University of Sheffield | School of Health & Related Research

# Smoking and the risks of adult diseases

Version 1.2.1

October 2018

Laura Webster[1], Colin Angus[1], Alan Brennan[1], Duncan Gillespie[1]

[1]School of Health and Related Research (ScHARR), The University of Sheffield

**Address for correspondence**:
Dr Duncan Gillespie
Section of Health Economics and Decision Science,
School for Health and Related Research,
The University of Sheffield,
Regent Court, Regent Street, Sheffield, S1 4DA, UK
Email: duncan.gillespie@sheffield.ac.uk

The code that accompanies this vignette can be found in the tobalcepi R package https://stapm.github.io/tobalcepi/ (Github code repository https://github.com/STAPM/tobalcepi).

This vignette is a reproduction of the content in: Webster, Laura; Angus, Colin; Brennan, Alan; Gillespie, Duncan (2018): Smoking and the risks of adult diseases. The University of Sheffield. https://doi.org/10.15131/shef.data.7411451.v1

Therefore the citation above should be used for this vignette. This vignette differs from the report cited above in being produced by the code within the tobalcepi R package. This vignette therefore presents the risk functions and acts as a means to quality assure the code in the tobalcepi R package.

# Contents

# 1 Acknowledgements

The authors would like to thank John Britton of the University of Nottingham and UK Centre for Tobacco and Alcohol Studies, Katrina Brown of Cancer Research UK for their advice and input at various stages of the preparation of this document.

# 2 Introduction

This document presents our list of **52** adult diseases related to smoking and the corresponding relative risks of disease due to smoking, explaining our choices of disease definitions and risk sources. Figure 1 shows the variation in disease-specific risks. We focus on the risks of current smoking and limit ourselves to diseases that affect the consumer themselves e.g. excluding secondary effects of smoking on children. We assume the equivalence of relative risks and odds ratios. Our starting point was the Royal College of Physician's (RCP) report "Hiding in plain sight: Treating tobacco dependency in the NHS" (Tobacco Advisory Group of the Royal College of Physicians 2018), which reviewed smoking–disease associations to produce an updated list of diseases that are caused by smoking and updated risk sources. We mainly keep to the RCP report's disease list, with any deviations from the RCP list and risk sources being for one of two reasons:

1. There are often slightly conflicting ICD-10 code definitions used for some conditions and we have sought to harmonise these consistently across both tobacco and alcohol, based on the Sheffield Alcohol Policy Model (SAPM) v4.0 disease list (Angus et al. 2018);
2. Since publication of the RCP report, Cancer Research UK (CRUK) produced their own disease list and risk sources for cancers attributable to modifiable risk factors, including tobacco and alcohol (Brown et al. 2018). Discussions with CRUK shaped the disease definitions in our updated Sheffield disease list for alcohol. Where there are differences in the risk sources used in the RCP report and CRUK's work, we take the estimate that matches most closely to our disease definitions, or the more recent estimate.

# 3 Tobacco–Alcohol interactions in disease risk

There is limited evidence for the risk of disease in someone who consumes both tobacco and alcohol ($RR_{ta}$) being higher than would be expected from combining the independent risks from tobacco ($RR_t$) and alcohol ($RRa$). This additional risk due to tobacco-alcohol interaction (over and above the combination of the independent contributions to risk from tobacco and alcohol) can be expressed as a "synergy factor" (1) (A. Prabhu, Obi, and Rubenstein 2014; Hashibe et al. 2009).

$$SF = \frac{RR_{ta}}{(RR_t - 1) + (RR_a - 1)} \tag{1}$$

We conducted a scoping review across all diseases for which tobacco and alcohol are causal factors to ascertain the extent of evidence on interaction effects. We include only interactions with a meta-analysis of effect size. The only diseases for which we have found suitable meta-analyses to inform the tobacco–alcohol interaction in risk are cancers of the oral cavity, pharynx, larynx and oesophagus. To evaluate the interaction between tobacco and alcohol and the risk of cancer of the oral cavity, pharynx and larynx, Hashibe et al. (2009) conducted a pooled analysis within the INHANCE consortium. For the oral cavity and pharynx, the SF was estimated to be 3.09 (CI 1.82–5.23) i.e. smoking and drinking together causes around a 3-fold increase in the risk of head and neck cancers over and about the independent contributions of tobacco and alcohol. For cancer of the larynx, Hashibe et al. (2009) estimate the SF to be 1.62 (CI 0.85–3.09). For cancer of the oesophagus, Prabhu et al. (A. Prabhu, Obi, and Rubenstein 2014) estimated the increase in risk of

Squamous Cell Carcinoma in people who both smoke and drink to be characterised by a synergy factor of 1.85 (CI 1.45–2.38).

