Associations between smoking and health outcomes in an economically deprived population: the Liverpool Lung Project

Sherratt FC[1], Field JK [2], Marcus MW [2]

[1] Department of Psychological Sciences, University of Liverpool, Whelan Building, Brownlow Hill, Liverpool, L69 3GB, United Kingdom.

[2] Roy Castle Lung Cancer Research Programme, Department of Molecular and Clinical Cancer Medicine, University of Liverpool, The William Henry Duncan Building, 6 West Derby Street, Liverpool, L7 8TX, United Kingdom.

Corresponding author:
Dr. Michael W. Marcus
Roy Castle Lung Cancer Research Programme,
The University of Liverpool
Department of Molecular and Clinical Cancer Medicine,
Institute of Translational Medicine,
The William Henry Duncan Building
6 West Derby Street
L7 8TX
Liverpool
UK

Tel: +44 151 794 9122
Email:m.w.marcus@liv.ac.uk

Abstract

Background: The association between smoking and several health outcomes among those from the most deprived communities in the UK, has not previously been detailed. The aim of this study is to examine the impact of smoking on health outcomes among individuals from Liverpool, one of the most deprived local authorities in England.

Methods: The Liverpool Lung Project recruited a prospective cohort of 8,753 participants from across Liverpool, aged 45-79 years between 1998 and 2008. Participants were followed annually through the hospital episode statistics until 31st January 2013. Logistic regression models were used to identify health outcomes of smoking.

Results: From our study population, 5,195 were smokers and 3,558 were non-smokers. Smoking was associated with male gender (OR 1.62, 95% CI 1.48-1.77), pneumonia (1.29, 95% CI 1.11-1.50), chronic obstructive pulmonary disease (1.26, 95% CI 1.11-1.43), emphysema (5.61, 95% CI 3.58-8.79), bronchitis (1.89, 95% CI 1.69-2.13), other cancers (1.72, 95% CI 1.47-2.02), lung cancer (5.55, 95% CI 3.51-8.76), diabetes (1.20, 95% CI 1.02-1.42) and cardiovascular disease (1.45, 95% CI 1.25-1.67).

Conclusions: Smokers from deprived backgrounds in Liverpool appear to have increased risk of developing pneumonia, emphysema, chronic obstructive pulmonary disease, bronchitis, lung cancer, other types of cancer, cardiovascular disease and diabetes. These findings are in line with the literature and may help to inform public health policies and ultimately work towards addressing smoking-related health inequalities.

Keywords: Smoking, lung cancer, health outcomes, cohort study, Liverpool Lung Project

Introduction

Deprivation has been used widely as a surrogate indicator of socio-economic status [1, 2]. In England, the Index of Multiple Deprivation (IMD) is a measure of deprivation experienced by people living in an area or neighbourhood [3]. It is a robust index that incorporates 37 separate indicators, based on weighted data from the following seven domains for quantifying deprivation: income deprivation (22.5%), employment deprivation (22.5%), health deprivation and disability (13.5%), education, skills and training deprivation (13.5%), barriers to housing and services (9.3%), crime and living environment deprivation (9.3%) [3, 4].

Liverpool is one of the most deprived local authorities in the whole of England [3, 5]. Numerous studies have reported that individuals from lower socioeconomic backgrounds have markedly poorer health outcomes compared to their counterparts from upper socioeconomic backgrounds [6, 7]. Smoking is a health inequalities concern, as smoking rates are frequently higher among lower socio-economic groups in most developed countries [8-10]. For example, in Great Britain, smoking prevalence among those with Managerial and Professional, Intermediate and Routine/Manual statuses was 14%, 20% and 33%, respectively [11].

Smoking was attributable to 17% (N = 79,700) of all mortalities in England alone in 2013 and it has been estimated that smoking cost the National Health Service (NHS) in England £2.7 billion in 2006 [12]. Since Doll and Hill [13] first identified the causal link between smoking and lung cancer, research continues to identify further associations between smoking, smoking cessation and various other diseases [14] and smoking-related mortality [15- 20]. In 2013, it was estimated that smoking was linked with 35%, 28% and 13% of all respiratory, cancer and cardiovascular disease mortalities, respectively [14].

