal of smoking in the entertainment media.[119]

1.5.7 Mass media campaigns

Mass media interventions use a range of methods to reach large numbers of people without being reliant on face-to-face contact often times involving local, regional or national television, radio, newspaper, leaflets, booklets, mobile phones, social networking and the internet. The National Institute for Health and Care Excellence (NICE) guidance on mass media suggests that mass media may have an influence on changing health behaviour; however it is not clear whether mass media independently prevents smoking uptake or encourages quitting behaviour.[150] Evidence about the effectiveness of mass media on quitting behaviour is mixed[151-154] and there is almost no evidence evaluating the effectiveness of mass media on preventing smoking uptake in youths. Most developed countries which have the

resources to conduct mass media campaigns usually also have comprehensive tobacco control policies, thus isolating the true effects of mass media on quitting behaviour or smoking uptake is extremely hard to quantify.

In the UK, mass media campaigns influencing smoking behaviour are funded by the government, charities or pharmaceutical companies. Although the pharmaceutical industry's primary goal is to increase pharmacotherapy sales by triggering quit attempts, this does complement the government's aim of increasing smoking cessation. The Department of Health 2009-2010 budget for smoking related marketing and communication totalled £38 million.[155] Due to budget cuts, the amount was decreased to £15 million in 2011-2012.[155] As a result, the Department of Health has prioritised the money to be spent on four key areas which includes smoking-related marketing and communication. However, more evidence is needed to evaluate the efficacy and cost-effectiveness of mass media campaigns on changing smoking behaviour.

1.5.8 Taxation

Taxation of tobacco products is the single most effective measure for influencing consumption. Most standard goods behave in a manner that if price increases then demand will decrease. It was once thought that the addictive nature of tobacco precluded it from a downward sloping demand curve. This was largely due to early arguments about smokers lacking self-control due to the addictive properties of nicotine and therefore the decision to smoke was not rational.[156] Consequently, taxation of cigarettes would result in little or no impact on consumption.[156] As empirical evidence on the effects of taxation on cigarette consumption developed, demand was shown to be negatively correlated with price. Estimates vary but international studies have shown that price elasticity (response in cigarette consumption to changes in price) of cigarettes range from -0.3 to -0.5 (1% increase in price results in between 0.3% to 0.5% fall in consumption).[157] Price elasticity in the UK was previously thought to be -0.5[158] which was within the range of the international estimates. However, a recent econometric analysis[159] conducted by the HMRC producing eight models using time-series data from 1982 to 2009 found price elasticity to be much larger than previously thought ranging from -1.17 to -0.92 after taking into account the effects of the smoking ban (2007) and the inception of the single EU market (1992).

Currently (2012), the UK has the second highest levels of cigarette taxation in the EU (Ireland has the highest levels of taxation) with a pack of 20 cigarettes typically costing £6.28; of which £4.82 is tax (77% of the total cost).[160] This generated £9.1 billion[112] from tobacco duties in 2010-2011. Under the current tobacco control plan, the government has proposed to maintain a high level of taxation but do not specify any specific increases in price on tobacco products.[119]

1.5.9 Illicit tobacco

One of the possible consequences of high tobacco prices is the rise in illicit tobacco. However, there is no evidence to directly attribute the rise in tobacco taxation to an increase in tobacco smuggling.[161] Tobacco smuggling grew in the mid-1990s after the integration of Member States into a single EU-market. In 2000, more than one in five cigarettes smoked in the UK was smuggled which cost over £3 billion per year in lost revenue.[162] Government efforts to combat illicit trade have since led to a decline but illicit tobacco is still a major problem. From 2007-2008, illicit tobacco accounted for £1.8 billion in lost revenue due to 10% of cigarettes and 47% of hand-rolled tobacco being smuggled.[161] Due to cheaper prices, illicit tobacco is most prevalent among youths from 14-17 years (one in three youths admit to buying illegal tobacco) and individuals from lower socio-economic classes (61% of illegal tobacco consumers).[161] Because poorer smokers are disproportionately more likely to buy illicit tobacco, combating illicit tobacco smuggling will also help reduce health inequalities.[162] Studies have also shown that smokers of illicit tobacco have significantly worse health outcomes and more likely to have financial difficulties than smokers of legal tobacco.[163] Economic analysis has shown using resources to combat illicit tobacco is extremely cost-effective generating a net monetary benefit of £5.7 billion (2007) and averting 760 deaths annually.[162] The current government's tobacco control plans calls for revising a work protocol between HMRC and local authorities as well as the development of a global protocol under the WHO FCTC.[119] These measures include marketing campaigns to reduce illicit tobacco use in certain communities, training local authorities to identify illegal products and examining the feasibility about restricting the amount of cheap tobacco products individuals can bring to the UK from abroad.[119]

1.5.10 NHS stop smoking services

For individuals that would like to quit smoking, the NHS offers stop smoking services free at the point of use. NHS stop smoking services were first introduced after the 1998 White Paper[117] 'Smoking Kills' as part of the first comprehensive tobacco control strategy. These services are provided locally in primary care, pharmacies or community centres. The counsellors provide a range of services such as brief advice, behavioural counselling and access to pharmacotherapy. From April 2011 to May 2012, there were 816,444 quit attempts in England made through NHS stop smoking services; of which 49% of the quit attempts were successful at 4 weeks follow-up (though longer term abstinence is unknown).[7] Total expenditure of the services in the same period was £88.2 million amounting to £220 per quitter (excluding costs of pharmacotherapy).[7] The service has been shown to be extremely cost-effective in a study of 92 specialist smoking cessation services in England.[164] However, the service has limited reach. In 2008, 67% of all smokers had reported that they wanted to give up smoking but only 26% had actually made a quit attempt.[165] Only 15% of those who had made a quit attempt sought professional advice while only 8% had been referred to a stop smoking service.[165] The majority of smokers who try to quit are unsupported. This is problematic as only an estimated 3% to 5% are successful with unaided quit attempts.[166] This is one of the key areas laid out in the UK tobacco control strategy to improve: methods in which NHS stop smoking services can maximise accessibility and outreach, particularly in groups with high rates of smoking prevalence.[119]

1.5.11 Point-of-sale displays

Tobacco companies have relied on point-of-sale displays as an effective means of branding and communicating affordability to youths. Studies have shown that tobacco companies have used large store displays to market cigarettes, often times behind counters and near other convenience items such as candy and magazines.[167] In addition, survey studies on school children have found children perceived stores with large point-of-sale displays to be less likely to ask for proof-of-age, recalled displayed cigarette brands more and increased susceptibility to smoke in the future.[168 169] There is also review evidence to suggest that point-of-sale promotion undermines smoking cessation attempts and promotes relapse among ex-smokers.[170] As a result, point-of-sale legislation in England prohibiting the display of cigarette packs came into effect in larger shops from April 2012 and will come into force for smaller shops from April 2015, effectively eliminating all visibility of cigarettes in retail

shops. In Northern Ireland, regulations have been issued to ban point-of-sale displays in the latter half of 2012 for large shops and in 2015 for smaller shops. The Welsh Government has also confirmed bans on point-of-sale displays from December 2012 in large stores and in all other businesses by April 2015. In Scotland, legislation to prohibit point-of-sale displays has passed but implementation is currently hindered by legal challenges by the tobacco industry.

1.5.12 Plain packaging

One of the last forms of brand advertising and promotion by the tobacco industry is through the cigarette pack itself. Australia was the first country in the world to implement plain packaging for products manufactured since October 2012 and on sale since December 2012. Brand logos and colours have been replaced by a standard size olive green pack with a common font for all brand variants. Health warnings in text and pictures will still remain on the majority of the packet surface area. There is no direct evidence that plain packaging will be effective in reducing smoking consumption and uptake as the empirical case in Australia had just come into force at the end of 2012. However, tobacco industry documents have revealed that companies view cigarette packs as integral to brand promotion supported by marketing studies carried out by the companies themselves which found that pack branding is designed to appeal to select target groups such as youths and women.[171] Tobacco field experts believe the most likely outcomes would be a reduction in smoking prevalence in adults and a greater reduction in the number of children trying smoking (although there is substantial variability in the estimated size of these impacts).[172] Recently, the Department of Health funded a systematic review on the impact of plain packaging which found that plain packaging reduced pack and product appeal, increased the salience of health warnings, improved recall of health warnings and reduced confusion about product harm.[173] The review also found some evidence that plain packs may have a deterrent effect for the onset of smoking in young people and may encourage existing smokers to quit.[173] The UK government has launched a public consultation in the spring of 2012 which has since ended in August 2012. The consultation report is expected to be released sometime in the near future.

1.5.13 Harm reduction

While pharmacotherapy can increase the probability of quitting significantly[101 103 107], successful smoking cessation is still low due to a low starting baseline of 3-5%[166] for unassisted quitting. Although the ideal for all smokers is to quit completely, a substantial proportion of smokers do not want to stop smoking or have not been able to do so despite many attempts.[174] For these heavily-addicted individuals, switching to alternative forms of nicotine without the major health risks of smoking may be a more positive option than continuing to smoke cigarettes. Two types of products that are currently being researched are electronic cigarettes and smokeless tobacco. Evidence has shown that smokeless tobacco (snus, chewing tobacco, snuff) confers about 0.1% to 10% of the overall risk of cigarette smoking.[175] There is evidence that suggests smokeless tobacco users have an increased risk of oral cancer but these results are due to discrepancies in product types from different locations.[176] Epidemiological data in Asia have shown an increased risk of oral cancer but the results are not confirmed in Swedish studies.[176] This is most likely due to the fact that the smokeless product snus used in Sweden has fewer contaminants than the chewing tobacco used in India.[177] Despite the mixed evidence, all smokeless tobacco products are banned throughout the EU with the exception being Sweden where there is a long history of smokeless tobacco use in the form of snus.

Electronic cigarettes are battery powered devices that deliver propylene glycol and nicotine in vapour form through inhalation which simulates the act of smoking. The device was first introduced on the Chinese domestic market in 2004 and later exported to the international market from 2005 onwards. The popularity of electronic cigarettes has risen in recent years due to an increase in internet marketing and product exposure. Little is known about the safety of electronic cigarettes. The WHO reported that there is currently no evidence or rigorous peer-reviewed studies that have been conducted showing that the electronic cigarette is safe but did not discount the possibility that the electronic cigarette could be useful as a smoking cessation aid.[178] Some online surveys have found that a large percentage of the smokers either cut-down or abstained from smoking altogether which suggests that electronic cigarettes may have the potential to act as a smoking cessation aid.[179] However, laboratory tests of electronic cigarettes by the US Food and Drug Administration had found in some products carcinogens and toxic chemicals such as diethylene glycol (compound used in antifreeze).[180] Debate about the safety and effectiveness of electronic cigarettes is ongoing in

the absence of peer-reviewed evidence. NICE is scheduled to release guidance around harm reduction mid-2013. Current UK tobacco control policy has suggested a review of the evidence around harm reduction before policy proposals will be made.

1.6 Smoking in the workforce

The previous sections have shown that tobacco use is an extremely complex issue. Comprehensive tobacco control involves a multifaceted approach involving the treatment of smoking-attributable disease, the treatment of the nicotine addiction, the evaluation of the economic consequences of smoking, government legislation and industry restrictions. Consequently, there are many research gaps which have been identified. In **Section 1.1.5**, there are no clear or effective policy solutions which would reduce the effects of passive smoking in children. In **Section 1.2.3**, smoking prevalence in low SES groups remains high and tobacco control policy seems ineffective to promote cessation in these groups. In **Section 1.5.12**, most tobacco control field experts believe that standard packaging will in fact reduce uptake and promote cessation; however, there is no direct evidence which has shown this effect. In **Section 1.5.13**, the safety and effectiveness of harm reduction products in aiding with smoking cessation is unclear. In **Section 1.3.2**, little is known about the economic impact of smoking in the workforce. Many of these research gaps highlighted require different approaches and addressing all of these gaps is beyond the scope of this thesis. However, the thesis does address the gap highlighted in **Section 1.3.2** as the evidence surrounding the economic impact of smoking in the workforce is extremely limited. The following sections describe why this is an important area to research.

1.6.1 Thesis rationale: The economic arguments

The WHO FCTC states that ultimately 'health and not economic arguments are the reason for tobacco control but economic arguments are raised as an obstacle to tobacco control policies'.[113] Government have raised three items[181] of concern over the negative economic consequences of tobacco control:

i. Lower tax revenues via reduced demand and increased illicit activities
ii. Decreasing employment in the manufacturing and retail sectors
iii. Impoverishing smokers with higher prices

Existing evidence from developed countries have suggested that economic fears over tobacco control policies are largely unfounded.[1] In **Section 1.5.8**, taxation was shown to be the most effective means to reducing consumption and there is no direct evidence that links increased illicit activities to increased taxation as described in **Section 1.5.9.**

There is little impact of effect of [182] decreasing employment in the manufacturing and retail sectors as employment in the UK tobacco industry has been falling over the past few decades.[88] There is little evidence to suggest that tobacco control policies are the reason for this decline. There is, however, evidence to show that the reduction in workforce is largely the result of mechanisation and rationalisation.[183] A study conducted in the UK found that 19,400 tobacco manufacturing jobs were lost between 1963 and 1985 in which 16,000 (82%) could be attributed to the improvement in productivity.[184] According to the Office for National Statistics, only 5,000 people were employed in UK tobacco manufacturing in 2010.[185]

Governments have raised the concerns over (iii) impoverishing smokers with higher prices due to the regressive nature of taxes on poor smokers. As the tax increases, the share of tobacco expenditure on household income also increases creating an extra burden on family budgets.[181] The counter-argument can be made that by implementing taxes to the level beyond the purchasing threshold of poor families, many simple will not be able to afford to smoke. Evidence has shown that poor smokers and young smokers are more responsive to price in which a 10% increase in price may reduce consumption by 4% or more.[186] In respect to poor smokers, the benefits of quitting are proportionally greater as there will be lower lifetime health costs and more resources for other essential goods such as food and education.[181]

Despite largely unfounded fears of negative economic consequences, there is still considerable difficulty in the legislation of tobacco control policies which promote cessation due to legal challenges by the tobacco industry. From 2009 to 2011, there were legal challenges by the tobacco industry in 18 countries on tobacco control legislation using the fear of negative economic consequences as part of the argument against measures such as point-of-sales displays, standard packaging and graphic warning labels.[187] One common argument against these measures is the reduction in tax revenue as described in the first item (i). However, the expectation of lower tax revenues due to stronger tobacco control policies

has not held true. From the period from 2002 to 2011, UK tobacco control policy has implemented health warning labels, introduced smoke-free public places, banned point-of-sales displays and increased taxation. In the same period, adult smoking prevalence has declined from 27% to 20%[7] while tax revenue has actually increased from £8.1 billion to £9.1 billion[188].

The common 'smoking pays for itself' argument used against implementation of tobacco control policies is that revenue from tobacco duty is considerably higher than the health care cost smoking imposes on society.[88] This point is true as tobacco revenue in the UK totalled £9.1 billion[188] while recent costs estimates of the treatment for smoking-attributable disease totalled £5.2 billion[87] to the NHS. However, this argument becomes unclear when indirect costs are incorporated. Indirect costs are costs resources which are not directly accountable to the cost object (smoking) but rather represent an opportunity cost or foregone benefit.[189] Indirect costs of smoking commonly include but are not limited to productivity loss, effects on other services and impact on patients, family and other stakeholders. This thesis has focussed on quantifying the indirect costs of productivity loss in the workplace in the UK due to smoking. The thesis uses the definition of productivity loss which can be described as lost ability to work as a result of the ill health caused by smoking. These costs are suspected to contribute substantially to the total cost smoking imposes on society.

In the UK, there were 29.2 million[190] employed adults in 2011 of which 20%[7] were current smokers. This equates to approximately 5.84 million employed adult smokers. As described in **Section 1.1**, there are significant health effects from smoking which are independent of employment status. However, there are no studies which have quantified the economic impact of smoking-attributable indirect costs such as productivity loss or absenteeism to both employers and the wider society in the UK. These indirect costs impose a large cost burden to society yet are difficult to quantify accurately. The sheer scale of the finances suggests that decreases in smoking prevalence may result in huge gains in productivity, possibly offsetting or even outweighing revenue generated by tobacco duties. Therefore, it is extremely vital for this research gap to be addressed in order to inform tobacco control policy at the national level.

1.6.2 Research gap

A literature review was conducted to identify and evaluate any previous studies that had reviewed the topic of smoking and indirect costs. The search for literature regarding smoking and indirect costs was conducted broadly through electronic database searches and cross-referencing between studies. The goal was to find any previous literature, narrative or systematic reviews on smoking and indirect costs. There were only six studies found that reviewed literature related to smoking and indirect costs; of which four studies were literature reviews[191-194]; one study was a narrative review[88]; and one study was a quantitative review[195]. There were three primary findings of the literature search:

- There is no standard methodology in which to quantify indirect costs due to smoking.
- Indirect costs were predominantly due to premature mortality or sickness absence.
- It is unknown whether interventions that promote smoking cessation are cost-effective in the workplace.

In order to address the economic arguments against stronger tobacco control, it is necessary to strengthen the evidence-base around these research gaps using robust and rigorous methods. This will help move forward tobacco control policy and improve both the economy and public health.

1.6.3 Aims and objectives

The aims of this thesis were to quantify the economic impact of indirect costs of smoking from productivity loss due to premature mortality and absenteeism in the UK and to evaluate possible solutions to decrease the burden of smoking in the workforce. These findings will complement existing direct cost-of-smoking studies conducted in the UK to better inform tobacco control policy at the national level. This is accomplished through seven specific objectives:

- To review all cost-of-smoking studies to inform best practice methodology for the estimation of population-level indirect costs (**Chapter 2**).
- To quantify productivity loss due to smoking using best practice cost-of-smoking methodology for the UK (**Chapter 3**).

- To evaluate the epidemiological association of smoking and absence from work by systematic review and meta-analysis of worldwide studies (**Chapter 4**).
- To quantify the cost of absenteeism in the UK (**Chapter 4**).
- To validate the indirect costs estimates derived from this thesis using an ecological model from worldwide studies (**Chapter 5**).
- To evaluate the cost-benefit of workplace smoking cessation interventions from an employer-based investment perspective using decision analysis and Markov simulation modelling (**Chapter 6**).
- To explore if the employer's decision strategy changes if the employers primarily valued maximising quitting using cost-effectiveness analysis (**Chapter 6**).

1.6.4 Study methods

The methods utilised in this thesis involve a number of statistical, epidemiological and health economic techniques drawing on multiple data sources. Outlined below are brief descriptions of the study methods used. More detailed information on methodology and data sources are provided in the individual methods sections of subsequent chapters and appendices.

1.6.4.1 Regression analysis

Regression analysis is a common statistical technique for estimating the relationship among variables. This technique was used in **Chapter 2** when examining the ecological association between indirect costs and smoking prevalence and in **Chapter 5** when exploring the ecological validity of UK cost estimates. In **Chapter 2**, stepwise linear regression was specifically used to determine the best ecological predictor model between indirect costs and smoking prevalence taking into account population-level covariates.

1.6.4.2 Cost-of-illness

Cost-of-illness methodology is commonly used to quantify the direct or indirect costs of particular diseases which are then reported as monetary values. As the focus of this thesis was on indirect costs, the methodology around the quantification of these costs was reviewed in **Chapter 2.** Subsequently, the methodological review informed the best practice technique for estimating productivity loss due to smoking in the UK in **Chapter 3.** There are two types of costing methods: prevalence and incidence approaches.[196] In this thesis, the prevalence-based approach was employed to calculate smoking-attributable mortality using population

fractions derived from smoking prevalence and smoking mortality risks. These figures were then combined with UK earnings data to estimate the annual value of lifetime income lost due to premature mortality.

1.6.4.3 Systematic review

Systematic review methodology was utilised in **Chapter 4** to identify, appraise, select and synthesize longitudinal evidence evaluating the association between smoking and absence from work. This thesis adhered to all PRISMA guidelines[197] to ensure a high level of quality assurance with regards to selecting and extracting data for the systematic review. Electronic searches were conducted using several databases for published studies while conference proceeding were searched for in grey literature. In addition, reference lists were assessed for potential studies. Quality assessment of the studies was carried out using a standardised form which evaluated important aspects of epidemiological quality such as study selection, minimisation of bias and attrition.

1.6.4.4 Meta-analysis

Meta-analysis methodology was used to synthesize the quantitative results from studies identified from the systematic review in **Chapter 4**. This thesis adhered to MOOSE guidelines[29] for meta-analysis of observational studies. The random effects model was used to determine the effect sizes for the smoking and risk or duration of absenteeism due to smoking. The random effects model was used to take into account heterogeneity in study location, study length, study year, workforce characteristics and other unknown factors. In addition, meta-regression was used to the test for differences in risk between subgroups.

1.6.4.5 Decision analysis

Decision analysis was used in **Chapter 6** for both cost-benefit and cost-effectiveness analysis of workplace interventions for smoking cessation. The decision analytical framework provides a formal technique to assessing and ranking workplace interventions for smoking cessation which maximise quitting and minimise absenteeism. From the employer's perspective, the outcomes were total costs (TC) incurred and return on investment (ROI) of interventions which reduce absenteeism and labour turnover. Additionally, some employers may choose to base their decision strategies on maximising quit rates. Therefore, **Chapter 6** used cost-effectiveness analysis to determine the optimal intervention strategy based on incremental cost-effectiveness ratios (ICERs) for maximising quitting.

1.6.4.6 Markov model

Representation of complex interventions may be difficult using conventional decision trees and often times requires simplifying assumptions. Instead, Markov models can be used to model complex interventions which involve risk that is continuous over time, incorporate time dependency and simultaneous events. In this thesis, workplace smoking cessation interventions were evaluated using a Markov state transition model which simulated a cohort of employed adult current smokers from 35 years to the age of retirement (**Chapter 6**). The Markov model was embedded in a decision tree to evaluate the cost-benefit and cost-effectiveness of multiple smoking cessation interventions (Markov-cycle tree).

1.6.4.7 Probabilistic sensitivity analysis

The incorporation of uncertainty into Markov models uses a Bayesian process by fitting prior probability distributions to model parameters. Probability distributions can be randomly sampled using the Monte Carlo method to generate posterior distributions of costs, effects, cost-effectiveness ratios, net monetary benefits or net health benefits. In **Chapter 6**, transition probabilities which govern the movement between Markov states were fit with appropriate probability distributions based on prior study information. The Monte Carlo method was used to simulate multiple trials of each Markov cohort simulation. This procedure tested for the robustness of the findings by incorporating all parameter uncertainty.

Chapter 2

Indirect costs of smoking: Comparison of methodology and results from population-level studies

2.1 Introduction

Smoking in the workplace has become an increasingly important public health issue in recent years. Although smoke-free workplaces have been implemented in many countries, employee smoking still remains a problem. Smoking is thought to contribute towards productivity loss and increased absenteeism due to ill health, death and early retirement.[198] Smoking may also reduce productivity as a result of smoking breaks and presenteeism (reduced productivity while at work).[198] Other costs include cleaning and fire damage to property and business.[198] All these components contribute substantial economic costs to society. One way of enhancing the awareness of the magnitude of these economic costs is to transform the health related consequences of smoking-related diseases to monetary values. Globally, the World Bank estimates that tobacco use results in a net economic loss of $200 billion (1998) USD (£132 billion) per year attributable to health care costs and lost productivity.[1] Due to the magnitude of these costs, governments have recognised the impact of smoking in the workplace. However, there is no consistent method used to measure indirect costs to facilitate informed decision making. Indirect costs of smoking are most commonly measured in terms of costs incurred from mortality, morbidity, absenteeism or reduced productivity at work.[199] Less frequently measured indirect costs include lost leisure time, lost household production, effects on family and friends or damage to business and property. The valuation of these costs depends on the perspective the study takes. Most cost-of-illness studies utilise either the human capital model[200] or friction cost method.[201] Human capital theory takes an individual (employee) perspective where indirect costs are estimated as foregone earnings and lost leisure time. Friction cost methodology takes the employer's perspective where indirect costs are presumed to be short-term or medium-term due to a firm's ability to restore the initial level of production depending on labour market conditions.

These differences in perspective have a profound impact on indirect cost estimates. For example, an Australian study (2008 costs) found that an absolute reduction in smoking prevalence of 8% from 23% resulted in workforce production gains of either AUD $415 million (£267 million) using the friction cost method or AUD $863 million (£556 million) according to the human capital model.[202] There have been a growing number of economic studies in the past decade on the cost of smoking, including the cost of absenteeism and reduced productivity due to illness. However, there have been no comparisons of results and methodologies of these studies.

2.2 Aims and Objectives

The aim of this chapter was to systematically examine the methodology and analyse the results from population-level studies which have quantified indirect costs due to smoking. This process informed the best methodology to conduct an indirect cost-of-smoking study for the UK in **Chapter 3**. A secondary aim was to explore the consistency among studies by examining the relationship between indirect costs and adult smoking prevalence. The results from the secondary aim allowed for the comparison of total indirect costs in the UK with other population-studies which formed the basis for a validation study in **Chapter 5**. These aims were achieved by completing the following objectives:

- Review of the international literature on indirect costs or productivity loss due to smoking
- Describe the cost components which contribute towards smoking-related indirect costs
- Summarise the methodology and compare the results of the indirect costs
- Carr out quality assessment of the included studies
- Investigate the ecological relationship between smoking and indirect costs using regression analysis

2.3 Methods

2.3.1 Data sources

Studies were identified (by SFW) through database searches of MEDLINE (1948 to December 2012), EMBASE (1974 to December 2012), Centre for Reviews and Dissemination (up to December 2012), Science Direct (1950 to December 2012) and EconLit (1980 to December 2012). In addition, reference lists from identified articles were reviewed for relevant literature. Keywords relating to 'smoking', 'indirect costs' and 'productivity loss' were used to search for all relevant publications (**Appendix 9.1**). Where available in the database, medical subject headings (MeSH) were used to identify related terms.

2.3.2 Inclusion criteria

The studies obtained from the electronic database search were screened for duplicates (by SFW). Titles and abstracts were assessed based on subject matter. Full-text articles were subsequently retrieved from the remaining studies. There were several key criteria for inclusion in the review:

(1) The designs considered in this review were economic cost-of-illness studies at the population-level. Population-level studies were classified as national, state or regional studies.
(2) The studies estimated the monetary value of indirect costs or productivity loss due to active smoking.
(3) Indirect costs of smoking could be made of several cost components: productive life lost due to mortality and morbidity; absenteeism due to sickness or behavioural issues; time spent on smoking breaks; reduced productivity at work due to presenteeism; or other smoking-related indirect costs reported in the study.

2.3.3 Data extraction and data synthesis

Studies were extracted (by SFW) for descriptive characteristics (study year, location, cost methodology, cost components and primary findings). In addition, underlying methodologies were described and compared. Only data pertaining to smoking-related indirect costs or productivity loss were extracted for this review. Results pertaining to direct costs (healthcare costs) of smoking were not extracted.

In order to compare monetary values of productivity loss across studies, a common unit of annual cost per capita was calculated. Size of the population was obtained in the study year using data from the World Bank Development Indicators (WDI)[203], US Census Bureau[204], General Register Office for Scotland[205] and National Statistics Republic of China (Taiwan)[206]. Cost per capita was exchange rate adjusted to US dollars by annual rates provided by the International Monetary Fund (IMF)[207] in the study year. Subsequently, the monetary values of costs were inflated to 2010 levels using a constructed earnings inflation index from data on annual average earnings from the Organisation for Economic Co-operation and Development (OECD)[208], Census and Statistics Department of Hong Kong[209] and National Statistics Republic of China (Taiwan)[210]. The year 2010 was selected as the

base year as this was the study year of the most recent studies identified. The costs were adjusted by the following equation:

$$Cost\ per\ capita_{2010} = \frac{Average\ annual\ earnings_{2010}}{Average\ annual\ earnings_{Study\ year}} \times Cost\ per\ capita_{Study\ year}$$

2.3.4 Quality assessment

To assess the methodological quality of selected studies, a scale was developed based on the Consensus on Health Economic Criteria (CHEC)[211] checklist. CHEC is a 19-point scale developed solely for clinical-effectiveness studies; thus the original scale was not appropriate to use for cost-of-smoking studies at the population-level. Therefore, an 8-point scale (**Appendix 9.2**) was adapted from the cost-side criteria of the CHEC checklist. The primary domains of the developed scale covered methodological quality of study objectives, study design, valuation of costs and sensitivity analysis. The quality assessment was conducted by one reviewer (SFW).

2.3.5 Statistical analysis

The association between cost per capita and smoking prevalence in the study year was tested by linear regression. Smoking prevalence rates for the included studies were obtained from multiple data sources: The WHO Tobacco Control Country Profiles[212-214]; The WHO Report on the Global Tobacco Epidemic[215 216]; CDC MMWR[217 218]; Canadian Report on National Strategy for Tobacco Control[219]; Hong Kong Thematic Household Survey[220]; Scottish Household Survey[221]; Taiwan National Health Interview Survey[222]; and Tobacco and Health in the European Union[223]. The smoking prevalence figures obtained from the data sources were the rates of current adult smoking in the study year.

For the regression analysis, non-inflated cost per capita amounts in US dollars were used instead of inflated cost per capita amounts. This was because all covariates were study-year variables to take into account study year differences. Study-year covariates were obtained from various official sources[203 208-210 224-232]. It was hypothesized that costs per capita or smoking prevalence may be associated with population size, earnings index (ratio of average

earnings in 2010 to earnings in the study year), GDP per capita, average monthly earnings, life expectancy at birth and age of the study. Initially, univariate associations between cost per capita or smoking prevalence and population-level covariates were explored. Associations giving *p-values* < 0.1 were included in a multivariate model. *P-values* < 0.1 were used as the cut-off as power of the analysis was expected to be relatively low (few studies). A smaller *p-value* would avoid missing potential univariate associations. Stepwise regression analysis was utilised to determine the best possible multivariable model incorporating smoking prevalence and cost per capita. Logarithmic and exponential transformations were made due to potential non-linear associations between smoking prevalence and covariates. The "best fit" model was determined by statistically significant *p-values* < 0.05. Two separate models were presented in the analysis: (1) Model 1 including all studies regardless of cost methodology; (2) Model 2 including only studies using the human capital model. The analyses were conducted in STATA 11 (Stata Corporation, College Station, Texas, USA).

2.4 Results

2.4.1 Description of included studies

Twenty-seven full-text articles were deemed potentially eligible (based on titles and abstracts) from a total search yield of 1,089 articles based on the inclusion criteria (**Figure 4**). Of the 27 studies, ten were excluded after full-text versions of the studies were obtained. Monetary costs of smoking were not reported in three studies[233-235]; five studies[182 236-239] were epidemiological studies which explored productivity loss in a specific sample of workers; and two subgroup studies[240 241] overlapped with another included study in this review where duplicate data were used. After excluding these studies, 17 population-level studies[89 110 202 242-255] were identified as fulfilling all the inclusion criteria and thus included in the review. **Table 1** shows the characteristics of the studies including location, study year, method, study currency, cost components, total indirect cost of smoking and quality score.

Nine studies[89 110 242 244 249 250 252-254] were from Europe,,four studies[243 245-247] were from North America, three studies[248 251 255] were from East Asia[248 251 255] and one study[202] was from Australia. All of the included studies were published within the last 15 years. The overall quality of studies was high with scores ranging from the lowest of six to the maximum of

eight. Most of the studies obtained a score of either six[89 243-246 250 251 255] points or seven[247-249 252 253] points. These studies most commonly lost quality points for not providing detailed descriptions of the study population or not conducting sensitivity analysis on reported cost estimates. There were four studies[110 202 242 254] which obtained the maximum quality score by fulfilling all elements of the quality criteria.

Figure 4. Search process and exclusion criteria

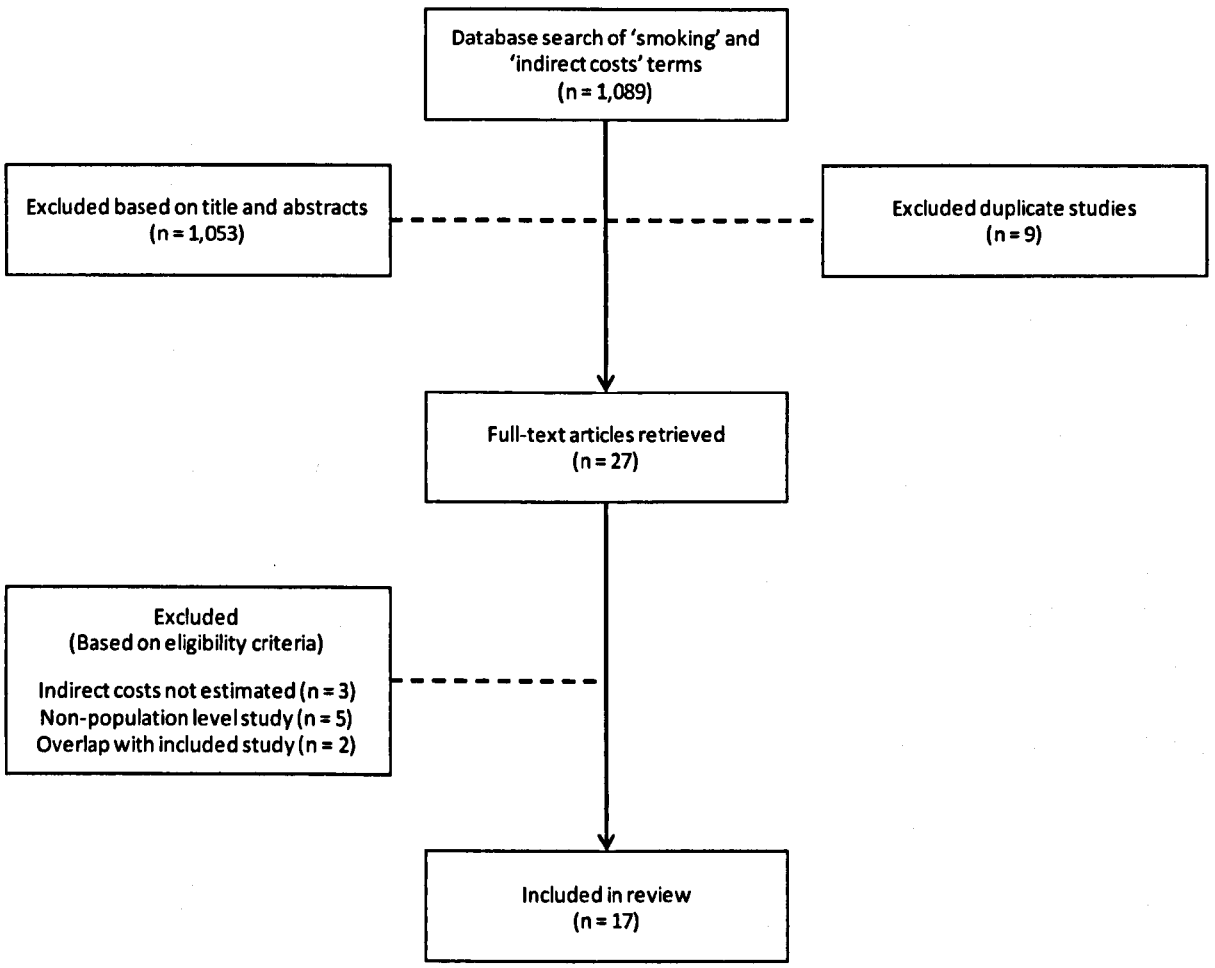


Table 1. Study characteristics and indirect costs per annum of smoking for 17 studies

First Author	Location	Study Year	Method	Study Currency	Cost Components (millions)				Total Cost (millions)	Quality Score (Max = 8)
					Productive Life Lost	*Absenteeism*	*Smoking Breaks*	*Other*		
Bolin 2007[242]	Sweden	2001	Human Capital	USD	592	--	--	--	592	8
CDC 2005[243]	USA	1997	Human Capital	USD	92,518	--	--	--	92,518	6
Jakubiak 2011[244]	Poland	2010	Human Capital	PLN	7,030	2,730	--	5,600[1]	15,360	6
Kaiserman 1997[245]	Canada	1991	Human Capital	CND	10,562	2,060	--	80[2]	12,702	6
Kayani 2007[246]	Missouri	2000	Human Capital	USD	2,419	--	--	--	2,419	6
Magnus 2004[202]	Australia	2008	Friction Cost	AUD	--	842		312[3]	1,154	8
Max 2004[247]	California	1999	Human Capital	USD	5,682	1,512	--	--	7,195	7
McGhee 2006[248]	Hong Kong	1998	Human Capital	USD	160	11	--	--	171	7
Neubauer 2006[249]	Germany	2003	Human Capital	EURO	9,652	3,893	--	--	13,545	7
Parrott 2000[89]	Scotland	1997	Human Capital	GBP	--	40	450	4[2]	494	6
Prenzler 2007[250]	Germany	2005	Human Capital	EURO	7,498	2,138	--	--	9,636	6
Rasmussen 2005[110]	Denmark	1999	Human Capital	DKK	8,347	5,616	--	--	13,963	8
Tsai 2005[251]	Taiwan	2000	Human Capital	USD	--	184	733	34[4]	950	6
Wegner 2004[252]	Germany	1999	Human Capital	EURO	10,284	4,196	--	--	14,480	7
Wegner 2005[253]	Germany	1999	Friction Cost	EURO	533	3,784	--	--	4,317	7
Welte 2000[254]	Germany	1993	Human Capital	DEM*	17,757	6,763	--	--	24,521	8
Yang 2005[255]	Taiwan	2000	Human Capital	USD	1,390	--	--	--	1,390	6

*Currency discontinued and replaced by EURO in 2002
[1]Cost of presenteeism
[2]Cost of fire damage to property
[3]Cost of household production and leisure
[4]Cost of occupational injuries

2.4.2 Human capital versus friction cost

The most common method of quantifying indirect costs of smoking was by the human capital model used in 15 studies[89 110 242-252 254 255]. Grossman's human capital model[200 256] provides a modelling framework for health and education and their relationship to labour supply, earnings and productivity. The theory is based on the notion that an increase in an individual's stock of knowledge and health increases his or her productivity in both market and non-market activities[257]. In health-related studies, the human capital model takes the perspective that an employee's income is related to their general health stock. The human capital accounts for all future income lost from an individual that leaves the workforce as result of death or disability. Therefore, negative behaviours such as smoking will likely have an impact on health and transitively, income and earnings.

Two studies[202 253] were identified which utilised the friction cost method. The friction cost method developed by Koopsmanschap *et al.*[201] is an alternative to the human capital model which takes into account the productivity loss from the employer's perspective. Taking the friction cost perspective, indirect costs estimated using the human capital approach are seen as *potential* lost production (or lost income) as a consequence of disease. *Potential* lost production can be calculated as the total income lost in the case of disability or premature death at a specific age until the potential age of retirement. The friction cost method considers that actual lost production is much smaller because employers will tend to reduce the impact of productivity loss from employee illness. This can be done through temporary or permanent replacement, redistribution of the workload or the ability for employees to make up work once they return. Therefore, the amount of lost production depends on the time-span employers need to restore the initial level of production known as the 'friction period'.[201]

2.4.3 Cost components

Seven cost components were identified in the 17 included studies (**Table 1**): future foregone earnings from productive life lost; foregone wages from absenteeism; reduced output from presenteeism; lost output due to smoking breaks; lost leisure time or household production due to smoking-related illness; damage to property due to smoking-related fires; and occupational injuries related to smoking. Future foregone earnings due to productive life lost was the most common component measured in 14 studies[110 242-250 252-255]. This component was

an estimate of discounted future earnings lost which were attributable to premature mortality. The estimation procedures routinely utilised smoking-attributable risk fractions (derived from the prevalence of smoking in the population and relative risk of mortality) for common disease classifications in combination with life expectancy data to calculate years of productive life lost. Years of productive life lost were translated into monetary amounts by age and sex-dependent wage data. Estimated future forgone earnings as a result of productive life lost from smoking ranged from 12%[253] to 100%[242 243 246 255] of total indirect costs with a median proportion of 78%. This was the single largest component of indirect costs in the majority of studies.

The absenteeism component of indirect costs was reported in 13 studies[89 110 202 244 245 247-254]. Absenteeism was a direct measure of forgone income due to short-term sick leave or temporary disability over the course of the study year. The monetary value of absenteeism was calculated from average hourly earnings and duration of illness absence found in survey data or previous literature. The cost of absenteeism ranged from 6%[248] to 88%[253] of total indirect costs with a median proportion of 22%. This was the second largest component of indirect costs in the majority of studies.

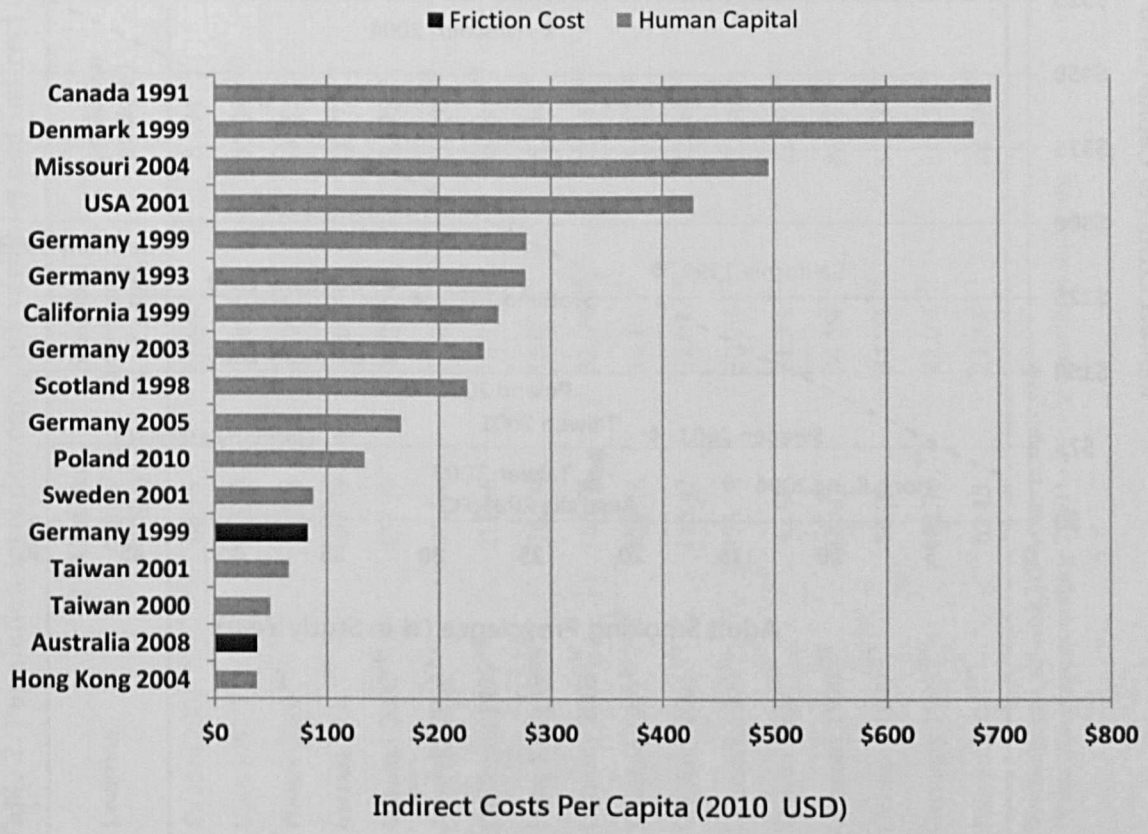
There were only two studies[89 251] that quantified the impact of smoking breaks at work. The method in which the costs of smoking breaks were estimated was similar in both studies. Assumptions were made on the time it took to smoke cigarettes based on previous literature and number of cigarettes smoked on a normal work day. Less commonly measured cost components were presenteeism[244], fire damage[89 245], lost leisure or household production[202] and occupational injuries[251]. Data on presenteeism and lost leisure or household production were quantified using questionnaire instruments. The costs of smoking-related fire damage to property were estimated based on insurance claims data. The cost of occupational injuries was based on relative risk estimates from previous epidemiological literature.

From the summary of the cost components, the two primary components of indirect costs which were estimated were future forgone earnings from productive life lost and foregone wages due to absenteeism (**Table 1**).

2.4.4 Indirect cost per capita due to smoking

For comparison across studies, indirect cost per capita due to smoking was exchange rate adjusted to US dollars and inflated to 2010 levels using a constructed earnings index. **Figure 5** shows in descending order cost per capita according to study location. Canada in 1991[245] had the highest cost per capita due to smoking at $694 USD (£455) while Hong Kong in 1999[248] had the lowest cost per capita at $28 USD (£18). The median cost per capita was $292 USD (£191). The friction cost studies[202 253] provided cost estimates on the lower end of the spectrum. There were two studies[252 253] conducted in Germany in 1999 by the same author. However, the first study[252] computed indirect costs using the human capital method while the latter study[253] used the friction cost method. Using the human capital method, the cost per capita of smoking in Germany in 1999 was $233 USD (£153).[252] Using the friction cost method, the cost per capita of smoking was $66 USD (£43).[253] There was a stark contrast in costs even though the populations were identical; the only difference being an assumption that workers on long-term disability were replaced by new labour in the latter study.