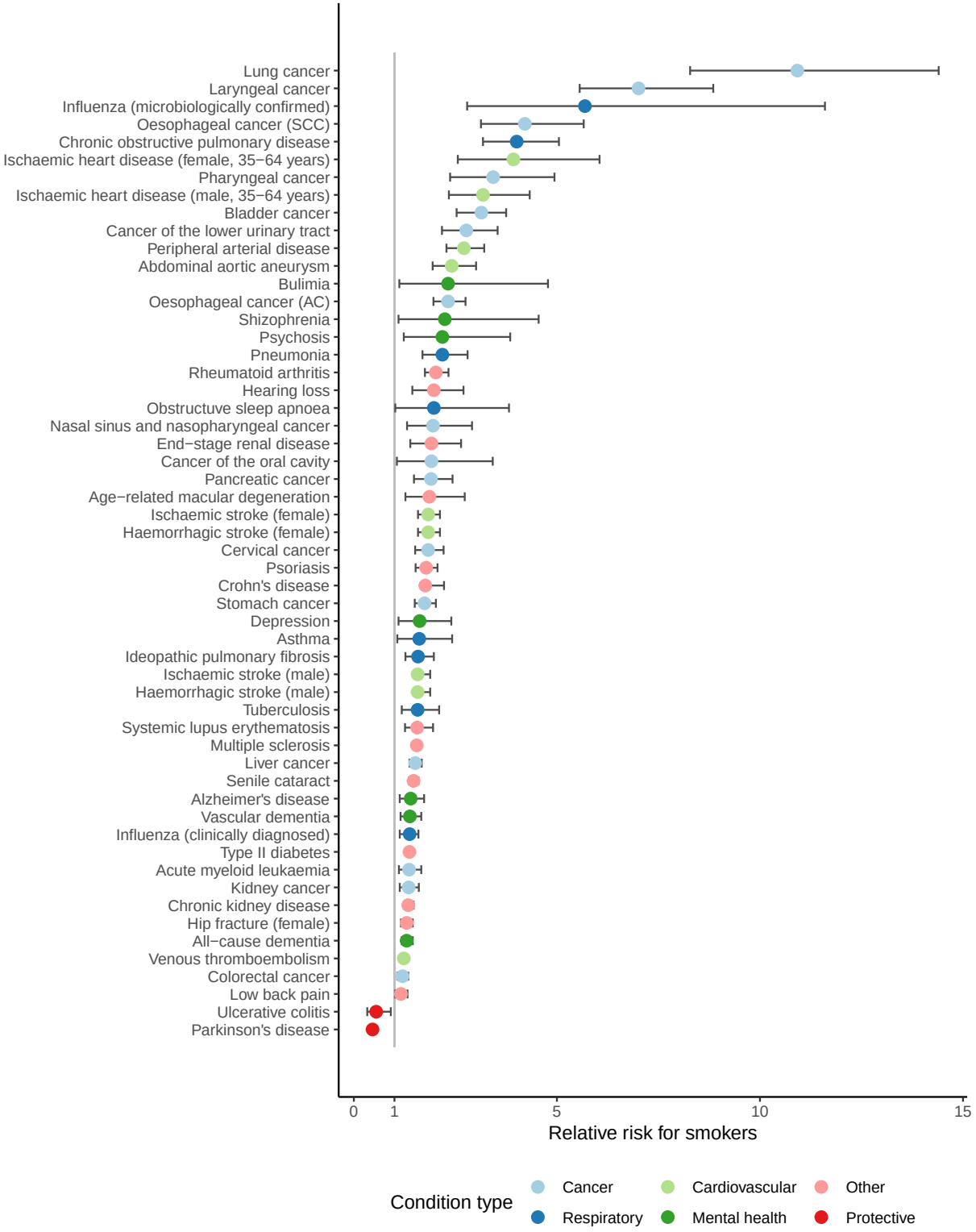


Figure 1: Relative risks and 95 percent confidence intervals in current smokers for 52 conditions attributable to smoking.

# 4 Cancers

We include all cancers attributable to tobacco as mentioned by CRUK (Brown et al. 2018), except ovarian cancer. Smoking only carries a risk for fully malignant mucinous ovarian cancers (13% of ovarian cancers are mucinous, and of these 57% are fully malignant). We excluded ovarian cancer due to the uncertainty involved in identifying the cases attributable to smoking based on the ICD-10 definitions used in our mortality data and hospital episode statistics.

Below we itemise each cancer type and explain how we have synthesised the definitions of cancers and the sources for the relative risk of smoking among the Sheffield alcohol disease list (Angus et al. 2018), RCP report (Tobacco Advisory Group of the Royal College of Physicians 2018), and CRUK's paper (Brown et al. 2018).

## 4.1 Oral cavity (C00–C06), and pharyngeal (C09, C10, C12–C14)

Gandini et al. (2008) estimated the relative risk of smoking for cancer in the oral cavity as 3.43 (95% Confidence Interval 2.37–4.94), and pharyngeal cancers as 6.76 (CI 2.86–16.0). Following Gandini, the RCP report associated the relative risk from Gandini for oral cavity (RR 3.43) with ICD10 code C10, and relative risk for pharyngeal cancer (RR 6.76) with ICD10 code C14. But in line with CRUK, we instead use the risk that Gandini associated with oral cavity cancer (RR 3.43) for pharyngeal cancers with ICD10 codes C09, C10, C12–C14. For oral cavity, we use the risk from Maasland et al. (2014) of 1.91 (CI 1.06–3.42) with ICD10 codes C00–C06.