In Liverpool, smoking prevalence in adults is 32.5%; substantially higher than the average in England (22.8%) [15]. Smoking related deaths in Liverpool are also among the highest rates in England; Liverpool’s directly age standardised rate is 428.3 per 100,000 population, aged 35 years and above, 2012-2014. England's worst level is 458.1 and average in England is 274.8 [15]. Previous research does not typically isolate and explore patterns in smoking-related disease within specific socio-economic groups and rather explores it between smokers and non-smokers, across the spectrum of socio-economic groups [16]. The benefit of exploring these risks within specific socio-economic groups (such as those most deprived) is that we will establish an in-depth understanding of the magnitude of risk between smokers and non-smokers among those who are specifically classified as most deprived. This is important to consider; a better understanding of risk across a multitude of diseases will help to guide and tailor future research and interventions designed to prevent and reduce smoking rates within the most deprived communities. For example, we know that completion of smoking cessation behavioural support programmes is generally lower for deprived smokers [17]; improved knowledge regarding the magnitude of various smoking related risks among the most deprived smokers in developed countries could better inform behavioural support programmes by focusing on specific-smoking related diseases that are of optimal relevance to the most deprived smokers from developed nations.

Method

Study Population

This study was performed as part of the Liverpool Lung Project. The objectives, methods, rationale and study design have been described previously [18]. The study protocol was approved by the Liverpool Research Ethics Committee and all participants provided informed consent in accordance with the declaration of Helsinki.

Briefly, 8,753 randomly selected healthy subjects aged 45-79 years were recruited between 1998 and 2008 and followed annually for health and mortality outcomes through the Office for National Statistics (ONS), Public Health England (the North West Cancer Intelligence Service) and hospital case-note review, until 31 January 2013. Because of the objective of this study i.e. to study the effect of smoking on various health outcomes, the socioeconomic status of our study population was ascertained from anonymised IMD obtained from postcodes provided by participants using a website developed by Mimas at the University of Manchester [19]. Using the English IMD 2015, IMD ranks for all participants were placed within deciles based on England-wide population data: decile 1 (D1; most deprived) = most deprived 10%; decile 2 (D2; 10-20%); decile 3 (D3; 20-30%); decile 4 (D4; 30-40%); decile 5 (D5; 40-50%); decile 6 (D6; 50-60%); decile 7 (D6; 60-70%); decile 8 (D8; 70-80%); decile 9 (D9; 80-90%); decile 10 (D10; least deprived 10%). Our study population fell within the most deprived including D1 and D2.

Data Collection and Extraction of Risk Factors

Self-reported information on demographics, medical history, family history of cancer and history of tobacco consumption were collected using a standardised questionnaire. Information on age, gender, smoking duration, prior history of other cancers and prior history of non-malignant lung disease such as asthma, chronic obstructive pulmonary disease (COPD), pneumonia, bronchitis, emphysema and tuberculosis were extracted from the questionnaire. Smoking duration was measured in years; an ever smoker was defined as someone who had smoked at least 100 cigarettes in their lifetime. Previous history of cancer (except melanoma) was coded as "yes" or "no". Information on diagnosis of non-malignant lung diseases such as asthma, COPD, pneumonia and tuberculosis were coded "yes" or "no". In addition, information about diagnosis of diabetes and cardiovascular disease (CVD) were obtained from the Hospital Episode Statistic (HES) database. HES is the national statistical data warehouse for the National Health Services that contain details of all admissions, outpatients' appointments and accident and emergences services in England [20].