Figure 5. Comparison of indirect costs per capita due to smoking inflated to 2010 US dollars by location



2.4.5 Relationship between indirect cost per capita and smoking prevalence

The ecological relationship between indirect cost per capita and smoking prevalence was examined using a regression model (**Figure 6**). The slope of the regression line was found to be \$8.57 (95% CI -\$6.60 to \$23.59, $p = 0.24$) [£5.62 95% CI -£4.33 to £15.48] for every 1% increase in adult smoking prevalence. The overall R^2 was 0.09 which meant a large variation was unexplained by the linear model. Although there seemed to be an overall positive relationship between adult smoking prevalence and cost per capita, this relationship was not necessarily linear. The non-linear association was explored further in the subsequent section.

Figure 6. Ecological relationship between smoking prevalence and indirect cost per capita for population-level studies

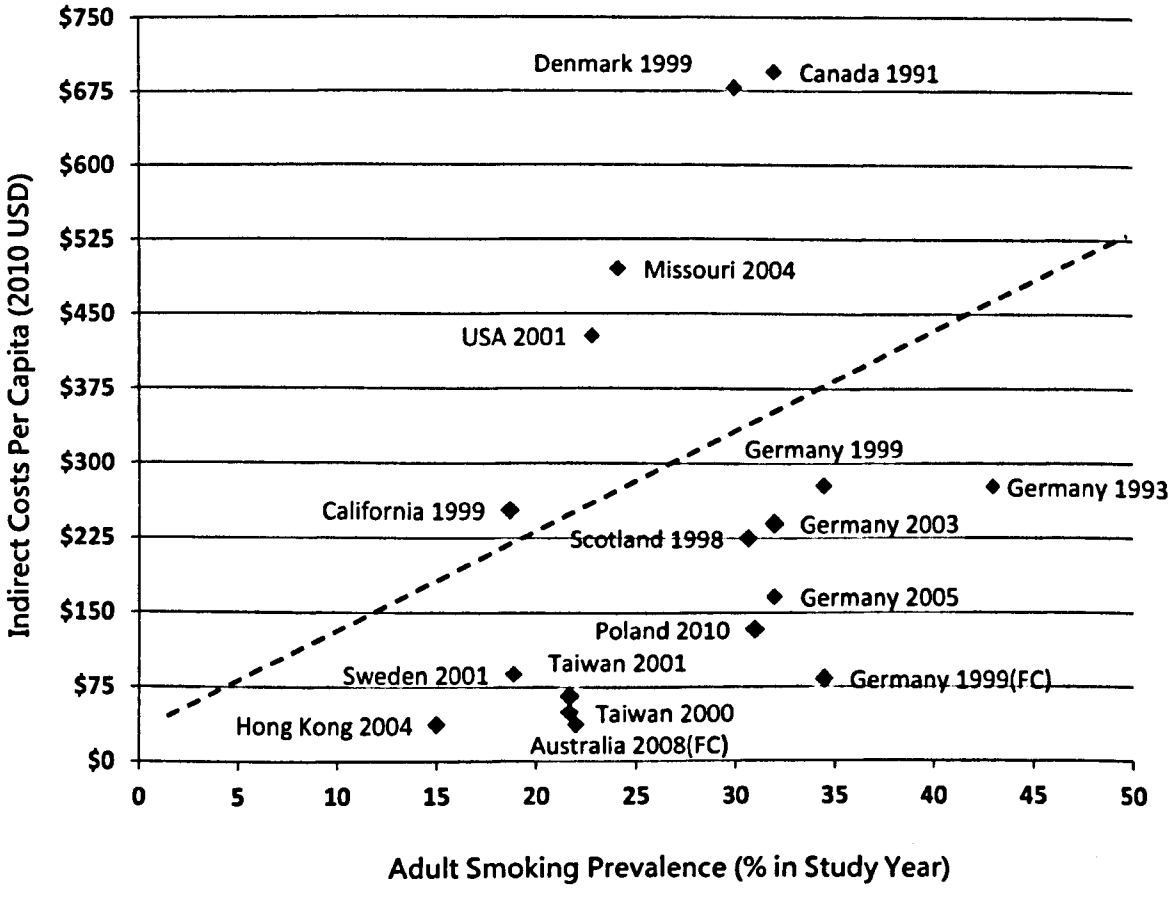


Table 2. Population-level demographic variables and indirect cost per capita due to smoking in the study year

Location	Cost per capita[+] (USD)	Smoking prevalence (% of adults)	Population (millions)	Earnings inflation index*	GDP per capita (USD)	Unemployment rate (% of labour)	Average monthly earnings (USD)	Life expectancy (years)
Sweden 2001[242]	66.56	18.9%[214]	8.894[203]	1.32[208]	25,563[203]	5.6%[203]	2,671[208]	80[203]
USA 1997[243]	324.53	22.8%[217]	285.082[203]	1.27[208]	30,282[203]	4.9%[203]	3,753[208]	76[203]
Poland 2010[244]	169.21	31.0%[216]	38.126[203]	1.06[208]	13,886[203]	7.1%[203]	1,514[208]	76[203]
Canada 1991[245]	393.39	32.0%[219]	28.172[203]	1.76[208]	21,234[203]	10.3%[203]	2,661[208]	78[203]
Missouri 2000[246]	432.39	27.2%[217]	5.595[204]	1.18[208]	32,349[225]	3.5%[224]	2,633[226]	76[228]
Australia 2008[202]	45.68	21.0%[216]	21.499[203]	1.04[208]	48,348[203]	4.2%[203]	3,526[208]	81[203]
California 1999[247]	211.66	18.7%[217]	33.995[204]	1.37[208]	35,599[225]	5.2%[224]	3,144[226]	78[228]
Hong Kong 1998[248]	26.13	15.0%[220]	6.544[203]	1.05[209]	25,507[203]	4.6%[203]	1,250[209]	80[203]
Germany 2003[249]	185.70	32.0%[216]	82.541[203]	1.10[208]	29,365[203]	9.3%[203]	3,184[208]	78[203]
Scotland 1997[89]	159.18	30.7%[221]	5.083[205]	1.60[208]	21,682[231]	5.8%[232]	2,227[230]	76[229]
Germany 2005[250]	145.47	32.0%[216]	82.469[203]	1.07[208]	33,543[203]	11.1%[203]	3,174[208]	79[203]
Denmark 1999[110]	376.38	30.0%[212]	5.319[203]	1.45[208]	32,702[203]	5.1%[203]	3,049[208]	76[203]
Taiwan 2000[251]	42.80	21.7%[222]	22.191[206]	1.06[210]	17,400[227]	3.0%[227]	1,327[210]	76[227]
Germany 1999[252]	188.09	34.5%[213]	82.087[203]	1.19[208]	25,961[203]	8.4%[203]	3,117[208]	78[203]
Germany 1999[253]	56.08	34.5%[213]	82.087[203]	1.19[208]	25,961[203]	8.4%[203]	3,117[208]	78[203]
Germany 1993[254]	182.76	43.0%[223]	81.156[203]	1.34[208]	24,605[203]	7.9%[203]	2,947[208]	76[203]
Taiwan 2001[255]	62.15	21.7%[222]	22.370[206]	1.06[210]	17,200[227]	4.5%[227]	1,331[210]	77[227]

[+]Exchange rate adjusted US dollars in study year
*Ratio of average earnings in 2010 to average earnings in study year

2.4.6 Cost-prevalence elasticity

In **Table 2**, cost per capita (USD) is shown without adjusting for inflation along with additional covariates in the reported study year. The adult smoking prevalence rates ranged from 15%[220] in Hong Kong (1998) to 43%[223] in Germany (1993) with a median of 30%. In **Table 3**, univariate analysis was conducted to test the relationship between indirect cost per capita and covariates. Since the variables appeared to have non-linear associations with cost per capita, logarithmic transformations were applied to all variables except for age of the study where an exponential transformation was used. Logarithmic and exponential transformations are routinely used to smooth continuous or time-element variables.[258] The regression coefficient of smoking prevalence was given as the cost-prevalence elasticity interpreted as a 1% change in smoking prevalence results in a Y% change in indirect cost per capita. In Models 1 and 2 (**Table 3**), indirect cost per capita was found to be significantly associated with smoking prevalence in univariate analysis (Model 1: $\beta = 1.60, p = 0.03$; Model 2: $\beta = 1.76, p = 0.02$). In addition, the covariates of earnings inflation, GDP per capita, average monthly earnings and life expectancy were associated with indirect cost per capita at the 10% level in both models (**Table 3**). Only the covariates of unemployment rate and life expectancy were associated with smoking prevalence at the 10% level in both models (**Table 3**).

Table 3. Regression coefficients from univariate analysis between population-level covariates and indirect cost per capita or smoking prevalence

Variables	Model 1 All Studies Included (N=17)		Model 2 Human Capital Studies Only (N=15)	
	Log(Cost Per Capita)	Log(Smoking Prevalence)	Log(Cost Per Capita)	Log(Smoking Prevalence)
Log(Smoking Prevalence)	1.599*	--	1.762*	--
Log(Population Size)	0.105	0.086	0.146	0.075
Log(Earnings Inflation Index)	3.124*	0.497	2.776*	0.458
Log(GDP Per Capita)	0.382^{+}	-0.123	1.219^{+}	-0.037
Log(Unemployment Rate)	0.660	0.484*	0.695	0.458*
Log(Average Monthly Earnings)	1.209*	0.292	1.657*	0.331
Log(Life Expectancy)	-21.85*	-5.809^{+}	-19.53^{+}	-6.479^{+}
Age of Study	0.059	0.012	0.040	0.006
Age of Study^2	0.003	0.001	0.002	0.001

Reported β Coefficients, $^{*}P < 0.05$, $^{+}P < 0.10$

Following stepwise model fitting (**Table 4**), the final regression model included only one covariate of GDP per capita when all studies were included and found that a 1% increase in smoking prevalence resulted in a 1.7% (95% CI 0.21 to 3.16, $p = 0.028$) increase in cost per capita (Model 1). The final regression model for human capital studies only included both GDP per capita and unemployment rate and found that a 1% increase in smoking prevalence resulted in a 2.1% (95% CI 0.46 to 3.81, $p = 0.017$) increase in cost per capita (Model 2). Model 2 which included only human capital studies had better fit ($R^2 = 0.540$) than Model 1 which included all studies ($R^2 = 0.313$). In monetary terms (back-transforming), the results show that on average a 1% increase in smoking prevalence results in a $5.42 USD (£3.55) increase in cost per capita across all population level studies and an $8.17 USD (£5.36) increase in cost per capita across human capital model studies only.

Table 4. Stepwise regression analysis for the relationship between the log of the indirect cost per capita and adult smoking prevalence with the addition of covariates

Step	Covariates	Beta Coefficient	95% Confidence Interval	*P-Value*
Model 1 – All Studies (N=17)				
1	GDP Per Capita, Inflation, Unemployment, Monthly Earnings, Life Expectancy	-0.91	-3.21, 1.38	0.396
2	GDP Per Capita, Unemployment, Monthly Earnings, Life Expectancy	-1.22	-3.47, 1.03	0.257
3	GDP Per Capita, Unemployment, Life Expectancy	-1.08	-3.29, 1.12	0.306
4	GDP Per Capita, Unemployment	1.91	-0.14, 3.96	0.065
5 (Final)	GDP Per Capita	1.69	0.21, 3.16	0.028
Model 2 – Human Capital Studies Only (N=15)				
1	GDP Per Capita, Inflation, Unemployment, Monthly Earnings, Life Expectancy	-0.36	-3.07, 2.35	0.766
2	GDP Per Capita, Unemployment, Monthly Earnings, Life Expectancy	-0.47	-3.13, 2.18	0.696
3	GDP Per Capita, Unemployment, Life Expectancy	-0.55	-3.32, 2.22	0.666
4 (Final)	GDP Per Capita, Unemployment	2.13	0.46, 3.81	0.017

2.5 Discussion

2.5.1 Summary of findings

In this literature review of health economic studies, 17 studies[89 110 202 242-255] on the indirect costs of smoking were identified from a comprehensive database search. The most common method of estimating indirect costs of smoking was by the human capital model. There were two studies[202 253] which used the friction cost method. There were a total of seven cost components identified: productive life lost, absenteeism, smoking breaks, presenteeism, lost leisure or household production, fire damage and occupational injuries. The most common component measured was foregone earnings due to productive life lost.

There was a positive and significant correlation between cost per capita and smoking prevalence after adjusting covariates. On average, a 1% increase in smoking prevalence resulted in a 1.7% increase in cost per capita across all population-level studies and a 2.1% increase in cost per capita across human capital studies only; with the latter model showing a better fit because the included studies used more similar study designs and methodology. Friction cost studies tended give more conservative cost estimates of smoking due to the model allowing for the firm's ability to find replacement work; thus foregone earnings due to productive life lost are minimised or negated altogether. In monetary terms (back-transforming), the results show that on average a 1% increase in smoking prevalence results in a $5.42 USD (£3.55) increase in cost per capita across all population level studies and an $8.17 USD (£5.36) increase in cost per capita across human capital model studies only.

2.5.2 Methodological implications

Although there were methodological differences in the estimation of cost components among studies, the transformed association between cost per capita and smoking prevalence was statistically significant. This suggests that there is a degree of consistency across population-level studies. As a result, the association between smoking prevalence and cost per capita could be utilised to validate future indirect cost-of-smoking studies at the population-level. This validation approach was taken in **Chapter 5** using UK indirect cost estimates derived from this thesis. In terms of comparability of other smoking-related studies, the human capital model offers the most comparable method of smoking-related costs and is relatively straightforward to conduct. The human capital approach was the approach used for UK

indirect costs estimates in **Chapter 3** due to having more comparability to existing studies and providing a theoretical basis consistent to neoclassical economic theory. The theoretical basis for the model lies in the concept of health capital, where an employee's stock of health determines the total amount of time he or she can spend producing money, earnings and commodities.[256] Broadly speaking, health defined by longevity and illness-free days in a given year is both produced and demanded by individuals. Therefore, behaviours such as smoking that have an impact on health will decrease health capital accumulation which will in turn affect an individual's ability to produce money, earnings and commodities. Most cost studies on smoking based on human capital theory capture productivity loss in terms of foregone earnings from the individual's perspective. The sum of all the individuals within a population or sample equals the total productivity loss due to smoking. There are criticisms of the human capital model and its ability to provide accurate estimates for the consequence of disease. When an employee becomes ill, several scenarios can potentially occur:[201]

I. The level and costs of production are unaffected due to the firm's ability to make up unperformed work when the employee returns or if the firm has internal labour reserves to make up for the loss.
II. The level of production remain unchanged but at higher costs due to colleagues working overtime or the firm hiring temporary workers.
III. The level of production falls while costs remain unchanged due to the firm not attempting to make up for the lost production.
IV. The level of production falls despite higher costs due to the firm attempting to make up for lost production but not able to achieve the levels of the ill employee.

Scenario III is representative of the human capital model where production is permanent wealth lost while scenarios I, II, IV are representative of the firm's ability to adjust production levels via the labour market. By valuing lost production as wealth lost to society, the human capital model overestimates the burden of disease in society as the method measures *potential* lost production and not *actual* lost production. This certainly has been suggested by several authors[259-261] that real production losses may in fact be much smaller.

Alternatively, the friction cost method[201] takes into account the short-term and medium-term effects of illness by the firm's ability to make up or draw on internal labour resources to

make up the level of production. Long-term costs are minimised by an employer's ability to replace ill employees. Koopmanschap *et al.*[201] suggests that the friction cost method better reflects the economic impact of the disease from the employer's perspective as firms will drive to maximize profits by reducing costs through worker replacement.[201] Empirically, friction cost studies utilise a variable of friction period (average time a firm takes to replace long-term vacancy due to illness). In addition, the friction cost approach takes into account macro-economic labour market conditions. If unemployment is low, then the friction period is longer than when unemployment is high. The friction cost method is relatively new (1995) compared to human capital model (1972) and there is substantial difficulty in obtaining valid data on both the frequency and length of friction periods. The friction cost model authors have themselves suggested that necessary labour parameters for the model are extremely scarce and a combination of data from time-surveys and patient questionnaires are needed to provide reliable estimation parameters. The main criticism of the friction cost model[262 263] is that there are assumptions which contradict neoclassical economic theory. According to the friction cost model, short-term and medium-term productivity losses are lower than the estimates provided by the human capital model due to diminishing returns to labour, internal labour reserves and sick employees restoring the level of work when they return from a period of absence. Consequently, to estimate productivity loss this way assumes that the price of labour (i.e. the opportunity cost of labour) is set close to zero after the friction period and is reduced during the friction period which is an implausible assumption.[263] If the same assumptions of the price of labour being set close to zero were consistently applied to direct healthcare cost estimation, then the costs of healthcare programmes would be drastically reduced. The friction cost method also takes into account diminishing returns to labour in the estimation procedure. However, this may actually be unnecessary as the human capital approach expects that a firm will hire labour until the marginal cost of labour equals the marginal value of the products produced by the worker. When the worker is absent, this represents a marginal loss of labour whose value of the firms equals the gross income of the worker. Therefore, the human capital model would correctly estimate the productivity loss according to neoclassical economic theory.

The friction cost model may also overestimate the ability of firms to draw upon internal labour reserves to restore production. According neoclassical theory, a firm would not hire additional workers unless the value of their production would exceed or be equal to the gross income of the workers.[263] If a firm has a labour surplus, then the firm is not maximising

profits because the same level of production could be achieved with fewer workers.[264] It is more likely that an increase in short-term absence would mean that the firm either loses production during absence or hires additional workers from the labour market where the price of labour should not be assumed to be close to zero. Finally, the friction cost model does provide the valid assumption that the sick worker may restore production levels after they return or other workers may make up this work through increasing working time or capacity. The model does not, however, take into account the opportunity cost of increasing working time or capacity such as lost leisure time and ill-health effects due to increased stress levels.[262]

This discussion of the human capital model and the friction cost model shows that there are clear limitations of both estimation procedures. Whilst the human capital model overestimates true lost production due to assumptions of achieving labour market equilibrium, the theoretical basis for the estimation procedure is consistent with neoclassical economic theory. Although, the friction cost approach attempts to address the reality of the labour market, the issue of zero cost replacement of labour may not only result in the underestimation of costs but is also based on an implausible assumption. As a result, this thesis did not address a friction cost approach. In addition, there was less comparability to existing studies and extremely limited data in the UK on friction periods at the employer-level. The two friction cost studies found in this chapter's review used national-level data in conjunction with assumptions on friction periods to estimate these costs as detailed data at the employer-level is difficult to obtain. The limitations of the friction cost method does not suggest this approach should not be utilised but rather it could be seen as an alternate costing approach in perhaps a sensitivity analysis given data availability. Given available data, the friction cost method can be used as a viable complement to the human capital model. This method can be seen as an alternative approach to the human capital model providing an additional perspective for cost-of-smoking studies.

2.5.3 Limitations

There were some limitations of the review. There are no published criteria for quality assessment of population-level cost studies. Thus, an 8-point scale was created to assess the methodological quality of population-level cost studies adapted from elements of the Consensus on Health Economic Criteria (CHEC)[211] checklist. However, the developed scale

has neither been validated nor used before. Additionally, the methods of searching, screening, quality assessment and data extraction of literature were conducted by only one reviewer (SFW). Another limitation was the regression models involving indirect cost per capita and smoking prevalence may have been underpowered to be able to detect a statistically significant relationship. The regression analysis took into account a maximum of 17 studies. Some of the multivariable models in the stepwise analysis showed a high level of predictability but the association between smoking prevalence and cost per capita was not significant at the 5% level most likely due to a lack of power. Also, the interpretation of the regression results should not be utilised to describe causal relationships between smoking prevalence and indirect costs per capita as the relationship is ecological and it is likely there are other confounding factors that influence the relationship. Finally, it is known that there are other potential indirect costs of smoking that have yet to be quantified or reported in published literature. These costs include the loss of vacation time, effect on family and friends, impact on motivation or teamwork and effects on co-workers.[199] However, these components are likely to have smaller impacts than the costs included in our models, therefore their effects on the findings are likely to be marginal.

2.6 Conclusion

In this chapter, the relationship between smoking prevalence and indirect cost per capita was found to be significant across 17 population-level cost-of-smoking studies. The findings suggests that a 1% increase in smoking prevalence results in a 1.7% increase in cost per capita across all population-level studies and a 2.1% increase in cost per capita across human capital model studies only. In monetary terms (back-transforming), the results show that on average a 1% increase in smoking prevalence results in a $5.42 USD (£3.55) increase in cost per capita across all population level studies and an $8.17 USD (£5.36) increase in cost per capita across human capital model studies only. The human capital model was the most commonly used method of quantifying costs while less commonly utilised was the friction cost method. While there are limitations of both methods, the human capital model provides a framework for estimating costs consistent with neoclassical economic theory. However, future research may involve the combination of both models but more empirical evidence is needed to validate the precision of the cost estimates.

Chapter 3

Productivity loss from foregone earnings due to smoking-attributable premature mortality in the UK

3.1 Introduction

In **Chapter 2**, the human capital model had been established as the primary methodology for conducting an indirect cost-of-smoking study in the United Kingdom due to its comparability with other indirect cost-of-smoking studies and strong theoretical underpinnings. This chapter describes the model methodology, results and potential limitations of such a model in the UK. There is a direct causal association between smoking and premature mortality.[8 9 265] A 50-year follow-up study of 34,439 male British doctors found that men who continued smoking died on average 10 years younger than lifelong non-smokers.[8] As many of these deaths come prematurely during working years, this creates a large economic burden for countries in terms of loss of productive life years.

To date, most economic studies evaluating the cost of smoking have focused only on healthcare costs. While many of these studies[81-83] have found that the lifetime healthcare costs of smokers (taking account of shorter life expectancy in smokers) are higher than those of non-smokers, other studies[84-86] have found the opposite. In the case of the UK, there have been three previous studies[87 266 267] which have estimated direct health care costs due to smoking. A recent study found that, despite a decline in adult smoking prevalence from 39% in 1980 to 21% in 2009[268], the direct healthcare costs to the UK NHS remained high at £5.2 billion.[87] This could be due a combination of factors such as healthcare cost inflation and improvement of treatments of complex cases. While studies in the US [240 241 247 269] and EU [242 244 250 270] have quantified productivity loss due to smoking, there are currently no studies in the UK that have taken this approach. Without accounting for lost productivity, the overall burden of smoking to society is likely to be underestimated.

3.2 Aims and Objectives

As there is a direct association between smoking and premature mortality, the aim of this chapter was to estimate the lost productivity cost of smoking in the UK due to premature mortality. This is the first study that has quantified the economic cost of lost productive life years associated with smoking in the UK. This study attempts to complement existing direct cost-of-smoking studies. These aims were achieved by completing the following objectives:

- Develop an economic model for productivity loss for the UK based on human capital theory

- Identify and obtain relevant parameters needed to populate the economic model from multiple UK data sources
- Quantify the productivity loss by implementing the developed model for the UK
- Conduct sensitivity analyses on the cost estimates obtained from the model

3.3 Methods

An economic model was developed based on Smoking-Attributable Mortality, Morbidity and Economic Costs (SAMMEC) methodology[271]. SAMMEC was developed by the CDC to permit the rapid calculation of deaths, years of potential life lost, direct health-care costs, indirect mortality costs and disability costs associated with cigarette smoking. For the mortality-related measures, age-specific and age-adjusted rates are also calculated. The pivotal epidemiologic measure in these calculations is the smoking-attributable fraction to calculate smoking-attributable mortality, years of potential life lost and smoking-attributable productivity costs. Unfortunately, SAMMEC does not take into consideration important labour market effects of unemployment and the full-time to part-time employment ratios in the calculation of economic costs. The economic model developed in this chapter uses SAMMEC equations to calculate smoking-attributable fractions (**Section 3.3.1**), smoking-attributable mortality (**Section 3.3.1**) and years of potential life lost (**Section 3.3.2**). SAMMEC equations were then modified to take into account age-adjusted employment rates when calculating years of productive life lost (**Section 3.3.2**) and income was adjusted by the full-time to part-time work ratios in the population (**Section 3.3.3**). The knock-on effect of this modification was that the model reflected labour market characteristics in calculating productivity loss which the original SAMMEC equations did not take into account.

This underlying approach is based on human capital theory[256] which views health as a durable capital stock that yields healthy life years, and therefore loss of life years results in lost production. The human capital model takes the perspective that income is related to the individual's general health stock. This accounts for all future income lost from an individual that leaves the workforce as result of death or disability. Therefore, negative behaviours such as smoking will likely have an impact on health and transitively, income and earnings. The cost of lost productivity due to premature mortality can be estimated by applying average wage rates to lost years during productive life. This approach was taken because of the comparability with previous cost-of-smoking studies[240-242 244 247 250 269 270] which had used

similar approaches in other countries and the availability of accurate population-level data to facilitate this estimation in the UK.

To implement the model, age and gender-specific UK life tables for disease-specific mortality[272-274] were used to calculate the total number of premature deaths (i.e. deaths that occurred before the average life expectancy) in the general population (irrespective of smoking status). For each premature death, the total number of productive life years lost was calculated as the difference between the age of death and the life expectancy in the general population adjusted by the employment rate. To calculate smoking-attributable loss of productive life years for each disease condition, epidemiological evidence on relative mortality risk for smoking-related diseases and smoking prevalence in the UK were used to generate mortality risk fractions. Following this, age and sex-specific gross earnings for men and women were applied to each person-year of premature death. The costs across all disease conditions were summed to estimate the total smoking-attributable loss of earnings due to premature mortality.

The year 2010 was set as the base year and the most recent data on disease-specific mortality, smoking prevalence, employment rate and annual income were used to populate the model. The study population included adults aged 35 years and older as most deaths due to smoking occur later in life and the risk of smoking attributable mortality is low in people under 35 years of age.[14] Further details on all aspects of the methodology and data sources are presented below.

3.3.1 Smoking-attributable mortality

The epidemiological approach to the economic model employs the use of smoking-attributable risk fractions (SAFs). In order to quantify smoking-attributable mortality, SAFs for both current and ex-smokers were calculated using a standard formula[275] based on smoking prevalence (p) and relative mortality risks (RR) for current, ex and never smokers:

$$SAF = \frac{[p_{ns} + p_{ex}(RR_{ex}) + p_{cs}(RR_{cs})] - 1}{p_{ns} + p_{ex}(RR_{ex}) + p_{cs}(RR_{cs})}$$

SAFs were calculated for sex-specific age-bands from 35 to 100 years. This process was repeated for 20 common smoking-related disease categories.[14] These disease categories were based on the International Classification of Diseases[276] (ICD-10). Smoking prevalence data for adults aged 35 years or over in England and Wales were extracted from the 2010 Health Survey for England.[277] [278] Smoking prevalence data for adults in Scotland and Northern Ireland were extracted using the 2010 Scottish Health Survey[279] (SHS) and the 2010 Northern Ireland Continuous Household Survey[280] (CHS). The percentage of adult current, ex and never smokers were stratified using the same age-bands and sex as used for SAF estimation. The length of each age-band was governed by the data available in each survey. The relative mortality risk parameters were used from the Cancer Prevention Study II[14] (CPS-II), a US prospective mortality study of over a million men and women enrolled in 1982. Data from the CPS-II were used because it was the largest prospective cohort study in which mortality risks from smoking was assessed in age, gender and ICD-10 strata. In addition, relative risk estimates from the CPS-II have been used extensively to estimate smoking-attributable mortality in nearly 50 countries.[265] [281] [282] The CPS-II provided relative mortality risk estimates for 19 common smoking-related diseases (**Table 5**). The relative risk of mortality for the 20th disease classification of "all other diseases" was based on Jha *et al.*[283] for current smokers and Jacobs *et al.*[284] for ex-smokers. Subsequently, smoking-attributable mortality [285] was calculated by multiplying age- and sex-specific SAFs by the number of deaths for each smoking-related disease:

$$SAM = Number\ of\ deaths\ x\ SAF$$

The annual number of deaths by sex and age was obtained from the 2010 national death registers[286-288] of England and Wales, Scotland, and Northern Ireland. The coding for underlying cause of death in the registers were based on ICD-10 and given in sex and age-specific categories.

3.3.2 Years of potential life lost

The SAM (discussed above) calculated the number of smoking-attributable deaths in each age category, stratified by sex and grouped by underlying cause of death. To calculate years of life lost (YLL), SAM was multiplied by the remaining life expectancy (RLE) at the age of

death. RLE was calculated as the difference between life expectancy and the midpoint of each 5 year age-band for both men and women:

$$Years\ of\ Life\ Lost\ (YLL) = SAM\ x\ RLE$$

Data for RLE was obtained from the most recent Office for National Statistics (ONS) life tables.[272-274] The YLL values were calculated irrespective of employment status. To adjust for the proportion of smokers in employment, YLL was multiplied by the age and sex-specific smoking-employment rate extracted from population health surveys[277 279 280] to obtain the years of productive life lost (YPLL):

$$Years\ of\ Productive\ Life\ Lost\ (YPLL) = YLL\ x\ Employment\ Rate$$

3.3.3 Cost of smoking-attributable productivity loss due to premature mortality

Smoking-attributable productivity loss was defined as the present value of future earnings (PVFE) from paid labour. In order to quantify smoking-attributable productivity loss, 2010 gross annual income data were used for both full-time (FT) and part-time (PT) work from the ONS Annual Survey of Hours and Earnings.[289-291] Earnings data from England and Wales were provided in 5-year age-bands while data for Scotland and Northern Ireland were given only as median income across all age-bands. The median income was used instead of the mean income to take into account the positively skewed distribution (that is, a long thin tail for those with high incomes). Therefore, the median income is necessarily correlated with income inequality and in fact is a better representation of 'average' income.[292] If median income inequality increases, then median income would decrease while the mean income would remain the same. Thus, the median income reflects both total income and income distribution whereas mean income only represents total income.

The median annual income was adjusted by the percentage of full-time and part-time (**Table 6, Table 7, Table 8**) workers for each sex, age-band and UK country using data from the 2010 UK Labour Force Survey[293]:

$$Adjusted\ Median\ Income = Median\ FT\ Income\ x\ \%\ FT + Median\ PT\ Income\ x\ \%\ PT$$

The PVFE for each age-band (b) was calculated by summing the adjusted annual median gross income (discounted) from the midpoint of each age-band to life expectancy from the midpoint of each age-band:

$$PVFE_b = \sum (Adjusted\ median\ income)_d$$

From t = (Midpoint of age-band) to (Life expectancy from mid-point)

The subscript d under adjusted median annual income represents the discounted PVFE. Discounting was based on the HM Treasury[294] recommended discount rate of 3.5% as the base-case scenario. The PVFE was then adjusted by the sex and age-specific employment rate for smokers in each age-band obtained from population health surveys[277 279 280] corresponding to each UK country:

$$Adjusted\ PVFE_b = PVFE_b x\ Employment\ Rate_b$$

Subsequently, $PVFE_b$ was then multiplied by age and gender-specific smoking-attributable mortality[271] to obtain smoking-attributable productivity loss for each age-band:

$$(Smoking\ attributable\ productivity\ loss)_b = SAM_b\ x\ Adjusted\ PVFE_b$$

The above calculation was repeated for each gender and age-group and each smoking-related disease category. This adjustment by the employment rates in smokers allowed for the estimation of earnings beyond the average age of retirement. The total smoking-attributable productivity loss was then summed for each smoking-related disease category by male and female strata. These costs were calculated for England and Wales, Scotland, and Northern Ireland separately and then combined for the UK estimate.

3.3.4 Sensitivity analysis

One-way sensitivity analysis was conducted to test the robustness of the results. Earnings loss was quantified by varying the underlying assumptions: (i) undiscounted future earnings [182] using the previous HM Treasury recommended 6% discount rate (iii) 25th percentile of annual income for low socio-economic status (iv) 75th percentile of annual income for high socio-economic status (v) assuming low production (100% part-time work) (vi) assuming high production (100% full-time work).

3.4 Results

3.4.1 Relative mortality risk parameters

The human capital model requires both epidemiological and economic components to quantify productivity loss due to smoking. Relative mortality risks provided by the CPS-II[14], Jha *et al.*[283] and Jacobs *et al.*[284] for 20 ICD-10 categories are shown in **Table 5**. Gender-specific mortality risks were extracted for both current and ex-smokers compared to the reference category of never smokers.

In males, the greatest mortality risk for smoking was due to cancer of the trachea, lung and bronchus (*RR* = 23.26 for current smokers, *RR* = 8.70 for ex-smokers, **Table 5**). In females, the greatest mortality risk from smoking was due to chronic obstructive pulmonary disease (*RR* = 13.08 for current smokers, *RR* = 6.78 for ex-smokers, **Table 5**). For ischemic heart disease and cerebrovascular disease, two separate relative risks were provided in individuals aged from 35-65 and individuals aged 65 or over due to significant differences in mortality risks between these age-groups. Ex-smokers generally had a reduction in relative risk of mortality compared to current smokers for most disease categories; however, the risks were almost always higher than that of never smokers.

Table 5. Relative mortality risks for 20 disease categories for current and ex-smokers compared to never smokers

Disease Category	ICD-10 Code	Male		Female	
		Current Smoker	*Ex Smoker*	*Current Smoker*	*Ex Smoker*
Malignant Neoplasm[1]					
Lip, Oral Cavity, Pharynx	C00-C14	10.89	3.40	5.08	2.29
Oesophagus	C15	6.76	4.46	7.75	2.79
Stomach	C16	1.96	1.47	1.36	1.32
Pancreas	C25	2.31	1.15	2.25	1.55
Larynx	C32	14.60	6.34	13.02	5.16
Trachea, Lung, Bronchus	C33, C34	23.26	8.70	12.69	4.53
Cervix Uteri	C53	--	--	1.59	1.14
Kidney and Renal Pelvis	C64, C65	2.72	1.73	1.29	1.05
Urinary Bladder	C67	3.27	2.09	2.22	1.89
Acute Myeloid Leukaemia	C92.0	1.86	1.33	1.13	1.38
Cardiovascular Disease[1]					
Ischemic Heart Disease					
Aged 35-64	I20-I25	2.80	1.64	3.08	1.32
Aged 65+		1.51	1.21	1.60	1.20
Other Heart Disease	I26-I52	1.78	1.22	1.49	1.14
Cerebrovascular Disease					
Aged 35-64	I60-I69	3.27	1.04	4.00	1.30
Aged 65+		1.63	1.04	1.49	1.03
Atherosclerosis	I70	2.44	1.33	1.83	1.00
Aortic Aneursym	I71	6.21	3.07	7.07	2.07
Other Arterial Disease	I77	2.07	1.01	2.17	1.12
Respiratory Disease[1]					
Pneumonia, Influenza	J09-J18	1.75	1.36	2.17	1.10
Bronchitis, Emphysema	J40, J43	17.10	15.64	12.04	11.77
Chronic Obstructive Pulmonary Disease	J44	10.58	6.80	13.08	6.78
All Other Disease (infection, endocrine, blood, nervous, digestive, musculoskeletal, skin, genitourinary)	A00-B99, D50-D89, E00-E90, G00-G99, K00-K93, L00-L99, M00-M99, N00-N99	1.30[2]	1.00[3]	1.70[2]	1.00[3]

[1]Relative mortality risks from CPS-II[14]
[2]Relative mortality risks from Jha *et al.*[283]
[3]Relative mortality risks from Jacobs *et al.*[284]

3.4.2 Demographic parameters

3.4.2.1 England and Wales

In **Table 6**, population-level demographic variables were provided for England and Wales from multiple data sources. Smoking-prevalence rates, annual gross earnings, remaining life years (life expectancy at midpoint of age-band), full-time/part-time work rates and employment rates in smokers were stratified by gender-specific age-groups. Men between the ages of 35-39 had the highest proportion of current smokers (27%) and lowest proportion of ex-smokers (21%). There was a sharp decrease in proportion of current smokers and a sharp increase in proportion of ex-smokers in men 60 years or over. In men aged 80 or over, only 3% were current smokers while 58% were ex-smokers. In women, current smoking prevalence was highest between the ages of 40-44 (21%) and then gradually declined thereafter. There were fewer ex-smokers in middle-aged females between 45-54 years. In terms of the economic component of human capital, annual gross earnings showed clear discrepancies in income levels between males and females across age-groups. For full-time work, the median income was highest in women between 35-59 years (£25,925 per annum) while the highest median income in men occurred between 40-49 years (£31,778 per annum). For part-time work, the median income was highest in women and men between 35-39 years (women: £9,776 per annum; men: £10,825 per annum). In men, the employment rate in smokers was highest between 35-39 years at 83.7% and dropped sharply after 65 years to 17.8%. In women, employment rates in smokers were lower than the employment rates in men across all age-groups peaking at 73.7% between 50-54 years. There were also gender discrepancies between the ratios of full-time to part-time workers. In men, the proportion of full-time workers was much higher than the proportion of part-time workers until 65 years. In women, the proportion of full-time workers was more similar to the proportion of part-time workers until 65 years.

Table 6. Population-level human capital model demographic variables for England and Wales in 2010

Sex	Age	Smoking Prevalence[1]			£ Medium Annual Gross Earnings[2] (InterQuartile Range)		Life Years Remaining[3]	FT/PT Work Rates[4]	Employment Rate in Smokers[1]
		Current	*Ex*	*Never*	*Full Time*	*Part Time*			
Male	35-39	0.27	0.21	0.52	29,698 (21,385 – 40,300)	10,825 (6,000 – 18,992)	43	0.94/0.06	0.837
	40-44	0.23	0.25	0.52	31,778 (22,893 – 44,998)	10,000 (5,838 – 18,409)	38	0.94/0.06	0.742
	45-49	0.19	0.26	0.55	31,778 (22,893 – 44,998)	10,000 (5,838 – 18,409)	33	0.94/0.06	0.839
	50-54	0.25	0.29	0.45	30,241 (21,849 – 42,763)	10,648 (6,165 – 19,096)	29	0.93/0.07	0.761
	55-59	0.25	0.32	0.43	30,241 (21,849 – 42,763)	10,648 (6,165 – 19,096)	24	0.87/0.13	0.678
	60-64	0.13	0.51	0.36	24,876 (18,502 – 34,903)	8,457 (4,862 – 14,227)	20	0.77/0.23	0.482
	65-69	0.16	0.55	0.29	24,876 (18,502 – 34,903)	8,457 (4,862 – 14,227)	16	0.46/0.54	0.178
	70-74	0.11	0.48	0.41	24,876 (18,502 – 34,903)	8,457 (4,862 – 14,227)	13	0.27/0.73	0.045
	75-79	0.06	0.51	0.42	24,876 (18,502 – 34,903)	8,457 (4,862 – 14,227)	10	0.32/0.68	0.037
	80-100	0.03	0.58	0.39	24,876 (18,502 – 34,903)	8,457 (4,862 – 14,227)	4	0.16/0.84	0.008
Female	35-39	0.17	0.24	0.59	25,925 (18,474 – 34,784)	9,776 (6,236 – 15,454)	46	0.55/0.45	0.614
	40-44	0.21	0.24	0.55	23,979 (17,003 – 34,837)	9,357 (6,000 – 14,201)	41	0.53/0.47	0.726
	45-49	0.20	0.19	0.61	23,979 (17,003 – 34,837)	9,357 (6,000 – 14,201)	37	0.58/0.42	0.714
	50-54	0.19	0.23	0.58	22,546 (16,686 – 33,597)	9,132 (5,893 – 13,476)	32	0.58/0.42	0.737
	55-59	0.19	0.27	0.55	22,546 (16,686 – 33,597)	9,132 (5,893 – 13,476)	28	0.54/0.46	0.601
	60-64	0.14	0.31	0.56	20,033 (15,504 – 29,329)	7,328 (4,414 – 11,479)	23	0.37/0.63	0.263
	65-69	0.16	0.37	0.47	20,033 (15,504 – 29,329)	7,328 (4,414 – 11,479)	19	0.23/0.77	0.190
	70-74	0.09	0.33	0.58	20,033 (15,504 – 29,329)	7,328 (4,414 – 11,479)	15	0.15/0.85	0.027
	75-79	0.07	0.28	0.65	20,033 (15,504 – 29,329)	7,328 (4,414 – 11,479)	11	0.06/0.94	0.001
	80-100	0.07	0.33	0.60	20,033 (15,504 – 29,329)	7,328 (4,414 – 11,479)	5	0.00/1.00	0.001

[1]Health Survey for England 2010
[2]Annual Survey of Hours and Earnings 2010
[3]ONS life tables 2008-2010. Life expectancy from the midpoint of each band
[4]ONS Labour Force Survey 2010. Proportion in full-time/part-time employment for England and Wales

3.4.2.2 Scotland

In **Table 7**, population-level demographic variables were provided for Scotland from multiple data sources. Smoking-prevalence rates, annual gross earnings, remaining life years (life expectancy at midpoint of age-band), full-time/part-time work rates and employment rates in smokers were stratified by gender-specific age-groups. Men between the ages of 35-44 had the highest proportion of current smokers (32%) and lowest proportion of ex-smokers (17%). As age-bands increased, there was a steady decline in the proportion of current smokers and increase in the proportion of ex-smokers in men. In women, current smoking prevalence was highest between the ages of 45-54 (28%) and then gradually declined thereafter. In terms of the economic component of human capital, annual gross earnings showed clear discrepancies in income levels between males and females. For full-time work, the median income in men was £27,331 per annum while the median income in women was £21,879 per annum. For part-time work, the median income in men was £7,976 per annum while the median income in women was £9,076 per annum. The employment rate in smokers was highest in men aged 45-54 years at 75.3% and dropped sharply after 65 years to 11.2%. In women, the employment rate in smokers was highest between 34-44 years at 69.9% and dropped sharply after 65 years to 5.4%. There were also gender discrepancies between the ratios of full-time to part-time workers. In men, the proportion of full-time workers was much higher than the proportion of part-time workers until 65 years. In women, the proportion of full-time workers was more similar to the proportion of part-time workers until 65 years.

Table 7. Population-level human capital model demographic variables for Scotland in 2010

Sex	Age	Smoking Prevalence[1]			£ Medium Annual Gross Earnings[2] (InterQuartile Range)		Life Years Remaining[3]	FT/PT Work Rates[4]	Employment Rate in Smokers[1]
		Current	*Ex*	*Never*	*Full Time*	*Part Time*			
Male	35-44	0.32	0.17	0.51	27,331 (20,048 – 37,506)	7,976 (4,996 – 12,942)	38	0.95/0.05	0.707
	45-54	0.30	0.19	0.51	27,331 (20,048 – 37,506)	7,976 (4,996 – 12,942)	29	0.96/0.04	0.753
	55-64	0.23	0.33	0.44	27,331 (20,048 – 37,506)	7,976 (4,996 – 12,942)	20	0.88/0.12	0.513
	65-74	0.15	0.50	0.35	27,331 (20,048 – 37,506)	7,976 (4,996 – 12,942)	13	0.39/0.61	0.112
	75-99	0.12	0.54	0.33	27,331 (20,048 – 37,506)	7,976 (4,996 – 12,942)	5	0.67/0.33	0.004
Female	35-44	0.27	0.20	0.53	21,879 (16,327 – 32,026)	9,076 (5,829 – 13,153)	41	0.55/0.45	0.699
	45-54	0.28	0.21	0.51	21,879 (16,327 – 32,026)	9,076 (5,829 – 13,153)	32	0.58/0.42	0.695
	55-64	0.26	0.27	0.48	21,879 (16,327 – 32,026)	9,076 (5,829 – 13,153)	23	0.57/0.43	0.391
	65-74	0.18	0.29	0.53	21,879 (16,327 – 32,026)	9,076 (5,829 – 13,153)	15	0.19/0.81	0.054
	75-99	0.10	0.34	0.56	21,879 (16,327 – 32,026)	9,076 (5,829 – 13,153)	6	0.00/1.00	0.004

[1]Scottish Health Survey 2010
[2]Annual Survey of Hours and Earnings (Scotland) 2010
[3]ONS life tables 2008-2010. Life expectancy from the midpoint of each band
[4]ONS Labour Force Survey 2010. Proportion in full-time/part-time employment for Scotland

3.4.2.3 Northern Ireland

In **Table 8**, population-level demographic variables were provided for Northern Ireland from multiple data sources. Smoking-prevalence rates, annual gross earnings, remaining life-years (life expectancy at midpoint of age-band and productive life years remaining (midpoint of age-band to retirement age) were stratified by age-groups and sex. Smoking prevalence figures were only able to be obtained for three age-bands of 35-49, 50-59 and 60-95 due to the coding structure of the Continuous Household Survey[295]. The overall smoking prevalence in Northern Ireland was 24% for men and 23% for women.[295] In terms of the economic component of human capital, annual gross earnings showed clear discrepancies in income levels between males and females. For full-time work, the median income in men was £23,364 per annum while the median income in women was £20,710 per annum. For part-time work, the median income in men was £7,361 per annum while the median income in women was £7,905 per annum. The employment rate in smokers was highest in men aged 35-49 years at 74.9% and dropped sharply after 60 years to 15.3%. In women, the employment rate in smokers was highest between 35-49 years at 68.6% and dropped sharply after 60 years to 11.3%. There were also gender discrepancies between the ratios of full-time to part-time workers. In men, the proportion of full-time workers was much higher than the proportion of part-time workers until 60 years. In women, the proportion of full-time workers was more similar to the proportion of part-time workers until 60 years.