## 4.2 Oesophageal (C15)

Gandini et al. (2008) estimated the relative risks of smoking for cancer of the oesophagus as 2.50 (CI 2.00–3.13). Differing from the RCP report but in-line with CRUK, we split oesophageal cancer into its two main histological types: Squamous Cell Carcinoma (SCC) and Adenocarcinoma (AC). CRUK use different relative risks of smoking for each subtype: following CRUK, for SCC, we use the risk from Prabhu et al. (2013) of 4.21 (CI 3.13–5.66); for AC, we use the risk from Tramacere et al. (2011) of 2.32 (CI 1.96–2.75). We apportion overall oesophageal cancer prevalence between AC and SCC using data on percentage prevalence by age and sex from cancer registries, supplied to us by CRUK.

## 4.3 Colorectal (C18–C20)

The RCP report used the CHANCES consortium (Ordóñez-Mena et al. 2016) estimate of the relative risk of smoking for colorectal cancer of 1.20 (CI 1.07–1.34). CRUK instead use the estimates of Cheng et al. (J. Cheng et al. 2015), who produce two separate risks of smoking for cancer of the colon and rectum (RR 1.11, 1.44). To align with the SAPM disease list, we define colorectal cancer as a single disease and use the CHANCES risk estimate in-line with the RCP report.

## 4.4 Liver (C22)

The RCP report used Lee et al.'s (2009) estimate of the risk of smoking for liver cancer of 1.51 (CI 1.37–1.67). CRUK use the same source but take the sex-specific effects: 1.61 (CI 1.38–1.89) for males and 1.86 (CI 1.33–2.60) for females. Due to the substantial overlap between the sex-specific confidence intervals, we use the overall estimate.

### 4.5 Pancreatic (C25)

CRUK used Bosetti et al.'s (2011) estimate from the PanC4 study that the risk of smoking for pancreatic cancer is 2.20 (CI 1.71–2.83). The RCP report used the CHANCES consortium (Ordóñez-Mena et al. 2016) estimate of 1.90 (CI 1.48–2.43), and we use this more recent estimate.

### 4.6 Laryngeal (C32)

The RCP report used Gandini et al.'s (2008) estimate for the relative risks of smoking for cancer of the larynx of 6.98 (CI 3.14–15.52). CRUK used the more recent estimate by Zuo et al. (2017) of 7.01 (CI 5.56–8.85). We use the estimate of Zuo.

### 4.7 Stomach (C16)

CRUK used the estimate of Ladeiras-Lopes et al. (Ladeiras-Lopes et al. 2008) that put the relative risk of stomach cancer among smokers at 1.62 (CI 1.50–1.75) for males and 1.20 (CI 1.01–1.43) for females. The RCP report used the CHANCES consortium (Ordóñez-Mena et al. 2016) estimate of 1.74 (CI 1.50–2.02), and estimates from Gandini et al. (2008) are similar. We use the CHANCES estimate.

### 4.8 Lung (C33–C34)

CRUK used Gandini et al.'s (2008) estimate of the relative risk of lung cancer among smokers of 8.96 (CI 6.73–12.11). The RCP report used the more recent 2016 meta-analysis by Jayes et al. (2016) estimates the risk to be 10.92 (CI 8.28–14.40). We use the Jayes estimate.

### 4.9 Cervical (C53)

Both CRUK and the RCP report use Gandini et al.'s (2008) estimate of the relative risk of cervix cancer among smokers of 1.83 (CI 1.51–2.21).

### 4.10 Kidney (C64)

The RCP report used Gandini et al.'s (2008) estimate of the relative risk of kidney cancer among smokers of 1.52 (CI 1.33–1.74). CRUK use the more recent meta-analysis by Cumberbatch et al. (2016) of 1.35 (CI 1.13–1.60) but associate this with ICD10 codes C64–C66, C68. We use the Cumberbatch estimate for C64.

### 4.11 Lower urinary tract (C65–C66)

In-line with the RCP report, we use Gandini et al.'s (2008) estimate of the relative risk of lower urinary tract (renal pelvis, bladder and ureter) cancer of 2.77 (CI 2.17–3.54).

### 4.12 Bladder (C67)

The RCP report used the estimate by van Osch et al. (2016) for the risk of bladder cancer among smokers of 3.14 (CI 2.53–3.75). CRUK used the same source but took the sex-specific estimates of 3.44 (CI 2.67–4.22) for males, and 3.56 (CI 2.76–4.36) for females. We use the overall estimate.

### 4.13 Acute myeloid leukaemia (C92)

CRUK used Fircanis et al.'s (2014) estimate of the relative risk of acute myeloid leukaemia among smokers of 1.47 (CI 1.08–1.98) but associate it with ICD10 codes C90–C95. The RCP report used the more recent meta-analysis by Colamesta et al. (2016), which produced a similar estimate of 1.36 (CI 1.11–1.66). In-line with the RCP report, we use the Colamesta estimate and associate it with ICD10 code C92.

### 4.14 Nasal-sinuses and nasopharynx (C11, C30–C31)

The RCP report and CRUK both used Gandini et al.'s (2008) estimate of the relative risk of smoking for nasopharyngeal (C11) and sino-nasal (C30, C31) cancers of 1.95 (CI 1.31–2.91).