Statistical analyses

Distribution in health outcomes between smokers and non-smokers was evaluated using Chi-square test for categorical variables and t-tests for normally distributed variables. To avoid complete case analysis i.e. removing participants in the datasets without complete information in the regression model, imputation of missing information was conducted for all missing covariates. Multiple imputation using chained equations (MICE) was conducted to impute missing information across multiple variables simultaneously [21]. Variable selection in the univariate analysis was informed by the literature and all available variables were included in the univariate analysis. Univariate logistic regression was used to examine the associations between health outcomes and smoking characteristics. All statistically significant covariates ($p < 0.05$) in the univariate analyses were included in the multivariable logistic regression model. Covariates that are not significant in the previous univariate logistic regression were subsequently included in multivariable logistic regression, in order to prevent excluding relevant covariates that may have been excluded by univariate pre-selection of significant covariates. The final multivariable regression was obtained after excluding covariates that were not statistically significant at $p < 0.05$. All analyses were performed using STATA® version 14.2 (StataCorp LP, College Station, Texas).

Results

In our study population (N = 8,753), 5,195 were smokers and 3,558 were non-smokers. Table 1 depicts the health outcomes and smoking characteristics of the study population. Smokers were older, more often male, and more frequently diagnosed with pneumonia, asthma, tuberculosis, COPD, emphysema, bronchitis, lung cancer, other tumours, diabetes and CVD than their non-smoking counterparts.

Table 1: Univariate analysis of Health outcomes and smoking characteristics of study population

Characteristics	Smokers (n=5195)	Non-smokers (3558)	Univariate analysis OR (95%CI)	*P*-values
Mean Age (SD)	62.0(8.3)	61.1(8.7)	1.01 (1.01-1.02)	<0.001
Gender			1.52 (1.11-1.45)	<0.001
Male	2724(52.4)	1461(41.1)		
Female	2471(47.6)	2097(58.9)		
Smoking duration (SD)	30.8(15.3)	-	-	-
Prior diagnosis of pneumonia			1.71 (1.49-1.97)	<0.001
No	4448(85.6)	3183(91.1)		
Yes	747(14.4)	312(8.9)		
Prior diagnosis of asthma			1.55 (1.37-1.75)	<0.001
No	4272(82.2)	3122(87.8)		
Yes	923(17.8)	436(12.2)		
Prior diagnosis of tuberculosis			1.26 (0.97-1.63)	<0.001
No	5031(96.8)	3468(97.5)		
Yes	164(3.2)	90(2.5)		
Prior diagnosis of COPD			2.02 (1.80-2.26)	<0.001
No	3959(76.2)	3081(86.6)		
Yes	1236(23.8)	477(13.4)		
Prior diagnosis of Emphysema			9.01 (5.82-13.95)	<0.001
No	4919(94.6)	3536(99.4)		
Yes	276(5.3)	22(0.6)		
Prior diagnosis of Bronchitis			2.19 (1.97-2.43)	<0.001
No	3603(69.4)	2960(83.2)		
Yes	1592(30.6)	598(16.8)		
Prior diagnosis of other tumours			1.87 (1.60-2.17)	<0.001
No	4566(76.2)	3313(91.9)		
Yes	629(12.1)	245(8.1)		
Diagnosis of lung cancer			7.30 (4.66-11.46)	<0.001
No	4979(95.8)	3537(99.4)		
Yes	216(4.2)	21(0.6)		
Prior diagnosis of diabetes			1.45 (1.24-1.70)	<0.001
No	4682(90.1)	3308(93.0)		
Yes	513(9.9)	250(7.0)		
Prior diagnosis of CVD			1.78 (1.56-2.03)	<0.001
No	4351(83.8)	3208(90.2)		
Yes	844(16.2)	350(9.8)		

Abbreviations: SD = Standard deviation; COPD = chronic obstructive pulmonary disease; CVD = Cardiovascular disease; *Numbers do not add up to total due to missing data

Table 2 shows the results of the final multivariable logistic regression analysis of all of the health outcomes associated with smoking. Male gender, pneumonia, COPD, emphysema, bronchitis, other cancers, lung cancer, diabetes and CVD were all associated with smoking.

Table 2: Multivariable analysis of health outcomes on smoking characteristics

Covariates	Odds ratios	95% confidence interval	*P*-value
Sex	1.62	1.48-1.77	<0.001
Pneumonia	1.29	1.11-1.50	0.001
COPD	1.26	1.11-1.43	<0.001
Emphysema	5.61	3.58-8.79	<0.001
Bronchitis	1.89	1.69-2.13	<0.001
Other cancers	1.72	1.47-2.02	<0.001
Lung cancer	5.55	3.51-8.76	<0.001
Diabetes	1.20	1.02-1.42	0.033
CVD	1.45	1.25-1.67	<0.001

Abbreviations: COPD = Chronic Obstructive Pulmonary Disease; CVD=Cardiovascular disease.