Table 8. Population-level human capital model demographic variables for Northern Ireland in 2010

Sex	Age	Smoking Prevalence[1]			£ Medium Annual Gross Earnings[2] (InterQuartile Range)		Life Years Remaining[3]	FT/PT Work Rates[4]	Employment Rate in Smokers[1]
		Current	*Ex*	*Never*	*Full Time*	*Part Time*			
Male	35-49	0.26	0.23	0.51	23,364 (17,221 – 33,753)	7,361 (4,498 – 11,227)	37	0.96/0.04	0.749
	50-59	0.22	0.27	0.52	23,364 (17,221 – 33,753)	7,361 (4,498 – 11,227)	25	0.94/0.06	0.642
	60-95	0.15	0.46	0.39	23,364 (17,221 – 33,753)	7,361 (4,498 – 11,227)	9	0.70/0.30	0.153
Female	35-49	0.27	0.19	0.53	20,710 (15,132 – 30,150)	7,905 (4,813 – 12,094)	41	0.64/0.36	0.686
	50-59	0.24	0.21	0.51	20,710 (15,132 – 30,150)	7,905 (4,813 – 12,094)	29	0.53/0.47	0.539
	60-95	0.13	0.25	0.63	20,710 (15,132 – 30,150)	7,905 (4,813 – 12,094)	10	0.36/0.64	0.113

[1]Continuous Household Survey (Northern Ireland) 2010
[2]Annual Survey of Hours and Earnings (Northern Ireland) 2010
[3]ONS life tables 2008-2010. Life expectancy from the midpoint of each band
[4]ONS Labour Force Survey 2010. Proportion in full-time/part-time employment for Northern Ireland

3.4.3 SAM, YPLL and productivity loss

Using the parameters provided in **Table 5, Table 6, Table 7** and **Table 8**, the SAM, YPLL, and productivity loss were calculated. Results of smoking-attributable lost productivity costs for England and Wales, Scotland, and Northern Ireland in 2010 by sex and disease category are presented in the subsequent sections.

3.4.3.1 England and Wales

There were 493,242 deaths[286] (all ages) registered in England and Wales in 2010 due to all causes. There were a total of 329,461 deaths in adults aged 35 years and over from 20 disease categories that have been known to carry higher risk in smokers. Of the total deaths, smoking was estimated to be responsible for 80,601 deaths annually (**Table 9**). The most common smoking-attributable deaths in both men and women were related to cancer of the trachea, lung, bronchus (males: 14,404 deaths; females: 10,296 deaths), ischemic heart disease (males: 7,073 deaths; females: 3,305) and COPD (males: 9,232 deaths; females: 8,123 deaths). Lung cancer, ischemic heart disease and COPD were responsible for 65% of all smoking-related deaths. Smoking was estimated to be responsible for 204,254 years of productive life lost in men and 96,513 years of productive life lost in women. Productivity lost was valued at £4.1 billion (£3.2 billion for men; £858 million for women). Men had higher values of productivity loss than women due to a higher prevalence of current smokers, higher income level, higher employment rate and larger proportion of full-time workers relative to part-time workers.

Table 9. Smoking-attributable mortality, years of potential life lost and productivity loss in England and Wales in 2010

Disease Category	Male				Female				Total			
	Deaths[1]	SAM[2]	YPLL[3]	PLoss[4] (000s £)	Deaths[1]	SAM[2]	YPLL[3]	PLoss[4] (000s £)	Deaths[1]	SAM[2]	YPLL[3]	PLoss[4] (000s £)
Malignant Neoplasm												
Lip, Oral Cavity, Pharynx	1,302	918	7,971	135,333	659	302	1,944	18,626	1,961	1,252	9,916	153,959
Oesophagus	4,475	3,133	16,357	262,490	2,162	1,171	3,606	31,759	6,637	4,304	19,963	294,249
Stomach	2,681	658	2,517	38,899	1,619	192	605	5,448	4,300	849	3,122	44,347
Pancreas	3,441	602	4,008	65,047	3,614	828	2,918	24,847	7,055	1,431	6,926	89,894
Larynx	508	410	2,184	34,041	130	130	498	4,470	638	540	2,682	38,511
Trachea, Lung, Bronchus	16,795	14,404	57,777	872,552	13,161	10,296	38,019	332,927	29,956	24,700	95,796	1,205,480
Cervix Uteri	--	--	--	--	754	80	1,022	9,934	754	80	1,022	9,934
Kidney and Renal Pelvis	2,054	726	4,437	72,675	1,306	57	272	2,452	3,360	783	4,709	75,127
Urinary Bladder	2,961	1,263	2,644	36,219	1,407	394	813	6,873	4,368	1,657	3,457	43,092
Acute Myeloid Leukaemia	1,070	215	973	14,580	931	109	370	3,173	2,001	324	1,343	17,754
Cardiovascular Disease												
Ischemic Heart Disease	40,633	7,073	51,752	886,724	29,444	3,305	9,715	91,518	70,077	10,378	61,467	978,243
Other Heart Disease	10,111	1,482	6,143	99,447	14,275	1,103	1,717	15,367	24,386	2,585	7,860	114,814
Cerebrovascular Disease	16,829	1,264	9,910	170,655	26,399	1,538	7,733	76,987	43,228	2,801	17,643	247,641
Atherosclerosis	152	31	55	774	247	14	12	108	399	45	68	882
Aortic Aneurysm	4,114	2,444	5,648	80,573	2,800	1,255	1,243	9,318	6,914	3,699	6,891	89,891
Other Arterial Disease	92	8	43	691	74	9	54	511	166	17	96	1,202
Respiratory Disease												
Pneumonia, Influenza	10,519	2,023	3,995	61,756	14,827	1,610	2,269	20,618	25,346	3,633	6,264	82,374
Bronchitis, Emphysema	665	598	1,762	26,293	443	362	990	8,469	1,108	960	2,752	34,763
COPD	11,685	9,232	16,394	218,526	10,973	8,123	11,494	87,655	22,658	17,355	27,888	306,181
All Other Disease	32,584	846	9,685	166,793	41,565	2,393	11,218	106,563	74,149	3,239	20,903	273,356
TOTAL	**162,671**	**47,330**	**204,254**	**3,244,070**	**166,790**	**33,271**	**96,513**	**857,624**	**329,461**	**80,601**	**300,768**	**4,101,694**

[1]ONS 2010 underlying cause of death by ICD-10 codes[286]
[2]Smoking-attributable mortality = deaths x smoking-attributable fraction
[3]Years of productive life lost = smoking-attributable mortality x remaining life expectancy x employment rate in smokers
[4]Productivity loss = smoking-attributable mortality x adjusted present value of future earnings (discounted at 3.5%)

3.4.3.2 Scotland

There were 53,967 deaths[287] (all ages) registered in Scotland due to all causes. There were a total of 36,324 deaths in adults aged 35 years and over from 20 smoking-related disease categories in 2010; of which smoking was estimated to be responsible for 12,397 deaths (**Table 10**). The most common smoking-attributable deaths in both men and women were related to cancer of the trachea, bronchus, lung (males: 1,847 deaths; females: 1,572 deaths), ischemic heart disease (males: 1,685 deaths; females: 936) and COPD (males: 899 deaths; females: 1,119 deaths). Lung cancer, ischemic heart disease and COPD were responsible for 64% of all smoking-related deaths. Smoking was estimated to be responsible for 24,040 years of productive life lost in men and 13,742 years of productive life lost in women. Productivity loss was valued at £564 million (£417 million for men; £146 million for women).

Table 10. Smoking-attributable mortality, years of potential life lost and productivity loss in Scotland in 2010

Disease Category	Male				Female				Total			
	Deaths[1]	SAM[2]	YPLL[3]	PLoss[4] (000s £)	Deaths[1]	SAM[2]	YPLL[3]	PLoss[4] (000s £)	Deaths[1]	SAM[2]	YPLL[3]	PLoss[4] (000s £)
Malignant Neoplasm												
Lip, Oral Cavity, Pharynx	191	141	1,025	18,317	88	45	237	2,505	279	186	1,263	20,822
Oesophagus	531	380	1,868	32,983	277	166	437	4,751	808	546	2,305	37,734
Stomach	334	90	278	4,785	169	22	75	763	503	112	353	5,548
Pancreas	346	76	430	7,551	323	86	319	3,347	669	162	748	10,898
Larynx	70	58	181	3,124	24	24	34	383	94	82	215	3,507
Trachea, Lung, Bronchus	2,106	1,847	6,688	116,528	1,946	1,572	4,997	53,940	4,052	3,419	11,685	170,468
Cervix Uteri	--	--	-	--	89	12	167	1,640	89	12	167	1,640
Kidney and Renal Pelvis	174	66	309	5,481	142	8	26	287	316	74	335	5,768
Urinary Bladder	269	125	268	4,647	171	53	105	1,103	440	178	372	5,750
Acute Myeloid Leukaemia	148	33	95	1,664	101	12	48	494	249	45	143	2,159
Cardiovascular Disease												
Ischemic Heart Disease	4,588	1,685	6,835	118,493	3,535	936	1,752	18,457	8,123	2,621	8,587	136,950
Other Heart Disease	844	152	727	12,214	1,209	115	225	2,332	2,053	267	952	14,546
Cerebrovascular Disease	1,879	461	1,369	23,326	2,880	880	1,188	12,519	4,759	1,341	2,557	35,845
Atherosclerosis	16	4	3	34	35	3	1	6	51	7	3	39
Aortic Aneurysm	302	193	425	7,156	200	103	65	689	502	296	489	7,845
Other Arterial Disease	13	2	19	307	11	2	0	3	24	4	20	311
Respiratory Disease												
Pneumonia, Influenza	980	213	323	5,477	1,345	191	256	2,744	2,325	404	579	8,221
Bronchitis, Emphysema	41	37	44	719	19	16	62	623	60	53	106	1,342
COPD	1,110	899	1,700	29,334	1,441	1,119	1,762	19,322	2,551	2,018	3,462	48,656
All Other Disease	3,743	162	1,453	24,993	4,634	408	1,988	20,560	8,377	570	3,441	45,552
TOTAL	**17,685**	**6,624**	**24,040**	**417,133**	**18,639**	**5,773**	**13,742**	**146,467**	**36,324**	**12,397**	**37,782**	**563,600**

[1]General Register Office for Scotland 2010 underlying cause of death by ICD-10 codes[287]
[2]Smoking-attributable mortality = deaths x smoking-attributable fraction
[3]Years of productive life lost = smoking-attributable mortality x remaining life expectancy x employment rate in smokers
[4]Productivity loss = smoking-attributable mortality x adjusted present value of future earnings (discounted at 3.5%)

3.4.3.3 Northern Ireland

There were 14,457 deaths[288] (all ages) registered in Northern Ireland due to all causes. There were a total of 9,539 deaths in adults aged 35 years and over from 20 smoking-related disease categories in 2010; of which smoking was responsible for 3,107 deaths (**Table 11**). The most common smoking-attributable deaths in both men and women were related to cancer of the trachea, lung, bronchus (males: 471 deaths; females: 369 deaths), ischemic heart disease (males: 460 deaths; females: 249) and COPD (males: 326 deaths; females: 236 deaths). Lung cancer, ischemic heart disease and COPD were responsible for 63% of all smoking-related deaths. Smoking was estimated to be responsible for 12,785 years of productive life lost in men and 6,496 years of productive life lost in women. Productivity loss was valued at £265 million (£200 million for men; £65 million for women).

Table 11. Smoking-attributable mortality, years of potential life lost and productivity loss in Northern Ireland in 2010

Disease Category	Male				Female				Total			
	Deaths[1]	SAM[2]	YPLL[3]	PLoss[4] (000s £)	Deaths[1]	SAM[2]	YPLL[3]	PLoss[4] (000s £)	Deaths[1]	SAM[2]	YPLL[3]	PLoss[4] (000s £)
Malignant Neoplasm												
Lip, Oral Cavity, Pharynx	42	31	187	2,785	34	16	127	1,184	76	47	314	3,969
Oesophagus	92	65	429	6,528	63	36	50	532	155	101	479	7,061
Stomach	76	20	228	3,479	53	6	107	1,041	129	26	335	4,520
Pancreas	88	19	222	3,505	97	22	116	1,185	185	41	337	4,689
Larynx	22	18	54	890	6	6	3	36	28	24	57	926
Trachea, Lung, Bronchus	539	471	1,393	22,390	369	287	784	7,697	908	758	2,177	30,087
Cervix Uteri	--	--	-	--	24	3	92	868	24	3	92	868
Kidney and Renal Pelvis	63	24	174	2,655	41	2	94	928	104	26	268	3,583
Urinary Bladder	71	32	143	2,350	34	9	50	497	105	42	193	2,846
Acute Myeloid Leukaemia	40	9	105	1,709	26	3	54	527	66	11	158	2,236
Cardiovascular Disease												
Ischemic Heart Disease	1,268	460	3,572	55,536	962	249	970	9,974	2,230	709	4,542	65,510
Other Heart Disease	223	40	529	8,360	307	27	320	3,264	530	68	849	11,624
Cerebrovascular Disease	488	133	1,042	16,829	748	237	753	7,737	1,236	369	1,796	24,567
Atherosclerosis	4	1	4	71	4	0	2	24	8	1	6	95
Aortic Aneurysm	68	43	87	1,535	47	24	56	556	115	67	143	2,091
Other Arterial Disease	3	0	3	53	5	1	18	167	8	1	21	220
Respiratory Disease												
Pneumonia, Influenza	283	62	536	8,732	450	68	437	4,508	733	130	973	13,241
Bronchitis, Emphysema	21	19	71	1,058	10	8	29	275	31	27	100	1,334
COPD	326	262	433	7,523	315	236	240	2,583	641	498	673	10,106
All Other Disease	942	45	3,573	54,199	1,285	113	2,194	21,485	2,227	158	5,767	75,684
TOTAL	**4,659**	**1,754**	**12,785**	**200,189**	**4,880**	**1,353**	**6,496**	**65,068**	**9,539**	**3,107**	**19,281**	**265,256**

[1]Northern Ireland Statistics & Research Agency 2010 underlying cause of death by ICD-10 codes[288]
[2]Smoking-attributable mortality = deaths x smoking-attributable fraction
[3]Years of productive life lost = smoking-attributable mortality x remaining life expectancy
[4]Productivity loss = smoking-attributable mortality x adjusted present value of future earnings (discounted at 3.5%)

3.4.3.4 United Kingdom

The number of combined deaths in the UK from all causes totalled 561,666. Smoking was estimated to be responsible for 96,105 (58% male) in adults aged 35 years and over in 2010 (**Table 12**). This amounted to 17% of all deaths resulting in 1.2 million years of life lost. For individuals who were in the workforce, premature deaths resulted in 357,831 years of productive life lost. The productivity cost of lost earnings due to smoking was valued at £4.93 billion per year (discounted 3.5%) after combining the estimates from England and Wales, Scotland, and Northern Ireland.

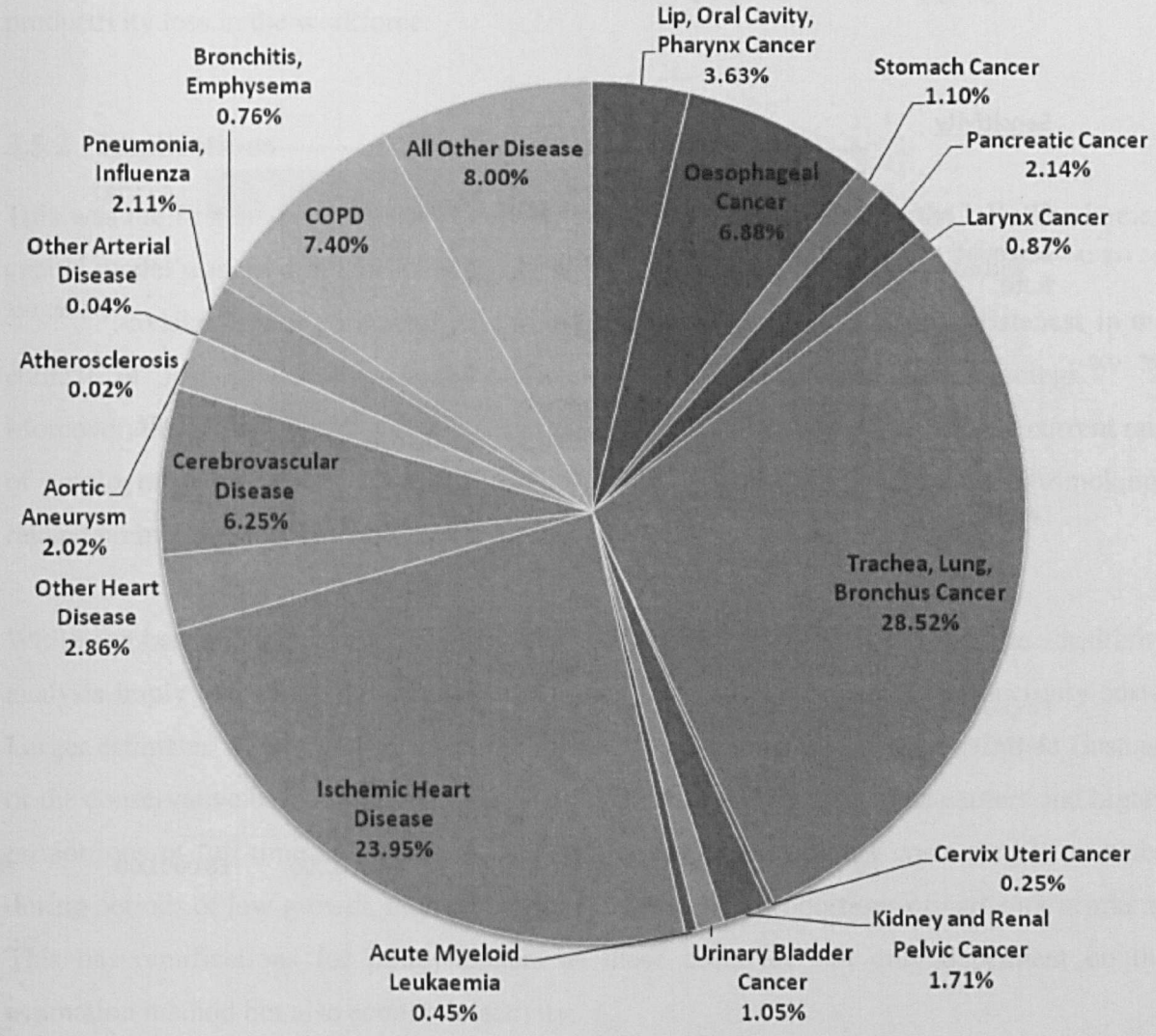
Table 12. Smoking-attributable mortality, years of potential life lost and productivity loss in the by UK country (2010)

Country	SAM[1]	YLL[2]	YPLL[3]	Productivity Loss[4] (000s £)
England and Wales	80,601	999,714	300,768	4,101,694
Scotland	12,397	139,749	37,782	563,600
Northern Ireland	3,107	66,483	19,281	265,256
United Kingdom	**96,105**	**1,205,946**	**357,831**	**4,930,550**

[1]Smoking-attributable mortality = deaths x smoking-attributable fraction
[2]Years of life lost = smoking-attributable mortality x remaining life expectancy
[3]Years of productive life lost = years of life lost x employment rate
[4]Productivity loss = smoking-attributable mortality x adjusted present value of future earnings (discounted 3.5%)

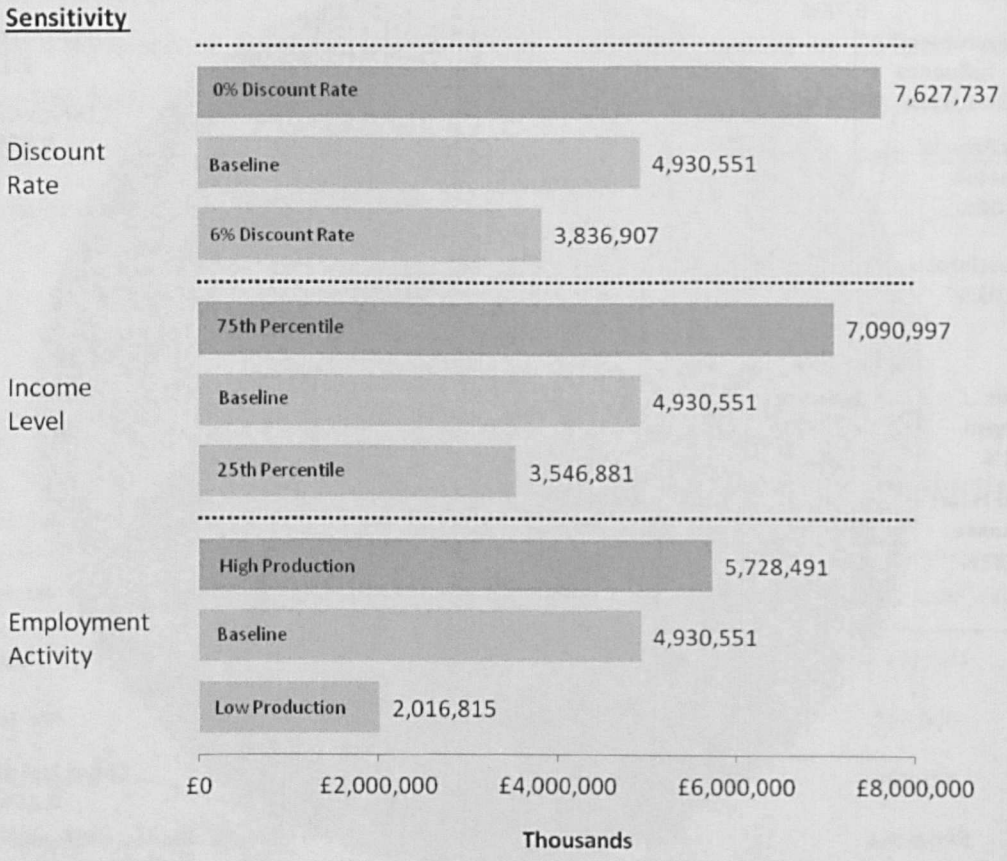
Figure 7 shows the proportion of smoking-attributable productivity loss in the UK by category of disease. Ischemic heart disease and cancer of the trachea, bronchus and lung made up of 53% total productivity loss. Oesophageal cancer, COPD and cerebrovascular disease made up of 21% of total productivity loss. Even though COPD was responsible for 21% of all smoking-attributable deaths, the monetary impact was only 7.4% of total productivity loss because deaths occurred in older individuals, many of whom were past the average age of retirement when employment rate dropped sharply.

Figure 7. Proportion of smoking-attributable productivity loss (£) in the UK (2010) by category of disease



One-way sensitivity analysis is shown in **Figure 8** by varying the parameter assumptions from the base-case productivity loss of £4.93 billion. By altering discount rates, the values ranged from £3.84 billion (0%) to £7.63 billion (6%). Using a low income level (25th percentile) resulted productivity loss of £3.55 billion while using a high income level (75th percentile) resulted productivity loss of £7.09 billion. By altering employment activity, the values ranged from £2.02 billion (low productivity) to £5.73 billion (high productivity).

Figure 8. One-way sensitivity analysis for UK productivity loss (£) with varying parameter assumptions from baseline



3.5 Discussion

3.5.1 Summary of findings

The analysis in this chapter demonstrates smoking was responsible for 96,105 deaths (17% of all deaths) in adults aged 35 years and over (58% male) in the UK in 2010. These deaths resulted in 1.2 million life years lost and 357,831 years of productive life lost. The analysis estimated that productivity loss was £4.93 billion discounted at the base-case rate of 3.5%. When combined with a recent estimate of the cost of smoking to the NHS (£5.2 billion)[87] and costs to the economy due to absenteeism (£1.46 billion)[296], the cost to the society from these components alone was estimated to be £11.6 billion due to smoking in 2010-2011. This amount is more than the total revenue generated of £9.1 billion[188] from tobacco duties in

2010-2011. The analysis suggests that reduction in smoking prevalence would result in fewer smoking-attributable deaths, increase in life-years saved and significantly reduce the productivity loss in the workforce.

3.5.2 Implications

This was the first study to quantify productivity loss due to smoking in the UK. The human capital model was used in this study due to its comparability with existing studies[240-242 244 247 250 269 270], availability of parameter data to populate the model and its appropriateness in the context of lost productivity analysis from its strong theoretical underpinnings.[200 256] Moreover, this study used the proportion of full-time to part-time workers and the current rate of employment in the UK to reflect the probability of being in employment if smoking-related premature mortality was avoided.

While the baseline costs reflect the current labour market, the results from the sensitivity analysis imply that economic activity may in fact have a large impact on productivity costs. Larger estimates were obtained when the following parameter values were assumed (instead of the conservative base-case assumptions): 0% discount rate, high income earners and higher proportions of full-time employment. This suggests that productivity costs may be reduced during periods of low growth, high unemployment and high proportions of part-time workers. This has ramifications for policy-makers as these costs are not only dependent on the estimation method but also economic activity.

To validate the death estimates from the model, smoking-attributable mortality estimated in this study was compared with previous studies conducted in the UK. The estimated number of 80,601 smoking-attributable annual deaths in England and Wales was similar to 81,700 deaths reported in the NHS report on smoking statistics.[297] In addition, the proportion of total deaths attributable to smoking in this study (17%) was similar to the 18.6% provided by Allender *et al.*[87] in 2005 and the 17.2% annually reported in Twigg *et al.*[5] for the period between 1998 to 2002 for the UK. This comparison suggests that our estimates are consistent with previous studies. Also, as in previous studies, this study has utilised population-attributable fractions (PAFs) to calculate the number of deaths. An important strength of this study is that the PAFs were based on the largest prospective cohort study that investigated the

mortality risks due to smoking. Moreover, the stratification of mortality estimates at the level of sex, age and disease condition was unique to the cohort.

3.5.3 Limitations

There are also some limitations of the study. First, productivity loss has only been quantified as lost earnings due to premature mortality. Hence, the estimates did not include other components of indirect costs such as absenteeism[296], presenteeism[244], smoking breaks[89], lost leisure time[202], fire damage[245] and passive smoking[248]. Including these costs in future studies will increase the costs of smoking. Second, the human capital approach taken in this study does not represent the employer's perspective of lost productivity. Calculating productivity loss from an employer's perspective would require a friction cost approach[201] taking into account employment costs and friction periods for restoring levels of initial production. Since the human capital model does not take into worker replacement as described in **Section 2.5.2**, the cost estimates in this chapter overestimate productivity loss. The alternate friction cost method was not utilised because of its implausible assumptions on zero-cost labour replacement (**Section 2.5.2**) and there was also substantial difficulty in obtaining valid population-level data on both the frequency and length of friction periods in the UK. Although human capital model overestimate costs, it was the current best practice method of estimating productivity loss due to the limitations of the friction cost method. Third, the relative risk in ex-smokers in the model was assumed to be constant and not a function of years of quitting due to data limitations. Previous evidence[298-300] has shown that the risk of smoking-related mortality declines in ex-smokers with longer durations of abstinence. Moreover, the analysis assumed that smokers dying early would most likely be in employment in the future had they survived. However, this assumption was strengthened by using the current employment rate in the UK to adjust for the probability of being in employment by age (conditional on survival). Fourth, the relative mortality risk from the final ICD-10 category of "all other diseases" was obtained from two case-control studies.[283 284] While a significant association was found in these studies, a causal relationship could not be determined due to the limitation in the study design. Fifth, the economic model in this chapter utilised median gross annual income for the estimation of costs to take into account the income distribution of the population. The costs estimates using this approach will underestimate costs when compared to using the mean income. However, the use of the median income provides a more robust estimate, having a breakdown point of 50% which is

resistant towards giving arbitrarily large results due to outliers. Finally, the economic model developed in this chapter estimates the costs of premature mortality in the workforce. It must be acknowledged, however, that significant cost-savings can arise from premature mortality in health and social care settings. Some modelling studies[84-86] have shown that although healthcare costs for smokers are on average higher than that of non-smokers, long-term costs savings for the health and social care services can result from smokers dying prematurely and not using health services in old age. Additionally, premature mortality may in fact increase the number of job vacancies and reduce unemployment rates when firms replace workers which may be especially relevant during economic recessions. Despite these limitations, a comprehensive and recent estimate has been provided for productivity loss in the UK using best practice methodology. These results will further facilitate the estimation of net societal costs of smoking to inform UK tobacco control policy.

3.6 Conclusion

In this chapter, smoking was found to be responsible for 96,105 deaths in adults aged 35 years and over (17% of all deaths) in the United Kingdom in 2010. These deaths resulted in nearly 1.2 million years of life lost and 357,831 years of productive life lost. The cost of productivity loss due to premature mortality was £4.93 billion discounted at base-case rate of 3.5%. These results suggest that reducing smoking prevalence is likely to result in substantial gains in economic productivity in the workforce. The scale of the cost burden stresses the importance of strong tobacco control policy at the national level.

Chapter 4

Smoking and absenteeism: Systematic review, meta-analysis of occupational studies and cost of absence in the UK

4.1 Introduction

In **Chapter 3**, the primary component of smoking-related indirect costs (productive life lost due to premature mortality) was estimated for the UK. Since the causal link between smoking and premature mortality has been well established in the UK[8 9] and globally[265], the indirect costs as a result of premature mortality could be estimated directly using the human capital model. In **Chapter 2**, the literature review found that absence from work due to illness was the second largest component of indirect costs of smoking. Absenteeism costs identified in 13 studies in **Chapter 2** were direct measures of foregone income due to short-term sick leave or temporary disability. These costs may provide motivation for employers to support smoking cessation programmes as potential near-term benefits may be gained by a reduction in absenteeism.

However, contrary to consistent evidence providing a causal association between smoking and premature mortality, there is limited review evidence to suggest smoking is associated with absenteeism.[88 191-195] To date, the epidemiological literature has not been systematically reviewed, evaluated for publication bias, assessed for quality or synthesised in a meta-analysis.

4.2 Aims and Objectives

The aim of this study was to evaluate and quantify the relationship between smoking and work absenteeism through a systematic review and meta-analysis of longitudinal and cohort studies. Establishing an epidemiological association between smoking and workplace absence provides stronger justification for the estimation of absenteeism costs in the UK. By providing this justification, the secondary aim of this study was to provide the parameters and estimate the recent absenteeism costs for the UK. These aims were achieved by completing the following objectives:

- Adhere to PRISMA[197] and MOOSE[29] guidelines to ensure a high level of quality assurance with regards to selecting and extracting data for the systematic review
- Develop search strategy and eligibility criteria
- Quality assessment of occupational cohort studies
- Summarise, extract and synthesize the evidence

- Conduct meta-analysis to quantify the association between smoking and absenteeism
- Assess for publication bias
- Use the results of the meta-analysis to estimate costs of absenteeism in the UK

4.3 Methods

4.3.1 Search strategy

A comprehensive search of electronic databases was conducted in MEDLINE (1948 to February 2012), EMBASE (1980 to February 2012), PubMed (1950 to February 2012), Science Direct (1950 to February 2012), NHS Economic Evaluation Database (1980 to February 2012). Grey literature were searched for in CAB Abstracts (1910 to February 2012) which includes all relevant conference proceedings. In addition, reference lists from included studies were checked for further potential studies. Keywords relating to "smoking" and "absenteeism" were used to search for all relevant articles (Search Terms: **Appendix 9.3**). Keywords were developed through group discussion and consensus (SFW, JLB, CQ, SA) and piloted in each individual database before the formal search process. Where available in the database, medical subject headings (MeSH) were used to identify related terms.

4.3.2 Inclusion criteria

Studies meeting all of the following key criteria were included in the review (Detailed eligibility checklist shown in **Appendix 9.4**):

(1) **Study design** – The designs included in the review were longitudinal studies, prospective cohorts or retrospective cohorts in order to evaluate the temporal relationship between smoking and absenteeism.

(2) **Population** – The studies including subjects who were full-time, part-time or self-employed adult wage earners in any occupation were included in the review.

(3) **Exposure** – Studies that established the primary exposure of smoking (cigarette, pipe, cigar) through one of the following methods were included: self-reported interview, self-reported survey, medical/employee records or validated biomarker such as cotinine or carbon monoxide.

(4) **Outcome** – The primary outcomes of interest were the following measurements of absenteeism established through self-reported interview, medical/employee records or self-reported survey: duration of absence (days, hours, percentage of work time lost) or risk of absence (risk, odds, hazard, rate).

4.3.3 Data extraction

Two authors (SW and JLB) independently selected studies based on titles and abstracts. Titles were excluded on the basis of subject matter while abstracts were excluded when inclusion criteria for study design or population were not met. Full-text articles were retrieved from the remaining studies. The full-text articles that were not written in English were translated using both a human translator (TL) and electronic language translator. Full-text articles were screened and independently selected for inclusion by two reviewers (SW and JLB; SW and CQ; or SW and SA) using a designed checklist based on eligibility criteria. The data extraction form was developed and independently piloted on five initial studies. Two reviewers (either SW and JLB; or SW and SA) independently extracted the data from the studies using a standardised form (**Appendix 9.6**) including data on study design, study population, location, sample size and reported results.

4.3.4 Quality assessment

To assess the methodological quality of selected studies, the Newcastle-Ottawa Scale[301] (NOS) was used. According to the NOS, studies were judged according to three domains i) selection of the study groups ii) comparability of the groups iii) ascertainment of the outcome of interest; with a maximum total score of nine. The original scale was modified slightly to account for specific aspects of the review (**Appendix 9.6**). The domains are described below:

i. The selection of the study groups (0-4): a score of four represents high representativeness of the cohort, validated assessment of the exposure and demonstration that the outcome of interest was not present at the start of the study.

ii. The comparability of the groups (0-2): a score of two represents high comparability due to controlling or stratifying for confounding factors.

iii. The ascertainment of the outcome of interest (0-3): a score of three represents validated assessment of the outcome, adequate duration of follow-up and low attrition rates (< 20%).

The quality assessment took into account most aspects of quality in epidemiological studies such as control of confounding variables, adequate sample size, minimisation of selection bias and clear definitions of exposures. Two reviewers (either SW and JLB; or SW and SA) independently assessed the quality of the included studies. Any disagreements were resolved by discussion and consensus.

4.3.5 Statistical analysis

Random effects meta-analysis was conducted to evaluate the following outcomes i) relative risk (*RR*) of absence and ii) mean difference in days absent per year (annualised). The extracted data for the effect size outcomes were in several formats: odds ratio, rate ratio, hazard ratio and mean difference. The difference in mean duration of absenteeism between the exposed (smokers) and non-exposed (non-smokers) groups was also reported in several different formats: days, hours and percentage of working time lost. The data transformation for mean duration of absenteeism was performed by annualising the data into days per year in both exposed and non-exposed groups. However, the transformations for the effects reported as odds ratios, rate ratios or hazard ratios were more complex. The most comparable method of comparison between the ratio measures was through risk ratios. While hazards and rate ratios are essentially special cases of risk ratios, odds ratios are fundamentally different. Rate ratios and hazard ratios were used directly as estimates of relative risk ratios[302] while odds ratios were transformed to risk ratios using the correction method[303]. Detailed methodology on the data transformation of reported effects from the studies to relative risk ratios is provided in **Appendix 9.10.**

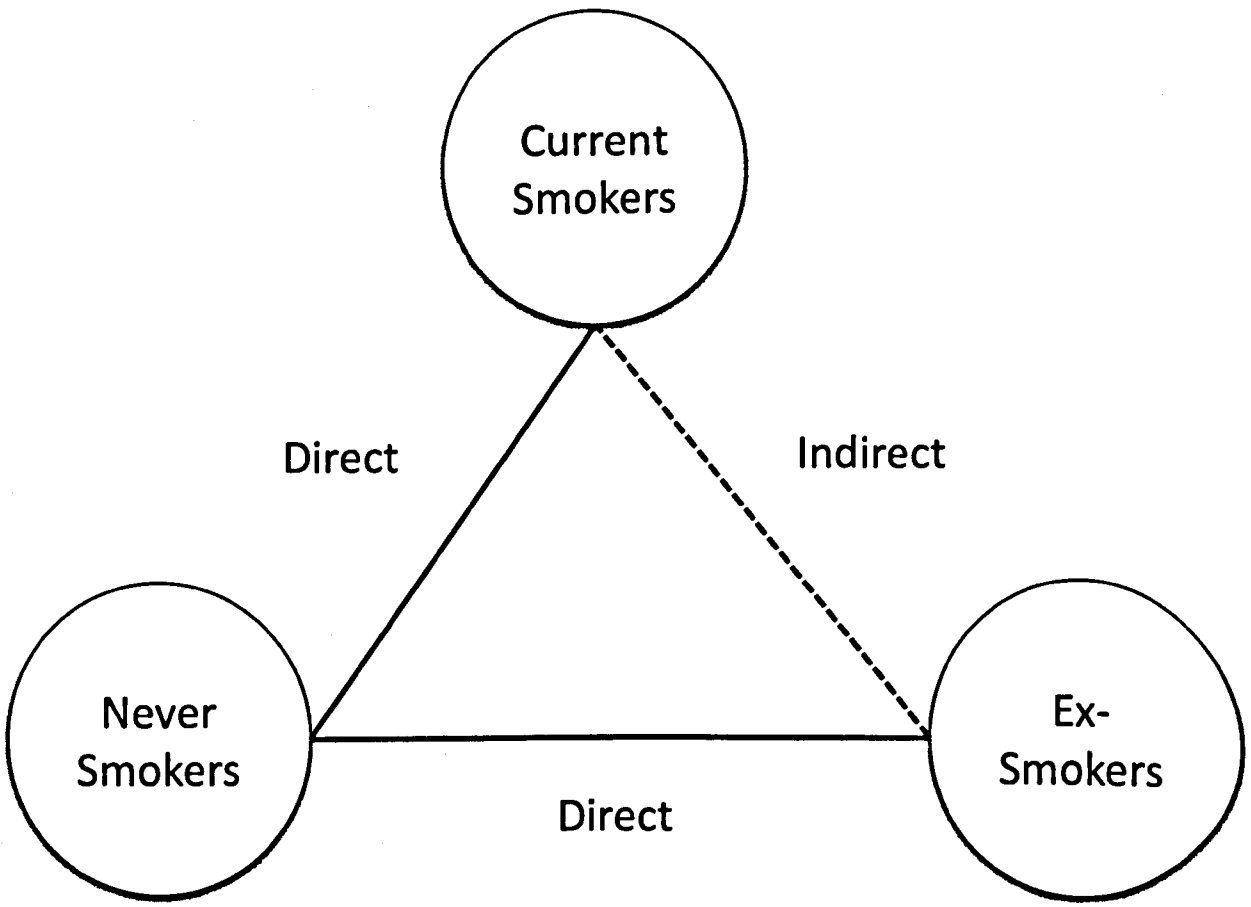
Separate analyses were conducted to assess the effects of smoking by comparing current smokers versus non-smokers, ex-smokers versus never smokers and current smokers versus ex-smokers. Random effects meta-analysis models were used to analyse the data from different studies and to account for differences in population characteristics, geography and study year. The heterogeneity between the studies was assessed using the I^2 statistic which measures the percentage of total variation across studies, derived from the Cochran's *Q*-

statistic[304]. Detailed methodology on the random effects meta-analysis and analysis of heterogeneity is provided in **Appendix 9.7.** All the analyses were completed in STATA 11 (Stata Corp, College Station, TX, USA).

4.3.5.1 Primary and sensitivity analyses

Three meta-analyses were performed using the extracted data: relative risk of absence for current smokers versus non-smokers (Model 1); mean difference in duration of absence for current smokers versus non-smokers (Model 2); and relative risk of absence for ex-smokers versus never smokers (Model 3). In addition, indirect comparison meta-analysis was performed using inverse variance weighting[305] to analyse the risk of absence between current smokers and ex-smokers to test for true effect of quitting smoking.

Figure 9. Diagram for indirect treatment comparison for meta-analysis



An adjusted indirect comparison[305] was utilised because all study results used never smokers or non-smokers as the reference group. **Figure 9** describes the process in which the indirect comparison was calculated based on smoking status. The solid lines represent direct relationships in which data was reported based on the reference group of never smokers while the dotted line describes the calculated indirect relationship based on meta-analysis results from the direct relationships. The detailed methodology on the adjusted indirect comparison is provided in **Appendix 9.9**.

Where available, adjusted relative risk estimates extracted from the studies were used opposed to unadjusted results to take into account additional individual-level covariates. The only outcome that was not able to be pooled using meta-analysis was the mean difference in duration of absence between ex-smokers and never smokers due to a limited number of studies (n = 4) and no reported measures of dispersion. Since none of the studies provided any measures of dispersion or test statistics to calculate the measures of dispersion, imputation procedures could not be utilised.

4.3.5.2 Missing parameters

Some studies in the meta-analysis had missing data for measures of dispersion (e.g. standard deviations or 95% confidence intervals). For some of these studies (n = 5), it was possible to obtain the measure of dispersion from the *p*-values or using the exact *t*-statistic or *F*-statistic. For other studies (n = 6) with insufficient data to enable estimation of dispersion, the measure of dispersion was imputed by first running an initial meta-analysis model with only those studies that had a measure of dispersion available and then imputing dispersion measure for the studies with insufficient data from the pooled standard error. Detailed imputation procedures on missing parameters are provided in **Appendix 9.11**. To evaluate the impact of the imputed dispersion parameters, sensitivity analysis was conducted by excluding the studies with imputed measures of dispersion.

4.3.5.3 Subgroup analyses and meta-regression

To explore reasons for heterogeneity, subgroup analyses were conducted using the above random effects models to evaluate effect size based on sex, work sector, type of absence and methodological quality of the study (based on the selection, comparability and ascertainment domains). The work sectors were sub-grouped by private, public or unclassified sector of work. The unclassified workers were usually from nationally representative samples or a

state-run company. Due to the diversity of the pooled workforce, the best classification was by public or private sectors. In terms of duration of absence, the NICE definitions[194] were used to define short- and long-term absence. The cut-offs were specified as < 4 weeks per year for short-term absence and ≥ 4 weeks per year for long-term absence.[194]

To evaluate statistical significance of difference in effect size based on subgroups, random effects meta-regression[306] was conducted for subgroups that appeared to have large differences in effect sizes. Gender, type of absence, work sector and quality score could be incorporated as dummy variables into multivariate models. Detailed meta-regression methodology is provided in **Appendix 9.8**.

4.3.5.4 Publication bias

Publication bias or "small-study bias" was assessed visually by funnel plot[307] and statistically by Egger's test for asymmetry[308] based on the distribution of effect sizes against standard errors. Funnel plots were used as a visual tool to investigate publication bias in meta-analysis. Funnel plots are scatter plots of the measure of effects estimated from individual studies on the horizontal axis against a measure of standard error on the vertical axis. In the absence of bias, results will scatter widely at the bottom of the graph (small studies, large standard error) and the spread narrowing among larger studies (large study, small standard error) resembling a symmetrical, inverted funnel.[307] Smaller studies without statistically significant effects can remain unpublished resulting to an asymmetrical funnel plot.

Asymmetry in the funnel plot was evaluated using Egger's test.[308] The method uses linear regression of the study effect estimates on their reciprocal of standard errors (precision). Under the null hypothesis of "no asymmetry", the line would be completely horizontal and the intercept term would be at zero. The greater the association between effect estimate and the standard error, the more the slope moves away from horizontal and the intercept term gets further away from zero[309] which results in greater asymmetry.

4.4 Results

4.4.1 Description of studies

The electronic database search yielded a total of 3,080 studies (**Figure 10**). After removing duplicates (n = 993) and excluding studies based on relevance of titles and abstracts (n = 1,906), 181 full-text articles were retrieved for evaluation. After screening full-text articles for eligibility, 29 studies[310-338] were identified for inclusion in the systematic review. The most common reason for exclusion was non-cohort or non-longitudinal study design (56 studies excluded) or smoking status was not reported (54 studies excluded). Other reasons for exclusion included no definition of absenteeism (18 studies), duplicates of the same participants (8 studies), non-adult participants (7 studies), unavailable full-text articles (7 studies) and protocols only (2 studies).

The study characteristics and study-effect estimates are presented in **Table 13**. The year of publication for the studies ranged from 1960[328] to 2011[335] with a median year of publication of 2003. Most studies were conducted in Western countries; though three studies[321 322 326] were from Eastern Europe; two studies[325 330] from Japan; and one study[318] was from Israel.