## 5 Cardiovascular conditions

Our cardiovascular disease list and risk sources are all in-line with the RCP report, which discusses the sources available. To align with the Sheffield alcohol disease list, we split stroke into haemorrhagic (I60–I62) and ischaemic (I63–I67) but use the same smoking risk for each.

## 6 Respiratory conditions

Our respiratory disease list and risk sources are all in-line with the RCP report. We expand the definition of 'Lower respiratory tract infections' (J09-J18) from the Sheffield alcohol disease list to accommodate the different risks of smoking that the RCP report identified for pneumonia (J12-J18), Influenza – clinically diagnosed (J11), and Influenza – microbiologically confirmed (J09, J10).

## 7 Mental health

Our mental health disease list and risk sources are all in-line with the RCP report.

## 8 Other adult diseases

We include 13 further diseases in-line with the RCP report.

## 9 Conditions less common among smokers

We include 2 diseases in-line with the RCP report.

## 10 Decline in risk over time after quitting smoking

To estimate the risk of disease for former smokers we used the findings of Kontis et al. (2014), who re-analysed the change in risk after smoking in the ACS-CPS II study from Oza et al.(2011), producing three functions to describe the decline in risk after quitting for each of cancers, CVD and COPD (Figure 2). The estimates were informed by data on former smokers with known quit dates who were disease-free at baseline. The results show the proportion of excess relative risk remaining at each time-point since cessation. A cross-check

showed that the figures for cancers were broadly consistent with the findings of the International Agency for Research on Cancer's (IARC) 2007 review of the decline in risk after quitting smoking (International Agency for Research on Cancer and World Health Organization 2007).

The remaining question is how risk declines after quitting smoking for diseases that are not cancers, CVD or COPD. Kontis et al. (2014) state that "Randomised trials also indicate that the benefits of behaviour change and pharmacological treatment on diabetes risk occur within a few years, more similar to the CVDs than cancers (Knowler et al. 2002). Therefore, we used the CVD curve for diabetes." In-line with Kontis, we apply the rate of decline in risk of CVD after quitting smoking to type 2 diabetes. For other diseases, we assume that the relative risk reverts to 1 immediately after quitting i.e. an immediate rather than a gradual decline in risk.

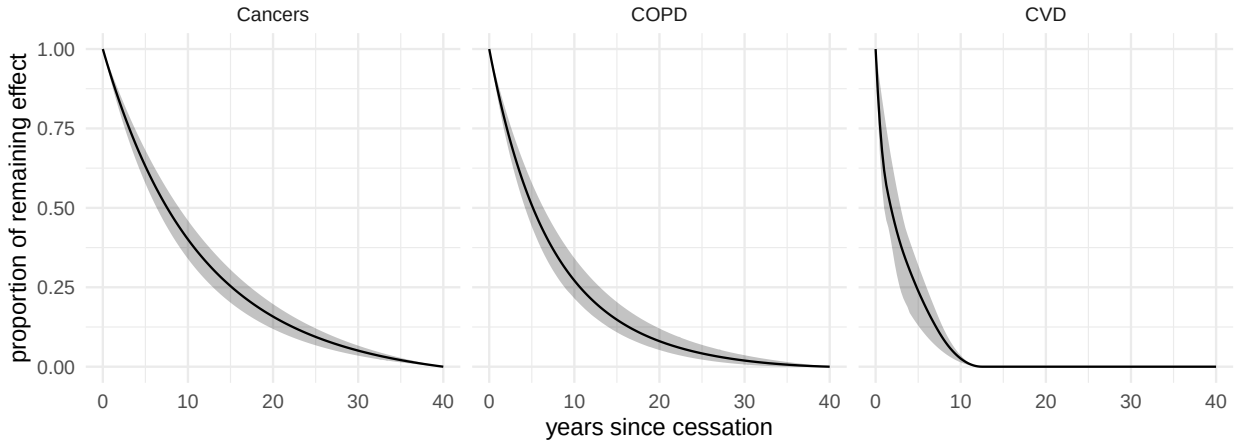


Figure 2: The proportion of remaining risk after quitting.

# 11 Tables

Table 1: Disease definitions and risk functions (with 95 percent confidence intervals) for current vs. never smoking.

| Category | Disease | ICD-10 | Relative risk | Source |
|---|---|---|---|---|
| | Oral cavity | C00-C06 | 1.91 (1.06–3.42) | (Maasland et al. 2014) |
| | Pharynx | C09, C10, C12-C14 | 3.43 (2.37–4.94) | (Gandini et al. 2008) |
| | Lung | C33, C34 | 10.92 (8.28–14.40) | (Jayes et al. 2016) |
| | Nasopharynx sinonasal | C11, C30, C31 | 1.95 (1.31–2.91) | (Gandini et al. 2008) |
| | Larynx | C32 | 7.01 (5.56–8.85) | (Zuo et al. 2017) |
| | Oesophageal (Adenocarcinoma) | C15 | 2.32 (1.96–2.75) | (Tramacere, La Vecchia, and Negri 2011) |
| | Oesophageal (Squamous cell carcinoma) | | 4.21 (3.13–5.66) | (A. Prabhu, Obi, and Rubenstein 2013) |