Discussion

The current study explored the relationships between smoking and several health outcomes in Liverpool, one of the most deprived local authorities in England. In this large prospective population-based study, smoking was associated with male gender, pneumonia, COPD, emphysema, bronchitis, lung cancer, other cancers, diabetes and CVD. The effect of smoking was much more pronounced for emphysema OR 5.61 (95% CI 3.58-8.79) and lung cancer 5.55 (95% CI 3.51-8.76) compared to other diseases reported.

The association between the effect of smoking on COPD, bronchitis and emphysema was found to be consistent with the results of an earlier published meta-analysis by Forey, Thornton and Lee [22]. In their study, based on random-effects meta-analyses of most-adjusted RR/ORs, the effect estimates for ever smokers compared to never smokers was 2.89 (95% CI 2.63-3.17) for COPD using 129 studies, 2.69 (95% CI 2.50-2.90) using 114 studies for chronic bronchitis and 4.51 (95% CI 3.38-6.02) for emphysema using 28 studies. The effect estimates for both COPD and chronic bronchitis is higher in magnitude than in our study. A plausible explanation for this observation is the design of the previous study, the large numbers of studies pooled in it and the statistical methodology employed in estimating the effect estimates in the meta-analysis. The effect estimate of emphysema in our study was slightly higher than that of the aforementioned meta-analysis, which suggests that the most deprived smokers are particularly vulnerable to emphysema, compared to their less deprived counterparts. However, there is a slight overlap in the effect estimates and confidence interval of both studies which further buttress the strong association between smoking and emphysema. Further research is needed to explore the relationship between smoking and emphysema in deprived communities to corroborate our results.

Regarding lung cancer, Lee, Foley and Coombs [23] conducted a random-effects meta-analysis, using 287 studies and reported the relative risk of lung cancer among ever smokers as 5.50 (95% CI 5.07-5.96). This effect estimate is slightly lower than the effect reported in the current study (OR 5.55, 95% CI 3.51-8.76). This suggests that incidence rates may be substantially higher among ever smokers in the current study, potentially due to socio-economic status. In another study, Sidorchuk, Agardh, Aremu, Hallqvist, Allebeck and Moradi [24] undertook a systematic review and meta-analysis to examine the relationship between socio-economic status and lung cancer incidence. They found that the greatest effect was present for studies exploring educational attainment and lung cancer incidence was significantly higher among those with the lowest level of educational attainment RR 1.61 (95% CI 1.40-1.85). Furthermore, studies investigating occupation and also, income displayed increased lung cancer incidence among the least affluent groups compared to the most affluent; RR 1.48 (95% CI 1.34-1.65), RR 1.37 (95% CI 1.06-1.77), respectively. The current study provides further insight into this relationship, as deprivation was considered and, more specifically, the English IMD. It is currently unclear if further factors might implicate the observed relationship between smoking, deprivation and lung cancer.

We also found that smoking was associated with other types of cancers (OR 1.72, 95%CI 1.47-2.02). This result was in accordance with earlier studies that have implicated smoking with 14 different types of cancer including nose and sinus, mouth and upper throat, larynx, oesophagus, liver, pancreas, stomach, kidney, bowel, ovary, bladder, leukaemia and cervical cancer, excluding lung cancer [25]. However, the current study provides an overview of the magnitude of risk among smokers from the most deprived communities, compared to their non-smoking counterparts.

In the present study, smoking was associated with diabetes (OR 1.21, 95% CI 1.02-1.43). This observation is also consistent with the literature, although there is currently limited research on the effect of smoking on diabetes among deprived communities and this finding adds to our knowledge. The Health Professionals' Follow-up Study showed that the risk for diabetes among men who smoked 25 cigarettes or more per day was RR 1.94 (95% CI 1.25-3.03) compared with non-smokers [26]. Other studies have also reported an association between smoking and diabetes in Japanese, United States and Chinese populations [26-31] .