Figure 10. Search flow chart and selection process

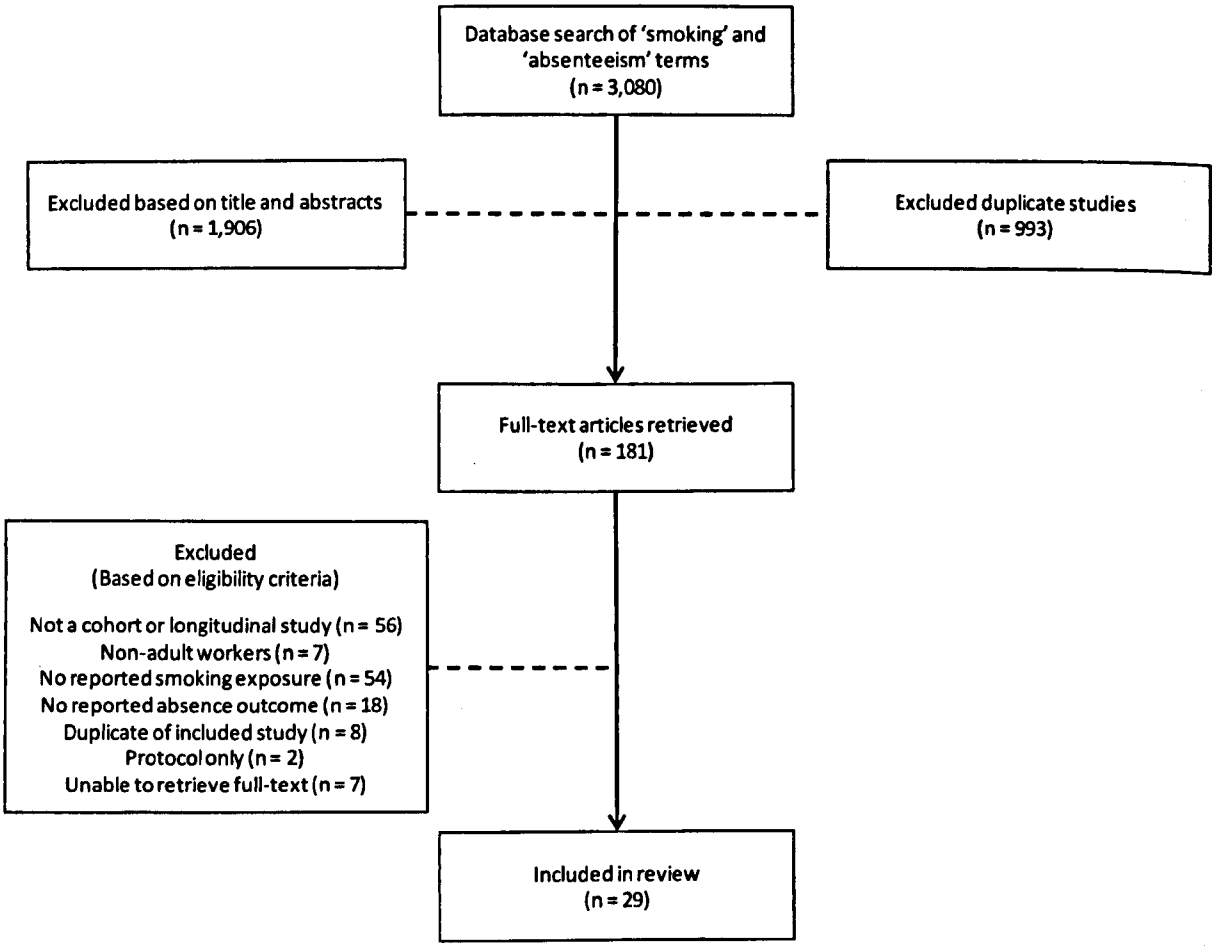


Table 13. Selected characteristics of studies included in the analysis of the relationship between smoking and absenteeism

First author/Year	Location	Sample Size	Start yr/ Duration (months)	Adjusted Results (Y/N)	Sex (M/F/Both)	Relative Risk of Absence (95% Confidence Interval)		Mean Diff. (SDpooled) [Days absent per yr]		Quality Score
						Current vs. Non/Never smoker	*Ex vs. Never smoker*	*Current vs. Non-smoker*	*Ex vs. Never smoker*	
Alavinia 2000[310]	Netherlands	5,867	2005/14	Yes	M	1.18 (1.07-1.30)	--	--	--	7
Andersen 2010[311]	Denmark	5,096	2000/24	Yes	Both	1.50 (1.29-1.75)	--	--	--	8
Athanasou 1979[312]	Australia	424	--/24	No	M F	--	--	5.62 (2.32) 0.24 (0.39)	--	3
Batenburg 1990[313]	New Zealand	892	1987/12	No	M F	--	--	0.60 (0.35) 0.75 (0.92)+	--	6
Christensen 2007[314]	Denmark	5,020	2000/18	Yes	M F	1.55 (1.00-2.40) 2.05 (1.36-3.08)	1.36 (0.85-2.19) 1.61 (1.07-2.42)	--	--	7
De Backer 2006[315]	Belgium	20,651	1994/12	Yes	M F	1.32 (1.21-1.43)* 1.21 (1.08-1.36)*	1.32 (1.21-1.43)* 1.21 (1.08-1.36)*	--	--	6
Eriksen 2004[316]	Norway	4,931	1999/3	Yes	Both	1.27 (1.04-1.53)*	--	--	--	7
Ferarrio 2007[317]	Italy	3,277	1992/24	Yes	Both	1.25 (1.09-1.43)*	1.06 (0.86-1.30)*	--	--	5
Green 1992[318]	Israel	5,826	1985/24	No	M F	--	--	1.30 (0.39) -0.47 (0.63)		6
Halpern 2001[319]	USA	292	--/3	No	Both	--	--	10.7 (2.16)	4.29 (1.47)	4
Holmberg 2010[320]	Sweden	836	1990/144	Yes	Both	1.05 (0.53-2.08)*	--	--	--	5
Indulski 1967[321]	Poland	2,874	1960/24	No	M F	--	--	1.72 (0.92)+ 3.10 (0.92)+	--	4
Jedrychowski 1976[322]	Poland	197	1968/72	No	M	--	--	0.72 (0.92)+	0.42 (--)	5
Karlsson 2010[323]	Sweden	341	2003/24	Yes	Both	0.79 (0.55-1.15)	--	--	--	6
Kivimaki 1997[324]	Finland	763	1994/24	Yes	Both	1.02 (0.67-1.55)	--	--	--	6

*Relative risk derived from odds ratio correction method[303]
+Proxy standard deviation obtained from meta-analysis of complete studies
-- Unreported data

Table cont. Selected characteristics of studies included in the analysis of the relationship between smoking and absenteeism

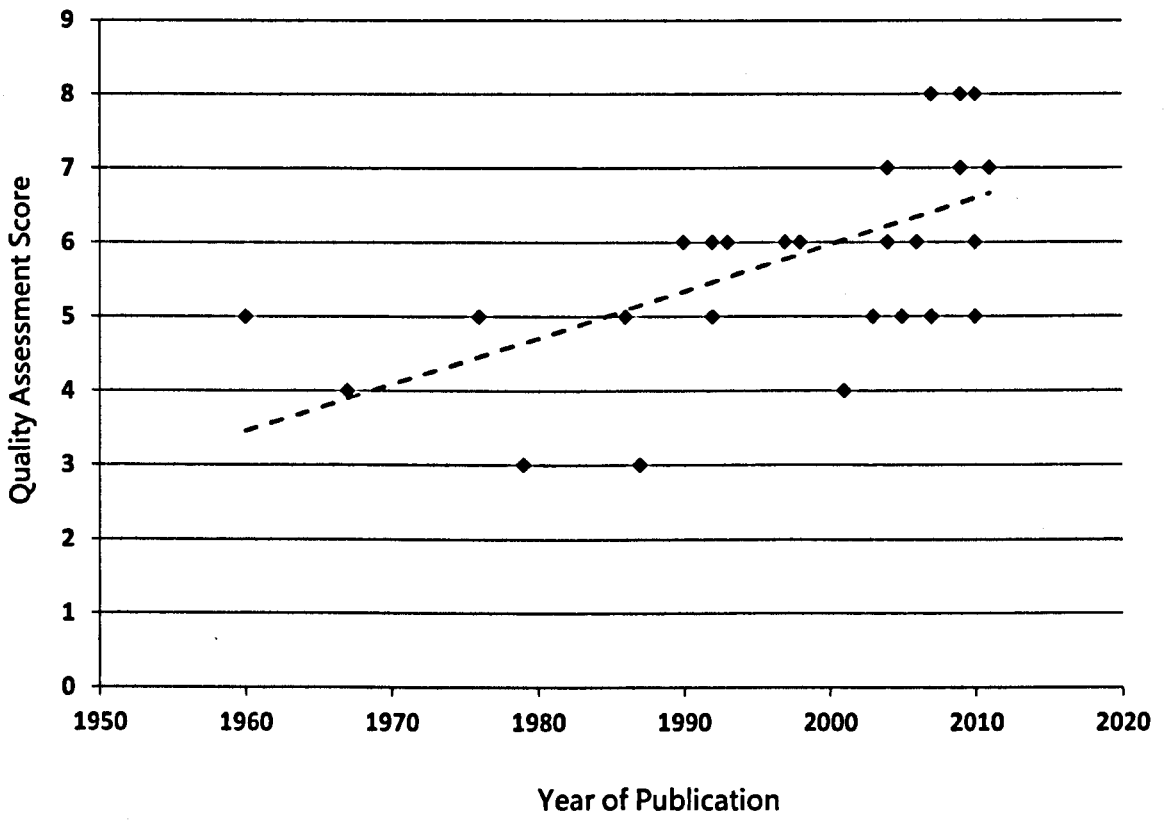
First author/Year	Location	Sample Size	Start yr/ Duration (months)	Adjusted Results (Y/N)	Sex (M/F/Both)	Relative Risk of Absence (95% Confidence Interval)		Mean Diff. (SDpooled) [Days absent per yr]		Quality Score
						Current vs. Non/Never smoker	*Ex vs. Never smoker*	*Current vs. Non-smoker*	*Ex vs. Never smoker*	
Kondo 2006[325]	Japan	529	1997/24	Yes	Both	1.85 (0.86-3.76)*	--	--	--	6
Kozak 1987[326]	Czech.	675	1981/48	No	M F	1.30 (1.00-1.57)* 1.24 (1.00-1.47)*	--	-1.70 (4.46) -3.50 (3.09)	--	3
Laaksonen 2009[327]	Finland	6,934	2000/47	Yes	M F	1.69 (1.44-1.97) 1.50 (1.40-1.60)	1.11 (0.98-1.27) 1.18 (1.12-1.25)	--	--	8
Lowe 1960[328]	UK	3,341	1957/12	No	M	--	--	1.33 (0.92)+	--	5
Lundborg 2007[329]	Sweden	14,272	1988/12	No	Both	--	--	14.1 (1.28)	4.55 (1.20)	8
Morikawa 2004[330]	Japan	2,504	1990/96	Yes	Both	1.43 (1.17-1.75)	1.39 (1.07-1.80)	--	--	6
Niedhammer 1998[331]	France	12,555	1995/12	No	M F	1.24 (1.10-1.38) 1.26 (1.11-1.41)	1.10 (1.00-1.20) 1.03 (0.96-1.10)	--	--	6
North 1993[332]	UK	7,715	1985/20	Yes	M F	1.61 (1.31-1.99) 1.22 (0.97-1.44)	--	--	--	6
Ryan 1992[333]	USA	2,537	1986/14	No	Both	--	--	4.75 (0.92)+	--	5
Skillgate 2009[334]	Sweden	6,532	1999/36	Yes	Both	1.80 (1.20-2.60)	1.80 (1.30-2.40)	--	--	8
Tsai 2011[335]	USA	6,551	2005/48	Yes	Both	1.18 (0.95-1.44)*	1.08 (0.91-1.26)*	--	--	7
Tsai 2005[336]	USA	2,203	1990/108	No	M F	--	--	6.30 (3.21) 11.0 (5.58)	1.70 (--) 0.20 (--)	5
Tsai 2003[337]	USA	2,550	1994/120	No	Both	--	--	2.90 (0.92)+	--	5
Van Tuinen 1986[338]	USA	406	1983/20	No	Both	--	--	1.50 (0.76)	--	5

*Relative risk derived from odds ratio correction method[303]
+Proxy standard deviation obtained from meta-analysis of complete studies
-- Unreported data

4.4.2 Quality assessment

The quality scores on NOS ranged from the lowest score of three to the highest score of eight with a median of six (InterQuartile Range: 5 to 7) (**Table 13**). There were no studies with the maximum score of nine because no studies achieved the maximum score of four in the "selection" criteria. To achieve this, studies must have assessed smoking status using a validated biomarker such as cotinine or a device such as a carbon monoxide reader. All 29 studies relied on self-reported smoking status either through interview or survey responses. Lower scores were generally related to studies not taking into account confounding variables and/or having high attrition rates (> 20%) without providing descriptions of those lost.

Figure 11. Improvement in quality score by publication year for 29 studies included in the systematic review



The relationship between quality and publication year was evaluated by scatter plot and linear regression. There was an upward trending relationship shown a scatter plot (**Figure 11**) between quality scores and year of publication where quality improved over time. On average, quality improved by 0.06 points per year from 1960 to 2011 ($\beta = 0.06$, 95% CI 0.03 to 0.10; $p = 0.001$).

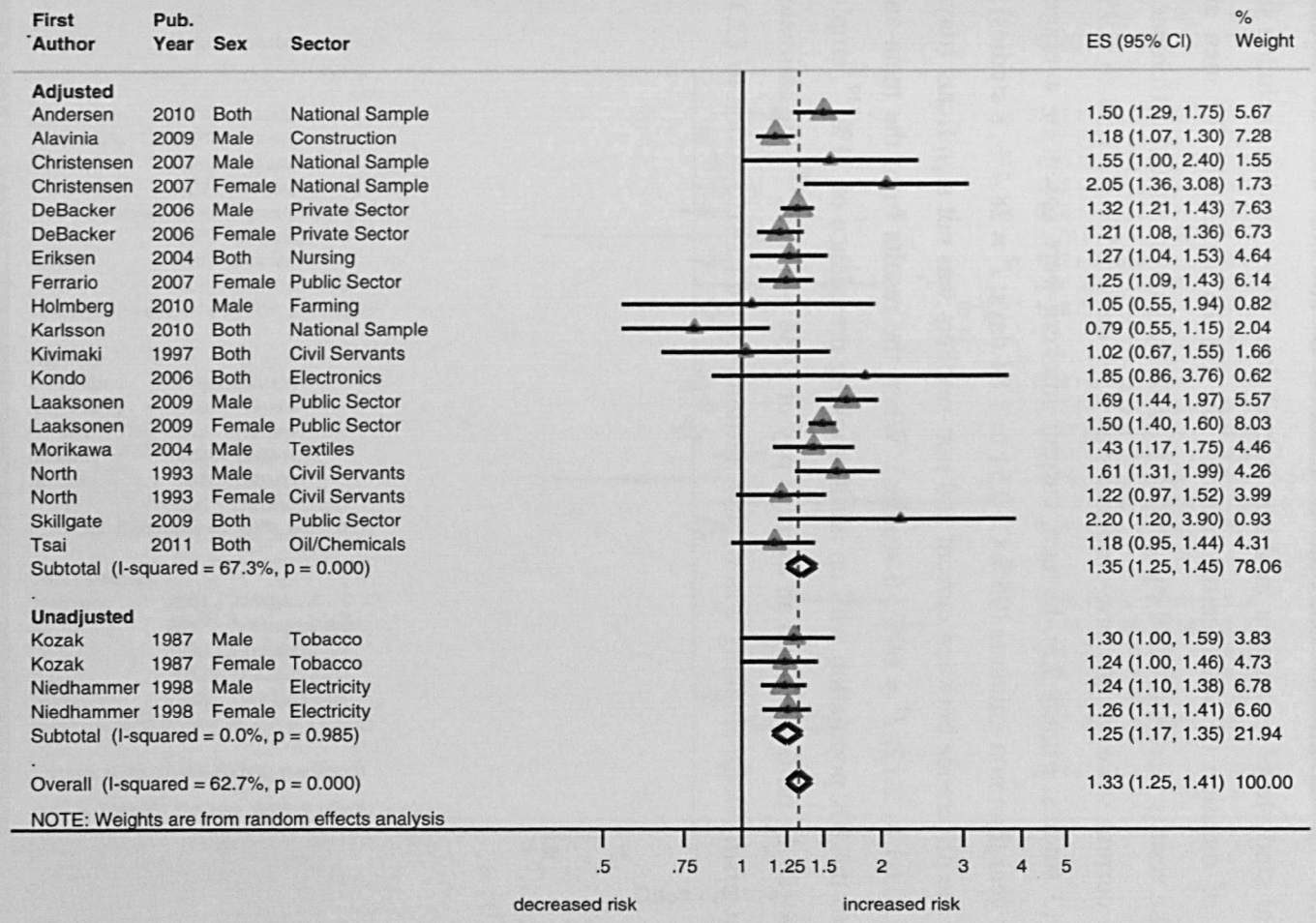
4.4.3 Current smokers versus non-smokers

4.4.3.1 Risk of absenteeism

Seventeen studies[310 311 314-317 320 323-327 330-332 334 335] compared the risk of work absenteeism for current smokers; of which 8 studies[314 315 317 327 330 331 334 335] compared the risk between current smokers and never smokers and 9 studies[310 311 316 320 323-326 332] compared the risk between current smokers and non-smokers (including ex-smokers). The follow-up duration ranged from 3 months[316] to 144 months[320] with a median duration of 24 months. There were 71,516 workers in the sample with an over-representation of men (60%) compared to women (40%). To test for the overall effect of current smoking, never smokers and non-smokers were combined in a single "non-smoking" group. The pooled meta-analysis showed that current smokers were 33% more likely to take work absence than non-smokers (RR = 1.33, 95% CI 1.25 to 1.41; $I^2 = 62.7\%$; 17 studies; **Figure 12**). When meta-analysis was stratified based on whether or not study-level covariates such as age, sex and lifestyle factors were adjusted for, the pooled estimates were similar to the overall relative risk (adjusted RR = 1.35 [95% CI: 1.25 to 1.45]; unadjusted RR = 1.25 [95% CI: 1.17 to 1.35]).

In the subgroup of 8 studies comparing the risk of absence between current and never smokers, almost identical results (RR = 1.36, 95% CI 1.27 to 1.47; $I^2 = 68\%$; 8 studies) to the overall analysis comparing the risk between current and non-smokers were obtained.

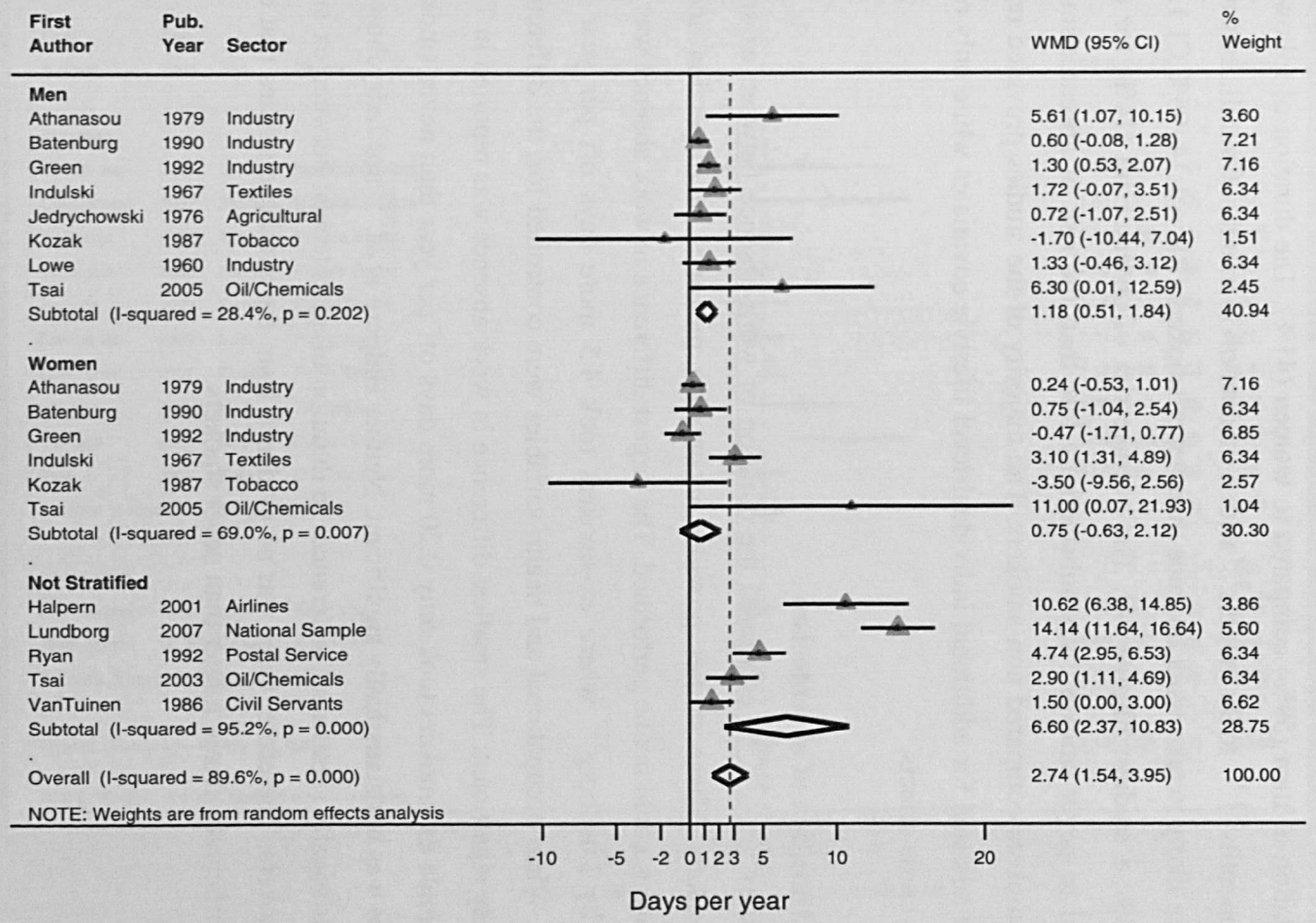
Figure 12. Pooled relative risk (RR of absence from work and 95% confidence interval (CI) of current smokers compared to non-smokers stratified by adjusted and unadjusted study-level characteristics



4.4.3.2 Duration of absenteeism

Thirteen studies[312 313 318 319 321 322 326 328 329 333 336-338] compared the duration of work absence between current smokers and non-smokers. There were a total of 30,978 workers in these studies. The follow-up duration ranged from 3 months[319] to 120 months[336] with a median of 24 months. The continuous outcome of duration of absence was not adjusted for any additional study-level covariates in the extracted data. Most studies included in the meta-analysis of duration of absenteeism reported the results separately for men and women; hence, the results were stratified by gender. The overall mean annual difference in absence between current smokers and non-smokers was 2.74 days (95% CI 1.54 to 3.95 days; I^2 = 89.6%; 13 studies; **Figure 13**). In men, current smokers were absent on average 1.18 more days per year than non-smokers (95% CI 0.51 to 1.84 days; I^2 = 28.4%; 8 studies); whereas in women, the difference between current and non-smokers was not significant (days/yr = 0.75; 95% CI -0.63 to 2.12; I^2 = 69%; 6 studies). When the results from the meta-analysis were applied to the UK population with an adult smoking prevalence of 21%[339], employment rate of 70.5% (29.17 million)[190] and an average pay of £434 per week[190], the estimated total cost of absenteeism due to smoking was £1,457 million (95% CI £819 million to £2,100 million) in 2011.

Figure 13. Pooled mean difference in absence (days per year) from work and 95% confidence interval (CI) of current smokers compared to non-smokers stratified by sex



4.4.4 Ex-smokers versus never smokers

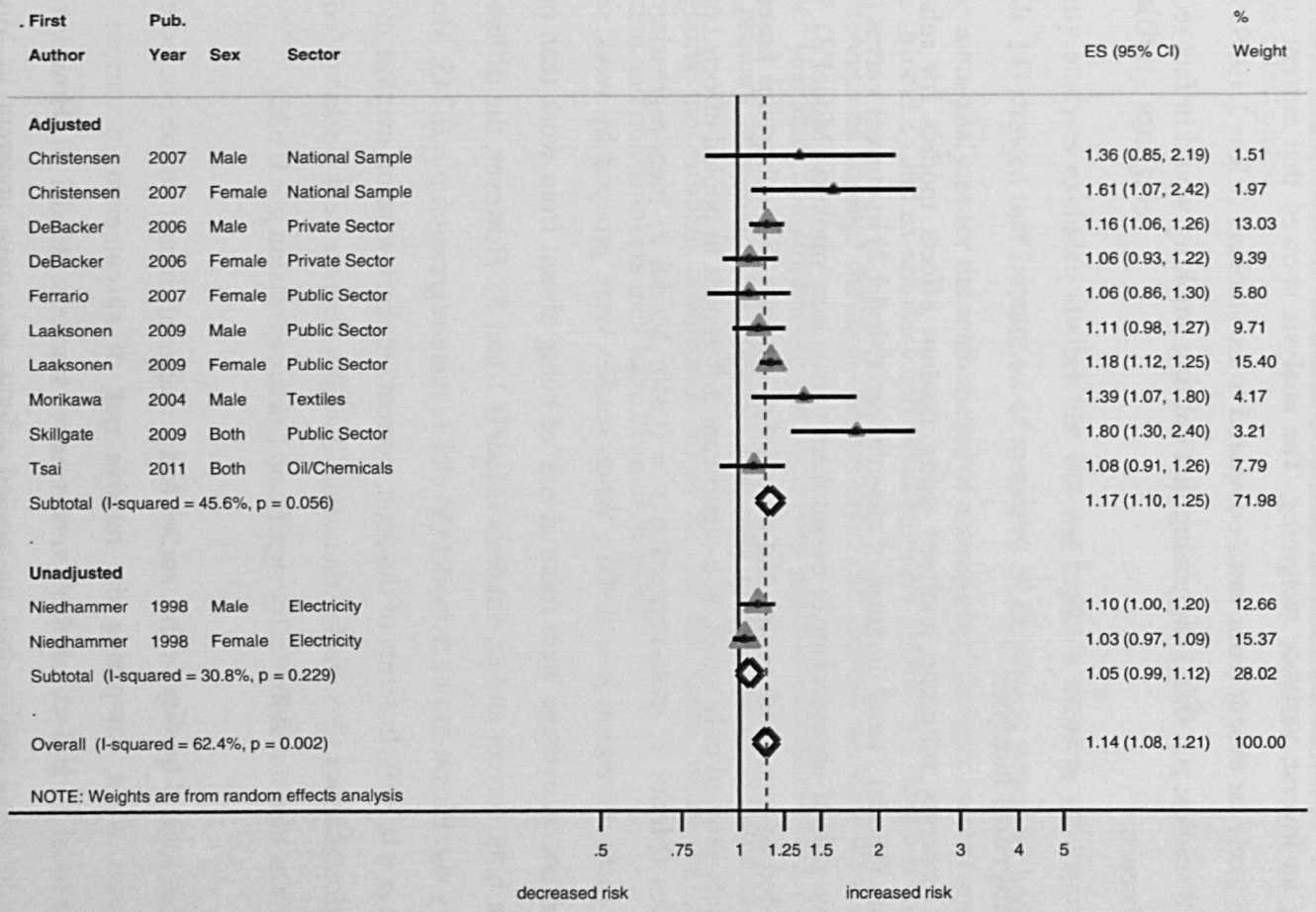
4.4.4.1 Risk of absenteeism

Eight studies[314 315 317 327 330 331 334 335] compared the risk of absenteeism for ex-smokers and never smokers comprising a total pooled sample of 48,645 workers with an over-representation of men (59%) compared to women (41%). The duration of follow-up ranged from 12 months[315 331] to 96 months[330] with a median of 30 months. Overall, ex-smokers were 14% more likely to take work absence than never smokers (RR = 1.14, 95% CI 1.08 to 1.21; I^2 = 62.4%; 8 studies; **Figure 14**). The average risk of absenteeism (14%) for ex-smokers compared to never smokers was substantially less than the risk of absenteeism (33%) for current smokers compared non-smokers. The majority of the studies provided relative risks that were adjusted for additional individual-level lifestyle covariates while only one study[331] provided crude effects.

4.4.4.2 Duration of absenteeism

Four studies[319 322 329 336] compared the duration of work absence between ex-smokers and never smokers. These studies provided incomplete measures of dispersion and therefore meta-analysis could not be performed. The largest difference in work absence was reported in a study by Lundborg[329] where ex-smokers took 4.5 more days off per year than never smokers. When occupational and health variables were controlled for, the difference was not statistically significant. The smallest difference in work absence was reported in Tsai *et al.*[336] where female ex-smokers took only 0.20 more days off per year than never smokers but the difference was not statistically significant. Neither Halpern *et al.*[319] nor Jedrychowski *et al.*[322] found statistically significant differences in duration of absenteeism between ex-smokers and never smokers. Therefore, there was no evidence from the available studies that ex-smokers were significantly absent longer than never smokers.

Figure 14. Pooled relative risk (RR) of absence from work and 95% confidence interval (CI) of ex-smokers compared to never smokers stratified by adjusted and unadjusted study-level characteristics



4.4.5 Current smokers versus ex-smokers (indirect comparison)

By using the meta-analyses comparing current smokers to never smokers (RR = 1.36, 95% CI 1.27 to 1.47; I^2 = 68%; 8 studies) and ex-smokers to never smokers (RR = 1.14, 95% CI 1.08 to 1.21; I^2 = 62.4%; 8 studies), indirect comparison meta-analysis was conducted (**Appendix 9.9**) using an inverse variance weighting. The analysis showed that current smokers were 19% more likely be absent from work compared to ex-smokers (RR = 1.19, 95% CI 1.09 to 1.32; n = 8 studies; $p < 0.01$) suggesting that quitting smoking would in fact reduce the risk of work absence.

4.4.6 Subgroup analysis

Table 14 presents subgroup analyses using random effects models for relative risk of absenteeism (Model 1) and duration of absenteeism (Model 2) in current versus non-smokers and relative risk of absenteeism in ex-smokers versus non-smokers (Model 3). The analysis was stratified by sex, work sector and duration of absence. For subgroups based on sex, all three models showed only small, non-significant differences in pooled effects between males and females (Model 1: meta-regression p = 0.940; Model 2: meta-regression p = 0.431; Model 3: meta-regression p = 0.906). When studies were grouped by work sector, public sector workers on average were more at risk of being absent from work than private sector workers in both current and ex-smokers (Models 1 and 3). However, the difference was not statistically significant in either model (Model 1: meta-regression p = 0.745; Model 3: meta-regression p = 0.709). In terms of duration, current smokers were on average more at risk of long-duration absence (≥ 4 weeks) than short-duration absence (< 4 weeks) (Model 1) but the difference was also not statistically significant (meta-regression p = 0.632).

The methodological quality of the studies had a marginal impact on the pooled effects of the meta-analyses when comparing the relative risk of absenteeism in current versus non-smokers (Model 1) and ex-smokers versus never smokers (Model 3). However, the impact that methodological quality had on pooled effects was most apparent in Model 2 when comparing the duration of absence between current and non-smokers. For the selection domain of the quality assessment, the average difference in pooled effects between studies with high scores and studies with low scores was 2.42 days per year (meta-regression p = 0.406). For the comparability domain, the average difference in pooled effects between

studies with high scores and studies with low scores was 2.67 days per year (meta-regression p = 0.401). In terms of the ascertainment domain, the average difference in pooled effects between studies with high scores and studies with low scores was 3.52 days per year (meta-regression p = 0.133). Overall, the analysis in Model 2 showed that low quality studies may have biased the average estimates downwards as high quality studies tended to demonstrate much stronger effect sizes.

4.4.7 Sensitivity analysis

The sensitivity analysis excluded studies that did not report a measure of dispersion. The results (**Table 14**) showed that imputation of measures of dispersion generally had marginal effects on the meta-analyses for the relative risk of absenteeism between current smokers and non-smokers (Model 1) and ex-smokers and never smokers (Model 3). However in Model 2, the mean difference of absence duration demonstrated that current smokers were absent 3.3 more days per year than non-smokers in the sensitivity analysis (compared to 2.74 days per year in the primary analysis). This suggests that data imputation procedures had a small impact weighting the estimate downwards when in fact the mean difference in absence between current and non-smokers may have been even greater.

Table 14. Summary relative risk ratios from primary and stratified random effects meta-analyses between smoking and absenteeism

Stratification	Pooled Effect Size		Heterogeneity	
Model 1: Current vs. Non-smokers	***Relative Risk of absenteeism***	***95% Confidence Interval***	***No. of studies***	I^2
Primary analysis	1.33	1.25, 1.41	17	62.7%
Sex				
Male	1.36	1.24, 1.49	9	62.2%
Female	1.32	1.19, 1.45	7	70.4%
Non-stratified	1.26	1.05, 1.52	7	63.6%
Work sector				
Private	1.25	1.20, 1.31	7	0.0%
Public	1.41	1.27, 1.57	6	62.8%
Unclassified	1.34	1.11, 1.62	4	67.1%
Type of absence				
Short (< 4 wks)	1.33	1.16, 1.52	4	91.2%
Long (≥ 4 wks)	1.55	1.37, 1.77	4	23.1%
Undefined	1.31	1.27, 1.43	13	62.3%
Selection				
High (≥ 3)	1.42	1.29, 1.56	6	66.2%
Low (< 3)	1.27	1.19, 1.36	11	43.2%
Comparability				
High (= 2)	1.33	1.23, 1.45	13	70.7%
Low (< 2)	1.30	1.21, 1.38	4	6.1%
Ascertainment				
High	1.40	1.29, 1.52	9	70.6%
Low	1.25	1.17, 1.33	8	12.4%
*Sensitivity analysis**	1.38	1.27, 1.50	12	70.7%
Current vs. never	1.36	1.27, 1.47	8	68.0%
Model 2: Current vs. Non-smokers	***Mean difference (days per yr)***	***95% CI***	***No. of studies***	I^2
Primary analysis	2.74	1.54, 3.95	13	89.6%
Sex				
Male	1.18	0.51, 1.84	8	28.4%
Female	0.75	-0.63, 2.12	6	69.0%
Non-stratified	6.60	2.37, 10.83	5	95.2%
Selection				
High	4.48	-0.13, 9.09	3	97.2%
Low	2.06	0.99, 3.13	10	78.1%
Comparability				
High	4.83	-0.72, 10.37	2	98.1%
Low	2.16	1.17, 3.16	11	76.4%
Ascertainment				
High	5.04	1.52, 8.57	6	93.7%
Low	1.52	0.59, 2.45	7	76.8%
*Sensitivity analysis**	3.30	1.51, 5.09	8	92.7%
Model 3: Ex- vs. Never smokers	***Relative Risk of absenteeism***	***95% CI***	***No. of studies***	I^2
Primary analysis	1.14	1.08, 1.21	8	62.4%
Sex				
Male	1.14	1.08, 1.21	5	0.0%
Female	1.11	1.01, 1.22	5	73.3%
Non-stratified	1.37	0.83, 2.26	2	88.0%
Work sector				
Private	1.10	1.03, 1.16	4	55.8%
Public	1.23	1.09, 1.39	4	45.6%
Unclassified	--	--	--	--
Selection				
High	1.14	1.04, 1.25	3	80.1%
Low	1.15	1.06, 1.24	5	21.8%
Comparability				
High	1.16	1.09, 1.24	6	45.7%
Low	1.10	0.99, 1.22	2	64.8%
Ascertainment				
High	1.17	1.08, 1.27	6	70.0%
Low	1.12	1.05, 1.20	2	0.0%
*Sensitivity analysis**	1.18	1.10, 1.27	6	49.0%

*Only included studies with reported measures of dispersion

4.4.8 Publication bias

No significant evidence of publication bias was found in the meta-analyses for the relative risk of absenteeism between current smokers and non-smokers (**Figure 15**; Egger's asymmetry test, $p = 0.951$); the mean difference in absenteeism between current smokers and non-smokers (**Figure 16**; Egger's asymmetry test, $p = 0.132$); and the relative risk of absenteeism between ex-smokers and never smokers (**Figure 17**; Egger's asymmetry test, $p = 0.104$).

Figure 15. Funnel plot of the log relative risk of absence and corresponding standard error between current smokers and non-smokers

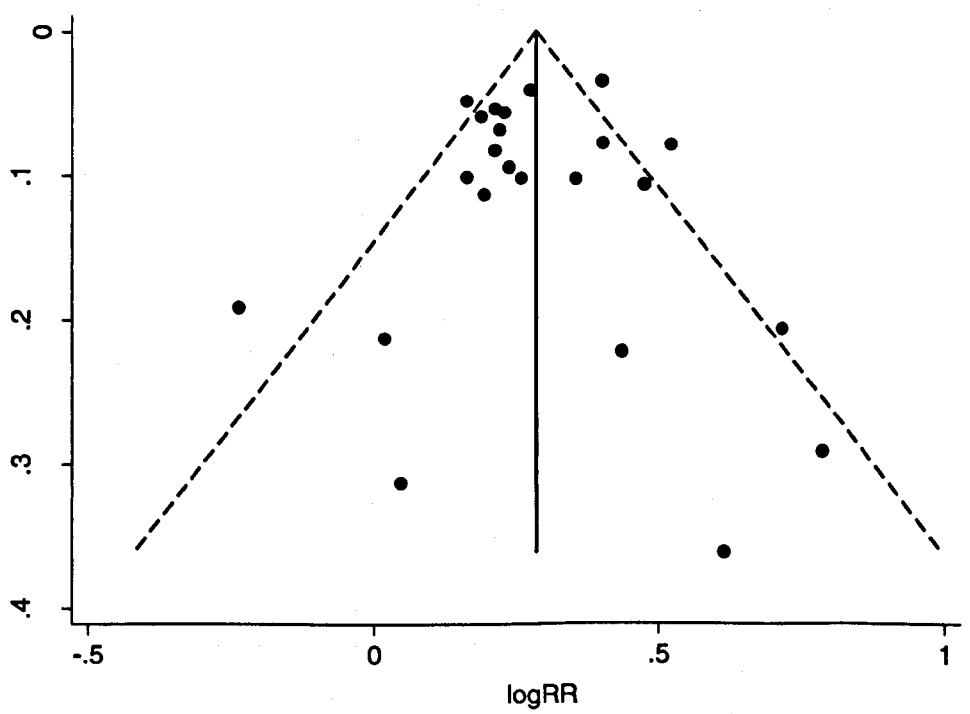


Figure 16. Funnel plot of the mean difference of absence and corresponding standard error between current smokers and non-smokers

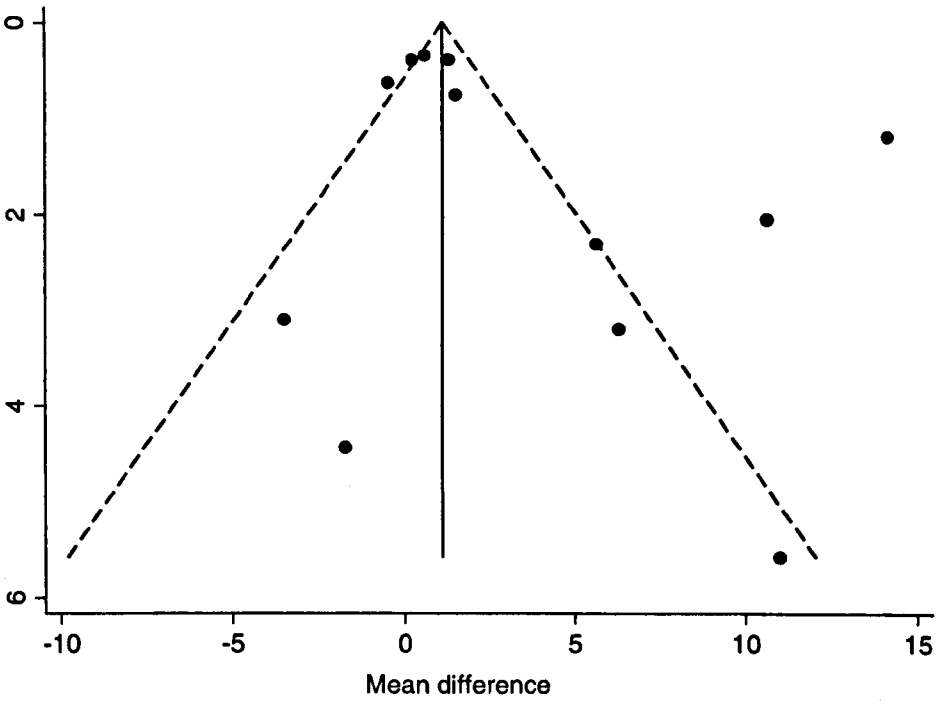
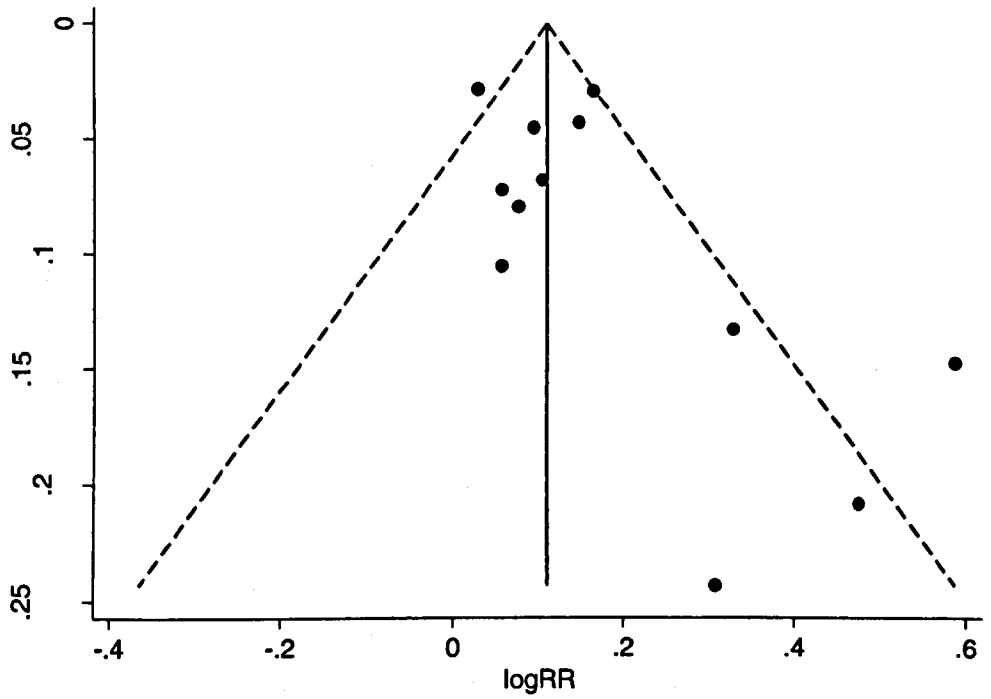


Figure 17. Funnel plot of the log relative risk of absence and corresponding standard error between ex-smokers and never smokers



4.5 Discussion

4.5.1 Summary of findings

There was consistent evidence from this systematic review and meta-analysis that smoking increased both the risk and duration of work absenteeism. This is the first systematic review assessing the impact of smoking on the risk and duration of absenteeism. In current smokers, the risk of work absenteeism was 33% greater than that of non-smokers. In terms of the duration of absence, current smokers were absent 2.74 days per year more than non-smokers. For ex-smokers compared to never smokers, the relative risk of absenteeism was 14% higher. For the mean duration of absence in ex-smokers compared to never smokers, there were only four studies available. There was no evidence in those four studies that smoking was significantly associated with absenteeism. The average number of days absent per year ranged from 0.2 days to 4.5 days but the study effects could not be pooled due to incomplete parameters. By comparing current smokers to ex-smokers indirectly, the relative risk of absenteeism was found to be 19% higher. Overall, the results were conservative in nature as quality assessment and sensitivity analysis showed that low quality studies and data imputations procedures weighted the pooled effect size downwards, suggesting that the strength of association between smoking and risk or duration of absenteeism may in fact be stronger.

4.5.2 Exploration of heterogeneity

High levels of heterogeneity ($I^2 > 60\%$) were generally seen in the meta-analyses as the studies differed in time periods, geographic location and population demographics. Additional reasons for heterogeneity were explored through further subgroups presented. When workers were stratified by sex, the relative risk and duration of absenteeism due to smoking were similar in men and women. Public sector workers had on average higher risk of absenteeism than private sector workers; however, the result was not statistically significant at the 5% level. The lack of significance could be due to a lack of power in the meta-regression analysis from a limited number of studies. A survey of 241 public and private sector organisations[340] found that absence was on average 2.5 days higher in the public sector than in the private sector. One of the reasons suggested was that public sector employees were in more challenging public-facing roles such as social work, policing, teaching and nursing where they often have to deal with people in difficult and emotionally

charged situations, putting pressure on their time and resilience.[341] Another reason may be that public sector workers have better job security than private sector workers. While the results were not statistically significant, there may be some indication to support the survey literature suggesting public sector workers on average were more at risk of absence.