Table 1: Disease definitions and risk functions (with 95 percent confidence intervals) for current vs. never smoking. *(continued)*

| Category | Disease | ICD-10 | Relative risk | Source |
|---|---|---|---|---|
| Malignant neoplasms | Stomach | C16 | 1.74 (1.50–2.02) | (Ordóñez-Mena et al. 2016) |
| | Pancreas | C25 | 1.90 (1.48–2.43) | (Ordóñez-Mena et al. 2016) |
| | Liver | C22 | 1.51 (1.37–1.67) | (Lee et al. 2009) |
| | Colorectal | C18-C20 | 1.20 (1.07–1.34) | (Ordóñez-Mena et al. 2016) |
| | Kidney | C64 | 1.35 (1.13–1.60) | (Cumberbatch et al. 2016) |
| | Lower urinary tract | C65, C66 | 2.77 (2.17–3.54) | (Gandini et al. 2008) |
| | Bladder | C67 | 3.14 (2.53–3.75) | (Osch et al. 2016) |
| | Cervical | C53 | 1.83 (1.51–2.21) | (Gandini et al. 2008) |
| | Acute myeloid leukaemia | C92 | 1.36 (1.11–1.66) | (Colamesta et al. 2016) |
| Circulatory system | Ischaemic heart disease | I20-I25 | Male 35–64: 3.18 (2.34–4.33), Male 65+: 1.96 (1.62–2.37), Female 35–64: 3.93 (2.56–6.05), Female 65+: 1.95 (1.60–2.37) | (Rostron 2012) |
| | Haemorrhagic stroke | I60-I62 | Male: 1.57 (1.49–1.88), Female: 1.83 (1.58–2.12) | (Peters, Huxley, and Woodward 2013) |
| | Ischaemic stroke | I63-I67 | | (Peters, Huxley, and Woodward 2013) |
| | Peripheral arterial disease | I73.9 | 2.71 (2.28–3.21) | (Lu, Mackay, and Pell 2014) |
| | Abdominal aortic aneurysm | I71 | 2.41 (1.94–3.01) | (Cornuz et al. 2004) |
| | Venous thromboembolism | I26,I80-I82 | 1.23 (1.14–1.33) | (Y.-J. Cheng et al. 2013) |
| | Chronic obstructive pulmonary disease | J40-J44,J47 | 4.01 (3.18–5.05) | (Jayes et al. 2016) |
| | Asthma | J45-J46 | 1.61 (1.07–2.42) | (Jayes et al. 2016) |
| | Tuberculosis | A15-A19 | 1.57 (1.18–2.10) | (Jayes et al. 2016) |
| | Obstructive sleep apnoea | G47.3 | 1.97 (1.02–3.82) | (Jayes et al. 2016) |

Table 1: Disease definitions and risk functions (with 95 percent confidence intervals) for current vs. never smoking. *(continued)*

| Category | Disease | ICD-10 | Relative risk | Source |
|---|---|---|---|---|
| Respiratory system | Pneumonia | J12-J18 | 2.18 (1.69–2.80) | (Tobacco Advisory Group of the Royal College of Physicians 2018) |
| | Influenza (clinically diagnosed) | J11 | 1.34 (1.13–1.59) | (Tobacco Advisory Group of the Royal College of Physicians 2018) |
| | Influenza (microbiologically confirmed) | J09, J10 | 5.69 (2.79–11.60) | (Tobacco Advisory Group of the Royal College of Physicians 2018) |
| | Idiopathic pulmonary fibrosis | J84.1 | 1.58 (1.27–1.97) | (Taskar and Coultas 2006) |
| Mental health | Alzheimers disease | G30 | 1.40 (1.13–1.73) | (Zhong et al. 2015) |
| | Vascular dementia | F01 | 1.38 (1.15–1.66) | (Zhong et al. 2015) |
| | All cause dementia | F02,F03 | 1.30 (1.18–1.45) | (Zhong et al. 2015) |
| | Depression | F32,F33 | 1.62 (1.10–2.40) | (Luger, Suls, and Vander Weg 2014) |
| | Psychosis | F28,F29 | 2.18 (1.23–3.85) | (Gurillo et al. 2015) |
| | Schizophrenia | F20-F25 | 2.24 (1.10–4.55) | (Tobacco Advisory Group of the Royal College of Physicians 2018) |
| | Bulimia | F50.2 | 2.32 (1.12–4.78) | (Solmi et al. 2016) |
| | Diabetes (type 2) | E11 | 1.37 (1.33–1.42) | (Pan et al. 2015) |
| | Multiple sclerosis | G35 | 1.55 (1.48–1.62) | (Zhang et al. 2016) |
| | Systematic lupus erythematosis | M32 | 1.56 (1.26–1.95) | (Jiang, Li, and Jia 2015) |
| | Low back pain | M54 | 1.16 (1.02–1.32) | (Shiri et al. 2010) |
| | Rheumatoid arthritis | M05,M06 | 2.02 (1.75–2.33) | (Di Giuseppe et al. 2014) |
| | Psoriasis | L40 | 1.78 (1.52–2.06) | (Armstrong et al. 2014) |
| | Age related macular degeneration | H35.3-H52.4 | 1.86 (1.27–2.73) | (Chakravarthy et al. 2010) |
| | Senile cataract | H25 | 1.47 (1.36–1.59) | (Ye et al. 2012) |