In our study, we observed that smoking was associated with CVD (OR 1.46, 95% CI 1.26-1.69). Smoking is regarded as the most preventable cause of cardiovascular morbidity and mortality [32] and there is overwhelming evidence from epidemiological studies showing association between smoking and CVD [33, 34]. In a recent study, Ehteshami-Afshar, Momenan, Hajshekholeslami, Azizi and Hadaegh [35] evaluated the impact of smoking status on CVD among Iranian men. In this prospective study, 3059 men aged ≥30 years, free of CVD at baseline were evaluated for a median of 9.3 years follow-up. Being a past smoker significantly increased the risk of CVD events HR 2.42 (95% CI 1.28–0.56), however, smoking had no effect on coronary heart disease (CHD) events, total and CVD mortality. Being a current smoker (more than 10 cigarettes a day) dramatically increased the risk of CVD/CHD events and total/CVD mortality. However, smoking less than 10 cigarettes per day was associated with a lower level of increased CVD risk 2.12 (95% CI 1.14–3.95) and its mortality 4.57 (95% CI 1.32–15.79). The current study adds to these findings as we report an estimation of CVD risk among smokers from a deprived population in the UK, providing an estimate of how the level of risk might differ to some other populations previously reported.

The current study provides a risk estimation for smoking-related disease among a deprived community in a developed country, however, other potentially mediating factors now need to be explored in addition to smoking, to fully understand the association between deprivation and smoking-related disease. As described, Sidorchuk, Agardh, Aremu, Hallqvist, Allebeck and Moradi [24] found that lung cancer incidence was highest among those with the lowest level of educational attainment, and those from the least affluent groups regarding occupation and income, even in some cases where smoking was controlled for. In considering these results with previous research regarding health outcomes and smoking, it should also be noted that some differences may be attributed to inconsistencies in international clinical practice over recent decades e.g. discrepancies in diagnosis definitions or misdiagnosis, or varying measures. However, further research is needed to fully understand the extent of smoking-related risk among deprived communities and to consider new strategies that might reduce this health inequality.

This research is novel in that it is focused specifically on a large cohort obtained from Liverpool, which was reported as one of the most deprived local authorities in England. To the best of our knowledge, there are currently no large cohort studies that have explored the relationship between smoking and smoking-related disease in deprived population from a developed country. The findings provide insight regarding smoking-related risks among specifically, the most deprived group within a developed country, providing better understanding of the magnitude of risk within such populations. In addition, we included data on a variety of health outcomes to truly explore the extent to which smoking affects health outcomes in a socio-economic deprived population.

Strengths of our study include the large number of participants, prospective study design, the long follow-up period, the reliability of the health outcome measures, the population-based setting and multiple imputation of missing data, which minimises bias. The findings of our study should be viewed in the light of some limitations. First, we used the IMD as a surrogate for socioeconomic status. IMD is not a perfect measure of deprivation. However, it represents a commendable advance in regard to the development of methods used to quantify deprivation in the English population [4]. Second, our study was based on a specific population in Liverpool which may limit generalisability. However, the city of Liverpool can be compared to other cities in England and in other developed countries so our study could be generalised both to the English and other communities in developed countries. Third, Smoking data was also gathered by extensively trained and closely supervised interviewers who used standardised questionnaires. Despite this, there is a possibility that recall and other biases may have influenced the results, as participants were required to report on smoking behaviours over a number of decades previous to the interview.