Compared to non-smokers, current smokers were on average at higher risk of taking longer durations of absence than shorter durations. However, this result was not statistically significant. Again, this lack of statistical significance could be due to a lack of power in the meta-regression as there were only four outcomes[310 317 327 332] that could be classified as short-duration and four outcomes[310 314 327 334] that could be classified as long-duration. In many of the included studies in the review, the reason for long-term absence was consistently due to chronic health problems while the reasons for short-term absence were due to short-term illness. Many of the smokers in the sample were persistent long-term smokers. Health problems related to smoking tend to be long-term and chronic conditions such as COPD and CVD where illness periods were longer and more frequent. This is further supported by a 19-year follow-up study in Finland which estimated that the smoking resulted in 2.6 productive work-years lost per person due to smoking-related chronic health problems.[182]

4.5.3 Implications

The results of this study suggest that smoking cessation in the workplace could potentially result in cost savings for employers from reduced absenteeism. Using the results of the meta-analyses, smoking was estimated to cost UK employers on average £1.46 billion in 2011 from absenteeism in the workplace. This large economic impact of smoking on absenteeism suggests that there is potentially great value in workplace smoking cessation programmes. This view is supported in several cost-of-smoking studies.[89 237 251 342]

There have been two systematic reviews[343 344] that have explored the impact of smoking cessation interventions in the workplace. A review of 22 prospective studies on the impact of work environment on smoking cessation by Albertsen *et al.*[343] found that highly demanding jobs were associated with higher amount smoked while social support at work was positively associated with cessation. In addition, a Cochrane Review by Cahill *et al.*[344] of 51 quasi-randomised controlled trials evaluated workplace interventions and found strong evidence that interventions directed towards individual smokers (such as individual or group

counselling and pharmacological treatment) increased the likelihood of quitting more than unassisted, self-help or social support interventions alone.[344] In both these reviews, the general conclusion was that workplace interventions aided employees to quit smoking. The number of quitters could be potentially increased by improving awareness of the workplace programmes. In order to improve quit rates, it would be necessary to increase participation by providing easier access and raising awareness of successful forms of workplace smoking cessation interventions.

4.5.4 Limitations

There were some limitations of the systematic review. The review found no significant evidence of publication bias in any of the meta-analyses; however some visual evidence of asymmetry was seen in the funnel plots. Asymmetry in the funnel plots could have been a result of poor methodological quality of the studies rather than publication bias.[345]
Furthermore, there were only a limited number of studies which had reported results by sub-groups, thus limiting the power of the subgroup analysis. As a result, meta-regression did not detect significant differences between gender subgroups, absence duration subgroups, work sector subgroups or quality assessment subgroups at the 5% level. This was most noticeable in quality assessment subgroups in Model 3 where the average pooled effects resulted in large effect sizes but wide 95% confidence intervals.

There were also limitations in terms of the quality of evidence and design of studies identified in the systematic review. Cohort studies may be the best type of evidence in terms of observational studies but some studies were subject to a high risk of attrition bias and confounding. A few of the studies experienced higher attrition rates and lacked description of those lost to follow-up. Many of these studies were retrospective and limited to what information was collected at the time. Some multivariate models included many covariates (e.g. demographics, lifestyle, health, work-related variables) and others included only a few (e.g. age and sex).

Additionally, relative risks ratios were computed from odds ratios in several studies for the meta-analysis using a common transformation method; however, this is known to overstate significance levels when outcomes are common.[346] Finally, there were seven studies which had old publication dates (1950-1970) where access full-text articles in print or electronic

form was unavailable. Several of these papers were in journals that have stopped circulation and contact with the study authors was not achievable. These studies presented findings within the range of the pooled results in this chapter and were unlikely to have a substantial impact on the pooled results due to small sample sizes.

4.6 Conclusion

The systematic review found that smoking increases both the risk and duration of absenteeism. Current smokers were on average 33% more likely to be absent from work than non-smokers. When current smokers did take absence, they were absent on average 2.74 more days per year than non-smokers. Ex-smokers were also on average 14% more likely to be absent from work than never smokers. There was no evidence to suggest there was a significant difference in duration of absence between ex-smokers and never smokers. Using an indirect comparison, current smokers were on average 19% more likely to be absent from work than ex-smokers. The increased risk and duration of absence was estimated to cost UK employers on average £1.46 billion in 2011. The results of this systematic review implicate that quitting smoking may reduce absenteeism and result in substantial cost-savings for employers.

Chapter 5

Validation of UK indirect cost estimates using population-level indirect cost-of-smoking studies

5.1 Introduction

One of the primary limitations of cost-of-illness studies is that there are no obvious methods in which to validate the cost estimates. This is due to methodological heterogeneity as described in **Chapter 2**. Whilst published guidance[347-349] has provided a conceptual framework for cost-of-illness methodology, many studies suffer from conceptual deficiencies and lack transparency in reporting. Most cost-of-smoking studies use some variant form of the 1960s framework[347] of combining 'direct' costs of medical care with 'indirect' costs of lost production from reduced working time. The differences in methodology were apparent in the 17 indirect cost-of-smoking studies identified in **Chapter 2**. Despite this, there was some degree of consistency across the studies. In **Chapter 2**, it was hypothesized smoking prevalence was directly proportional to indirect costs across populations. The ecological relationship between smoking prevalence and indirect cost was tested and found to be significant. The significant association was not surprising because in spite of methodological heterogeneity, prevalence was in fact the primary driver of all 17 cost-of-smoking studies. The multiplicative effects of individual-level costs (i.e. lost productive life years, absenteeism) were propagated to population-level estimates by the degree of smoking within a population. In other words, the greater the number of people in a population who smoke the more indirect costs the population incurs.

Chapter 2 also identified the primary components of indirect costs. The two major contributors to indirect costs were foregone income due to productive life lost and absenteeism from work. This was the rationale for quantifying the indirect costs of foregone income due to productive life lost (**Chapter 3**) and indirect costs of absenteeism from work (**Chapter 4**). The results in those chapters showed that smoking resulted in £4.93 billion in foregone income due to productive life lost and £1.46 billion in absenteeism in the UK in 2010-2011. These two primary components of indirect costs totalled £6.39 billion in 2010-2011.

5.2 Aims and Objectives

In this chapter, the aim was to validate the calculated indirect costs of smoking in the UK. The aim was achieved by completing the following objectives:

- Derive regression equations from the ecological analysis of 17 population-level cost-of-smoking studies identified in **Chapter 2.**
- Include the thesis estimate of indirect costs into the ecological regression analysis
- Compare the predicted indirect cost estimate to the observed indirect cost estimate

5.3 Methods

The methodology for validating the UK indirect cost estimate involved transforming the UK indirect cost estimate to reflect the common US dollar currency in the base-year of 2010 similar to the methods used in **Chapter 2.** Since the UK cost estimate reflected the year 2010-2011, it was not necessary to inflate the amount by the labour cost index. The combined indirect cost of £6,387,550,000 in foregone income from productive life lost (**Chapter 3**) and absence from work (**Chapter 4**) was first converted to indirect cost per capita. From a UK population of 62,231,336 in 2010[203], the indirect cost-per-capita was calculated to be £102.64. This value then had to be exchange rate adjusted to US dollars to coincide with the regression analysis in **Chapter 2** in which the cost estimates were based on 2010 US dollars. Using the 2010 annual dollar to pound exchange rate of 1.55 (USD:GBP) provided by the IMF[207], the indirect cost per capita was converted to $159.10 USD. Subsequently, the exchange rate adjusted indirect cost per capita was compared to the indirect cost per capita derived from published studies in **Chapter 2.**

Regression analysis was conducted on smoking prevalence in the study year and indirect cost per capita with the inclusion of the UK estimate. Previously in **Chapter 2,** the 'best-fit' logarithmic model was specified using stepwise regression analysis for the multivariate association between smoking prevalence and indirect cost per capita. The results of that particular analysis included the covariate of GDP per capita and found that a 1% increase in smoking prevalence resulted in a 1.7% (95% CI 0.21 to 3.16, p = 0.028) increase in cost per capita across all studies and a 2.1% (95% CI 0.46 to 3.81, p = 0.017) increase in cost per capita across human capital model studies only. The results of this regression analysis yielded two logarithmic functions:

Function 1. All studies (17 studies):

$$Ln(CostperCapita) = 1.69 * Ln(Prevalence) + 0.59 * Ln(GDPperCapita) - 6.66$$

Function 2. Human capital studies (15 studies):

$$Ln(CostperCapita) = 2.13 * Ln(Prevalence) + 1.35 * Ln(GDPperCapita) - 0.38 * Ln(Unemployment\ Rate) - 14.76$$

Using the logarithmic functions, a predicted logarithmic value of indirect cost per capita could be calculated using the log of smoking prevalence, log of GDP per capita and log of the unemployment rate (human capital studies only). To predict indirect cost per capita in the UK, the smoking prevalence of 20%[7], GDP per capita (2010) of USD $36,356[203] (£25,886) and annual (2010) unemployment rate of 7.8%[350] were substituted in the logarithmic functions. The predicted indirect cost per capita for the UK was then back-transformed from the logarithmic scale to reflect the monetary amount:

Function 3. All studies (17 studies):

$$CostperCapita = \exp[1.69 * Ln(Prevalence) + 0.59 * Ln(GDPperCapita) - 6.66]$$

Function 4. Human capital studies (15 studies):

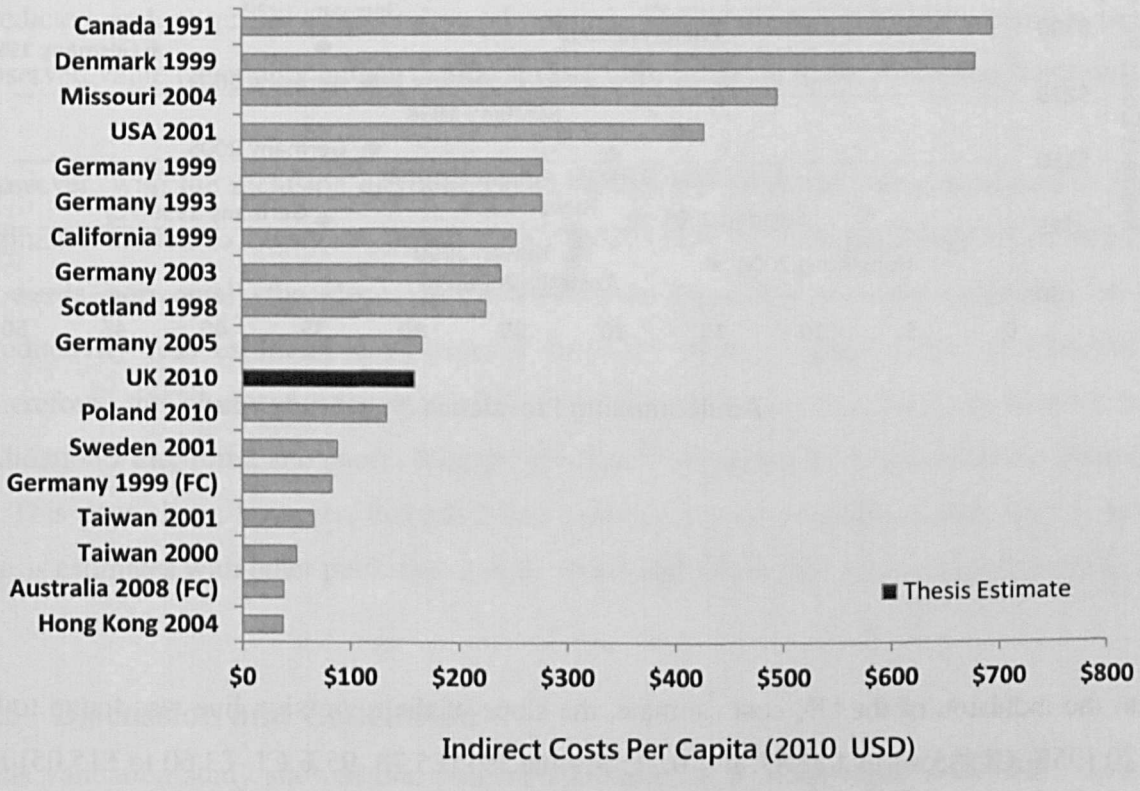
$$CostperCapita = \exp[2.13 * Ln(Prevalence) + 1.35 * Ln(GDPperCapita) - 0.38 * Ln(Unemploymen\ Rate) - 14.76]$$

The predicted monetary values were then compared to the observed indirect cost-per-capita amount for the UK of $159.10 USD (£102.64).

5.4 Results

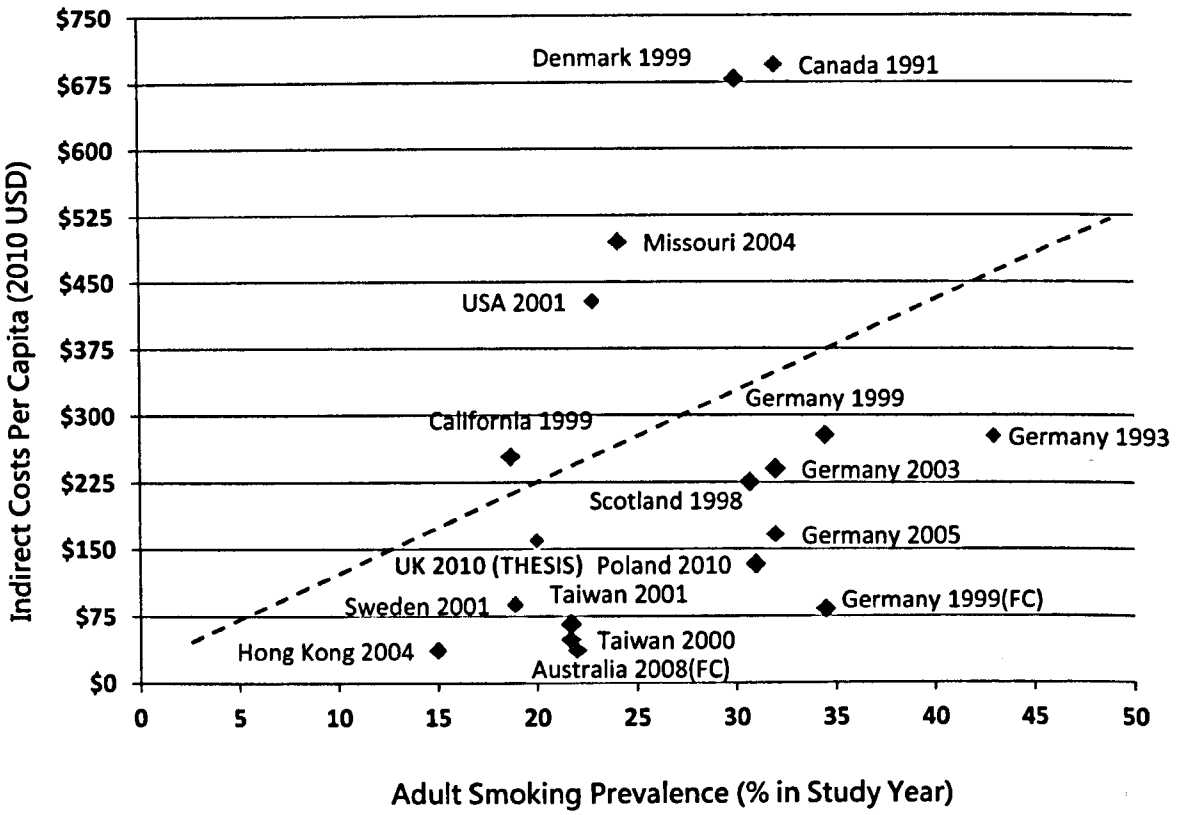
When compared to other studies, the indirect cost per capita due to smoking for the UK in 2010 reflected the lower half of the cost spectrum as shown in **Figure 18**.

Figure 18. Comparison of indirect costs per capita due to smoking inflated to 2010 US dollars by location



This was due to the UK adult smoking prevalence of 20% in 2010 was below the median prevalence rate of 27% among all studies. Since smoking prevalence was the primary driver of the estimates and it was not surprising the UK cost estimate for the most part was less than that of populations with higher smoking prevalence. The ecological relationship between indirect cost per capita and smoking prevalence was examined using a regression model (**Figure 19**).

Figure 19. Ecological relationship between smoking prevalence and indirect cost per capita for population-level studies



With the inclusion of the UK cost estimate, the slope of the regression line was found to be \$8.70 (95% CI -\$5.44 to \$22.83, $p = 0.21$; **Figure 19**) [£5.73, 95% CI -£3.60 to £15.05] for every 1% increase in adult smoking prevalence. In **Chapter 2**, without the inclusion of the UK cost estimate, the slope of the regression line was found to be \$8.57 (95% CI -\$6.60 to \$23.59, $p = 0.24$; **Figure 6**) [£5.62 95% CI -£4.33 to £15.48] for every 1% increase in adult smoking prevalence. The inclusion of the UK cost estimate only slightly changed slope of the regression line. In addition, the estimate seemed was consistent with other population-level cost estimates seen visually in **Figure 19**. Similar to the association found in **Chapter 2**, there seemed to be an overall positive relationship between adult smoking prevalence and cost per capita; however, this relationship was not linear, nor statistically significant. Therefore, logarithmic transformations were used for the validation functions.

By substituting the 2010 UK adult smoking prevalence of 20%, 2010 GDP per capita of $36,356 USD (£25,886) and 2010 unemployment rate of 7.8% into the logarithmic functions provided in the methods, the predicted value of indirect cost for the UK could be estimated. Using regression function derived from all studies (**Function 1** and **Function 3**), the predicted cost per capita was $99.33 USD (£65.47). When the regression function derived only from human capital model studies was used (**Function 2** and **Function 4**), the predicted cost per capita was $150.93 USD (£99.49). When the predicted costs were compared to the observed cost per capita of $159.10 USD (£102.64), there was a 5% difference between predicted and observed costs across human capital studies and a 34% difference between predicted and observed costs across all studies. The predicted value was similar to the observed value when only human capital studies were included in the prediction function.

However, with the inclusion of friction cost studies, the predicted value decreased as these estimates tended to be more conservative. The friction cost estimates negatively affected (towards horizontal) the slope of the prediction line. This was not surprising as the productivity loss estimates were derived from the human capital model in **Chapter 3**. Therefore, the observed values converged well with the predicted values derived from validation **Function 2** and poorly with the predicted values derived from validation **Function 1**. This does show, however, that there was some degree of consistency and validity in the thesis estimates with other published studies which had utilised the human capital method.

5.5 Discussion and Conclusion

This validation study showed that cost methodology used in this thesis provided a level of consistency and validity when compared to other published studies which had used the human capital method. This study employed an ecological approach to validate the UK cost estimates. The main limitation of this approach was that there was no method of incorporating the effects of methodological heterogeneity into the regression analysis. A random-error term could have been included in the regression analysis to try to capture differences among studies; however, there were doubts regarding whether the methodological heterogeneity was completely random. All the included studies used variant forms of prevalence-based approaches to estimate indirect costs. Dummy variables were also considered to group potentially similar studies; however, the analysis lacked power due to the limited number of studies. Furthermore, no clear, defensible grouping of the studies could be

made. Finally, weighting the cost outcomes by the number of cost components was considered but this process only decreased the predictability of the model. Thus, the final model chosen was based on the log-log transformation function between smoking prevalence and indirect cost per capita with one covariate (GDP per capita) for all studies and two covariates for human capital studies (GPD per capita and unemployment rate). Ultimately, this approach provided the 'best-fit' model suitable for validation.

Chapter 6

Economic evaluation of workplace smoking cessation interventions: Markov model from the employer's perspective

6.1 Introduction

On the basis of current consumption patterns, 450 million adults will be killed by smoking between 2000 and 2050 where over half of these deaths will occur between the ages of 30 and 69 years losing years of productive life.[4] The analysis in **Chapter 3** found smoking was responsible for 96,105 deaths (17% of all deaths of adults aged 35 and over) in the UK in 2010. As many of these deaths come prematurely during working years, this creates a large economic burden in terms of loss of productive life years. The cost-of-smoking study conducted in **Chapter 3** showed that smoking cost the UK economy £4.93 billion in foregone income due to productive life lost. Smoking has also been established to be associated with a higher probability of absenteeism from work. The systematic review conducted in **Chapter 4** found that smokers were estimated to have 33% more risk of being absent from work than non-smokers due to sick leave and absent on average 2.74 days a year more than non-smokers, costing UK employers £1.46 billion per year. When the cost of smoking to the NHS (£5.2 billion)[87], costs to the employers due to absenteeism (£1.46 billion)[351] and costs of foregone income due to productive life lost (£4.93 billion)[6] are combined, the cost to the society from these components alone was estimated to be £11.6 billion in 2010-2011.

The large economic burden suggests that smoking cessation would lead to fewer lives lost, fewer productive years lost, less foregone income and fewer absences at work resulting in large cost-savings for both employers and the wider society. A potential solution is for employers to adopt smoking cessation interventions in the workplace. Previous systematic reviews[352 353] have found there is strong evidence that interventions directed towards individual smokers increase the likelihood of quitting smoking including advice from a health professional, individual and group counselling and pharmacological treatment. It has been established that smoking cessation interventions are cost-effective[266 354 355] for increasing life years or quality adjusted life years (QALYs) in individuals. However, previous studies have only taken a health service perspective on costs and outcomes. In order for employers to adopt smoking cessation interventions, any proposed model must analyse the cost-benefits from a firm's perspective to maximise profits and minimise absenteeism-related costs (including labour turnover, disability and mortality) by increasing quit rates in the workforce. These costs have been established in well-known business surveys[356-358] as contributing significantly to operating expenses.

Cost-benefit analysis is commonly used to measure all positive or negative consequences of interventions including the effects on users and non-users, externality effects and other social benefits. The analysis in this chapter measures the positive and negative consequences of the smoking cessation interventions with regards to the employer and employees. This is technically a cost-offset analysis because this analysis does not measure the effects on non-users, externality effects and other social benefits. However, the analysis retains the cost-benefit terminology due to it being commonly used in reporting monetary outcomes for costs and benefits in evaluating investment decisions.

6.2 Aims and Objectives

The aim of this chapter was to conduct a cost-benefit analysis of several common workplace smoking cessation interventions from the employer's perspective for minimising costs and maximising returns on investment. A secondary aim was to conduct cost-effectiveness analysis of workplace smoking cessation interventions if the employer valued maximising quitting instead. The aims were achieved by completing the following objectives:

- Develop the decision analytic framework for comparing cost-benefits and cost-effectiveness of workplace interventions from the employer's perspective: no intervention, brief advice, individual counselling, individual counselling with nicotine replacement therapy (NRT)
- Construct a Markov model to simulate a cohort of workers taking into account smoking cessation interventions, smoking status, absenteeism, labour turnover, death and disability
- Conduct deterministic analysis to obtain total costs incurred and return on investment
- Conduct probabilistic sensitivity analysis taking into account parameter uncertainty
- Conduct additional sensitivity analysis on costs and alternate discount rates
- Re-sample the Markov model using cost-effectiveness analysis to determine the employer's optimal smoking cessation strategy for maximising quitting

6.3 Methods

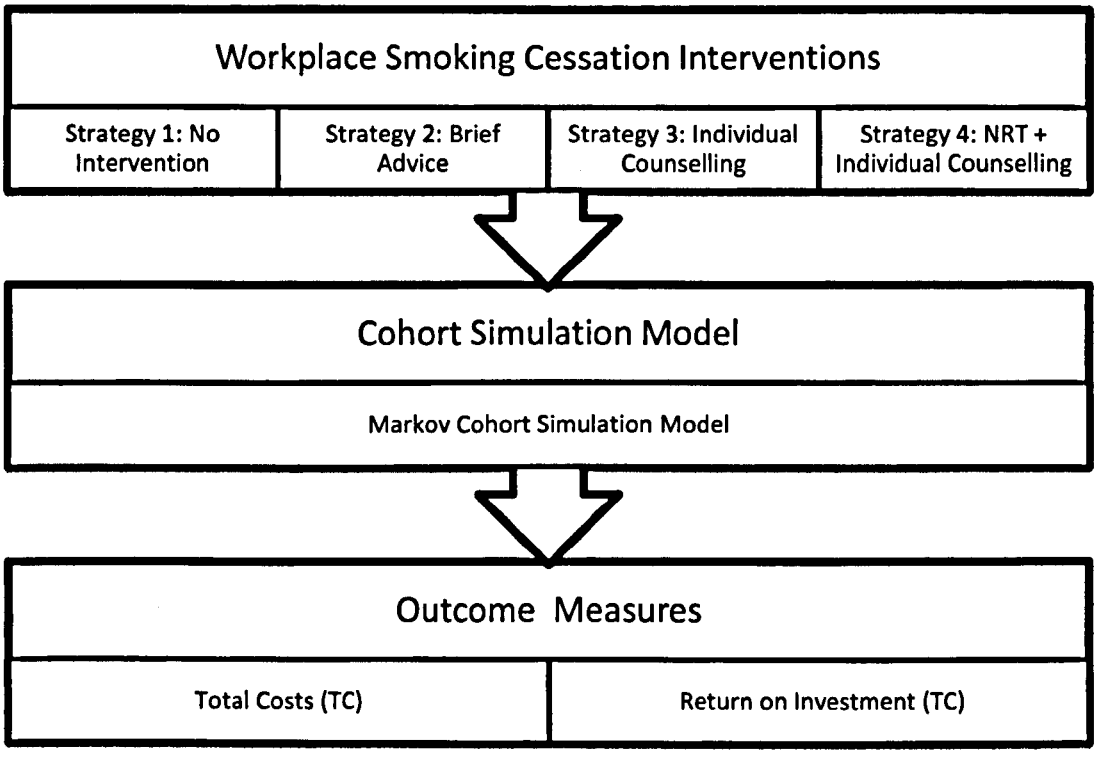
6.3.1 Decision analysis

The study used a decision analytic framework[359] based on a Markov model[360] to assess the effects of workplace interventions for smoking cessation to reduce absenteeism and labour turnover (due to disability and death). Four workplace smoking cessation strategies were evaluated based on prior comprehensive reviews[344 361] and NICE guidance[361] on the effectiveness of workplace smoking cessation interventions:

I. Strategy 1: No intervention (base-case scenario)
II. Strategy 2: Brief advice from an occupational health nurse
III. Strategy 3: Individual counselling with an occupational health nurse
IV. Strategy 4: Nicotine replacement therapy (patch) and individual counselling with an occupation health nurse

Other forms of pharmacotherapy such as varenicline and buproprion were not evaluated as there is limited evidence on the practicality and effectiveness of these interventions in a workplace setting. Each strategy was evaluated using a Markov state transition model simulating a cohort of adult smokers (aged 35 and older) participating in a particular workplace smoking cessation strategy. The decision analysis framework involved comparing the total costs (TC) incurred and returns on investment (ROI) derived from each individual strategy simulated from the Markov models in reducing absenteeism, disability and death in the workplace cohort (**Figure 20**).

Figure 20. Decision analytical framework for evaluating workplace smoking cessation interventions from the employer's perspective



Two outcomes were presented to allow the decision-maker (employer) to decide on which outcome to use. The strategy with the lowest total cost and largest return on investment was considered to be the optimal choice in the primary analysis. Many economic evaluation studies use net benefits (net monetary benefit, net health benefits) to determine optimal strategies from a health services perspective. Cost-effectiveness analysis from this perspective often use outcomes such as QALYs or life years where the most cost-effective strategy is usually determined by the maximisation of the effects (QALYs or life years) and minimisation of the costs, often times given a willingness-to-pay threshold. However, from an employer's perspective, it is common to evaluate alternate investment options using total cost (TC) incurred and return on investment (ROI).[362] Total cost (TC) incurred is simply the combined expected value of expenditure from smoking cessation intervention, absence costs and labour turnover costs. The optimal strategy selection for the employer would be the strategy which minimised total costs.

ROI can be interpreted as the amount of additional money an employer gains per pound spent. In the calculation below, the net present value (NPV) of benefits gained is quantified as the monetary value saved from a reduction of absence and labour turnover costs while the net present value (NPV) of costs is the investment expenditure of adopting a particular smoking intervention strategy:

$$Return\ On\ Investment = \frac{(NPV\ of\ benefits - NPV\ of\ costs)}{NPV\ of\ costs}$$

Both NPV of costs and NPV of benefits are incremental values calculated from the baseline strategy of no intervention. Strategies with positive ROI compared to a baseline strategy will offer a better investment for the employer while strategies with negative ROI will offer a worse investment. Investment choices made on the basis of TC and ROI are identical (strategy with the lowest TC incurred results with the highest ROI). Both outcomes were utilised in the primary analysis.

In a secondary analysis, cost-effectiveness analysis was used to determine whether the employer's optimal selection strategy would differ if the employer valued maximising quitting. In this scenario, the outcome used was cost per quitter and the evaluation of intervention strategies were ranked based in the incremental cost-effectiveness ratio (ICER):

$$ICER = \frac{Total\ Costs_{Strategy\ i} - Total\ Costs_{Strategy\ i-1}}{Number\ of\ Quitters_{Strategy\ i} - Number\ of\ Quitters_{Strategy\ i-1}}$$

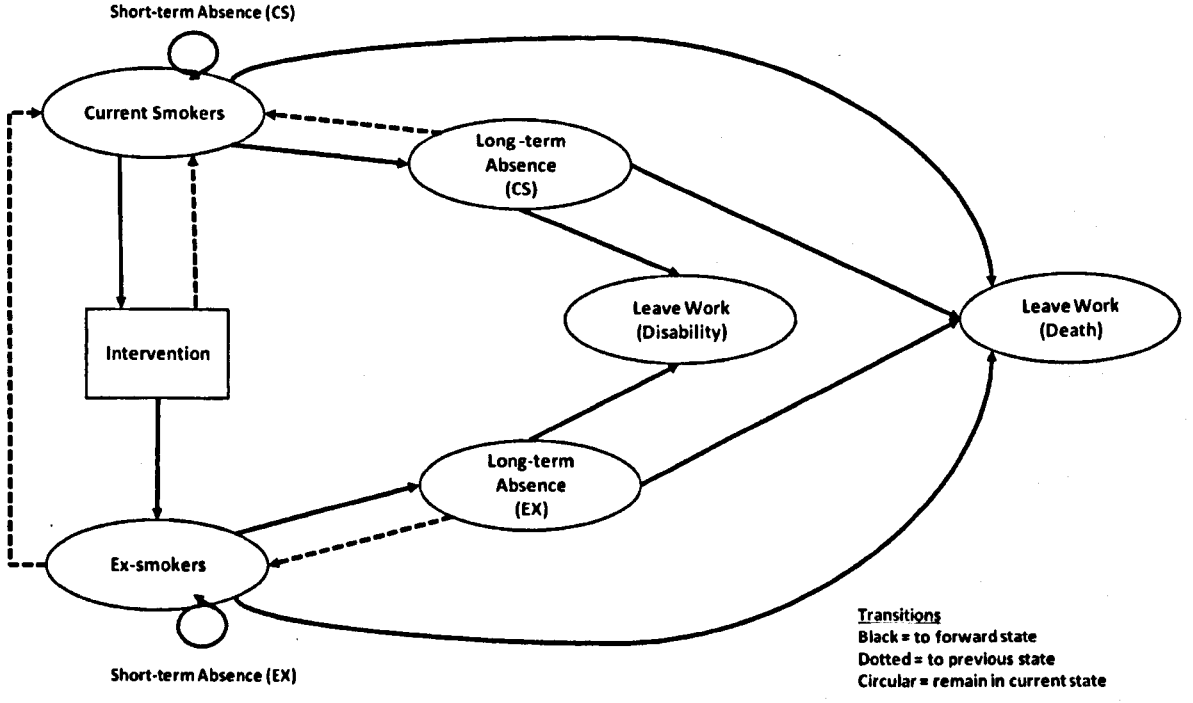
The ICER was calculated as the ratio of the change in costs (from current strategy to previous strategy) to the change in number of quitters (from current strategy to previous strategy). The ICER allows for the ranking of all four intervention strategies according to cost-effectiveness.

6.3.2 Markov state transition model

A Markov model was constructed which simulated a hypothetical cohort of 1,000 current smokers in the workplace (**Figure 21**). The direction and likelihood of a worker moving between states was governed by transition probabilities. Solid lines describe forward progressions, dotted lines describe return progressions and circular arrows represent remaining in the same state.

There were two 'present at work' states: current smokers and ex-smokers; and four 'absence from work' states: long-term absence for current smoker, long-term absence for ex-smokers, leaving work due to disability and leaving work due to death. In **Figure 21**, the smoking cessation intervention can be visualised as a rectangle to illustrate the probability of participation in the intervention by current smokers who subsequently had either a successful or unsuccessful quit attempt. For the 'no intervention' strategy, cessation interventions were removed from the model and the transition between current and ex-smokers was shown as a successful unassisted quit attempt.

Figure 21. Markov state transition model for smoking cessation interventions

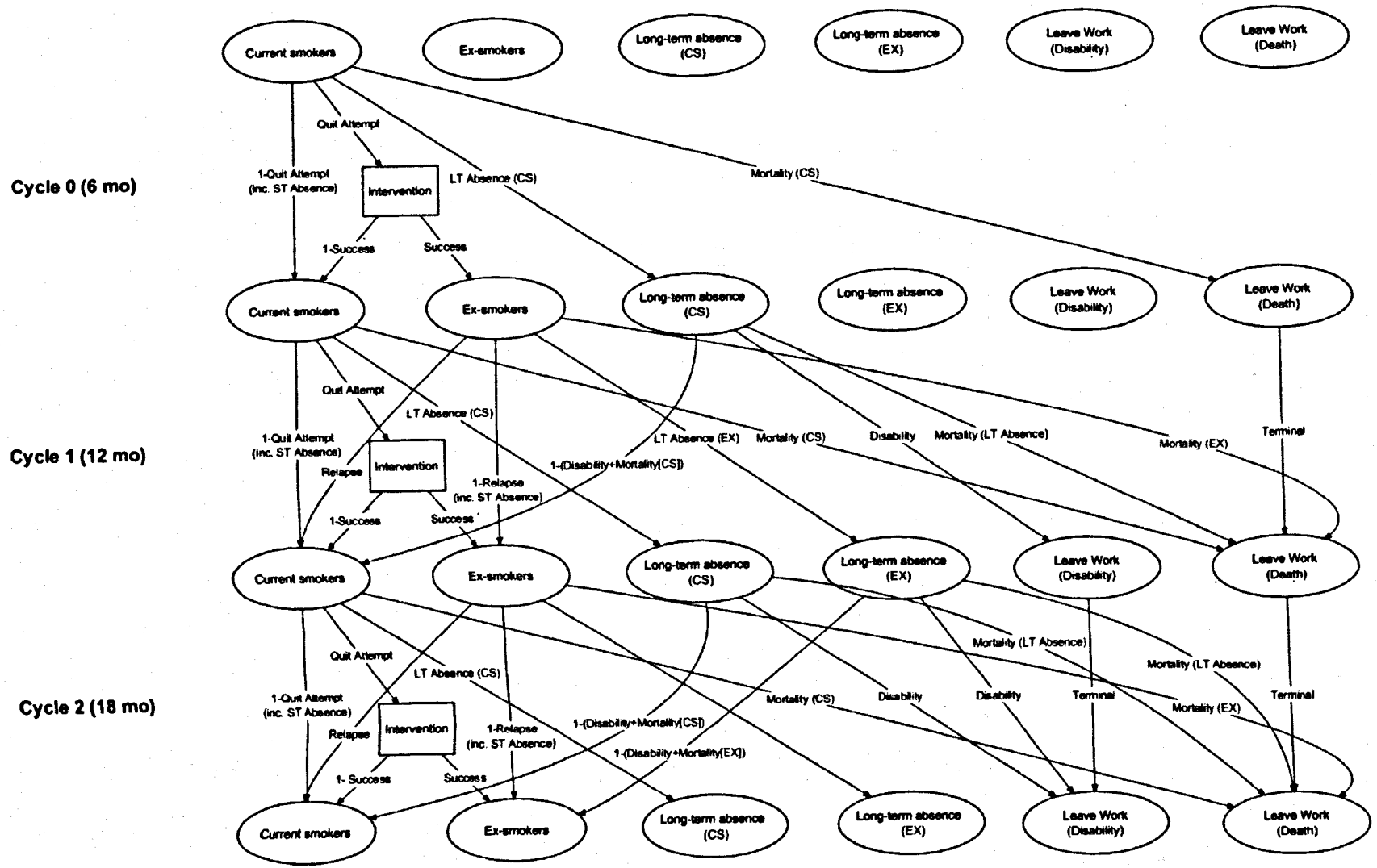


The key characteristics of the model are summarised below:

- The workers were followed up from 35 years until the average age of retirement[363] in the UK (64.6 years for men and 62.3 years for women).
- Cycle lengths of six months (26 weeks) were implemented corresponding to sustained smoking cessation quit rates at six months because smokers who can quit and remain abstinent for six months are likely to have a very high probability of remaining long-term ex-smokers.[364]
- When an individual left work due to disability or death, it was assumed that the individual would not be able to return to work as a member of the original cohort.
- Short-term absences were defined as absent workers who did not qualify for long-term statutory sick pay in the UK.
- Long-term absences were defined as absences that qualified for long-term statutory sick pay by the employer (up to 26 weeks).
- Current and ex-smokers are allowed to have short-term absences without having to leave the state as short-term absences are usually much shorter than the cycle length
- Transition to the disability state could only happen from long-term absence (i.e. workers cannot directly enter disability state from long-term absence) because the UK labour market definition of disability[365] was applied where individuals must be on long-term absence greater than 26 weeks to be able to qualify for disability or incapacity benefits.
- Costs were taken from the employer's perspective as companies and firms behave to minimise the costs of absenteeism and labour turnover.
- All future costs were discounted by 3.5% in accordance to HM Treasury recommended guidelines.[294]

The simulation was conducted separately for men and women as there were gender differences in costs, absence rates, death rates and disability rates. The cohort simulation results took into account all probabilistic parameters for transition probabilities (methodology in **Section 6.3.3**) in conjunction with baseline costs (methodology in **Section 6.3.4**). Probabilistic analysis employed random sampling technique of 1,000 Monte Carlo simulations (methodology in **Section 6.3.5.2**). One-way sensitivity analysis was also conducted to take into account the maximum and minimum values of costs and alternate discount rates of 0% and 6% (methodology in **Section 6.3.5.1**). The analyses were conducted using TreeAge Pro 2012 Decision Analytic Modelling Software.

Figure 22. Cycle tree describing movement between states governed by transition probabilities



6.3.3 Transition probabilities

Transition probabilities governed movement between states during cycles. The Markov model in **Figure 21** is shown in a linear cycle tree in **Figure 22** which shows all the possible transitions between states. The total time for all the possible transitions to occur was exactly three cycles (18 months). Cycle zero had relatively few pathways as all individuals in the cohort started as current smokers (base cohort). Cycle one was the first cycle in which ex-smokers could transition to other states and cycle two was the first full cycle where all possible transitions could be made. In order to simulate the hypothetical cohort, the model required the following probabilities corresponding to a six-month cycle length: quit attempts, intervention specific quit rates, relapse rates, mortality rates, absence rates and disability rates. Most transition parameters in the literature were given as proportions over a particular study period or rates over a period of time. If a proportion was given over a study period of six months, then it was used directly as a six-month probability. However, if a proportion was given over study or follow-up periods other than six months, then a transformation was made using two formulae[366]; one which converts probabilities (corresponding to the length of particular study periods) to an instantaneous event rate and another which converts the instantaneous event rate into a six-month probability:

$$Rate = \frac{-\ln(1 - Probability)}{Time_{years}}$$

where $Time_{years}$ is the study period or length of follow-up

$$6\ month\ probability = 1 - e^{(-Rate\ x\ Time_{years})}$$

where $Time_{years}$ is 0.5 corresponding to a six-month cycle length

Details about how specific transition probabilities were obtained are provided in the subsequent sections.

6.3.3.1 Probability of making a quit attempt

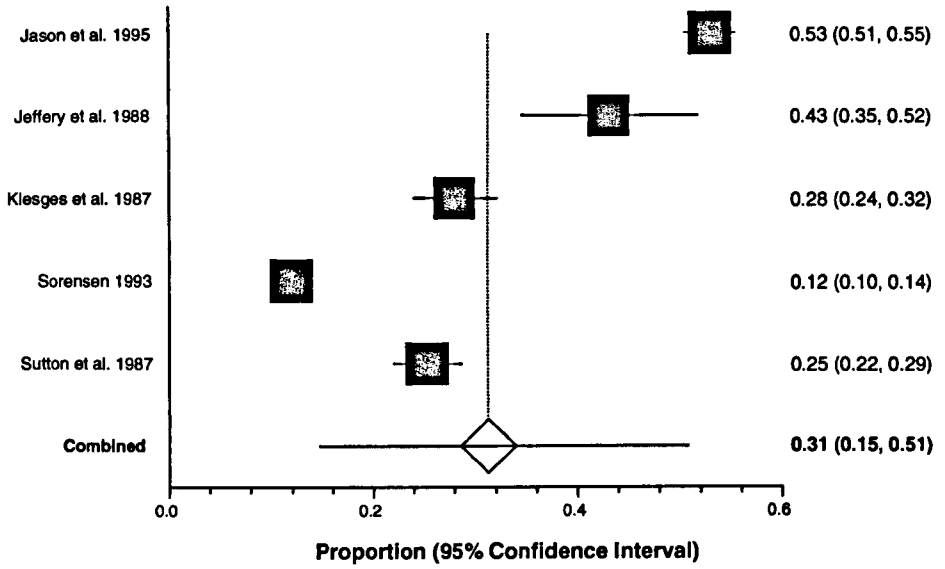
The probability of making a quit attempt varied between intervention strategies. Evidence from a review of smoking cessation interventions in the workplace[352] suggests that the availability of assisted interventions in the workplace increases participation rates among workers. For strategy one (no intervention), the Omnibus Survey[165] informed that the proportion of unassisted quit attempts made in a random sample of 950 UK smokers in 2008 was 26%, which was transformed (**Section 6.3.3**) into a six-month probability of 14%. For strategies two through four (brief advice, individual counselling, NRT with individual counselling), the pooled probability was calculated for using intervention participation rates from five randomised control trials[367-371] identified in a Cochrane Review of workplace smoking cessation interventions[352] shown in **Table 15.**

Table 15. Participation in workplace smoking cessation interventions

Participants	Total Smokers	Proportion	Reference
844	1,592	0.53	Jason *et al.*[367]
59	137	0.43	Jeffery *et al.*[368]
486	136	0.28	Klesges *et al.*[369]
143	1,193	0.12	Sorensen *et al.*[370]
172	681	0.25	Sutton *et al.*[371]

For each study, the raw proportions were calculated using the number of participants divided by the total number of smokers in each study. The variances of the raw proportions were stabilised using the Freeman-Tukey variant of the arcsine square root transformation.[372] The pooled analysis was conducted using the random effects model to allow for heterogeneity between studies. In **Figure 23**, results of the meta-analysis of proportions show that the six-month probability of participation in workplace interventions was 31% (95% CI 15% to 51%) from a pooled sample of 3,739 workers. There was a large amount of heterogeneity seen due to the outcomes being absolute (rather than relative) and worksite interventions differed across locations. Detailed methodology on the meta-analysis of proportions is provided in **Appendix 9.12.**

Figure 23. Random effects meta-analysis for workplace smoking cessation intervention probability of participation



6.3.3.2 Probability of quitting smoking

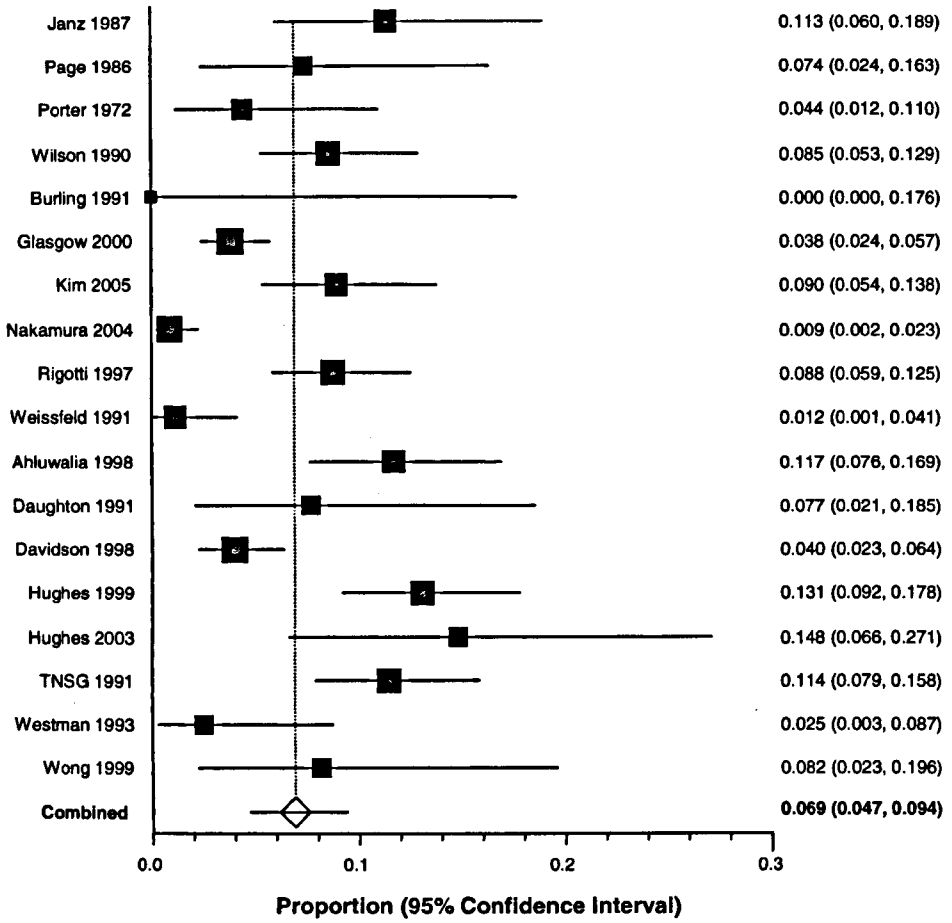
The baseline probability of sustained quitting at six months was obtained by pooling the proportion of quitters from the control/no intervention groups identified in three separate Cochrane Reviews[97 98 101] on the effectiveness of smoking cessation interventions. For each study, the raw proportions were calculated using the number of quitters at six months divided by the total number of smokers in the control arm of the trial. The variances of the raw proportions were again stabilised using the Freeman-Tukey variant of the arcsine square root transformation.[372] There were 18 total studies[373-390] extracted from the Cochrane Reviews where the outcome reported was a six-month sustained quitting outcome validated by biomarker.