Table 1: Disease definitions and risk functions (with 95 percent confidence intervals) for current vs. never smoking. *(continued)*

| Category | Disease | ICD-10 | Relative risk | Source |
|---|---|---|---|---|
| Other adult diseases | Crohns disease | K50 | 1.76 (1.40–2.22) | (Mahid et al. 2006) |
| | Hip fracture | S72.0-S72.2 | 1.30 (1.16–1.45) | (Shen et al. 2015) |
| | Chronic kidney disease | N18.1,N18.2,N18.3, N18.4,N18.8,N18.9 | 1.34 (1.23–1.47) | (Xia et al. 2017) |
| | End-stage renal disease | N18.5,N18.0 | 1.91 (1.39–2.64) | (Xia et al. 2017) |
| | Hearing loss | H90,H91 | 1.97 (1.44–2.70) | (Nomura, Nakao, and Morimoto 2005) |
| Conditions less common among smokers | Ulcerative colitis | K51 | 0.55 (0.33–0.91) | (Dias et al. 2015) |
| | Parkinson | G20 | 0.46 (0.42–0.51) | (Breckenridge et al. 2016) |

# References


Angus, Colin, M Henney, L Webster, and Duncan Gillespie. 2018. "Alcohol-Attributable Diseases and Dose-Response Curves for the Sheffield Alcohol Policy Model Version 4.0." https://doi.org/10.15131/shef.data.6819689.v1.

Armstrong, A. W., C. T. Harskamp, J. S. Dhillon, and E. J. Armstrong. 2014. "Psoriasis and Smoking: A Systematic Review and Meta-Analysis." Journal Article. *Br J Dermatol* 170 (2): 304–14. https://doi.org/10.1111/bjd.12670.

Bosetti, C, E Lucenteforte, DT Silverman, G Petersen, PM Bracci, BT Ji, E Negri, D Li, HA Risch, and SH Olson. 2011. "Cigarette Smoking and Pancreatic Cancer: An Analysis from the International Pancreatic Cancer Case-Control Consortium (Panc4)." Journal Article. *Annals of Oncology* 23 (7): 1880–88.

Breckenridge, Charles B., Colin Berry, Ellen T. Chang, Jr. Sielken Robert L., and Jack S. Mandel. 2016. "Association Between Parkinson's Disease and Cigarette Smoking, Rural Living, Well-Water Consumption, Farming and Pesticide Use: Systematic Review and Meta-Analysis." Journal Article. *PLOS ONE* 11 (4): e0151841. https://doi.org/10.1371/journal.pone.0151841.

Brown, Katrina F., Harriet Rumgay, Casey Dunlop, Margaret Ryan, Frances Quartly, Alison Cox, Andrew Deas, et al. 2018. "The Fraction of Cancer Attributable to Modifiable Risk Factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015." Journal Article. *British Journal of Cancer* 118 (8): 1130–41. https://doi.org/10.1038/s41416-018-0029-6.

Chakravarthy, Usha, Tien Y Wong, Astrid Fletcher, Elisabeth Piault, Christopher Evans, Gergana Zlateva, Ronald Buggage, Andreas Pleil, and Paul Mitchell. 2010. "Clinical Risk Factors for Age-Related Macular Degeneration: A Systematic Review and Meta-Analysis." Journal Article. *BMC Ophthalmology* 10 (1): 31.

Cheng, Jiemin, Yi Chen, Xiaolin Wang, Jianhua Wang, Zhiping Yan, Gaoquan Gong, Guoping Li, and Changyu Li. 2015. "Meta-Analysis of Prospective Cohort Studies of Cigarette Smoking and the Incidence of Colon and Rectal Cancers." Journal Article. *European Journal of Cancer Prevention* 24 (1): 6–15.

Cheng, Yun-Jiu, Zhi-Hao Liu, Feng-Juan Yao, Wu-Tao Zeng, Dong-Dan Zheng, Yu-Gang Dong, and Su-Hua Wu. 2013. "Current and Former Smoking and Risk for Venous Thromboembolism: A Systematic Review and Meta-Analysis." Journal Article. *PLoS Medicine* 10 (9): e1001515.

Colamesta, Vittoria, Silvia D'Aguanno, Massimo Breccia, Sara Bruffa, Claudio Cartoni, and Giuseppe La Torre. 2016. "Do the Smoking Intensity and Duration, the Years Since Quitting, the Methodological

Quality and the Year of Publication of the Studies Affect the Results of the Meta-Analysis on Cigarette Smoking and Acute Myeloid Leukemia (AML) in Adults?" Journal Article. *Critical Reviews in Oncology/Hematology* 99: 376–88.

Cornuz, Jacques, Claudio Sidoti Pinto, Heindrik Tevaearai, and Matthias Egger. 2004. "Risk Factors for Asymptomatic Abdominal Aortic Aneurysm: Systematic Review and Meta-Analysis of Population-Based Screening Studies." Journal Article. *The European Journal of Public Health* 14 (4): 343–49.