Since the results suggest that health outcomes are particularly prominent amongst ever smokers compared to never smokers within deprived communities, we should consider future directions. As described, further analyses may benefit from the integration of additional variables associated with both smoking and socio-economic status, to explore any mediating effect which is independent of smoking. In doing so, it may be possible to identify other avenues by which health inequalities could be reduced. In comparison to previous data, it seems that health outcomes remain substantially poorer among smokers and those from less affluent socio-economic groups to present day within a developed country such as England; which leads us to explore how far the health inequalities margin has narrowed and what more can be done. A review by Hiscock, Bauld, Amos, Fidler and Munafo [17] suggested that differences in smoking prevalence between socioeconomic groups could be the result of factors including: lower social support for quitting, poorer motivation to quit, greater addiction to tobacco, decreased likelihood of completing a pharmacotherapy or behaviour support programme for quitting smoking, psychological differences e.g. lower self-efficacy. The current study adds to understanding of the magnitude to which individuals from the most deprived communities in developed countries exhibit smoking-related risk. A better understanding of the risks associated with smoking among the most deprived communities and consideration of psychosocial factors associated with smoking prevalence among the most deprived individuals from developed nations, could help to inform more tailored and robust smoking cessation communications; ultimately, tailored communications have been referred to as the most promising approach to smoking cessation interventions [36].

What is already known on this subject:

- Smoking has been associated with deprivation and smoking-related risk is higher among deprived populations.
- Previous research on smoking often focuses on specific outcomes in diverse socioeconomic status, as opposed to focusing on specific socio-economic groups.
- Exploration of a range of smoking-related risks within a specifically deprived population, will improve understanding of risk and help to inform future smoking cessation approaches.

What this study adds:

- Deprived smokers are substantially more at risk of developing lung cancer, other types of cancers, pneumonia, bronchitis, emphysema, CVD, COPD and diabetes, than their non-smoking counterparts.
- Risk estimates for some smoking-related disease among participants in the current study were observed to be substantially higher than some reported elsewhere, which has implications for the tailoring of future smoking cessation interventions.
- Further research is required to fully understand other substantial factors in the relationship between smoking, deprivation and disease; this would help to inform public health policies that could help narrow this prominent health inequality.

Acknowledgement

We thank the individuals who participated in this research and all the clinicians and support staff who made this study possible. The Liverpool Lung project was principally funded by the Roy Castle Lung Cancer Foundation,

Competing Interest: None declared

References

1 Galobardes B, Shaw M, Lawlor DA, *et al.* Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;**60**:7-12.

2 Kim JY, Kim SH, Cho YJ. Socioeconomic status in association with metabolic syndrome and coronary heart disease risk. *Korean J Fam Med* 2013;**34**:131-8.

3 Government DfCaL. The English Indices of Deprivation 2015. 2015.

4 Deas I, Robson B, Wong C, *et al.* Measuring neighbourhood deprivation: a critique of the Index of Multiple Deprivation. *Environment and Planning C: Government and Policy* 2003;**21**:883-903.

5 Liverpool City Council. The Index of Multiple Deprivation 2010: A Liverpool Analysis. Liverpool, United Kingdom: Liverpool City Council 2011.

6 Embrett MG, Randall GE. Social determinants of health and health equity policy research: exploring the use, misuse, and nonuse of policy analysis theory. *Soc Sci Med* 2014;**108**:147-55.

7 Low L, Hodson J, Morris D, *et al.* Socioeconomic deprivation and serious ocular trauma in Scotland: a national prospective study. *Br J Ophthalmol* 2017.

8 Barnett R, Pearce J, Moon G. Community inequality and smoking cessation in New Zealand, 1981-2006. *Soc Sci Med* 2009;**68**:876-84.

9 Cavelaars AE, Kunst AE, Geurts JJ, *et al.* Educational differences in smoking: international comparison. *BMJ* 2000;**320**:1102-7.

10 Pampel FC, Krueger PM, Denney JT. Socioeconomic Disparities in Health Behaviors. *Annu Rev Sociol* 2010;**36**:349-70.

11 Office for National Statistics. Opinions and Lifestyle Survey, Smoking Habits Amongst Adults, 2012. Office for National Statistics 2013.

12 Callum C, Boyle S, Sandford A. Estimating the cost of smoking to the NHS in England and the impact of declining prevalence. *Health economics, policy, and law* 2011;**6**:489-508.

13 Doll R, Hill AB. Smoking and carcinoma of the lung; preliminary report. *British medical journal* 1950;**2**:739-48.

14 Health and Social Care Information Centre. Statistics on Smoking: England 2014. Health and Social Care Information Centre, 2014.