Table 16. Baseline proportion of sustained quitters at six months follow-up from no intervention groups (controls)

Sustained Quitters (6 mo. validated)	Total Smokers (N)	Proportion	Reference
12	106	0.113	380
5	68	0.074	383
4	90	0.044	384
20	234	0.085	389
0	19	0.000	374
22	576	0.038	377
18	201	0.090	381
4	447	0.009	382
27	308	0.088	385
2	173	0.012	387
24	205	0.117	373
4	52	0.077	375
16	401	0.040	376
34	260	0.131	378
8	54	0.148	379
31	271	0.114	386
2	80	0.025	388
4	49	0.082	390

The proportions were then pooled using random effects meta-analysis using the methodology detailed in **Appendix 9.12** to obtain the probability of unaided sustained quitting at six-months. In **Figure 24**, the results of the meta-analysis show that the sustained six-month probability of unaided quitting was 6.9% (95% CI 4.7% to 9.5%) from an aggregate pool of studies with a total sample of 3,594 smokers.

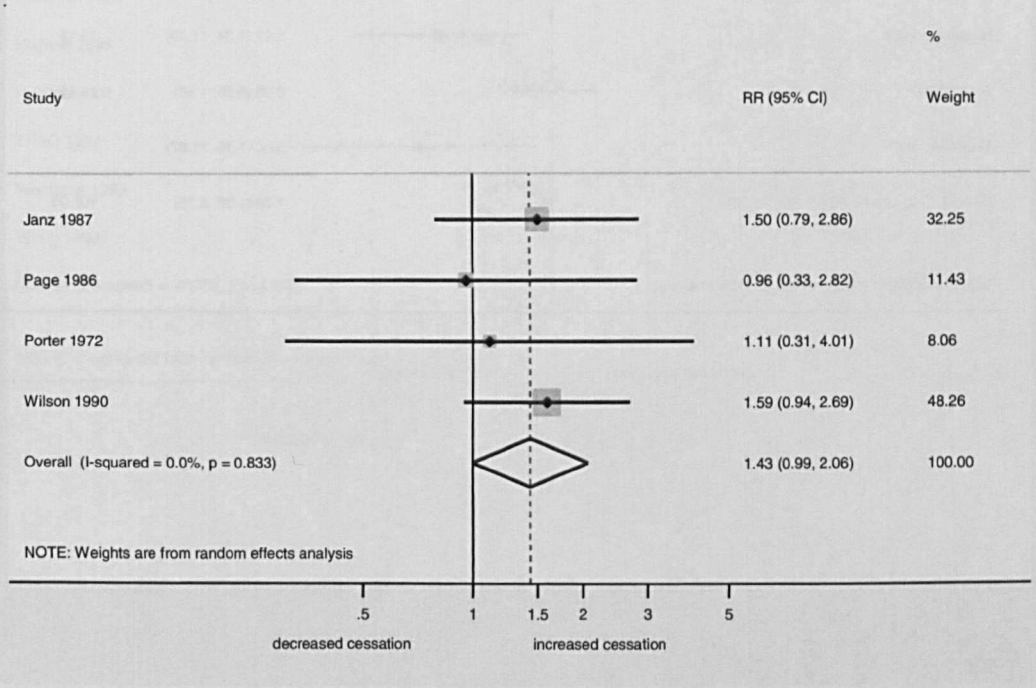
Figure 24. Random effects meta-analysis for sustained six-month probability of unaided quitting



Once the baseline probability of quitting was calculated, the treatment effect of each smoking cessation intervention was applied by multiplying the risk ratios to the baseline probability of quitting smoking. Cochrane Reviews provided the treatment effects through meta-analysis for brief advice[97], individual counselling[98] and NRT patches with individual counselling[101]. However, the risk ratios could not be directly used as too much methodological heterogeneity was detected between studies. The reviews pooled together multiple types of smoking cessation endpoints and intervention groups. To solve this problem, only studies from the Cochrane Reviews that closely mirrored the smoking cessation interventions evaluated in this particular study and reported a six-month sustained quit rate validated by biomarker (carbon monoxide and salivary cotinine) were re-extracted. Random effects meta-analysis was used to re-pool together the extracted studies to obtain weighted treatment effects for brief advice,

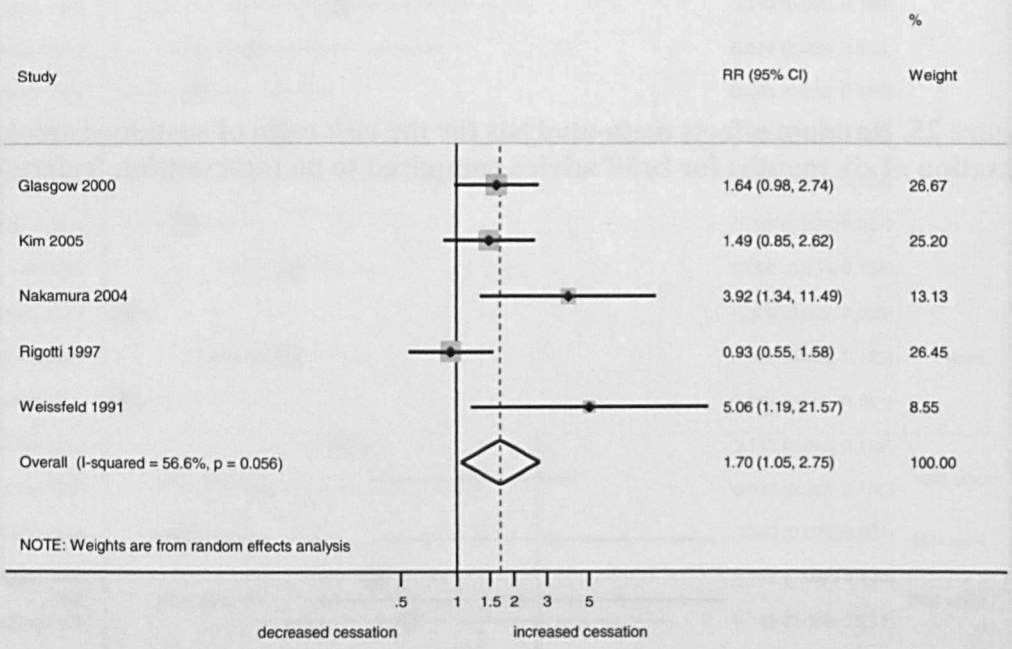
individual counselling and NRT (patches) with individual counselling while accounting for heterogeneity between studies. Both male and female participants were combined in the meta-analyses as most of the extracted studies did not report sex-specific quit-rates.

Figure 25. Random effects meta-analysis for the risk ratio of sustained smoking cessation at six months for brief advice compared to no intervention (reference)



In the pooled analysis for smokers who received brief advice, the level of sustained quitting at six months was 43% greater than in smokers who received no intervention (RR = 1.43, 95% CI 0.99 to 2.06, n = 4 studies, $I^2 = 0\%$; **Figure 25**).

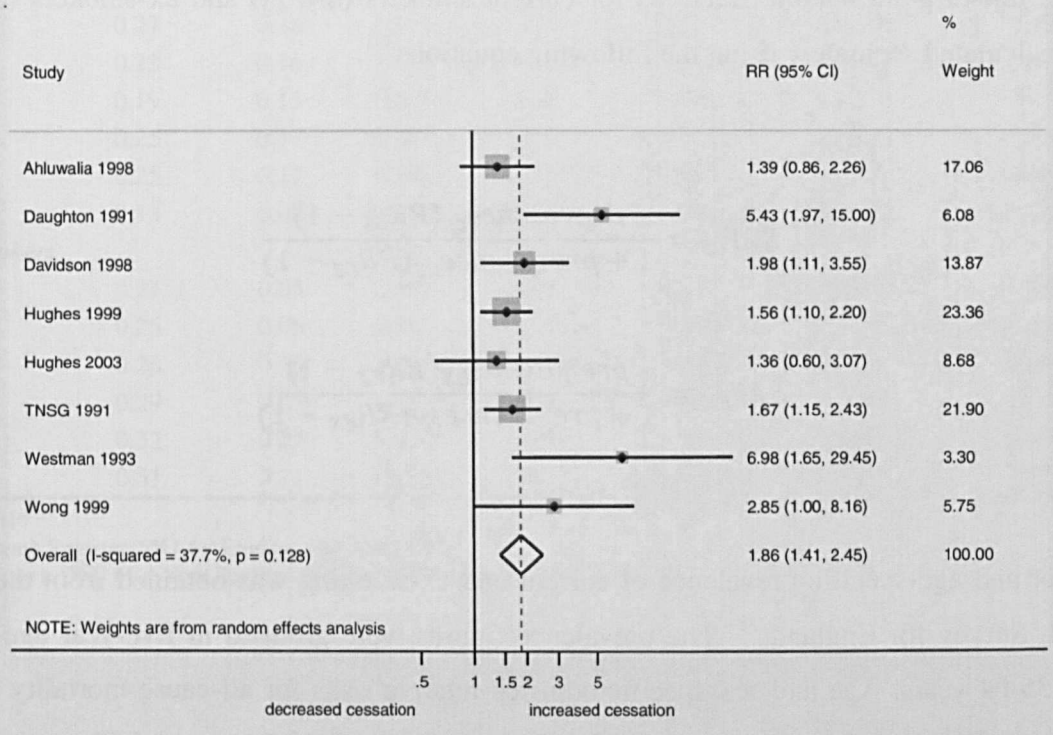
Figure 26. Random effects meta-analysis for the risk ratio of sustained smoking cessation at six months for individual counselling compared to no intervention (reference)



For smokers who received individual counselling, the level of sustained quitting at six months was 70% greater than in smokers who received no intervention (RR = 1.70, 95% CI 1.05 to 2.75; n = 5 studies, I^2 = 56.6%; **Figure 26**).

For smokers who received NRT patches and individual counselling, the level of sustained quitting at six months was 86% greater than in smokers who received a placebo or no intervention (RR = 1.86, 95% CI 1.41 to 2.45, n = 8 studies, I^2 = 37.7%; **Figure 27**). Applying the average treatment effects of the smoking cessation interventions to the baseline probability of quitting of 6.9%, the probability of quitting at six months was calculated as 9.9% for brief advice, 11.7% for individual counselling and 12.8% for NRT with individual counselling.

Figure 27. Random effects meta-analysis for the risk ratio of sustained smoking cessation at six months for NRT patches with individual counselling compared to placebo or no intervention (reference)



6.3.3.3 Probability of relapse

For smokers who made a successful quit attempt, a probability of relapse after six months was estimated. Because of the cycle length, the model assumed that smokers can only relapse after six-months sustained quitting. Relapse rate used in the Markov model was obtained from a cohort study of 1,266 ex-smokers who had recently quit smoking after six months.[364] The study found that only 7.3% of smokers who had abstained from smoking for a continuous six months had actually relapsed.

6.3.3.4 Probability of mortality

To obtain gender-specific mortality for current and ex-smokers, smoking-attributable risk fractions (SAFs) were calculated for all-cause mortality in five-year age-bands from 35-64 years. Smoking-attributable fractions for current smokers (SAF_{CS}) and ex-smokers (SAF_{EX}) were calculated separately using the following equations[391]:

$$SAF_{CS} = \frac{prevalence_{cs}(RR_{CS} - 1)}{1 + prevalence_{CS}(RR_{CS} - 1)}$$

$$SAF_{EX} = \frac{prevalence_{EX}(RR_{EX} - 1)}{1 + prevalence_{EX}(RR_{EX} - 1)}$$

Gender and age-specific prevalence of current and ex-smoking was obtained from the 2010 Health Survey for England[278]. The prevalence figures were grouped in five-year age-bands from 35-64 years. Age and sex-specific adjusted relative risks for all-cause mortality due to current and ex-smoking were provided by Doll *et al.*[8] for British men and Pirie *et al.*[9] for British women. These were used to calculate SAFs in five-year age-bands. SAFs were then multiplied by total number of deaths in each five-year age-band to obtain smoking-attributable mortality [285]. The total number of deaths in England and Wales required to calculate SAM was obtained from the 2011 Death Register[392] provided by the Office for National Statistics (ONS). SAM was in turn used to calculate the annual probability of mortality (as explained below).

The annual probability of mortality for current and ex-smokers required SAM and population-level estimates for the population of current and ex-smokers using the ONS 2011 Mid-Year Population Estimates[393] of England and Wales. These population estimates were obtained by multiplying smoking prevalence with the number of current and ex-smokers in the population in each 5-year age-band. The annual probabilities of mortality were then obtained by dividing SAM from current smoking by the number of current smokers and SAM from ex-smoking by the number of ex-smokers. Finally, annual probabilities were converted to the six-month probabilities using transformation equations[366] (**Section 6.3.3**). This process described above is shown in **Table 17** for men and **Table 18** for women.

Table 17. Probability of all-cause mortality in men from current and ex-smoking

Age	Prevalence[1]	SAF	Total Deaths[2]	SAM	Smokers[3]	Annual Probability Mortality	6-Month Probability Mortality
Current Smokers							
35-39	0.27	0.18	2,197	405	504,266	0.0008	0.0004
40-44	0.23	0.16	3,514	555	460,127	0.0012	0.0006
45-40	0.19	0.13	5,005	664	376,383	0.0018	0.0009
50-54	0.25	0.17	6,878	1,197	458,412	0.0026	0.0013
55-59	0.25	0.17	9,726	1,679	398,092	0.0042	0.0021
60-64	0.13	0.09	15,766	1,488	208,405	0.0071	0.0036
Ex-Smokers							
35-39	0.21	0.05	2,197	109	389,685	0.0003	0.0001
40-44	0.25	0.06	3,514	203	504,904	0.0004	0.0002
45-40	0.26	0.06	5,005	301	529,377	0.0006	0.0003
50-54	0.29	0.07	6,878	459	522,975	0.0009	0.0004
55-59	0.32	0.07	9,726	701	497,575	0.0014	0.0007
60-64	0.51	0.11	15,766	1,768	848,166	0.0021	0.0010

[1]HSE 2010[394]
[2]ONS Death Register 2011 for England and Wales[395]
[3]Prevalence x ONS Mid-Year Population Estimates for England and Wales[396]

Table 18. Probability of all-cause mortality in women from current and ex-smoking

Age	Prevalence[1]	SAF	Total Deaths[2]	SAM	Smokers[3]	Annual Probability Mortality	6-Month Probability Mortality
Current Smokers							
35-39	0.17	0.23	1,219	282	317,718	0.0009	0.0004
40-44	0.21	0.27	2,201	593	433,702	0.0014	0.0007
45-40	0.20	0.26	3,369	873	412,938	0.0021	0.0011
50-54	0.19	0.25	4,736	1,185	346,506	0.0034	0.0017
55-59	0.19	0.25	6,480	1,598	300,204	0.0053	0.0027
60-64	0.14	0.19	10,736	2,087	235,003	0.0088	0.0044
Ex-Smokers							
35-39	0.24	0.05	1,219	55	442,761	0.0001	0.0001
40-44	0.24	0.05	2,201	102	505,054	0.0002	0.0001
45-40	0.19	0.04	3,369	123	395,274	0.0003	0.0002
50-54	0.23	0.04	4,736	210	422,858	0.0005	0.0002
55-59	0.27	0.05	6,480	326	428,033	0.0008	0.0004
60-64	0.31	0.06	10,736	621	526,400	0.0012	0.0006

[1]HSE 2010[394]
[2]ONS Death Register 2011 for England and Wales[395]
[3]Prevalence x ONS Mid-Year Population Estimates for England and Wales[396]

The Markov model also needed to be populated with the probability of mortality of workers who were on long-term absence. The Whitehall Study II[397] of British civil servants provided estimates of long-term absence as a predictor of all-cause mortality. The study compared number of deaths over a three year period for workers who had a spell of long-term absence to number of deaths for workers who had not had a spell of long-term absence over a three year period. There were 127 deaths during 3-year follow-up of 1,906 British workers who had a spell of long-term absence. Therefore, the 3-year probability of mortality for those workers who were on long-term absence was 6.7%. The 3-year probability was converted using transformation equations[366] (**Section 6.3.3**) to a six-month probability of 1.14%.

6.3.3.5 Probability of disability

The parameter which dictated the transition of workers on long-term absence to leaving work due to disability was obtained from a large population-based cohort study[398] predicting disability pension in workers who were on long-term absence. Over a five-year period, there were 2,318 cases of disability pension in 8,283 men and 3,122 cases of disability pension in 11,096 women. Therefore, the five-year probability of disability in individuals on long-term absence was 28.0% for men and 28.1% for women. The five-year probability was converted to six-month probabilities (**Section 6.3.3**) of 5.3% for men and 5.4% for women.

6.3.3.6 Probability of absence from work

Both short-term and long-term probabilities of absenteeism in current and ex-smokers were obtained from a population-based cohort of workers followed-up over 12 months.[327] The study provided person-years for the length of follow-up. Therefore, the absence rates could be calculated over a 12-month period for 375 male current smokers and 498 male ex-smokers. Similarly, absence rates were calculated for 1,242 female current smokers and 1,182 female ex-smokers. The annual rates were converted using transformation equations[366] (**Section 6.3.3**) to six-month probabilities. These parameters are illustrated in **Table 19** for men and **Table 20** for women.

Table 19. Probability of short-term and long-term absence from work in men by smoking status

Smoking Status	Absence Incidence	Person-Years	Absence Rate	Annual Probability	6-Month Probability
Short-term Absence					
Current Smoker	285	1,434	0.199	0.180	0.095
Ex-Smoker	86	1,907	0.045	0.044	0.022
Long-term Absence					
Current Smoker	167	1,434	0.116	0.110	0.057
Ex-Smoker	57	1,907	0.030	0.029	0.015

Table 20. Probability of short-term and long-term absence from work in women by smoking status

Smoking Status	Absence Incidence	Person-Years	Absence Rate	Annual Probability	6-Month Probability
Short-term Absence					
Current Smoker	400	4,822	0.083	0.080	0.041
Ex-Smoker	166	4,590	0.036	0.036	0.018
Long-term Absence					
Current Smoker	232	4,822	0.048	0.047	0.024
Ex-Smoker	90	4,590	0.020	0.019	0.010

6.3.4 State costs

Transitioning from states in the Markov model shown in **Figure 21** may incur state costs. The expected value of these costs can be characterised as the sum-product of the state cost and the proportion of the cohort in each cycle. There are several transition states in the Markov model that incurred costs (discussed below). The year 2011-2012 was set as the base-year for the model to reflect the most recent costs derived from literature. Details about how the state costs were obtained from existing literature are provided below.

6.3.4.1 Costs of smoking cessation interventions

The duration and intervals for brief advice and individual counselling for the interventions were based on similar interventions used in other workplace smoking cessation studies.[352] Brief advice was modelled to be given in the first month while individual counselling was

modelled to be given over two months (2 sessions per month). Nicotine replacement therapy (NRT) was modelled in accordance with NICE guidance[399] on recommended usage and duration based on a maximum three month supply. NICE guidance[399] has also suggested that it is possible to give combination NRT therapy to heavy smokers; however there was uncertainty on length of usage, type of NRT combinations and adherence in the workplace setting. Existing workplace interventions have all relied on single therapy NRT and therefore, there was considerable difficulty modelling the usage of combination therapy accurately.[344] Therefore, single therapy nicotine patches were modelled as they are commonly used in workplace interventions[344] known to be effective and one of the cheapest forms of NRT available.[400] The descriptions of each strategy are presented in **Table 21.**

Table 21. Routine workplace smoking cessation interventions

Strategy	Description	Costs
No Intervention	None	None
Brief Advice	10 minute session with an occupational health nurse (Initial consultation in first month)	Consultation time, wages/salary, national insurance, qualifications, overheads, travel and working time
Individual counselling	Four 10 minute sessions with an occupational health nurse (Initial consultation and every two weeks for two months)	Consultation time, wages/salary, national insurance, qualifications, overheads, travel and working time
Nicotine Replacement Therapy + Individual Counselling	Four 10 minute sessions with an occupational health nurse and NRT (Initial consultation and every two weeks for two months + NRT supply for three months)	Consultation time, NRT patches, wages/salary, national insurance, qualifications, overheads, travel and working time

The human resource cost elements for each smoking cessation strategy were consultation costs for nurse-led smoking cessation counselling obtained from Table 10.7 of the 2011 PSSRU report[401] for unit costs of health care use in the UK and unit costs for nicotine patches. Nurse-led counselling cost £1.45 per minute in 2011. For one 10-minute session of brief advice, this amounted to £14.50 per person. For individual counselling, four sessions amounted to £58 per person. These costs include wages/salary, national insurance,

qualifications (training), overheads (management, administration, non-staff and capital expenses), travel and working time (including annual leave, sick days, study days).

For NRT patches, data provided in the 2012 British National Formulary[400] were used. The unit costs were calculated for 13 well-known branded patch products manufactured by McNeill, Novartis and GSK (**Table 22**). The average unit cost of one 24-hour nicotine patch was £1.34. There was little variation in unit costs between products and dose strengths. A standard adherence model[402] was implemented where 50% of individuals were likely to use NRT for only 4 weeks and 50% of individuals were likely to use NRT for a full 12 weeks. Further sensitivity analyses were conducted using a low adherence model where all individuals use NRT for only 4 weeks and a high adherence model were individuals use NRT for the full 12 weeks. A worker was given one 24-hour patch per day (dose strength dependent on amount smoked) over the intervention period. The average cost per worker of NRT usage totalled £75.17 with standard adherence, £37.58 with low adherence and £112.75 with high adherence.

Table 22. Baseline costs of NRT patches from well-known branded products (2012)

Product	Costs	Units	Unit Cost	Cost Per Worker*
Nicorette®				
5 mg patch	£9.07	7	£1.30	£72.56
10 mg patch	£9.07	7	£1.30	£72.56
15 mg patch	£9.07	7	£1.30	£72.56
Nicotinell®				
7 mg patch	£9.12	7	£1.30	£72.96
14 mg patch	£2.57	2	£1.29	£71.96
14 mg patch	£9.40	7	£1.34	£75.20
21 mg patch	£2.85	2	£1.43	£79.80
21 mg patch	£9.97	7	£1.42	£79.76
21 mg patch	£24.51	21	£1.17	£65.36
NiQuitin®				
7 mg patch	£9.97	7	£1.42	£79.76
14 mg patch	£9.97	7	£1.42	£79.76
21 mg patch	£9.97	7	£1.42	£79.76
21 mg patch	£18.79	14	£1.34	£75.16
Average	--	--	**£1.34**	£75.17

*Standard adherence for 12 weeks[402] [50% of individuals use for 4 weeks; 50% of individuals use for 12 weeks]

By combining NRT costs with nurse-led counselling costs, total intervention costs were calculated in **Table 23**. An employer would incur no intervention costs if they elected not to have a smoking cessation intervention. Brief advice was relatively cheap at £14.50 per worker while individual counselling costs the employer £58 per worker. NRT combined with individual counselling was the most expensive strategy at £133.17 per worker.

Table 23. Baseline intervention costs per worker who choose to join a smoking cessation strategies

Strategy	Description	Costs Per Worker
No Intervention	None	£0
Brief Advice	10 minute session with an occupational health nurse (Initial consultation in first month)	£14.50
Individual counselling	Four 10 minute sessions with an occupational health nurse (Initial consultation and sessions every two weeks for two months)	£58.00
Nicotine Replacement Therapy + Individual Counselling	Four 10 minute sessions with an occupational health nurse and NRT (Initial consultation and sessions every two weeks for two months + NRT supply for three months)	£133.17

6.3.4.2 Costs of absenteeism

In **Chapter 4**, a meta-analysis was conducted on the duration of absence between current smokers and non-smokers. The results of the meta-analysis showed the mean annual difference in absence between current smokers and non-smokers was 2.74 days (95% CI 1.54 to 3.95 days; I^2 = 89.6%; 13 studies; **Figure 13**) from a pooled sample of 30,978 workers. This particular meta-analysis provided the mean difference in annual duration of absence which informed the costs of absenteeism needed to populate the Markov model. Instead of mean difference in absence, the raw number of days absent was needed to populate the model. This was done by specifying the random effects meta-analysis to output the pooled average mean for current smokers and non-smokers separately instead of mean difference. The output showed that current smokers were absent 12.53 days per year from a pooled

sample of 14,267 current smokers and non-smokers were absent 9.79 days per year from a pooled sample of 16,711 non-smokers. **Section 4.4.4.2 (Chapter 4)** found no evidence of a significant difference in the number days of absence per year between ex-smokers and never smokers; hence, the mean absence days from the overall non-smoking group was used for days of absence in ex-smokers. The absence days per six months (corresponding to the model cycle length) combined with UK gender-specific wage rates were used to calculate the productivity loss for the employer due to short-term absence. The wages during the short-term absence period which an employer pays to a worker was used to value for productivity lost in the workplace. The 2012 UK Annual Survey of Hours and Earnings[403] was used to obtain median gross hourly wages (Men: £12.6 per hour; Women: £10.05 per hour) and hours worked per day (Men: 7.76 hours per day; Women: 7.46 hours per day). The median hourly wage was used to estimate baseline costs due to having heavily skewed distribution. This process is illustrated in **Table 24.**

Table 24. Baseline costs of short-term absence days in the workplace

Smoking Status	Annual absence days[1]	Absence days per 6 month	Hours per day[2]	Hourly wage[2]	Daily Earnings[3]	Foregone production[4]
Men						
Current Smoker	12.53 days	6.27 days	7.76	£12.60	£97.78	£612.57
Ex/Non Smoker	9.79 days	4.90 days	7.76	£12.60	£97.78	£478.71
Women						
Current Smoker	12.53 days	6.27 days	7.46	£10.05	£74.97	£469.71
Ex/Non Smoker	9.79 days	4.90 days	7.46	£10.05	£74.97	£366.99

[1]Weng et al. 2013[351]
[2]Annual Survey of Hours and Earnings 2012[404]
[3]Hours per day x hourly wage
[4]Absence per 6 month x daily earnings

In men, the cost of short-term absence was valued at £612.57 for current smokers and £478.71 for ex/non-smokers. In women, the cost of short-term absence was valued at £469.71 for current smokers and £366.99 for ex/non-smokers. Sensitivity analyses was also conducted using the inter-quartile range of hourly wages[403] to determine short-term absence costs if individuals were in the lowest 25th percentile of hourly wage (Men: £8.7 per hour; Women: £7.4 per hour) or highest 75th percentile of hourly wage (Men: £19.17 per hour; Women:

£15.47 per hour). If a male worker was in the bottom 25th percentile of wage earners, the cost of short-term absence would be £423.90 for current smokers and £331.20 for ex/non-smokers while for female workers in the bottom 25th percentile, the cost of short-term absence would be £344.90 for current smokers and £269.50 for ex/non-smokers. If a male worker was in the top 75th percentile of wage earners, the cost of short-term absence would be £931.98 for current smokers and £728.18 for ex/non-smokers while for female workers in the top 75th percentile, the cost of short-term absence would be £723.02 for current smokers and £564.91 for ex/non-smokers.

To obtain costs for long-term absence (absences up to 26 weeks), the 2012 weekly rate of £85.85 for statutory sick pay in the UK[405] was combined with the median cost of temporary vacancy cover provided by a survey of 124 UK businesses.[358] The cost of vacancy cover is provided in **Table 25** for several occupational groups.

Table 25. Costs of vacancy cover and other costs per employee due to absence

Occupation Group	2012 Cost (per worker absence)
Manufacturing and production	£456
Private sector services	£513
Public services	£647
Non-profit	£700
All employees	**£600**

The responsibility of statutory sick pay in the UK lies with the employer.[405] Many employers have higher payment amounts per week with privately managed sick pay schemes.[356 358] However, the UK government scheme provides the lowest amount per week. A worker can qualify for statutory sick pay if they are absent greater than 4 days per spell up to a maximum of 26 weeks. Since the Markov model has a 26 week (6 month) cycle length, workers who transition to long-term absence states incur the full 26 week costs of statutory sick pay before they can transition back to work or out of work. Therefore, the cost of statutory sick pay for the full 26 weeks was £2,232.10 per person. The cost of statutory sick pay (£2,232.10) was

then added to the median cost of temporary vacancy cover (£600, **Table 25**). This resulted in the total baseline cost of long-term absence to be £2,832.10 per worker. Additional sensitivity analysis was conducted using the lowest vacancy cost occupational group (manufacturing and production) and the highest vacancy cost occupational group (non-profit). Therefore, total long-term absence costs ranged from £2,688.10 per worker to £2,932.10 per worker.

6.3.4.3 Cost of labour turnover

For individuals who transitioned from long-term absence to leaving work through death or disability, the employer incurred *the cost of replacing the labour.* The costs of labour turnover were obtained from the annual survey[356] of 308 UK businesses in 2009. **Table 26** shows the costs of labour turnover by occupational group.

Table 26. Costs of labour turnover per employee

Occupation Group	2009 Cost (per worker)	2011 Cost (per worker)*
Senior managers/directors	£9,000	£9,375
Managers and professionals	£6,500	£6,771
Administrative, secretarial and technical	£3,445	£3,589
Service(customer, perspective, protective, sales)	£3,723	£3,878
Manual and craft workers	£3,150	£3,281
All employees	**£6,125**	**£6,380**

*Inflated to 2011 levels by UK labour cost index[406]

The costs of labour turnover included vacancy cover, redundancy, recruitment, selection, training and induction. The cost of labour turnover in 2009 for all occupational groups was £6,125 per worker. The 2009 cost was inflated to 2011 levels with the most recent labour cost index[406] for the UK. The 2011 cost of labour turnover totalled £6,380 per worker. Sensitivity analysis was conducted using the lowest cost occupational group (manual and craft workers) and the highest cost occupational group (senior manager/directors). Therefore, the cost of labour turnover ranged from £3,281 per worker to £9,375 per worker.

6.3.5 Sensitivity analysis

6.3.5.1 One-way sensitivity analysis for costs

The process in which state costs were obtained to populate the Markov model was detailed in **Section 6.3.4**. The baseline, minimum and maximum state costs summarised in **Table 27** were used to populate the Markov model for the calculation of total costs (TC) and return on investment (ROI). The baseline cost values were used as the primary parameters in the Markov model. All future costs were discounted at a base-case rate of 3.5%. The maximum and minimum values of costs were used for one-way sensitivity analyses in a secondary analysis. The only possible distribution that could be fit with maximum and minimum values was the triangular distribution.[407] Due to limitations described in **Appendix 9.13.1**, the triangular distribution was not utilised. Instead, one-way sensitivity analysis was conducted because costs obtained from literature provided little information on sample moments (mean and variance) and therefore could not be fit with a more informed distribution (i.e. *gamma* or *log*-normal). The one-way sensitivity on the cost parameters was modelled in conjunction with the probabilistic probability parameters. In addition, alternate discount rates of 0% and 6% for future costs were utilised to examine the robustness of the results.

Table 27. Summary state costs used to populate the Markov model

Parameter	Description	Baseline	Min	Max	Source
Intervention Strategies					
No Intervention	None	£0	--	--	--
Brief Advice	10 minute session with an occupational health nurse	£14.50	--	--	401
Individual Counselling	Four 10 minute sessions with an occupational health nurse	£58.00	--	--	401
NRT	Four 10 minute sessions with an occupational health nurse and NRT (patch)	£133.17	£96.56	£170.75	400 401
Short Term Absence	Productivity Loss (Foregone Earnings)				351 403
Men: Current Smoker		£612.57	£423.94	£931.98	
Men: Ex-Smoker		£478.61	£331.23	£728.18	
Women: Current Smoker		£469.71	£344.92	£723.02	
Women: Ex-Smoker		£366.99	£269.49	£564.91	
Long Term Absence	Statutory sick pay paid by the employer and vacancy cover	£2,832.10	£2688.10	£2,932.10	358 405
Labour Turnover	Vacancy cover, Redundancy, Recruitment, Selection, Training and Induction Costs	£6,380.21	£3,281.25	£9,375.00	356

6.3.5.2 Probabilistic sensitivity analysis

The methods for obtaining transition probabilities to populate the Markov were described in **Section 6.3.3. Table 28** shows the summary of all transition probabilities. Probabilistic sensitivity analysis (PSA) is essentially a Bayesian process. The primary purpose of PSA was to incorporate parameter uncertainty into the model by specifying prior probability distributions for the purpose of generating posterior distributions of total costs (TC) incurred. PSA was conducted using transition probabilities and their respective distribution parameters provided in **Table 28** combined with base-line state costs provided in **Table 27**. With the exception of all-cause mortality in current smokers and ex-smokers, all transition probabilities parameters were obtained from studies which had provided finite sample sizes. Distributions for the probabilities of all-cause mortality in current and ex-smokers were not required as the probabilities were obtained from UK aggregate population-level sources. The remaining parameters were from finite and often small sample sizes. Therefore, those probabilities were fit with *beta* distributions using the method of moments approach.[407] Detailed methodology and justification for using the *beta* distribution is described in **Appendix 9.13.2**. The random sampling was conducted using 1000 Monte Carlo simulations. The Monte Carlo method recalculates expected values in the Markov model multiple times by randomly sampling of the probability density function of individual parameter distributions. The advantage of this technique is that any number of parameter uncertainties can be incorporated into the analysis allowing for the estimation of the total impact of uncertainty on the model. PSA was conducted using TreeAge Pro 2012 Decision Analytic Modelling Software.

Table 28. Summary transition probabilities with *beta* distribution parameters for probabilistic sensitivity analysis

Parameter	Probability	N	StD Error	α	β	Source
Quit Attempt						
No Intervention	0.140	950	0.011	133	816	165
Strategy 2-4	0.310	3,739	0.008	1159	2579	352
Sustained Quit						
No Intervention	0.069	3,831	0.004	264	3566	97 98 101
Brief Advice	0.099	596	0.012	59	536	97
Individual Counselling	0.117	1,898	0.007	223	1674	98
NRT + Counselling	0.128	2,218	0.007	285	1932	101
Relapse	0.073	1,266	0.007	92	1173	364
Mortality: CS						
Men						*8 394-396*
35-39	0.0004	--	--	--	--	
40-44	0.0006	--	--	--	--	
45-49	0.0009	--	--	--	--	
50-54	0.0013	--	--	--	--	
55-59	0.0021	--	--	--	--	
60-64	0.0036	--	--	--	--	
Women						9 394-396
35-39	0.0004	--	--	--	--	
40-44	0.0007	--	--	--	--	
45-49	0.0011	--	--	--	--	
50-54	0.0017	--	--	--	--	
55-59	0.0027	--	--	--	--	
60-64	0.0044	--	--	--	--	
Mortality: EX						
Men						8 394-396
35-39	0.0001	--	--	--	--	
40-44	0.0002	--	--	--	--	
45-49	0.0003	--	--	--	--	
50-54	0.0004	--	--	--	--	
55-59	0.0007	--	--	--	--	
60-64	0.0010	--	--	--	--	
Women						9 394-396
35-39	0.0001	--	--	--	--	
40-44	0.0001	--	--	--	--	
45-49	0.0002	--	--	--	--	
50-54	0.0002	--	--	--	--	
55-59	0.0004	--	--	--	--	
60-64	0.0006	--	--	--	--	
Mortality: LT Absence	0.011	1,906	0.002	22	1883	397
ST Absence: CS						327
Men	0.095	375	0.015	35	338	
Women	0.041	1,242	0.006	50	1190	
ST Absence: EX						327
Men	0.022	498	0.007	11	486	
Women	0.018	1,182	0.004	21	1159	
LT Absence: CS						327
Men	0.057	375	0.012	21	353	
Women	0.024	1,242	0.004	29	1211	
LT Absence: EX						327
Men	0.015	498	0.005	7.37	489.39	
Women	0.010	1,182	0.003	11.52	1169.00	
Disability						398
Men	0.053	8,283	0.002	441	7841	
Women	0.054	11,096	0.002	594	10501	

6.3.5.3 Maximisation of quitting: cost-effectiveness analysis

One of the key assumptions in the primary analysis is that the employer will optimise strategy selection based on total costs incurred and return on investment as described in **Figure 20.** Decision making based on these financial metrics[233 362] are the most commonly employed strategy for businesses and employers for evaluating investments such as workplace interventions. However, there are other metrics which are also considered when businesses make investments. To address the secondary aim in this chapter, an assumption was made that the employer may value maximising quitting instead of minimising total costs. This was a plausible assumption as smoking cessation interventions are implemented in some workplaces with the primary purpose of maximising quit rates.[344] Therefore, cost-effectiveness analysis was conducted by re-assessing the Markov model using number of quitters as the primary outcome. Cost per quitter was utilised instead of cost per quality adjusted life-year (QALYs) due to having more relevance in an employer-based setting for smoking cessation interventions. The method of ranking interventions by QALYs implies a quasi-utilitarian perspective which is commonly used to determine who will or will not receive certain treatments.[408] This metric is extremely useful from a health services perspective in the provisioning of healthcare based on willingness-to-pay per QALY. From an employer-based perspective of workplace interventions, QALYs may be less intuitive for decision-making as the valuation of how much a QALY is worth is not standard practice. This is supported in a review[409] evaluating the cost-effectiveness of workplace policies for smoking cessation where all of the included studies used a cost per quitter metric.

Each strategy was ranked based on ICERs as described in **Section 6.3.1** calculated as the ratio of incremental costs over the incremental number of quitters of each workplace intervention compared to the previous intervention. ICERs were utilised because the workplace interventions were mutually exclusive options in this analysis. The ICER allows for the ranking of these mutually exclusive strategies to determine optimal strategy given a specific budget constraint (Willingness-To-Pay). However, in this analysis, there was no specified budget constraint as willingness-to-pay differs among employers (due to differences in size, overheads, efficiency). In addition, there was no literature to specify what UK employers were currently willing to pay per quitter. Therefore, an optimal strategy selection was provided for different scenarios of budget constraints.

6.4 Results

6.4.1 Effectiveness of interventions

The Markov model simulation was conducted using a cohort of 1,000 men and 1,000 women separately starting at the age of 35 and followed until the average age of retirement, disability or death (whichever occurred first) for each smoking cessation strategy.

Table 29. Cumulative number of current smokers, quitters, dead or disabled and total number of absence spells incurred for each workplace smoking cessation intervention

Strategy	Current Smokers	Total Quitters	Death or Disability	Absence Spells[1]
Men (N = 1000)				
No Intervention	685	80	235	7,186
Brief Advice	574	214	212	6,474
Individual Counselling	550	243	207	6,314
NRT + Individual Counselling	537	260	204	6,224
Women (N = 1000)				
No Intervention	761	98	141	3,195
Brief Advice	630	245	125	2,930
Individual Counselling	591	288	121	2,872
NRT + Individual Counselling	575	306	119	2,839

[1]Short-term absence, long-term absence, leaving work through death or disability

The number of workers in each state at the average age of retirement is reported in **Table 29** for separate smoking cessation strategies. In both men and women, the number of current smokers decreased while the number of quitters increased for more comprehensive smoking cessation strategies. NRT with individual counselling provided the highest number of sustained quitters (260 men; 306 women), lowest number of workers who left work due to death or disability (204 men; 119 women) and fewest absence spells incurred (men: 6,224 cases; women: 2,839 cases). The baseline 'no intervention' strategy resulted in the lowest number of sustained quitters (80 men; 98 women), highest number of workers who left work

due to death or disability (235 men; 141 women) and most absence spells incurred (7,136 men; 3,195 women). Brief advice and individual counselling were ranked between the effectiveness of 'no intervention' and NRT with individuals counselling in terms of increasing number of sustained quitters and reducing death, disability or absence spells. If strategy selection was purely based on effectiveness of increasing the number of quitters and reducing the number of deaths, disabilities or absence spells, then NRT with individual counselling was the optimal choice for an employer without budget constraints.

6.4.2 Cost-benefit analysis

6.4.2.1 Deterministic

Despite being the most effective strategy for increasing quitting and reducing death, disability or absenteeism, NRT with individual counselling was not the optimal choice when effectiveness was evaluated alongside cost implications for the employers (i.e. the cost of intervention, absence and labour turnover). The cost-benefit analysis based on the total cost (TC) incurred and return on investment (ROI) for each smoking intervention strategy were provided in **Table 30**.

Table 30. Total costs (TC) incurred and return on investment (ROI) of workplace smoking cessation interventions per 1,000 individuals (deterministic)

Strategy	Total Cost (£)	Absence and Labour Turnover (£)	Intervention Cost (£)	Net Benefit[1] of Absence and Labour Turnover (£)	Net Cost[2] of Intervention (£)	ROI (£)
Men **(N = 1,000)**						
No Intervention	£5,253,219	£5,253,219	£0	--	--	--
Brief Advice	£4,875,484	£4,801,137	£74,347	£452,082	£74,347	£5.08
Individual Counselling	£4,975,282	£4,696,842	£278,440	£556,377	£278,440	£1.00
NRT + Individual Counselling	£5,264,242	£4,637,535	£626,706	£615,684	£626,706	-£0.02
Women **(N = 1,000)**						
No Intervention	£2,294,834	£2,294,834	£0	--	--	--
Brief Advice	£2,196,534	£2,113,734	£82,800	£181,100	£82,800	£1.19
Individual Counselling	£2,381,797	£2,072,774	£309,023	£222,060	£309,023	-£0.28
NRT + Individual Counselling	£2,743,785	£2,049,620	£694,165	£245,214	£694,165	-£0.65

[1]Net benefit = net savings from absence and labour turnover costs compared to no intervention (baseline)
[2]Net cost = net costs of workplace smoking cessation intervention compared to no intervention (baseline)

Total cost (TC) was the combined expected value of absence, labour turnover and intervention for each workplace intervention over the productive lifetime. According to **Table 30**, brief advice for both men and women was the optimal strategy if the strategy selection was based on the minimisation of total costs (men: £4,875,484; women: £2,196,534). NRT with individual counselling had the largest total costs incurred for both men and women compared to all other strategies (men: £5,253,219; women: £2,743,785) due to having the most expensive intervention costs (men: £626,706; women: £694,165).

In terms of the monetary returns on investment, brief advice also provided the largest returns on investment (ROI) for men and women. For every £1 the employer expends, brief advice resulted in additional returns of £5.08 for men and £1.19 for women. Individual counselling provided positive but smaller return than brief advice for men with a ROI of £1. However, in women, individual counselling provided a negative ROI of -£0.28. NRT with individual counselling provided the employer with negative ROIs for both men (-£0.02) and women (-£0.28). For the employer, brief advice resulted in the lowest TC and highest ROI compared to all other strategies for both men and women.

6.4.2.2 One-way cost sensitivity analysis

Maximum and minimum values for state costs were used to calculate the change in total costs incurred from baseline for men in **Figure 28** and for women in **Figure 29.** The graphs illustrate the monetary change from baseline estimates of total cost in thousands of GBP. Sensitivity in NRT adherence costs only affected the total costs for the smoking cessation strategy which provided NRT. There was no difference in total costs for other smoking cessation strategies which did not provide NRT.