Cumberbatch, Marcus G, Matteo Rota, James WF Catto, and Carlo La Vecchia. 2016. "The Role of Tobacco Smoke in Bladder and Kidney Carcinogenesis: A Comparison of Exposures and Meta-Analysis of Incidence and Mortality Risks." Journal Article. *European Urology* 70 (3): 458–66.

Di Giuseppe, Daniela, Andrea Discacciati, Nicola Orsini, and Alicja Wolk. 2014. "Cigarette Smoking and Risk of Rheumatoid Arthritis: A Dose-Response Meta-Analysis." Journal Article. *Arthritis Research & Therapy* 16 (2): R61.

Dias, C. C., P. P. Rodrigues, A. da Costa-Pereira, and F. Magro. 2015. "Clinical Predictors of Colectomy in Patients with Ulcerative Colitis: Systematic Review and Meta-Analysis of Cohort Studies." Journal Article. *J Crohns Colitis* 9 (2): 156–63. https://doi.org/10.1093/ecco-jcc/jju016.

Fircanis, Sophia, Priscilla Merriam, Naushaba Khan, and Jorge J Castillo. 2014. "The Relation Between Cigarette Smoking and Risk of Acute Myeloid Leukemia: An Updated Meta-analysis of Epidemiological Studies." Journal Article. *American Journal of Hematology* 89 (8): E125–32.

Gandini, Sara, Edoardo Botteri, Simona Iodice, Mathieu Boniol, Albert B Lowenfels, Patrick Maisonneuve, and Peter Boyle. 2008. "Tobacco Smoking and Cancer: A Meta-analysis." Journal Article. *International Journal of Cancer* 122 (1): 155–64. https://onlinelibrary.wiley.com/doi/pdf/10.1002/ijc.23033.

Gurillo, Pedro, Sameer Jauhar, Robin M. Murray, and James H. MacCabe. 2015. "Does Tobacco Use Cause Psychosis? Systematic Review and Meta-Analysis." Journal Article. *The Lancet Psychiatry* 2 (8): 718–25. https://doi.org/10.1016/S2215-0366(15)00152-2.

Hashibe, M., P. Brennan, S. C. Chuang, S. Boccia, X. Castellsague, C. Chen, M. P. Curado, et al. 2009. "Interaction Between Tobacco and Alcohol Use and the Risk of Head and Neck Cancer: Pooled Analysis in the International Head and Neck Cancer Epidemiology Consortium." Journal Article. *Cancer Epidemiology Biomarkers & Prevention* 18 (2): 541–50. https://doi.org/10.1158/1055-9965.epi-08-0347.

International Agency for Research on Cancer and World Health Organization. 2007. "Reversal of Risk After Quitting Smoking." Report.

Jayes, Leah, Patricia L. Haslam, Christina G. Gratziou, Pippa Powell, John Britton, Constantine Vardavas, Carlos Jimenez-Ruiz, and Jo Leonardi-Bee. 2016. "SmokeHaz: Systematic Reviews and Meta-Analyses of the Effects of Smoking on Respiratory Health." Journal Article. *CHEST Journal* 150 (1): 164–79.

Jiang, Fan, Suyun Li, and Chongqi Jia. 2015. "Smoking and the Risk of Systemic Lupus Erythematosus: An Updated Systematic Review and Cumulative Meta-Analysis." Journal Article. *Clinical Rheumatology* 34 (11): 1885–92.

Knowler, William C, Elizabeth Barrett-Connor, Sarah E Fowler, Richard F Hamman, John M Lachin, Elizabeth A Walker, and David M Nathan. 2002. "Reduction in the Incidence of Type 2 Diabetes with Lifestyle Intervention or Metformin." Journal Article. *The New England Journal of Medicine* 346 (6): 393–403.

Kontis, Vasilis, Colin D Mathers, Jürgen Rehm, Gretchen A Stevens, Kevin D Shield, Ruth Bonita, Leanne M Riley, Vladimir Poznyak, Robert Beaglehole, and Majid Ezzati. 2014. "Contribution of Six Risk Factors to Achieving the 25× 25 Non-Communicable Disease Mortality Reduction Target: A Modelling Study." Journal Article. *The Lancet* 384 (9941): 427–37.

Ladeiras-Lopes, Ricardo, Alexandre Kirchhofer Pereira, Amanda Nogueira, Tiago Pinheiro-Torres, Isabel Pinto, Ricardo Santos-Pereira, and Nuno Lunet. 2008. "Smoking and Gastric Cancer: Systematic Review and Meta-Analysis of Cohort Studies." Journal Article. *Cancer Causes & Control* 19 (7): 689–701.

Lee, Yuan-Chin Amy, Catherine Cohet, Yu-Ching Yang, Leslie Stayner, Mia Hashibe, and Kurt Straif. 2009. "Meta-Analysis of Epidemiologic Studies on Cigarette Smoking and Liver Cancer." Journal Article. *International Journal of Epidemiology* 38 (6): 1497–1511.

Lu, L, DF Mackay, and JP Pell. 2014. "Meta-Analysis of the Association Between Cigarette Smoking and Peripheral Arterial Disease." Journal Article. *Heart* 100 (5): 414–23.