15 England PH. Liverpool Health Profile 2016. 2016.

16 Thun MJ, Apicella LF, Henley SJ. Smoking vs other risk factors as the cause of smoking-attributable deaths: confounding in the courtroom. *JAMA* 2000;**284**:706-12.

17 Hiscock R, Bauld L, Amos A, *et al.* Socioeconomic status and smoking: a review. *Annals of the New York Academy of Sciences* 2012;**1248**:107-23.

18 Cassidy A, Myles JP, van Tongeren M, *et al.* The LLP risk model: an individual risk prediction model for lung cancer. *Br J Cancer* 2008;**98**:270-6.

19 Mimas. GeoConvert. Manchester: Mimas 2014.

20 Service NH. Health Episode Statistics. 2016.

21 Azur MJ, Stuart EA, Frangakis C, *et al.* Multiple imputation by chained equations: what is it and how does it work? *Int J Methods Psychiatr Res* 2011;**20**:40-9.

22 Forey BA, Thornton AJ, Lee PN. Systematic review with meta-analysis of the epidemiological evidence relating smoking to COPD, chronic bronchitis and emphysema. *BMC Pulmonary Medicine* 2011;**11**:36-.

23 Lee PN, Foley BA, Coombs KJ. Systematic review with meta-analysis of the epidemiological evidence in the 1900s relating smoking to lung cancer. *BMC cancer* 2012;**12**:385-474.

24 Sidorchuk A, Agardh EE, Aremu O, *et al.* Socioeconomic Differences in Lung Cancer Incidence: A Systematic Review and Meta-Analysis. Springer 2009:459.

25 Baan R, Grosse Y, Straif K, *et al.* A review of human carcinogens--Part F: chemical agents and related occupations. *The lancet oncology* 2009;**10**:1143-4.

26 Rimm EB, Chan J, Stampfer MJ, *et al.* Prospective study of cigarette smoking, alcohol use, and the risk of diabetes in men. *BMJ* 1995;**310**:555-9.

27 Uchimoto S, Tsumura K, Hayashi T, *et al.* Impact of cigarette smoking on the incidence of Type 2 diabetes mellitus in middle-aged Japanese men: the Osaka Health Survey. *Diabet Med* 1999;**16**:951-5.

28 Manson JE, Ajani UA, Liu S, *et al.* A prospective study of cigarette smoking and the incidence of diabetes mellitus among US male physicians. *Am J Med* 2000;**109**:538-42.
29 Ko GT, Chan JC, Tsang LW, *et al.* Smoking and diabetes in Chinese men. *Postgrad Med J* 2001;**77**:240-3.
30 Sairenchi T, Iso H, Nishimura A, *et al.* Cigarette smoking and risk of type 2 diabetes mellitus among middle-aged and elderly Japanese men and women. *Am J Epidemiol* 2004;**160**:158-62.
31 Pan A, Wang Y, Talaei M, *et al.* Relation of active, passive, and quitting smoking with incident type 2 diabetes: a systematic review and meta-analysis. *Lancet Diabetes Endocrinol* 2015;**3**:958-67.
32 Lakier JB. Smoking and cardiovascular disease. *The American journal of medicine* 1992;**93**:8s-12s.
33 Kenfield SA, Stampfer MJ, Rosner BA, *et al.* Smoking and smoking cessation in relation to mortality in women. *JAMA - Journal of the American Medical Association* 2008;**299**:2037-47.
34 Preston SH, Glei DA, Wilmoth JR. A new method for estimating smoking-attributable mortality in high-income countries. *International journal of epidemiology* 2010;**39**:430-8.
35 Ehteshami-Afshar S, Momenan A, Hajshekholeslami F, *et al.* The impact of smoking status on 9.3 years incidence of cardiovascular and all-cause mortality among Iranian men. *Annals of Human Biology* 2014;**41**:249-54.
36 Thun MJ, Hannan LM, Stefanek M. Risky business: tools to improve risk communication in a doctor's office. *Journal of the National Cancer Institute* 2008;**100**:830-1.