Figure 28. Tornado diagram showing the change in total costs incurred from baseline due to one-way sensitivity analysis of state costs for male workers (£ Thousands)

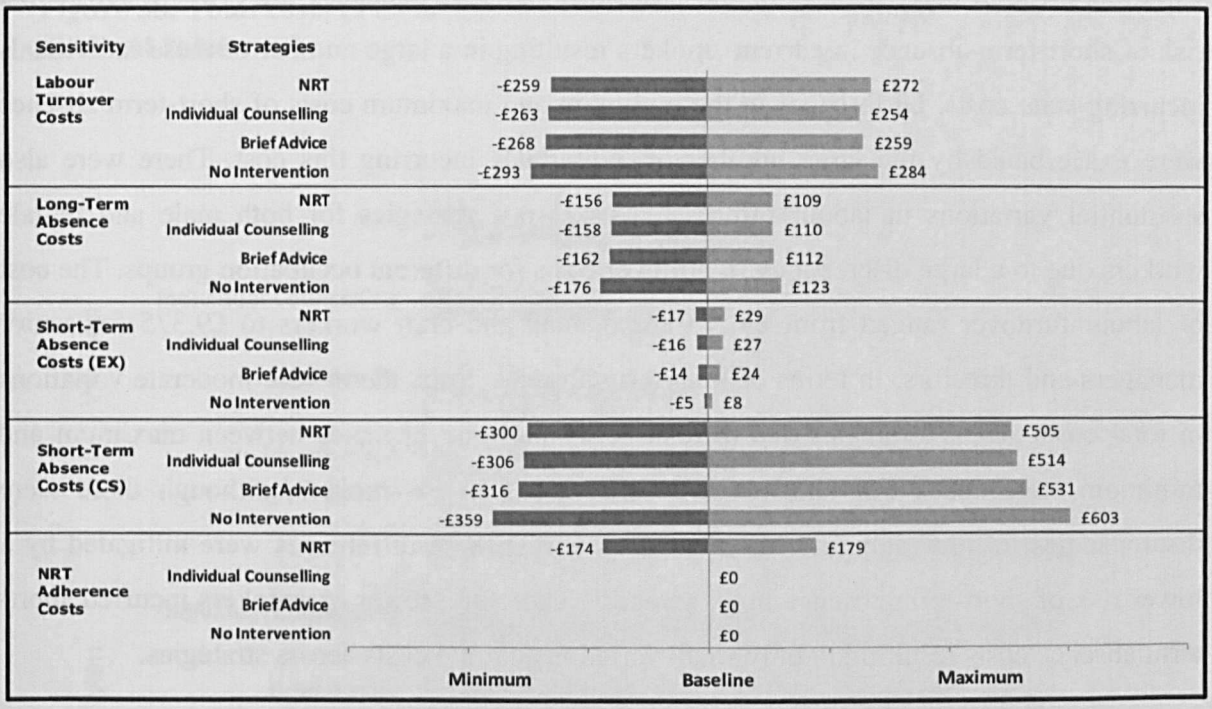
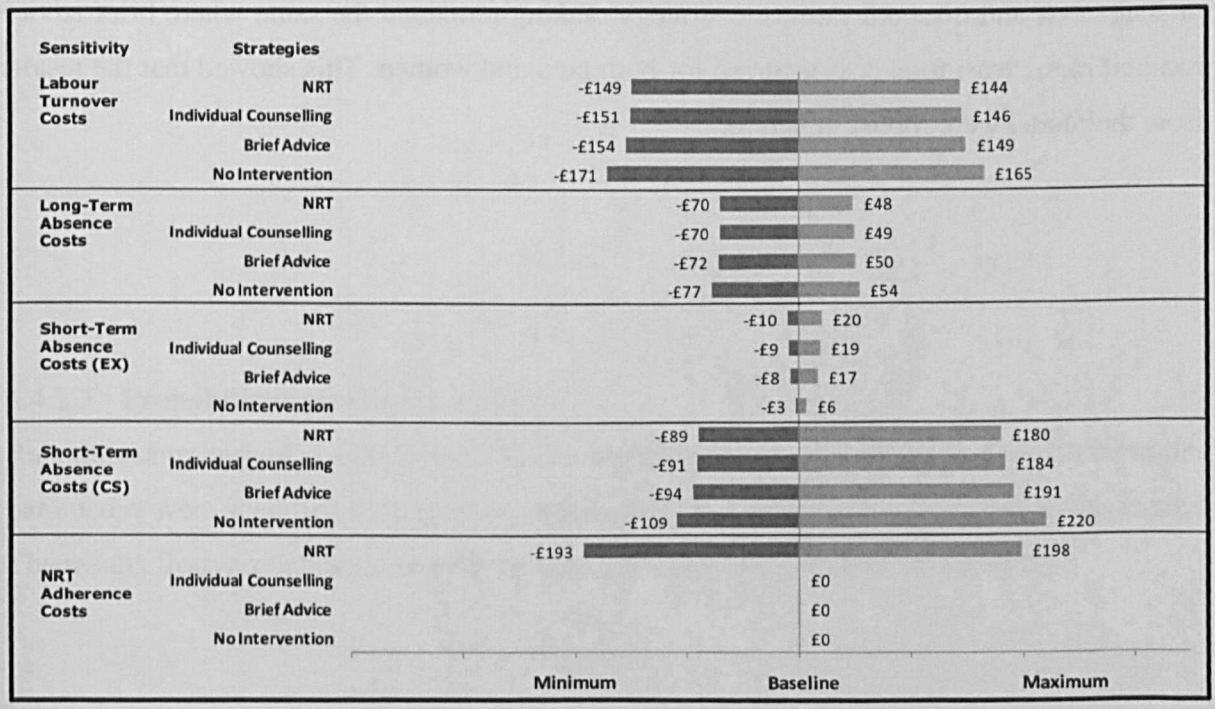


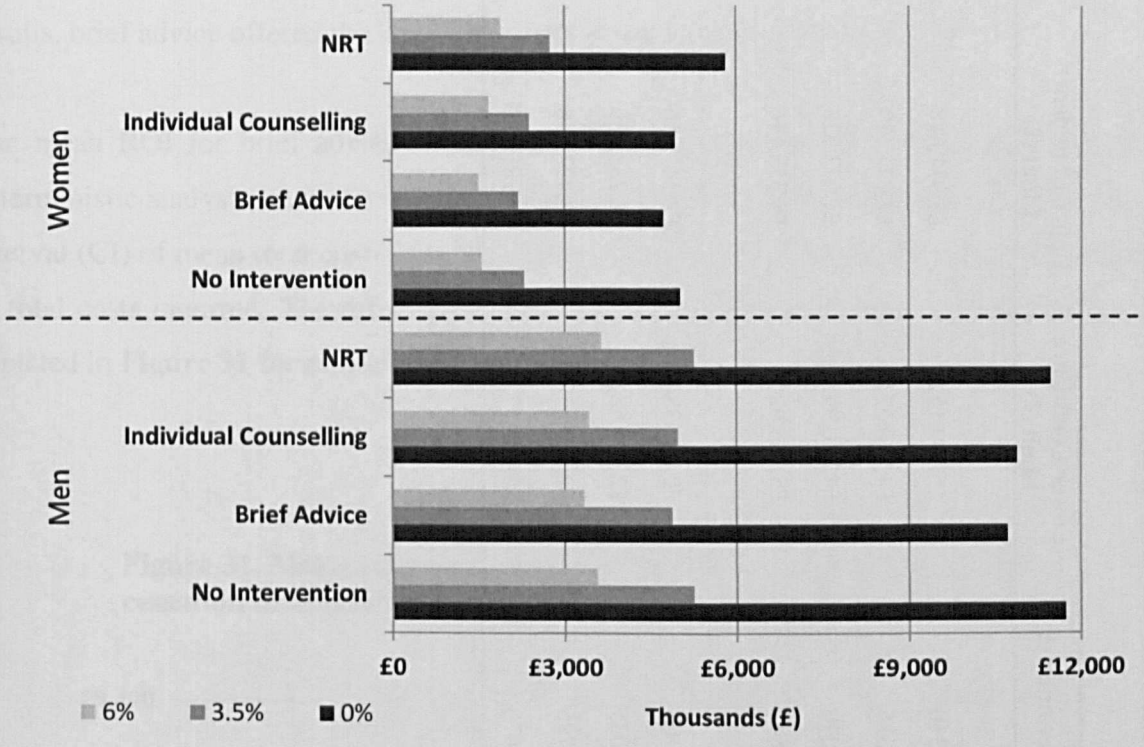
Figure 29. Tornado diagram showing the change in total costs incurred from baseline due to one-way sensitivity analysis of state costs for female workers (£ Thousands)



For both men and women, short-term absence costs for current smokers resulted in the largest variations in total costs across all four strategies. This was because there was a substantial risk of short-term absence in current smokers resulting in a large number of these individuals incurring state costs. Differences in the minimum and maximum costs of short-term absence were exacerbated by the large number of individuals incurring this cost. There were also substantial variations in labour turnover costs across strategies for both male and female workers due to a large discrepancy in turnover costs for different occupation groups. The cost of labour turnover ranged from £3,281 for manual and craft workers to £9,375 for senior managers and directors. In terms of long-term absence costs, there were moderate variations in total costs across strategies due to relatively small discrepancies between maximum and minimum state costs. For short-term absence costs in ex-smokers, although there were discrepancies in maximum and minimum state costs, these differences were mitigated by a lower risk of short-term absence in ex-smokers. Therefore, fewer ex-smokers incurred short-term absence costs resulting in only small variations in total costs across strategies.

Sensitivity analysis using alternate discount rates is shown in **Figure 30**. For both men and women, total costs were smallest for all strategies when costs were undiscounted. Total costs were largest when discounted by 6%. Despite the variations in total costs due to differences in state costs and discount rates, the strategy ranking remained the same where brief advice resulted in the least total cost incurred for both men and women. This showed that the results from the model were robust in nature.

Figure 30. Total costs (TC) incurred of smoking cessation strategies using alternate discount rates



6.4.2.3 Probabilistic sensitivity analysis

Random sampling of 1,000 Monte Carlo simulations was conducted after distributions parameters were specified for transition probabilities to evaluate the uncertainty in the results. The results from probabilistic sensitivity analysis (PSA) are provided in **Table 31**.

Table 31. Mean total costs (TC) incurred with 95% confidence interval (CI) and mean return on investment (ROI) of workplace smoking cessation interventions (PSA)

Strategy	Mean Total Cost (£)	Standard Deviation (£)	Lower Confidence Limit (£)	Upper Confidence Limit (£)	Mean ROI
Men **(N = 1,000)**					
No Intervention	£5,255,400	£59,310	£5,139,152	£5,371,648	--
Brief Advice	£4,872,170	£52,015	£4,770,221	£4,974,119	£5.16
Individual Counselling	£4,977,110	£49,040	£4,880,992	£5,073,228	£1.00
NRT + Individual Counselling	£5,259,400	£47,845	£5,165,624	£5,353,176	-£0.01
Women **(N = 1,000)**					
No Intervention	£2,296,670	£23,105	£2,251,384	£2,341,956	--
Brief Advice	£2,196,910	£21,035	£2,155,681	£2,238,139	£1.20
Individual Counselling	£2,381,390	£20,795	£2,340,632	£2,422,148	-£0.27
NRT + Individual Counselling	£2,742,730	£19,670	£2,704,177	£2,781,283	-£0.64

From the probabilistic results provided in **Table 31,** the optimal strategy selection did not differ from the deterministic analysis. Brief advice for both men and women had the lowest mean total costs incurred (men: £4,872,170; women: £2,196,910). NRT with individual counselling had the largest mean total costs incurred for both men and women compared to all other strategies (men: £5,259,400; women: £2,742,730). Similar to the deterministic results, brief advice offered the largest mean ROI (men: £5.16; women: £1.20).

The mean ROI for brief advice from probabilistic analysis was similar to the ROI from deterministic analysis (men: £5.08; women: £1.19). **Table 31** also shows the 95% confidence interval (CI) of mean total costs incurred which was constructed using the standard deviation of total costs incurred. The mean total costs and 95% CI for each intervention strategy are depicted in **Figure 31** for men and in **Figure 32** for women.

Figure 31. Mean total cost (TC) and 95% CI for workplace smoking cessation interventions for men

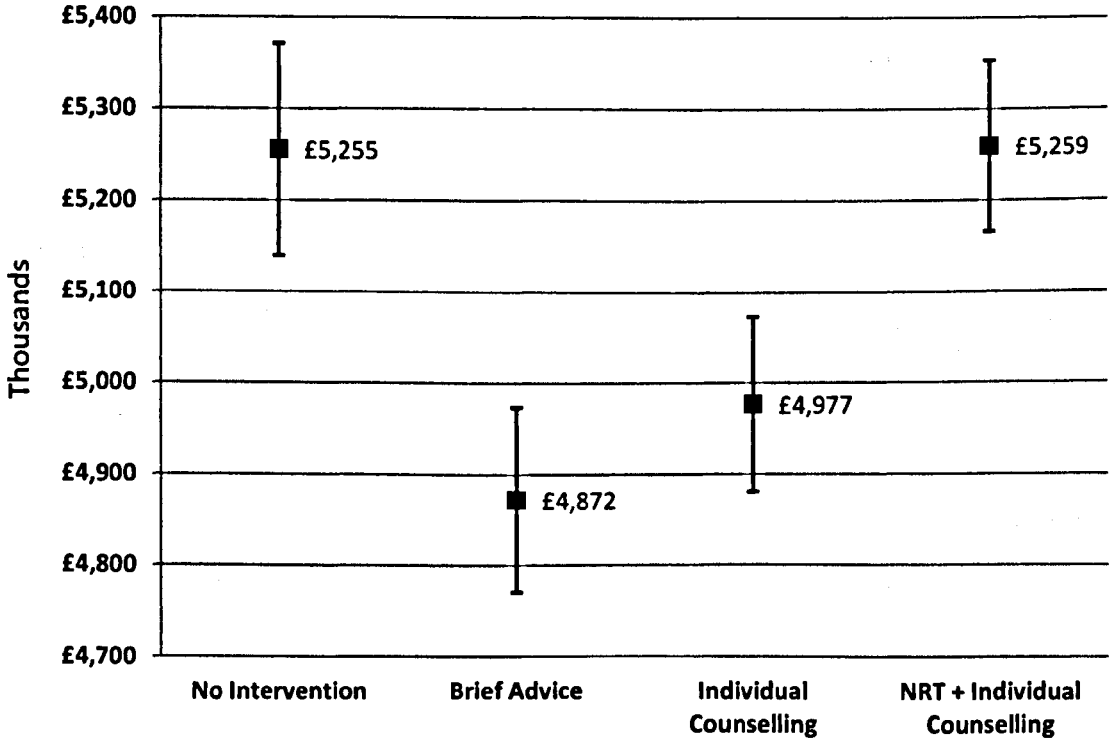
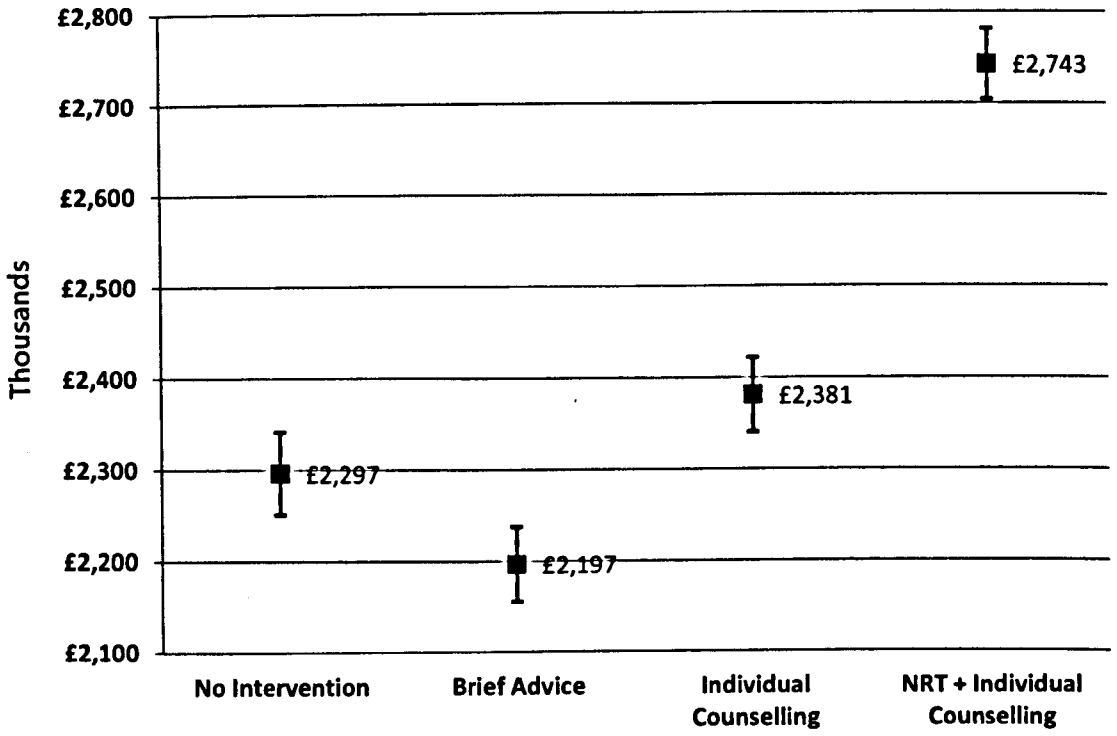


Figure 32. Mean total cost (TC) and 95% CI for workplace smoking cessation interventions for women

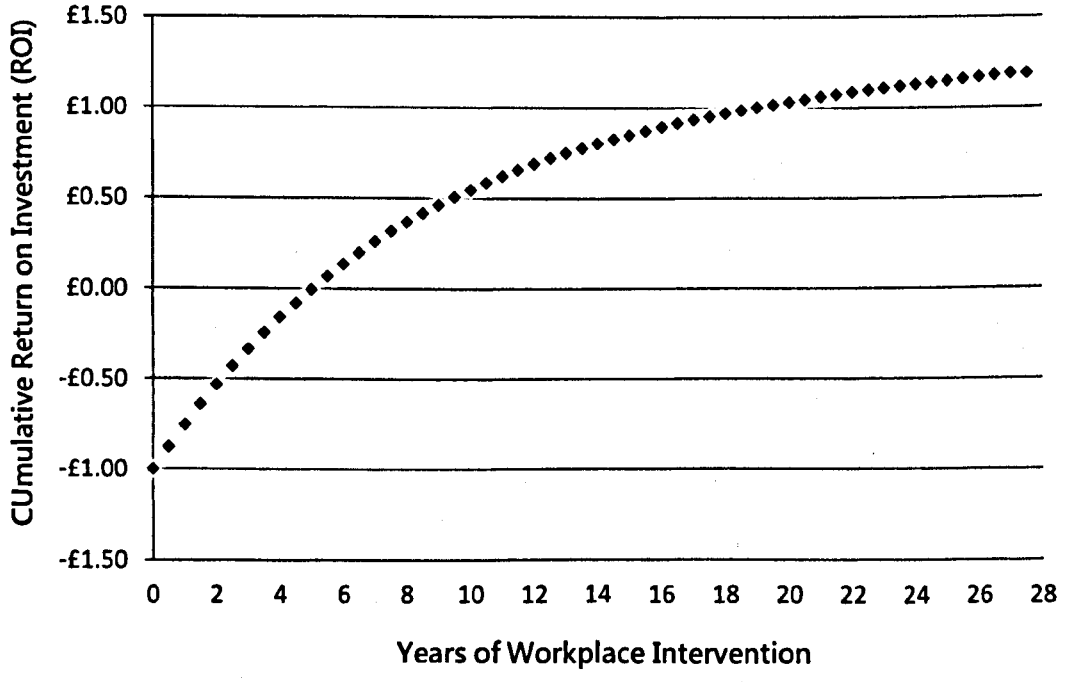


In men (**Figure 31**), total cost incurred for brief advice (£4,872,170; 95% CI £4,770,221 to £4,974,119) was significantly different from total cost incurred for no intervention (£5,255,400; 95% CI £5,139,152 to £5,371,648) and NRT with individual counselling (£5,259,400; 95% CI £5,165,624 to £5,353,176) but was not significantly different from total cost incurred for individual counselling (£4,977,110; 95% CI £4,880,992 to £5,353,176). In women (**Figure 32**), total cost incurred for brief advice (£2,196,910 95% CI £2,155,681 to £2,238,139) was significantly different from total cost incurred for no intervention (£2,296,670; 95% CI £2,251,384 to £2,341,956), individual counselling (£2,381,390; 95% CI £2,340,632 to £2,422,148) and NRT with individual counselling (£2,742,730; 95% CI £2,704,177 to £2,781,283). The results from PSA suggest that brief advice was the optimal strategy for women and either brief advice or individual counselling could be the optimal strategy for men.

6.4.2.4 Average cumulative returns on investment over time

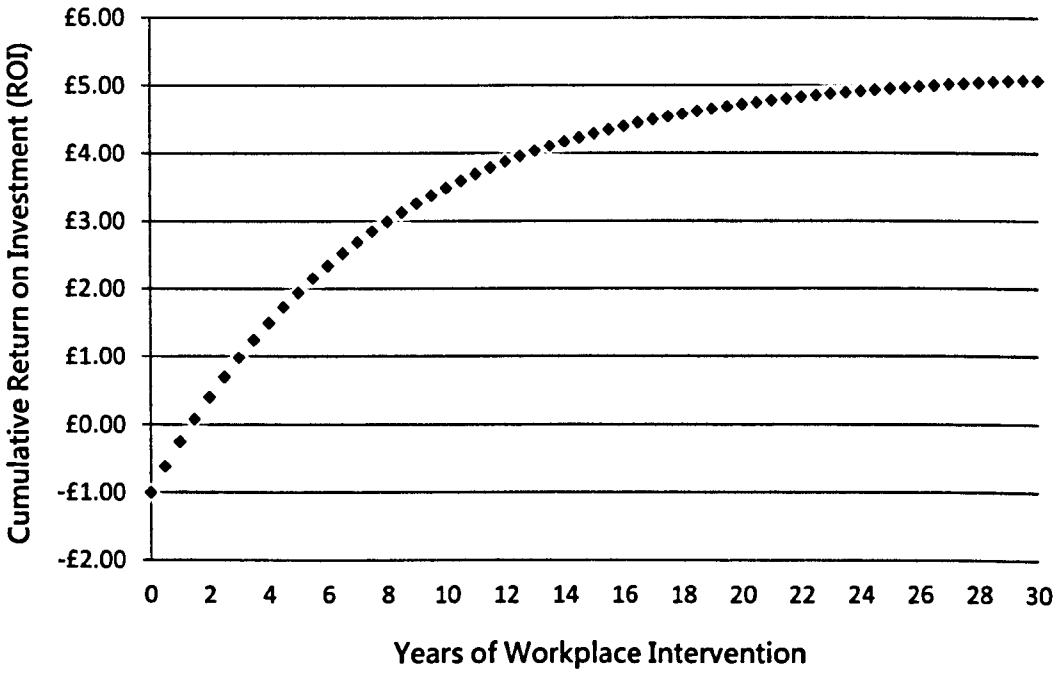
With the inclusion of parameter uncertainty in PSA, the total costs incurred for brief advice was significantly different than all other interventions for women. Therefore, brief advice was the single optimal option for women. In men, total costs incurred for brief advice and individual counselling were significantly different than all remaining interventions. However, brief advice and individual counselling did not differ significantly in total costs incurred. Thus, either brief advice or individual counselling could be the optimal option. The results for the optimal decisions were the result of cumulative costs incurred over a productive life time. Consequently, it was unknown whether brief advice or individual counselling resulted in positive returns on investment (ROI) in the short-term or long-term. In **Figure 33**, average cumulative ROI (from PSA) for brief advice was plotted in years for women.

Figure 33. Average cumulative returns on investment (from PSA) for brief advice in women over years of workplace smoking cessation intervention



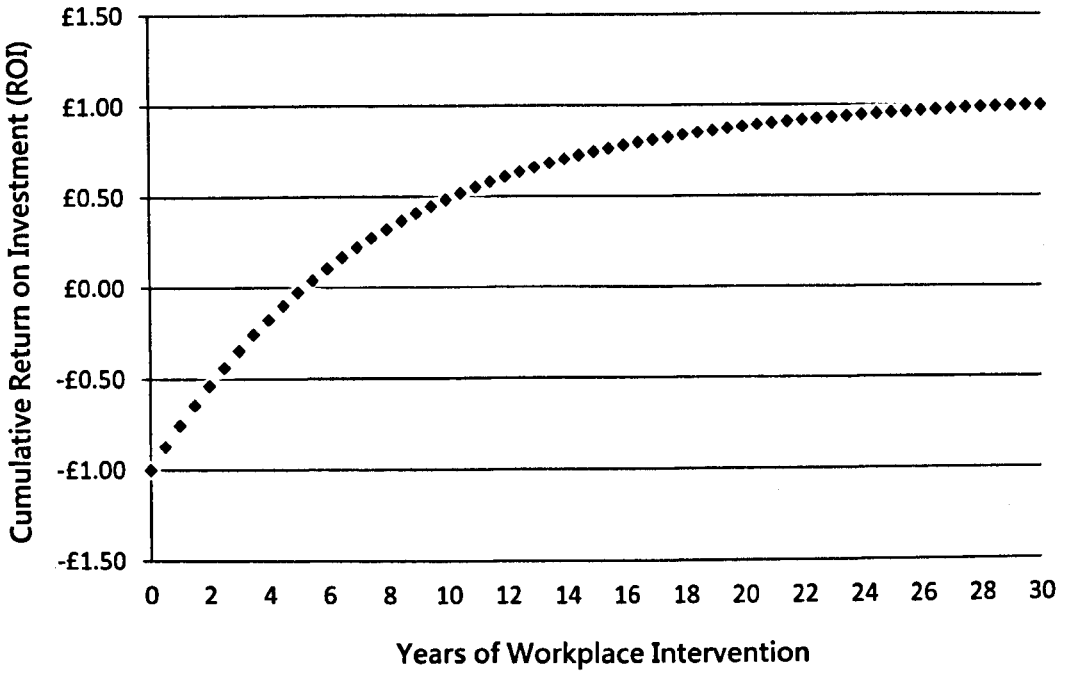
The results in **Figure 33** showed that positive returns on investment from brief advice in women occurred after 5.5 years since the inception of the programme. Not only was brief advice the optimal strategy over the productive lifetime of the intervention but was also the optimal strategy in a relatively short amount of time. In **Figure 34**, a similar plot of average cumulative ROI against intervention time in years was analysed for brief advice in men.

Figure 34. Average cumulative returns on investment (from PSA) for brief advice in men over years of workplace smoking cessation intervention



The results **Figure 34** in showed that positive returns on investment from brief advice in men occurred in a shorter time than in woman. Brief advice in men resulted in positive returns in investment almost immediately after the inception of the programme from 1.5 years onwards. Individual counselling was also analysed in men in **Figure 35** due to the fact that the total cost incurred was not significantly different than total incurred of brief advice.

Figure 35. Average cumulative returns on investment (from PSA) for individual counselling in men over years of workplace smoking cessation intervention



The returns on investment for individual counselling were on average less than that of brief advice in men but did provide positive returns after 5 years since programme inception. Overall, brief advice is likely to provide positive returns on investment in men at a much faster and larger amount than individual counselling. However, this difference may not be significant. Nevertheless, both options of brief advice and individual counselling provide employers with good investment opportunities compared to current practice (no intervention). In addition, the law of diminishing returns shapes all three figures in the long-term. Long-term returns gradually decrease as the pool of current smokers becomes smaller as quitting increases. Thus, incremental returns on investments decrease due to fewer numbers of current smokers in the work cohort as time increases.

6.4.3 Cost-effectiveness analysis

The secondary aim of this chapter was to examine whether the decision strategy changed had the employer valued maximising quit rates as the primary outcome. The Markov model was re-assessed using number of quitters as the primary outcome and each strategy was ranked based on ICERs. **Table 32** shows the ICERs of the Markov simulation model using number of quitters as the primary outcome.

Table 32. ICERs (£/Quitter) for each workplace smoking cessation strategy compared to the previous strategy from Markov simulation modelling

Strategy	Total Costs (£)	Total Quitters	Incremental Costs (£)	Incremental Quitters	ICER (£/Quitter)
Men **(N = 1000)**					
No Intervention	£5,255,400	80	£0	£0	--
Brief Advice	£4,872,170	214	-£383,230	134	-£2,859.75
Individual Counselling	£4,977,110	243	£104,940	29	£3,623.66
NRT + Individual Counselling	£5,259,400	260	£282,290	16	£17,457.81
Women **(N = 1000)**					
No Intervention	£2,296,670	98	£0	£0	--
Brief Advice	£2,196,910	245	-£99,760	147	-£678.12
Individual Counselling	£2,381,390	288	£184,480	43	£4,298.60
NRT + Individual Counselling	£2,742,730	306	£361,340	18	£19,837.79

Table 32 shows that no intervention was the dominated strategy in both men and women. Brief advice was less costly and more effective at maximising number of quitters than no intervention. Therefore, the baseline strategy of no intervention was never cost-effective so this could be excluded from as a decision option immediately. This can be easily visualised using incremental cost-effectiveness planes (**Figure 36** for men and **Figure 37** for women).

Figure 36. ICER plane for workplace smoking cessation strategies compared to the previous strategy in men

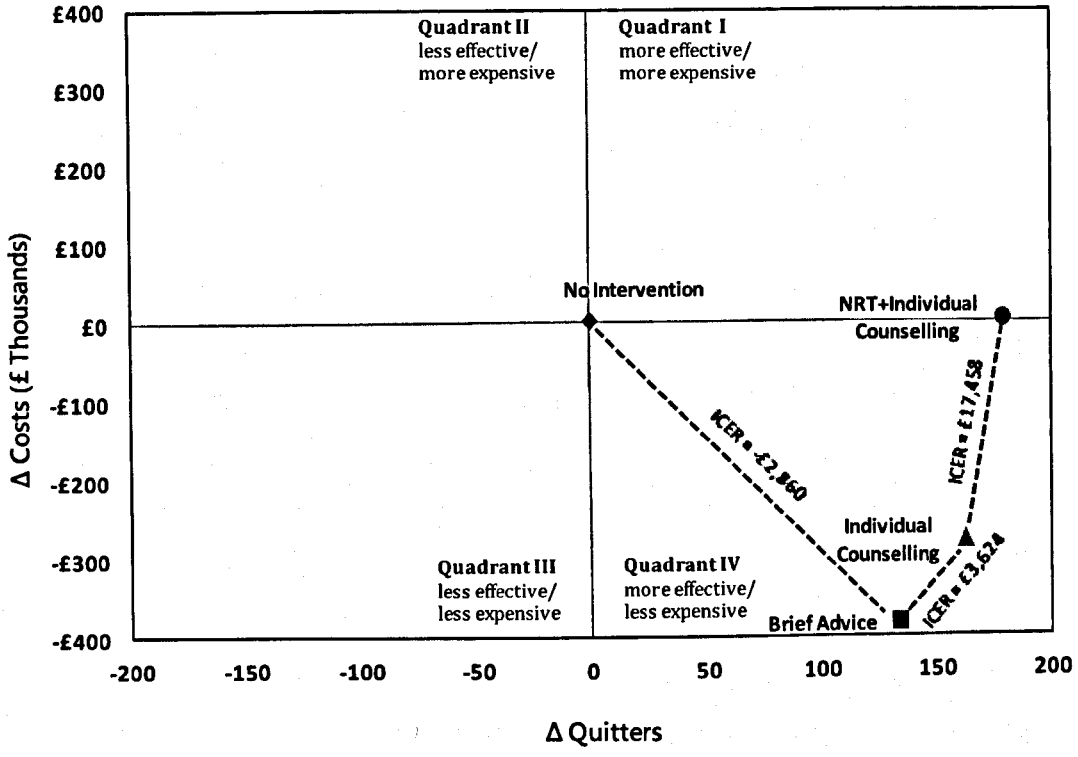
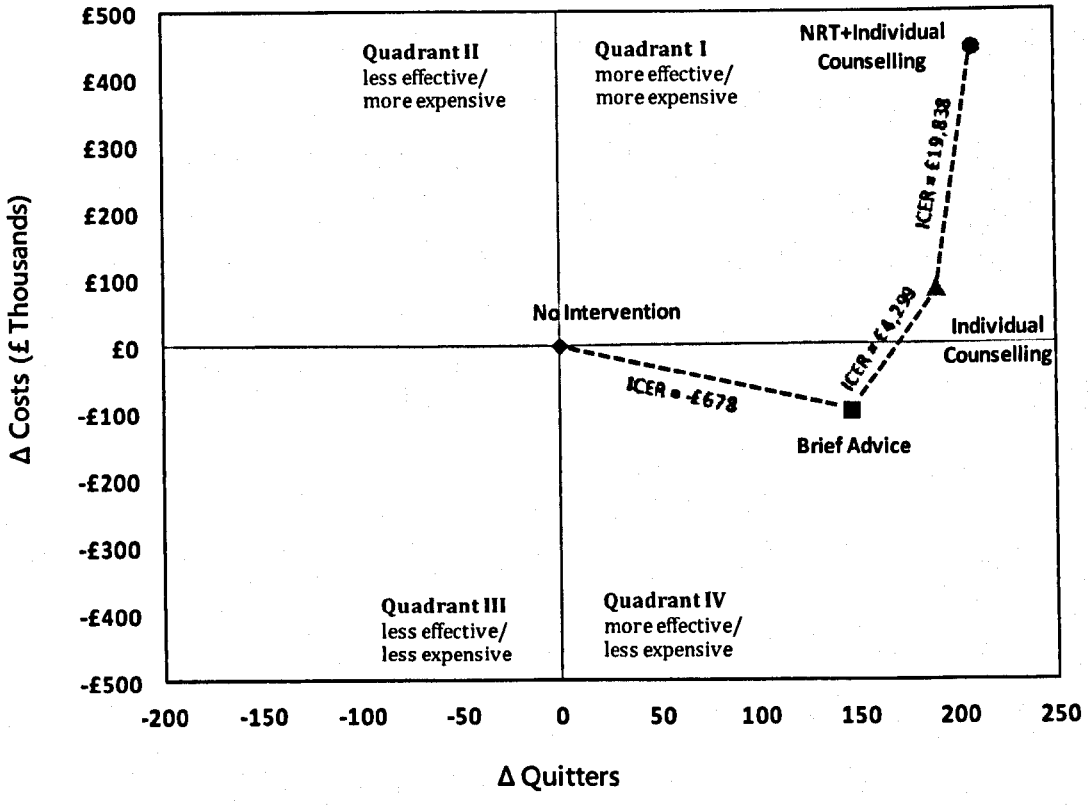


Figure 37. ICER plane for workplace smoking cessation strategies compared to the previous strategy in women



The origin of the incremental cost-effectiveness planes represents the baseline strategy of no intervention. The incremental costs and quitters were plotted relative to the origin and ranked based on the ICER from the previous strategy. Brief advice and individual counselling appeared in quadrant IV for men meaning that both strategies were less expensive and more effective than no intervention (**Figure 36**). Brief advice was the only strategy that appeared in quadrant IV for women which dominated no intervention (**Figure 37**).

In terms of ranking the cost-effectiveness of brief advice, individual counselling and NRT with individual counselling, there was no clear dominated strategy. For individual counselling compared to brief advice an additional male quitter costs £3,624 (**Figure 36**) while an additional female quitter costs £4,299 (**Figure 37**). For NRT with individual counselling compared to individual counselling, an additional male quitter cost costs £17,458 (**Figure 36**) while an additional female quitter costs £19,838 (**Figure 37**).

The most cost-effective strategy for these remaining interventions will be dependent on budget constraints or willingness-to-pay. The current willingness-to-pay for employers in the UK is unknown so therefore a hypothetical scenario analysis was implemented to rank the remaining strategies. Budget constraints or willingness-to-pay can be determined based on total costs shown in **Table 32** per person (divided by N = 1,000). If the total budget constraint was £4,872 per male worker and £2,197 per female worker then brief advice would the most cost-effective option. If the total budget constraint was £4,977 per male worker and £2,381 per female worker then the more effective intervention of individual counselling would be the most cost-effective option. If the total budget constraint was £5,259 per male worker and £2,743 per female worker or if there was no budget constraint, then the most effective option of NRT with individual counselling would be the most cost-effective option.

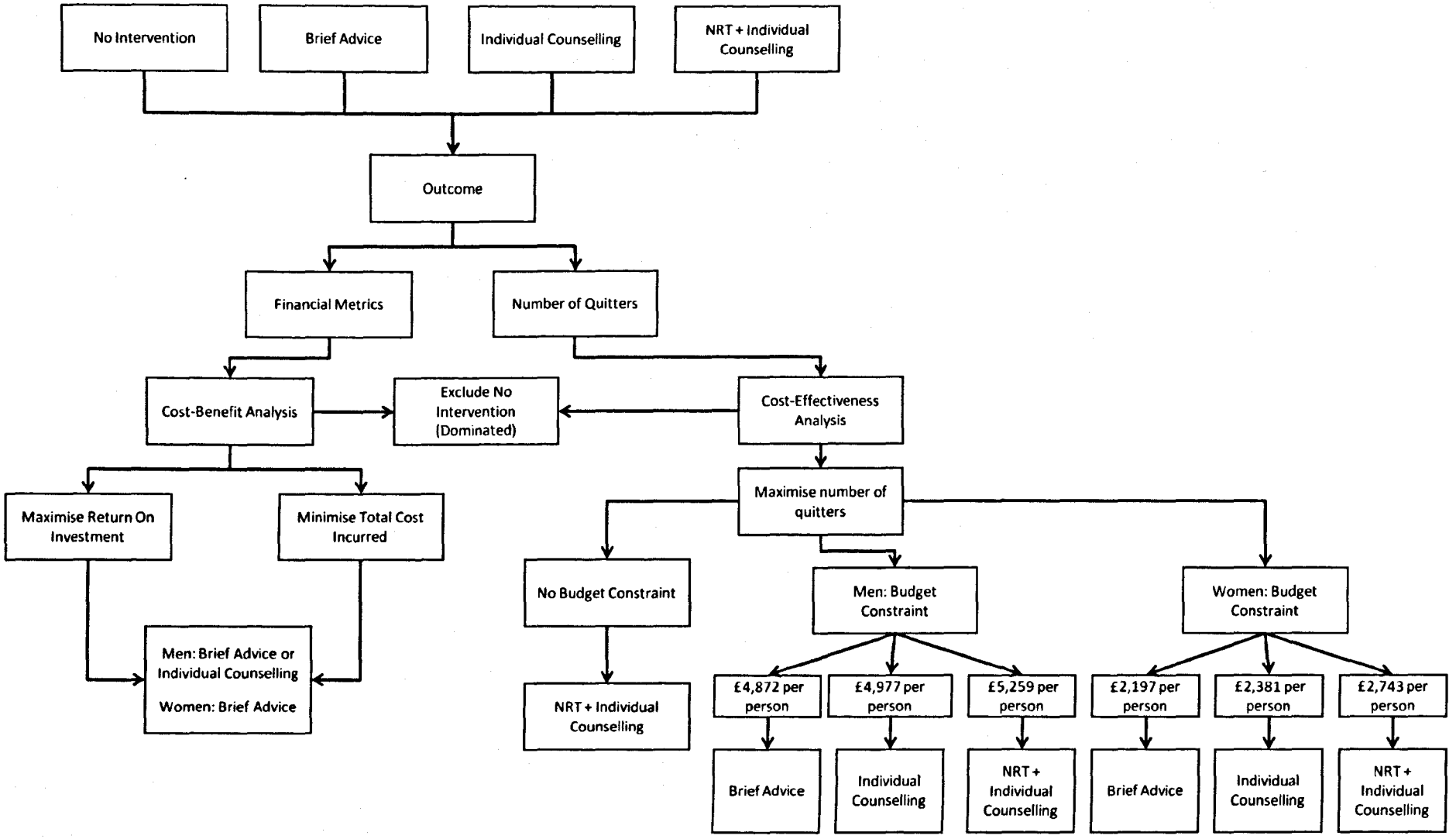
6.5 Discussion

6.5.1 Summary

The results of the simulation of workers over the course of a productive life-time showed that NRT with individual counselling provided the highest number of quitters, the lowest number of workers who left work due to death or disability and fewest cases of absence spells compared to no intervention, brief advice or individual counselling alone. However, once costs were factored in, brief advice was the optimal strategy for minimising the total costs incurred and maximising return on investment for the employer. Probabilistic sensitivity analysis showed that total costs incurred were significantly different from all other interventions in women while brief advice and individual counselling were both viable investment options in men (**Figure 38**). Brief advice in women resulted in average additional returns of £1.20 per pound expended while brief advice in men resulted in average additional returns of £5.16 per pound expended. Individual counselling in men resulted in average additional returns of £1.00 per pound expended. Additionally, positive returns occurred only a few years after the interventions were implemented suggesting the interventions did not just provide long-term financial benefits. One-way sensitivity analysis of costs and alternate discount rates (0% and 6%) did not change the strategy ranking process showing that the results were robust.

One of the key assumptions for the primary analysis was that employers are optimising decisions based on financial metrics such as total cost (TC) incurred and return on investment (ROI). Cost-benefit suited this analysis as investment decisions for cessation interventions were based purely on financial benefits. However, there are other outcomes employers may base decision making on. In the constructed decision flow chart in **Figure 38**, it was assumed that employers may try to maximise number of quitters. Instead of cost-benefit analysis, cost-effectiveness analysis was used to evaluate the workplace interventions.

Figure 38. Decision flow chart for optimal workplace smoking cessation intervention selection from the results of the analysis



The decision options in the scenario analysis were dependent on budget constraints. If the total budget constraint was £4,872 per male worker and £2,197 per female worker then brief advice would the most cost-effective option. If the total budget constraint was £4,977 per male worker and £2,381 per female worker then the more effective intervention of individual counselling would be the most cost-effective option. If the total budget constraint was £5,259 per male worker and £2,743 per female worker or if there was no budget constraint, then the most effective option of NRT with individual counselling would be the most cost-effective option.

The large discrepancies in total costs, return on investment and budget constraints between men and women were due to gender differences between absence costs and absence probabilities. Average hourly wages (used to value short-term absence costs) for women were less than that of men (described in **Section 6.3.4.2**). Additionally, absenteeism in women was less problematic than absenteeism in men as there was less risk of short-term and long-term absence (described in **Section 6.3.3.6**). Therefore, the transitions probabilities and state costs of both short-term and long-term absenteeism reflected this difference in the Markov model results.

6.5.2 Implications

This is the first study that has evaluated the cost-benefit/cost-effectiveness of smoking cessation interventions in the workplace from an employer's perspective in the UK. The results suggest that employers who adopt workplace smoking cessation programmes will in fact save money assuming that turnover not shorter than 2-5 years per employee. From an employer's perspective, not having a workplace intervention was not optimal for either returns on investment or maximising quitting. This suggests there is common ground for employers to contribute towards the net social welfare of society. The selection between brief advice, individual counselling and NRT with individual counselling depends on a multitude of factors such as outcome metrics or budget constraints as shown in **Figure 38**. From a societal perspective, the maximisation of quit rates would contribute the most towards net social welfare due to overwhelming health and economic benefits of smoking cessation (**Section 1.4**). The employer's strategy selection, however, may not necessarily maximise social welfare from a societal perspective. For instance, if an employer chooses to base the decision process on financial metrics, then brief advice would be an optimal intervention

from the employer's perspective offering the best returns on investment. While brief advice certainly will contribute towards increasing the number of quitters, it would not be the intervention that would maximise quitting. Even if employers valued maximising quitting, the decision strategy will be largely dependent on individual budget constraints. However, if budget constraints were maximised or eliminated, then the most effective intervention NRT with individual counselling would be the optimal option resulting in the alignment of the societal and employer's perspective. This has some potential policy implications.

This suggests that policy-makers could consider promoting or supporting employers that choose to start a workplace smoking cessation intervention. Tax incentives, subsidies or support for employers for setting up smoking cessation interventions in the workplace may offer better returns on investments by cutting costs of more expensive yet more effective interventions. A survey of 1,344 British workplaces[410] found that only 40% undertook at least one major health-related activity per year. However, activity was particularly low in small and medium sized companies, lacked structure and organisation to be effective. One of the reasons cited for smaller and medium sized companies was the overhead costs of setting up interventions were proportionally more than that of larger corporations.[410] Another key issue which may affect whether or not employers adopt smoking cessation interventions is workforce turnover rates. The economic model presented in this chapter was modelled on a stable population of workers. However, workforce turnover rates can significantly differ between employers. For employers with low turnover rates (employees stays greater than 2-5 years), the model shows that there are clear benefits of smoking cessation interventions. For employers with high turnover rates (employees stays less than 2-5 years), it may not be cost-effective to implement a smoking cessation intervention as the long-term benefits of reducing absenteeism, disability and death may not be realised by the employer.

In addition, there are several reasons why interventions in the workplace can contribute to the net social welfare of society which the model does not consider due to using an employer's perspective[352]: (i) protection of non-smokers from the harmful effects of tobacco smoke [182] reduced direct costs of health care (iii) reduced costs of life insurance (iv) reduced cleaning costs (v) reduced risk of fires (vi) increased productivity. There are also several potential advantages of interventions in the workplace. First, more people may be reached and thereby participation and cessation may be increased.[352] Second, the workplace provides access to relatively large number of people who make up a stable population.[344] Third, there is a good

opportunity to target young men who traditionally have low general practitioner visiting rates.[344] Finally, many workplaces (apart from small businesses) already have occupational health staff and travel time is minimal.[344]

While this study is particularly relevant to UK employers and policy makers, the results are transferable to other developed countries where the smoking prevalence, labour costs and mortality rates are similar. The key parameters in the model are the treatment effects of smoking cessation interventions obtained from randomised clinical trials which are likely to be similar across populations. The model itself is extremely flexible and can be used at an aggregate-level or individual employer-level. The model can be easily populated with country-specific parameters or even employer-specified parameters.

6.5.3 Limitations

There were several limitations of the study – most of which involve model assumptions around parameter or structural uncertainty. First, the baseline unassisted quit rate of 6.9% pooled from the control groups of the clinical trials may be higher than the general population. The unassisted quit rate from the control groups was used so individuals from the control groups could be compared to the treatment groups which allowed for the pure treatment effect to be obtained. In clinical trials outcomes tend to be optimistic due to individuals knowing they are in a clinical trial. Survey estimates of six-month quit-rates from other studies ranged only between 3-5%[166]. However, the probabilistic analysis took into account this discrepancy as the *beta* distribution for the baseline quit rate of 6.9% ranged from 3% to 9%. Second, the random-effects meta-analysis which provided baseline cessation rates combined the control arms of brief advice, individual counselling and NRT with individual counselling to generate a larger pooled sample from which estimates could be obtained. The pooled baseline quit rate of 6.9% (95% CI 4.7% to 9.4%, N = 18 studies) was then applied to risk ratios from meta-analysis to determine quit rates for brief advice (9.9%), individual counselling (11.7%) and NRT with individual counselling (12.8%). In order to determine if the pooling of all control arms in a meta-analysis affected the quit rates for each smoking cessation strategy, meta-analyses were conducted separately for each smoking cessation strategy. The baseline quit rate for brief advice was 6.6% (95% CI 4.1% to 8.0%, N = 4 studies); for individual counselling was 6.8% (95% CI 5.5% to 7.8%, N = 6 studies); and for NRT with individual counselling was 7.1% (95% CI 5.8% to 8.4%, N = 8 studies). The

baseline quit rates for individual smoking cessation strategies were very similar to the pooled baseline quit rate of 6.9%. Therefore, the effects of using the quit rates from the individual smoking cessation strategies would have only marginally changed the results of the analysis. Third, the treatment effects from the random effects meta-analysis of brief advice, individual counselling and NRT with individual counselling were combined for both men and women. Men and women may in fact have different treatment effects which the Markov model did not capture. Individual studies in the meta-analysis did not report gender subgroups and therefore could not be pooled separately. Fourth, the probability of mortality, disability and absence was not dependent on time since an individual became an ex-smoker due to Markov memory limitation and parameter uncertainty. For probability of mortality, the model could not determine how long an individual had become a non-smoker. A way around this is to build multiple ex-smoking states; however, this would have made the model overly complex with little added value. For probability of disability and absence, there were no parameters in the literature which addressed time dependency. Fifth, the structural assumption was made that individuals would remain in the cohort until they retire or exits due to disability or death. It is likely that individuals in the workplace could quit or leave for other employment. There was no literature around how long individuals typically remained at one employer at the population-level. Sixth, distributions for state costs could not be fit due to limited data. Although sensitivity analysis was conducted using maximum and minimum costs, the probabilistic analysis assumed infinite probability density for cost parameters. Finally, there were no parameters in the literature which could inform a sensitivity analysis on size of the employer. Financial outcome metrics such as return on investment may depend on size as smaller business may have relatively larger overheads compared to larger businesses.

6.6 Conclusion

In this chapter, the economic evaluation of workplace interventions resulted in brief advice being the optimal decision strategy for women and both brief advice and individual counselling were the optimal decision strategies for men in terms of minimising total costs and maximising return on investment. If the employer valued maximising quitting, then NRT with individual counselling was the most cost-effective strategy given a budget constraint greater than or equal to £5,259 per worker. These results, however, are dependent on employer workforce turnover rates. Nevertheless, this analysis shows that employers can contribute to net social welfare of society. Policy which aligns employers' interest to societal

interest may maximise net social welfare to society. Future research also needs to examine the cost-benefit/cost-effectiveness of other forms of pharmacotherapy (varenicline or bupropion) and financial incentives for smoking cessation.

Chapter 7

Summary Conclusions and Future Research

7.1 Introduction

The overall aims of this thesis were to quantify the economic impact of indirect costs of premature mortality and absenteeism in the UK and to evaluate possible solutions to decrease the burden of smoking in the workforce.

This concluding chapter summarises the key findings from the research presented in the thesis and how these findings fulfil the objectives described in **Section 1.6.3**. In addition, there were several key lessons learned relating to the methods which were applied to evaluating the impact of smoking in the workforce. Finally, this chapter also highlights impact of the work and avenues of future research relating to evaluating the impact of smoking in the workforce.

7.2 Summary of findings

7.2.1 Objective 1: Review of indirect cost-of-smoking methodology

In **Chapter 2**, the aim was to review cost-of-smoking methodology on the estimation of population-level productivity loss or indirect costs. An electronic database search was conducted in MEDLINE, EMBASE, CRD, Science Direct and EconLit. Included in the analysis were population-level economic studies that had quantified the indirect costs of smoking. Stepwise regression analysis determined the association between adult smoking prevalence and cost per capita with the inclusion of population-level covariates.
Seventeen economic studies were included in the review; of which 15 studies used the human capital model while only two studies used the friction cost method to quantify the indirect costs of smoking. After adjusting for covariates, regression analysis showed that a 1% increase in smoking prevalence resulted in a 1.7% (95% CI 0.21 to 3.16, $p = 0.028$) increase in cost per capita across all studies and a 2.1% (95% CI 0.46 to 3.81, $p = 0.017$) increase in cost per capita across human capital model studies only.

The findings in **Chapter 2** suggest that on average a 1% increase in smoking prevalence results in a $5.42 USD (£3.55) increase in cost per capita across all studies and an $8.17 USD (£5.36) increase in cost per capita across human capital model studies only. Despite methodological differences among studies, there was a degree of consistency. In terms of comparability, the human capital model serves as the most common template for indirect

cost-of-smoking studies but tends to overestimate the consequence of disease. The friction cost method is not as widely used and there are questions on the assumptions on zero-cost labour replacement.

7.2.2 Objective 2: Quantify productivity loss of smoking in the UK

In **Chapter 3**, the aim was to quantify productivity loss (indirect costs) due to smoking using cost-of-smoking methodology for the UK. An epidemiological approach was taken to calculate disease-specific smoking-attributable risk fractions for mortality from national-level data. The risk fractions were then combined with UK death register data to calculate smoking-attributable mortality. Based on age and sex-specific earnings data, the monetary value of future foregone income was estimated (discounted at 3.5%) due to smoking-attributable mortality.

Smoking was found to be responsible for 96,105 deaths in adults aged 35 years and over (17% of all deaths) in the United Kingdom in 2010. These deaths resulted in nearly 1.2 million years of life lost and 357,831 years of productive life lost. The cost of productivity loss due to premature mortality was £4.93 billion discounted at base-case rate of 3.5%.

The results in **Chapter 3** suggest that there may be large gains in productivity of the workforce by reductions in smoking prevalence. The sheer scale of the financial loss stresses the importance of strong tobacco control policy at the national level.

7.2.3 Objective 3: Evaluate the association between smoking and absenteeism

In **Chapter 4**, the aim was to evaluate the epidemiological association of smoking and absence from work by systematic review and meta-analysis. A systematic review and meta-analysis was performed by electronic database searches in MEDLINE, EMBASE, CAB Abstracts, PubMed, Science Direct and National Health Service Economic Evaluation Database. Longitudinal, prospective cohorts or retrospective cohorts were included in the review. Summary effect estimates were calculated using random effects meta-analysis. Heterogeneity was assessed by I^2 and publication bias was investigated.

A total of 29 longitudinal or cohort studies were included. Compared with non-smokers, current smokers had a 33% increase in risk of absenteeism. Current smokers were absent for an average of 2.74 more days per year compared with non-smokers. Compared with never smokers, ex-smokers had a 14% increase in risk of absenteeism; however, no increase in duration of absence could be detected. Current smokers also had a 19% increase in risk of absenteeism compared with ex-smokers. There was no evidence of publication bias. The results in **Chapter 4** showed that there was in fact a strong epidemiological association between smoking and absence from work. Therefore, these findings could be used to quantify the monetary costs of absence due to smoking.

7.2.4 Objective 4: Quantify costs of absence in the UK

A secondary aim in **Chapter 4** was to quantify the cost of absenteeism in the UK using the results from the meta-analysis comparing the duration of absence from current smoker and ex-smokers. Smoking was estimated to cost UK employers on average £1.46 billion in 2011 from absenteeism in the workplace. This large economic impact of smoking on absenteeism suggests that there is potentially great value in workplace smoking cessation programmes.

7.2.5 Objective 5: Validate indirect costs of smoking

In **Chapter 5**, the aim was to validate the indirect costs or productivity loss estimates using an ecological model. The method for validation used the regression equations derived from the ecological analysis of 17 population-level cost-of-smoking studies identified in **Chapter 2**. When the regression function derived from human capital model studies was used, the predicted cost per capita was $150.93 USD (£99.49). When the predicted costs were compared to the observed cost per capita of $159.10 USD (£102.64), there was only a 5% difference between predicted and observed values. This validation procedure in **Chapter 5** showed that the results of the cost estimates in this thesis were consistent with the results of other published human capital studies.

7.2.6 Objective 6: Cost-benefit analysis of workplace interventions

In **Chapter 6**, the primary aim was to evaluate the cost-benefit of workplace smoking cessation interventions to reduce absenteeism and labour turnover from the employer's perspective via decision analysis and Markov simulation model. A simulated cohort of UK

workers was analysed using Markov modelling techniques. Decision analysis was used to optimise strategy selection based on minimising total costs and maximising return on investment for the employer.

Cost-benefit analysis of workplace interventions resulted in brief advice being the optimal decision strategy for women and both brief advice and individual counselling being the optimal decision strategies for men in terms of minimising total costs and maximising return on investment. Brief advice in women resulted in average additional returns of £1.20 per pound expended while brief advice in men resulted in average additional returns of £5.16 per pound expended. Individual counselling in men resulted in average additional returns of £1.00 per pound expended.

The results in **Chapter 6** suggest that employers who adopt workplace smoking cessation programmes will in fact save money. However, this may largely depend on workforce turnover rates. There are clear benefits for employers with low labour turnover rates for adopting smoking cessation interventions but the results are unclear when labour turnover is high. In addition, the strategies selection may not necessarily maximise social welfare from a pure societal perspective. If employers choose to base the decision analysis on financial metrics, then brief advice would be an optimal intervention from the employer's perspective offering the maximum returns on investment. While brief advice certainly will contribute towards increasing quitters, it would not be the intervention that would maximise quitting from a pure societal perspective.

7.2.7 Objective 7: Cost-effectiveness analysis of workplace interventions

A secondary aim of **Chapter 6** was to explore if the decision strategy changes if the employer valued maximising the number of quitters. In this cost-effectiveness analysis, the selection between brief advice, individual counselling or NRT with individual counselling was dependent on budget constraints. If the total budget constraint was £4,872 per male worker and £2,197 per female worker then brief advice would be the most cost-effective option. If the total budget constraint was £4,977 per male worker and £2,381 per female worker then the more effective intervention of individual counselling would be the most cost-effective option. If the total budget constraint was £5,259 per male worker and £2,743 per female worker or if there was no budget constraint, then the most effective option of NRT

with individual counselling would be the most cost-effective option. Maximising budget constraints would align the societal and employer's perspective by selecting the most effective smoking cessation strategy.

Policy-makers could consider promoting or supporting employers that choose to start a workplace smoking cessation intervention. Tax incentives, subsidies or support for employers for setting up smoking cessation interventions in the workplace may offer better returns on investments by reducing costs for more expensive yet more effective interventions. This suggests there is common ground for employers to contribute towards the net social welfare of society.

7.3 Key lessons learned

The methods used in this thesis span a range of statistical, epidemiology and health economic methods. Through the research process several key lessons were learned.

7.3.1 Flexibility and focus

The overarching theme of the thesis revolves around the economic impact of smoking in the workforce. When this topic was in its inception, there were several avenues of research which could have been pursued. The thesis had to be focussed on specific areas of research due to the broadness of the economics of smoking while simultaneously allow flexibility due to limitations in data availability.

In this thesis, quantifying the indirect costs of smoking was limited to the monetary value of productivity loss from premature mortality and the cost of absenteeism. While these two components are two primary components, indirect costs are theoretically comprised of many other components as described in **Chapter 2.** However, quantifying the non-health related components (i.e. presenteeism, smoking breaks, lost leisure time, lost household production) require detailed data and complex econometric methods beyond the scope of public health. Therefore, the research objective was focussed on the primary cost components of premature mortality and absenteeism. Once the idea was devised to examine indirect costs due to premature mortality and absenteeism, flexibility was also needed. In these particular areas of research, there were a multitude of methods. The methodology used was largely dependent

on data availability in the UK. In **Chapter 2**, the methodological review identified the human capital model and friction cost model as possible methods for estimating productivity loss due to premature mortality. Research into data availability showed that it was possible to use the human capital model for estimating costs in the UK using a prevalence based approach. However, the friction cost methodology required survey instruments from employers to determine exact turnover times (friction periods). This data was not available and therefore, this avenue of research could not be pursued.

Another instance where the balance between flexibility and focus was vital was in the construction of the Markov model in **Chapter 6.** The building the model was dependent on perspective. The idea was proposed to focus on employers as this was an area which research gaps exist on the economic evaluations of workplace interventions. Once the perspective was decided, flexibility was needed in the model building phase. The construction of the model was an iterative process. For instance, the initial model constructed included the idea of having time varying components based on duration of ex-smoking. However, time varying parameters on absence and labour turnover risk by smoking status did not exist. Therefore, assumptions had to be made about the model structure.

7.3.2 Impact of thesis work

The ultimate goal of research in public health, epidemiology or health economics is to influence public policy and provide solutions to prevent ill-health and improve the health of the individual or population. This is the most important lesson learned – the research questions addressed in the field of public health should be translational and have the potential to benefit the welfare of the individual or society. The research in this thesis attempts to add to tobacco control economics. The economic arguments for and against tobacco control need to be examined using an evidence-based approach to strengthen the research base around tobacco control policy. While it was impossible to address all areas of research on the economics of smoking, this thesis does provide a clearer picture about indirect costs, productivity loss, absenteeism and workplace smoking cessation interventions. The implications of the research provided in the thesis are particularly relevant for UK smoking policy and has already contributed towards tobacco control policy in the UK.

Parts of this thesis have been published in peer-reviewed journals. **Chapter 3** has been submitted to *The European Journal of Health Economics*. **Chapter 4** was published in *Addiction*. **Chapter 6** will soon be submitted to the *Journal of Health Economics* for peer-review. The publication in *Addiction* was fortunate enough to receive press coverage in media outlets such as *Reuters, New York Post, Daily Mail, The Guardian* and *The Telegraph*. In addition, the findings in **Chapter 4** have been requested by the Department of Health for an on-going budget impact assessment.

Furthermore, most of the research conducted in this thesis has been disseminated at international conferences and University seminars. **Chapter 3** has been presented at ***Tackling Smoking in 21st Century Britain*** which took place in York in November 2012. **Chapter 4** has been presented at the ***15th World Conference on Tobacco or Health*** in Singapore in March 2011 and also presented as a seminar for the ***Epidemiology, Public Health and Primary Care Joint Seminar Series*** at the University of Nottingham in September 2011. The economic model in **Chapter 6** has been presented as a seminar for ***The Department of Health Sciences Spring Seminar Series*** at the University of York in January 2013.

7.3.3 Developing transferable research skills

The range of methods used in this thesis helped me develop research skills which were transferable to other areas of public health. During my time as a PhD student at the UK Centre for Tobacco Control Studies, I simultaneously worked as a NIHR- CLAHRC funded research associate in developing risk prediction models for paediatric obesity with an interdisciplinary team based at the Institute of Mental Health (University of Nottingham). After completing **Chapter 4** and publishing the contents of the systematic review, I applied the transferable skills in meta-analysis and indirect treatments to my paediatric obesity research which investigated the risk factors of childhood obesity. I subsequently was able to publish the systematic review and meta-analysis in *Archives of Disease in Childhood* with substantial press interest. In **Chapter 3**, the economic models relied on obtaining many parameters from large population-level surveys in the UK which required a substantial amount of large database management. I applied those database management skills to the UK Millennium Cohort Study; from which I developed a risk prediction algorithm for paediatric obesity based on predictors in infancy. I wrote a publication disseminating this research which has now been accepted by *Pediatrics* for publication. I have since conducted a

validation study of my risk prediction algorithm using the Avon Longitudinal Study of Parents and Children which will soon be submitted to *The British Medical Journal.*

7.4 Future research

As mentioned earlier, the economic impact of smoking in the workforce is extremely broad. The research in this thesis provided aspects that can contribute to the evidence-base. However, there are several areas in which there is potential for future avenues of research.
In **Chapter 2,** besides productivity loss due to foregone income and absence costs from work, there were several other components of indirect costs identified such as presenteeism, smoking breaks, lost leisure time, fire damage and passive smoking. These elements made up of smaller proportions of total indirect costs. Furthermore, the methods around the quantification of these costs are less developed and there is no consensus on best practice methods due to a limited number of studies. Therefore, this thesis did not attempt to address those elements. However, it must be acknowledged that future research should address these components in order to facilitate the estimation of total societal costs of smoking.

In **Chapter 3,** productivity loss due to premature mortality was estimated using the human capital method for the UK. The friction cost is not as widely used but if data is available from UK employer-based surveys on friction periods (replacement time) it would possible to quantify indirect costs due to premature mortality using this method. This method assumes an employer's perspective and therefore costs would be reduced due to replacement of labour. This would add an important perspective to complement the human capital method.

In **Chapter 4,** the epidemiological association was based on absence from work due to sickness and illness. This type of absence was solely based on the health effects consequences of smoking. Absenteeism related to behaviour was not excluded from the review but there were no longitudinal studies identified which have investigated this effect. There are some indications that in addition to the health effects of smoking, there may be possible differences in behavioural characteristics associated with smokers that contribute towards absenteeism, similar to perhaps the truancy effect observed in children who smoke.[411] This link between smoking and absence related to behavioural effects could be investigated in the future using an occupational cohort.

In **Chapter 6**, the economic evaluation of four workplace strategies for smoking cessation was conducted; of which only one form of NRT was tested. Other forms of NRT which could be evaluated for cost-benefit or cost-effectiveness in the future include gum, inhaler, lozenges, tablets or combination therapy. In addition, other forms of pharmacotherapy such as varenicline and buproprion offer substantially higher rates of quitting[103 107]; however it is unknown due to lack of evidence as to whether these therapies are effective or cost-effective in the workplace setting. Another area of potential research is the effectiveness and cost-effectiveness of financial incentives in the workplace for smoking cessation. A recent review found that rewarding participation and compliance in cessation programmes may have the potential to deliver higher absolute numbers of quitters, but long-term success of quitting through financial incentives is mixed.[412] This is an area that needs much more research into types of programmes, scale and longevity of cash rewards within a variety of smoking populations before cost-effectiveness can be assessed.

7.5 Overall conclusions

This thesis has used a range of methodology to quantify the impact of smoking in the workplace. In addition, this research has provided possible solutions to decrease the burden of smoking in the workplace. The results have highlighted that a variety of methodologies are needed to evaluate the economics of smoking. Although significant research gaps still remain, the research provided contributed towards narrowing this gap. In particular, this thesis has provided the first indirect cost-of-smoking study quantifying the productivity loss due to premature mortality in the UK; the first systematic review and meta-analysis which has explored the association between smoking and absence from work; and the first cost-benefit and cost-effectiveness analysis of workplace interventions for smoking cessation in the UK. The findings are particularly relevant for UK policymakers and employers for justifying stronger tobacco control and promoting cessation. However, these methods are not unique to the UK. The research in this thesis has provided the framework and methodology for studies that can strengthen the evidence on the economics of smoking in other countries as well. Finally, these methods are also not unique to tobacco control field. The burden-of-illness and economic evaluation methodologies can be translated for research in other disease epidemics.

Chapter 8

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Chapter 9

Appendices

9.1 Chapter 2 Methods: Search terms

smoking
nicotine
tobacco
tobacco dependence
tobacco smoke
cigarette smoking
exp smoking
exp "smoking and smoking related phenomena"
smok$
tobacco$
cigarette$
cotinine$
cigar$
pipe$
adult smok$
former smok$
current smok$
ex smok$
non smok$
indirect
indirect cost$
mortality
morbidity
premature mortality
smoking-attributable$
life years lost
productive life years
absenteeism
sick$ absence
ill$ absence
sick$ absenteeism
ill$ absenteeism
work$ absence
prevalence approach
incidence approach
human capital
friction cost
work$ absenteeism
product$ lost
product$ loss
presenteeism

9.2 Chapter 2 Methods: Health economic quality assessment form

Checklist Questions (Max = 8 points)	Yes (1 point)	No (0 points)
1. Is a well-defined research question posed in an answerable form?		
2. Is the study population clearly described?		
3. Is the economic study design appropriate to the stated objective?		
4. Are costs measured appropriately in physical units?		
5. Are costs valued properly?		
6. Are all future costs discounted appropriately?		
7. Do the conclusions follow the data reported?		
8. Are costs subject to additional sensitivity analysis?		
Total Score		

9.3 Chapter 4 Methods: Search terms

Smoking
Nicotine
smoking cessation
Tobacco
tobacco dependence
tobacco smoke
cigarette smoking
Cotinine
exp smoking
exp tobacco smoke pollution
exp "smoking and smoking related phenomena"
exp parental smoking
exp passive smoking
exp smoking habit
exp smoking cessation
smok$
tobacco$
cigarette$
cotinine$
cigar$
pipe$
second hand smok$
environmental tobacco smoke
adult smok$
former smok$
current smok$
ex smok$
non smok$
smoking status
absenteeism
"period of absence"
sick$ absence
ill$ absence
sick$ absenteeism
ill$ absenteeism
sick$ leave
sick$ day$
work$ absence
work$ absenteeism
employee absence
employee absenteeism
work$ ill$
work$ sick$
product$ lost
product$ loss
"risk of absenteeism"
"risk of absence"
presenteeism

9.4 Chapter 4 Methods: Eligibility checklist

Area 1. Study Design

I. The article presents a study that is longitudinal in design, where participants were recruited at the beginning of the study, and then reassessed at a later interval or end of the study (Y/N) ____

II. The article presents a study that is a prospective cohort, where participants were recruited in the beginning of the study, and followed-up over regular intervals (Y/N) _____

III. The article presents a study that is a retrospective cohort, where participants were recruited, and then data was gathered on the participants from previous records (Y/N) _____

If the answer was "yes" to any of these (I-III) statements, then the study satisfies the study design criteria (Area 1): _____

Area 2. Population

I. The participants in the study are full time workers and wage earners in the any of the following occupational categories below (Y/N) ____

II. The participants in the study are part time workers and wage earners in any of the following occupational categories below (Y/N) ____

III. The participants in the study are self employed workers and wage earners in any of the following occupational categories below (Y/N) ____

Agriculture and fishing	Energy and waster
Manufacturing	Construction
Distribution, hotels, and restaurants	Transport and communication
Banking, finance, and insurance	Public admin, education, health
Other services	

If the answer was "yes" to any of these statements (I-III), then the study satisfies the population criteria (Area 2): _____

Area 3. Exposure of interest - Smoking

I. The study assesses the participant's smoking status absenteeism occurs (Y/N) ____

II. The study assesses the participant's smoking dosage before absenteeism occurs (Y/N) ____

If the answer was "yes" to any of these statements (I-II), then the study satisfies the exposure criteria (Area 3): _____

Area 4. Outcome of interest – Absenteeism

I. The study assesses the participants work absenteeism record after smoking status has been established (Y/N) ____

II. The study assesses the participants work sickness/illness record after smoking status has been established (Y/N) ____

III. The study assesses the participants work attendance records after smoking status has been established (Y/N) ____

If the answer was "yes" to any of these statements (I-III), then the study satisfies the outcome criteria (Area 4): _____

Overall Inclusion:

If the study satisfies Areas 1-4, then include study in the systematic review: ___Yes/No___

9.5 Chapter 4 Methods: Data extraction form

DESCRIPTION OF STUDY

Title	
Study Design	Prospective Cohort Retrospective Cohort Longitudinal
Timing of Study	Duration of Study (days/months/years): Study year(s):
Definition of Smoking (Smoking Status)	Yes/No: Current: Ex/Former: Non: Heavy: Light: Moderate: Other:
Attainment of Smoking	Validated test (Cotinine, Blood test, CO test) Self reported Employer reported Medical record Other:
Measurement of Absenteeism	Days: Hours: Ratio Measure: Other:
Attainment of Absenteeism	Self reported Employer reported Registry Not Stated Other:
Setting/Location	

PARTICIPANTS

General characteristics (Descriptive statistics)	
Inclusion/Exclusion	
Occupational characteristics (Industry sector – LFS)	Occupation as defined by study: Full-time (≥ 30 hours/week) Part-time (< 30 hours/week) All Industries Agriculture & fishing Energy & water Manufacturing Construction Distribution, hotels & restaurants Transport & communication Banking, finance & insurance Public admin, education, health Other services
Initial Sample Size	
Follow-up rate	
Final Sample Size	

RESULTS

Absenteeism	Unadjusted (Inc 95% CI)	Adjusted (Inc 95% CI)	Adjusted Significance
Time Element (Days/Hours) Ratio (Risk/Odds/Rate) Other			

Covariates:

9.6 Chapter 4 Methods: Quality assessment form

Newcastle - Ottawa Scale	Cohort studies	☆
Selection (Max – 4 stars)	1) Representativeness of the exposed cohort a. Truly representative of the average worker in the field/industry ☆ b. Somewhat representative of the average worker in the field/industry ☆ c. Selected group of users (volunteers) d. No description of the derivation of the cohort 2) Selection of the non exposed cohort a. Drawn from the same field/industry as the exposed cohort ☆ b. Drawn from a different source c. No description of derivation of non exposed cohort 3) Ascertainment of exposure a. Biomarker or validation test (Cotinine/Blood sample/ CO test) ☆ b. Medical/employer/survey reported c. Self report or interview d. No description 4) Demonstration that the outcome of interest was not present at start of study a. Yes ☆ b. No	
Comparability (Max – 2 stars)	1) Comparability of cohorts on basis of the design or analysis a. Study controls/stratifies for age or sex ☆ b. Study controls/stratifies for any additional factor (at least one more) ☆	
Exposure / Outcome (Max – 3 stars)	1) Assessment of absenteeism a. GP/Medical record ☆ b. Employer/National record ☆ c. Self report or interview d. No description 2) Was follow-up long enough for outcomes to occur a. Yes (≥ 1 year) ☆ b. No 3) Adequacy of follow up cohorts a. Complete follow up – all subjects accounted for ☆ b. Subjects lost to follow up unlikely to introduce bias (follow-up rate >80%) or description provided of those lost ☆ c. Follow up rate < 80% and no description of those lost d. No statement	

9.7 Chapter 4 Methods: Random effects meta-analysis

The random effects model was used to pool the effect sizes from the extracted data using inverse variance weighting[413]. The study i of a total of n studies provided the estimated effect of interest y_i, such as the log odds ratio, log risk ratio or difference in means. The estimated effect of interest y_i as a function of the effect size θ_i was assumed to be distributed normally with mean of θ_i and study variance of σ_i^2:

$$y_i \mid \theta_i \sim N(\theta_i, \sigma_i^2)$$

Additionally, the random effects meta-analysis allowed the true effects θ_i to vary between studies assuming a normal distribution around the true mean effect θ with variance τ^2:

$$\theta_i \sim N(\theta, \tau^2)$$

Transitively, the effect size of interest y_i was normally distributed around a mean effect θ with variance $\sigma_i^2 + \tau^2$:

$$y_i \sim N(\theta, \sigma_i^2 + \tau^2)$$

Equivalently in functional form:

$$y_i = \theta + u_i + \varepsilon_i \quad where\ u_i \sim N(0, \tau^2)\ and\ \varepsilon_i \sim N(0, \sigma_i^2)$$

The variance τ^2 was estimated as the between-study variance through the method of moments approach[414]. Each effect size was given a weight, the reciprocal of its variance. In effect, studies with smaller sample sizes resulted in larger variances, which translated into smaller weights. The weight ω_i was denoted by the following:

$$\omega_i = \frac{1}{\sigma_i^2 + \tau^2}$$

Subsequently, the pooled estimate of the effect size $\hat{y}$ was calculated as the sum of the weights multiplied by the estimated effect of each study y_i, divided by the sum of the weights from all studies:

$$\hat{y} = \frac{\sum_{i=1}^{k} \omega_i y_i}{\sum_{i=1}^{k} \omega_i}$$

The variance $\hat{\sigma}^2$ of the pooled effect size was given by:

$$\hat{\sigma}^2 = \frac{1}{\sum_{i=1}^{k} \omega_i}$$

To assess heterogeneity between studies, the I^2 statistic was calculated as a proportion of total variability in the model:

$$I^2 = \frac{Q - (k-1)}{Q}$$

The measure of heterogeneity Q was given by:

$$Q = \sum_{i=1}^{k} \omega_i (\theta_i - \hat{\theta})^2$$

The component $(\theta_i - \hat{\theta})$ was the difference of the study effect and the pooled effect and ω_i was the study weight. I^2 values lie between 0 to 100%, with higher percentage variation suggesting more heterogeneity or differences among the studies.

9.8 Chapter 4 Methods: Random effects meta-regression

Random effects meta-regression extends random effects meta-analysis by replacing the mean effect size θ with a linear predictor $x_i\beta$. This assumes that the true effects follow a normal distribution around the linear predictor:

$$y_i \mid \theta_i \sim N(\theta_i, \sigma_i^2) \quad where \ \theta_i \sim N(x_i\beta, \tau^2)$$

Therefore,

$$y_i \sim N(x_i\beta, \sigma_i^2 + \tau^2)$$

Written in functional form:

$$y_i = x_i\beta + u_i + \varepsilon_i \quad where\, u_i \sim N(0, \tau^2) \ and\ \varepsilon_i \sim N(0, \sigma_i^2)$$

The model was extended into a multivariate form to incorporate covariates:

$$\hat{y} = \beta_0 + x_{1i}\beta_{1i} + x_{2i}\beta_{2i} + \cdots + x_{ki}\beta_{ki} + u_i + \varepsilon_i$$

Using the equations directly above, the covariates of gender, type of absence and work sector were incorporated as dummy variables for into three separate multivariate models. All algorithms for random effects meta-regression first estimate the between study variance τ^2 and then estimate the coefficient β by weighted least squares using weight $1/(\sigma_i^2 + \tau^2)$. The algorithm for meta-regression uses restricted maximum likelihood (REML) to estimate τ^2 based on maximisation of the residual log likelihood.[306]

9.9 Chapter 4 Methods: Adjusted indirect comparisons

The random effects model in **Chapter 4** makes two direct comparisons due to never smokers as the reference group: (1) current smokers versus never smokers (2) ex-smokers versus never smokers. It is possible to take an indirect comparison between current smokers and ex-smokers from information available using adjusted indirect meta-regression methods[305]. The natural log of the relative risk of absence between current and ex-smokers ($LnRR_{CS\ vs\ EX}$) for indirect comparison can be estimated as the exponential of the difference in log relative risk of current smokers versus never smokers ($LnRR_{CS\ vs\ NS}$) and ex-smokers versus never smokers ($LnRR_{EX\ vs\ NS}$):

$$LnRR_{CS\ vs\ EX} = exp(LnRR_{CS\ vs\ NS} - LnRR_{EX\ vs\ NS})$$

Furthermore, the standard error of the indirect comparison ($SE_{CS\ vs\ EX}$) can be estimated from the square root of the sum of the squared standard errors:

$$SE_{CS\ vs\ EX} = \sqrt{SE_{CS\ vs\ NS} + SE_{EX\ vs\ NS}}$$

Using the indirect comparison results of the standard error and log relative risks, the 95% confidence interval can be computed:

$$95\%\ CI = exp(LnRR_{CS\ vs\ EX}) \pm 1.96 \times lnSE_{CS\ vs\ EX}$$

The above analysis produces inverse variance estimates. Alternative indirect meta-analysis models can be obtained by using the Mantel–Haenszel fixed-effect model, the DerSimonian and Laird random effects model, weighted linear meta-regression or random effects meta-regression.[305] The differences between the methods resulted in less than 1% difference in pooled indirect effects and standard errors. Therefore, the choice of methodology had a marginal impact on the results so the most straightforward method was used.

9.10 Chapter 4 Methods: Data transformations

9.10.1 Rate ratio to risk ratio

Rates ratios and incidence rates are specified by:

$$Rate\ Ratio = \frac{Incidence_{Exposed}}{Incidence_{Nonexposed}}$$

$$Incidence = \frac{Event}{Person - time}$$

The Poisson distribution is the preferred method for calculation of rates as a discrete probability distribution that expresses the probability of a given number of events occurring in a fixed interval of time if these events occur with a known average rate. The rate ratio is a consistent estimator of the risk ratio provided that the ratio of persons at risk between exposed and non-exposed groups are constant over time.[302] The theory suggests that the rate ratio will converge to the risk ratio if size of the sample at the beginning of the study approaches the size of the sample at the end of the study. The rate ratio can in effect be considered a special case of the risk ratio taking into account individual follow-up time. Thus, rate ratios were used as estimates of risk ratios due to sufficient sample sizes and follow-up rates.

9.10.2 Hazard ratio to risk ratio

Hazard ratios are measurements of instantaneous risk. The hazard ratio is specified by:

$$Hazard\ Ratio = \frac{Hazard_{Exposed}}{Hazard_{Nonexposed}}$$

The studies included in the systematic review used the Cox proportional hazards model. In the Cox model, the hazard rate is the probability that if the event in question (absenteeism) has not yet occurred, it will occur in the next time interval, divided by the length of the interval.[285] As the time interval decreases, the rate becomes instantaneous. The hazard ratio is a ratio of hazard rates; the assumption in the Cox model being that the ratio remains constant over time. In contrast to hazard ratios, the risk ratio is expressed as the proportion of events

occurring in the exposed group compared to that of the non-exposed group calculated at the end of the study having occurred over an average or median duration of the study.[415] When the study is short in length, then hazard ratio converges on the risk ratio. When the study is long in length, the hazard ratio becomes a more precise estimator of the risk ratio. In essence, the hazard ratio is a special case of the risk ratio that takes into account length of time for the event to occur. Therefore, the studies that reported hazard ratios as outcomes were used directly as estimates of the risk ratio.

9.10.3 Odds ratio to risk ratio

Odds ratios, unlike hazards and rate ratios are structurally different from risk ratios. If the prevalence of outcome is high (common outcome), odds ratios will overestimate the risk ratio when the measure of effect is greater than one and will underestimate the risk ratio when the measure of effect is less than one.[416] Even if the outcome is uncommon, the odds ratios may not approximate the risk ratio well if adjustment are made for confounding variables.[416] Therefore, odds ratios were transformed into relative risk using a correction method[303].

$$Risk\ Ratio = \frac{Odds\ Ratio}{(1 - P_0) + (Odds\ Ratio \times P_0)}$$

$$P_0 = \frac{Cases}{Total\ Nonexposed}$$

This method has been used to estimate adjusted risk ratio using P_0, the number of cases of absenteeism events in the non-exposed group. For studies that did not provide enough information to compute P_0, the weighted average $\bar{P}_0$ was used calculated from the known studies with known P_0:

$$\bar{P}_0 = \frac{\sum_{i=1}^{k} n_i P_{0i}}{\sum_{i=1}^{k} n_i}$$

9.11 Chapter 4 Methods: Missing parameter imputation

In order to use meta-analysis to pool a measure of effect, several parameters are needed. For categorical exposures, this required individual studies to provide: the relative risk ($lnRR$), lower confidence limit ($lnLCI$), upper confidence limit ($lnUCI$); or the standard error of the relative risk ($se[lnRR]$). For studies that were missing the upper or lower confidence limit, certain techniques were used to impute the values.

For continuous exposures, six parameters are needed. The pooled difference in means estimation required individual studies to provide: the mean of the exposed group ($\bar{x}_{Exposed}$), sample size of the exposed group ($n_{Exposed}$), standard deviation of the exposed group ($sd_{Exposed}$); mean of the non-exposed group ($\bar{x}_{Nonexposed}$), sample size of the non-exposed group ($n_{Nonexposed}$), standard deviation of the non-exposed group ($sd_{Nonexposed}$); or separately the difference in the means ($\bar{x}_{Exposed} - \bar{x}_{Nonexposed}$) and the standard error of the mean difference. Studies that did not provide the sample sizes of the exposure groups were excluded from the meta-analysis but not from the systematic review. For studies that were missing standard deviations, certain techniques were used to impute the values.

9.11.1 Imputing 95% confidence interval

For studies that did not report a 95% confidence interval (CI), it was possible to impute the lower and upper bounds from exact p-values or p-value cut-offs. The reported p-value needed either to be an exact or an upper bound cut-off. In studies that reported the exact p-value, the exact values of the lower and upper bound 95% CI were calculated. In studies that reported an upper bound cut-off of the p-value, only a conservative estimate of the 95% CI was obtained. The z-score from the corresponding p-value was obtained from the normal distribution. The log of the standard error ($lnSE_i$) was calculated from the z-score and study effect size θ_i, using the following formula:

$$lnSE_i = \frac{\theta_i - 1}{z_i}$$

In some cases where rate ratios were reported as the effect size and *p*-values were not given, studies providing number of absenteeism events in both exposed and non-exposed groups could be used to compute the log of the standard error[417]:

$$lnSE_i = \sqrt{\frac{1}{E_{Exposed_i}} + \frac{1}{E_{Nonexposed_i}}}$$

The variable $E_{Exposed_i}$ was the number of absence events in the exposed group and $E_{Nonexposed_i}$ was the number of absence events in non-exposed group. Subsequently, the 95% CI of the effect size was obtained from the log of the standard error:

$$95\%\ CI_i = \theta_i \pm 1.96 \times lnSE_i$$

However, when *p*-values were not given, were insignificant or when information about the number of absence events in exposure groups were not given, an alternative method was used: the standard error from the pooled effect size of all the other studies with available confidence intervals in the random effects meta-analysis could be used as a proxy for individual study standard errors.[418] In essence, the missing confidence intervals were given the standard error of the entire pooled population. The log of the pooled standard error $\widehat{lnSE}$ could be obtained from the estimated pooled effect size $\hat{\theta}$ and pooled 95% CI:

$$\widehat{lnSE} = \frac{95\%\ \widehat{CI} - \hat{\theta}}{1.96}$$

From a slight variation, the 95% confidence interval of the individual study could be imputed from the log of the pooled standard error:

$$95\%\ CI_i = \theta_i \pm 1.96 \times \widehat{lnSE}_i$$

9.11.2 Imputing standard deviation

For studies that did not report standard deviations of the mean duration of absence in both exposed and non-exposed groups, it was possible to impute standard deviations from the *F*-statistic, *t*-statistic, or *p*-value.[419] The *F*-statistic is derived from analysis of variance (ANOVA), which tests for the equality of the means by the variance. The *t*-statistic was derived from the *F*-statistic by:

$$t = \sqrt{F}$$

If and only if:

$$df = k - 1 = 1$$

This condition was only satisfied when $k = 2$ and the degrees of freedom was 1. Therefore, the above process can only be used when comparing two means. In this case, the analysis was based on comparison of mean difference of absence between the exposed and the non-exposed group satisfying the assumption of two means. The *t*-statistic can also be derived from the *p*-value using the student's *t* distribution and degrees of freedom. The degrees of freedom for the *t*-statistic was derived by:

$$df = n_{Exposed} + n_{Nonexposed} - 2$$

Once the *t*-statistic was obtained, the standard error was calculated where $\bar{x}_{Exposed_i}$ and $\bar{x}_{Nonexposed_i}$ were the mean absence durations of the exposed and non-exposed groups respectively:

$$se_i = \frac{\bar{x}_{Exposed_i} - \bar{x}_{Nonexposed_i}}{t}$$

The within-group standard deviation was obtained from a standard error using the following formula where $n_{Exposed_i}$ and $n_{Nonexposed_i}$ were the sample sizes of the exposed and non-exposed groups respectively for study *i*:

$$\overline{SD_i} = \frac{se_i}{\sqrt{\frac{1}{n_{Exposed_i}} + \frac{1}{n_{Nonexposed_i}}}}$$

The standard deviation ($\overline{SD_i}$) was the average of the standard deviations of the both the exposed and non-exposed group. Thus, the average standard deviation was used as a proxy for the individual standard deviations from groups as shown:

$$\overline{SD_i} = sd_{Exposed_i} = sd_{Nonexposed_i}$$

For studies that did not provide a test statistic or *p*-value to impute standard deviations, an alternative method was used to impute standard deviations from the pooled mean difference using random effects meta-analysis of studies with known standard deviations.[418] The degrees of freedom could be computed for the entire pooled sample. The *t*-statistic was obtained from the student's *t* distribution using the computed degrees of freedom and *p*-value cut-off of 0.05. From the pooled mean difference, *t*-statistic and 95% confidence interval; the standard error of the pooled mean difference was calculated using:

$$\widehat{se} = \frac{(\bar{x}_{pooled} - LCI_{pooled})}{t}$$

The pooled standard error was used as a proxy for the standard error of each individual study. From a slight variation of an above equation, the within group standard deviation was derived from the pooled standard error:

$$\overline{SD_i} = \frac{\widehat{se}}{\sqrt{\frac{1}{N_{Exposed_i}} + \frac{1}{N_{Nonexposed_i}}}}$$

9.12 Chapter 6 Methods: Random effects meta-analysis of proportions

The process of pooling proportions across studies relied on similar meta-analytic techniques used in previous sections. In **Chapter 4**, relative risks were pooled using inverse variance weighting[413]. However, this process assumes a normal distribution for effect sizes as described in **Appendix 9.7.** The assumption of normality cannot be assumed for proportions as proportions have binomial characteristics.

In order to pool proportions, data transformations must be used. This is done by first transforming the raw proportions into a quantity suitable for random effects meta-analysis. Let n_i be the sample size and p_i be the raw proportion of study i. The Freeman-Tukey[372] variant x_i of the study proportion can be calculated by an arcsine square root transformation:

$$x_i = \sin^{-1}\sqrt{\frac{p_i}{n_i+1}} + \sin^{-1}\sqrt{\frac{p_i+1}{n_i+1}}$$

The aim behind this transformation is to use the arcsine function to create a new set of variables such that the variability in the values do not relate to the mean value. The arcsine transformation is a common transformation which applies to source data in the range from [0,1] which naturally characterises binomial data. The transformation spreads the data across the range from [-π/2, π/2] which adjusts the data to make the distributions more similar to a normal distribution. Next, the individual transformed proportions x_i can be pooled across studies:

$$\hat{x} = \frac{\sum x_i w_i}{\sum w_i}$$

The DerSimonian-Laird weight[414] w_i for each study i incorporates the random effects variable τ^2 characterised as the between-study variance calculated by the method of moments approach[414]:

$$w_i = \frac{1}{\tau^2 + \sigma_x^2}$$

The variance σ_x^2 of transformed study proportion x_i can be estimated as the square of the standard error of study proportion x_i using study sample size n_i:

$$\sigma_x^2 = se_x^2 = \sqrt{\frac{1}{(n_i + 1)}}$$

Once the pooled transformed proportion $\hat{x}$ is calculated, the parameter can be back-transformed to obtain the original pooled proportion $\hat{p}$ by using sine squared:

$$\hat{p} = sin^2\left(\frac{\hat{x}}{2}\right)$$

This analysis was carried out using the statistical software StatsDirect Version 2.

9.13 Chapter 6 Methods: Probability Distributions

9.13.1 Limitations of the triangular distribution

Costs typically can be fit as *gamma* or *log*-normal distributions constraining costs to non-negative values while also reflecting potential skewness in the data.[407] However, fitting a *gamma* or *log*-normal distribution requires sample moments (mean and variance) which none of the literature which informed the cost estimates provided. In scenarios where only maximum and minimum costs elements are provided, there are two possible solutions: (1) fit a triangular distribution (2) or conduct one-way sensitivity analysis. The triangular distribution is easily fitted as a unit area triangle which can be represented by three parameters: a minimum, a maximum and a mode. Despite being easy to fit, the distribution is extremely limited. The distribution is non-symmetric and the mean will not equal the mode. The distribution also has three points of discontinuity at each of the minimum, mode and maximum (zero probability of values above or below the minimum and maximum). Minima and maxima are also poor statistics in that the range of the variation measured tends to increase with sample size as there is more of a chance of observing and extreme value. This is contrary to what is generally considered desirable for the variance of the parameter distribution to decrease when greater information on the parameter of interest is provided. These limitations bring more *arbitrary* uncertainty rather than *informed* uncertainty into the model by using the triangular distribution. Therefore, the latter choice of conducting one-way sensitivity analyses on the maximum and minimum values of transitions costs was the desired strategy.

9.13.2 Fitting the *beta* distribution

When parameters are obtained from finite and small sample sizes, the natural probability distribution for probability parameters is the *beta* distribution. The *beta* distribution was fit using the method of moments approach[407]:

$$(\alpha + \beta) = \frac{\bar{u}(1-\bar{u})}{s^2} - 1$$

$$\alpha = \bar{u}(\alpha + \beta)$$

The system of equations requires two sample moments: the mean ($\bar{u}$) and the standard error (s) to solve for distribution parameters alpha (α) and beta (β). The mean was provided as the six-month transition probability and the standard error (se) was calculated using the following formula with known sample size (n):

$$se = \sqrt{\frac{p(1-p)}{n}}$$

The *beta* distribution is the natural choice for representing uncertainty in a probability parameter when the data informing the parameters is binomial as the *beta* distribution is conjugate to binomial data.[407] The selection of the *beta* distribution was an informed choice as the *beta* distribution constrains probabilities to their natural endpoints – from zero to one. Since many of the probabilities populating the Markov model in **Chapter 6** were near zero and had small sample sizes, standard errors were often large relative to the mean. If a normal distribution was applied to those parameters, the tail ends of the distribution would have been less than zero. This would have been problematic for probabilistic sensitivity analysis as probabilities cannot be negative.