Luger, Tana M., Jerry Suls, and Mark W. Vander Weg. 2014. "How Robust Is the Association Between Smoking and Depression in Adults? A Meta-Analysis Using Linear Mixed-Effects Models." Journal

Article. *Addictive Behaviors* 39 (10): 1418–29. https://doi.org/http://doi.org/10.1016/j.addbeh.2014.05.011.

Maasland, Denise HE, Piet A van den Brandt, Bernd Kremer, R Alexandra Sandra Goldbohm, and Leo J Schouten. 2014. "Alcohol Consumption, Cigarette Smoking and the Risk of Subtypes of Head-Neck Cancer: Results from the Netherlands Cohort Study." Journal Article. *BMC Cancer* 14 (1): 187.

Mahid, S. S., K. S. Minor, R. E. Soto, C. A. Hornung, and S. Galandiuk. 2006. "Smoking and Inflammatory Bowel Disease: A Meta-Analysis." Journal Article. *Mayo Clin Proc* 81 (11): 1462–71. https://doi.org/10.4065/81.11.1462.

Nomura, Kyoko, Mutsuhiro Nakao, and Takeshi Morimoto. 2005. "Effect of Smoking on Hearing Loss: Quality Assessment and Meta-Analysis." Journal Article. *Preventive Medicine* 40 (2): 138–44.

Ordóñez-Mena, José Manuel, Ben Schöttker, Ute Mons, Mazda Jenab, Heinz Freisling, Bas Bueno-de-Mesquita, Mark G O'Doherty, Angela Scott, Frank Kee, and Bruno H Stricker. 2016. "Quantification of the Smoking-Associated Cancer Risk with Rate Advancement Periods: Meta-Analysis of Individual Participant Data from Cohorts of the CHANCES Consortium." Journal Article. *BMC Medicine* 14 (1): 62.

Osch, Frits HM van, Sylvia HJ Jochems, Frederik-Jan van Schooten, Richard T Bryan, and Maurice P Zeegers. 2016. "Quantified Relations Between Exposure to Tobacco Smoking and Bladder Cancer Risk: A Meta-Analysis of 89 Observational Studies." Journal Article. *International Journal of Epidemiology* 45 (3): 857–70.

Oza, Shefali, Michael J Thun, S Jane Henley, Alan D Lopez, and Majid Ezzati. 2011. "How Many Deaths Are Attributable to Smoking in the United States? Comparison of Methods for Estimating Smoking-Attributable Mortality When Smoking Prevalence Changes." Journal Article. *Preventive Medicine* 52 (6): 428–33.

Pan, An, Yeli Wang, Mohammad Talaei, Frank B Hu, and Tangchun Wu. 2015. "Relation of Active, Passive, and Quitting Smoking with Incident Type 2 Diabetes: A Systematic Review and Meta-Analysis." Journal Article. *The Lancet Diabetes & Endocrinology* 3 (12): 958–67.

Peters, Sanne AE, Rachel R Huxley, and Mark Woodward. 2013. "Smoking as a Risk Factor for Stroke in Women Compared with Men: A Systematic Review and Meta-Analysis of 81 Cohorts, Including 3 980 359 Individuals and 42 401 Strokes." Journal Article. *Stroke* 44 (10): 2821–28.

Prabhu, A., K. O. Obi, and J. H. Rubenstein. 2014. "The Synergistic Effects of Alcohol and Tobacco Consumption on the Risk of Esophageal Squamous Cell Carcinoma: A Meta-Analysis." Journal Article. *American Journal of Gastroenterology* 109 (6): 821–27. https://doi.org/10.1038/ajg.2014.71.

Prabhu, A, KO Obi, and JH Rubenstein. 2013. "Systematic Review with Meta-analysis: Race-specific Effects of Alcohol and Tobacco on the Risk of Oesophageal Squamous Cell Carcinoma." Journal Article. *Alimentary Pharmacology & Therapeutics* 38 (10): 1145–55.

Rostron, Brian. 2012. "Smoking-Attributable Mortality by Cause in the United States: Revising the CDC's Data and Estimates." Journal Article. *Nicotine & Tobacco Research* 15 (1): 238–46.

Shen, Guang Si, Yong Li, GuoYang Zhao, Hai Bin Zhou, Zong Gang Xie, Wei Xu, Hai Nan Chen, Qi Rong Dong, and You Jia Xu. 2015. "Cigarette Smoking and Risk of Hip Fracture in Women: A Meta-Analysis of Prospective Cohort Studies." Journal Article. *Injury* 46 (7): 1333–40.

Shiri, Rahman, Jaro Karppinen, Päivi Leino-Arjas, Svetlana Solovieva, and Eira Viikari-Juntura. 2010. "The Association Between Smoking and Low Back Pain: A Meta-Analysis." Journal Article. *The American Journal of Medicine* 123 (1): 87. e7–35.

Solmi, Marco, Nicola Veronese, Giuseppe Sergi, Claudio Luchini, Angela Favaro, Paolo Santonastaso, Davy Vancampfort, et al. 2016. "The Association Between Smoking Prevalence and Eating Disorders: A Systematic Review and Meta-Analysis." Journal Article. *Addiction* 111 (11): 1914–22. https://doi.org/10.1111/add.13457.

Taskar, Varsha S, and David B Coultas. 2006. "Is Idiopathic Pulmonary Fibrosis an Environmental Disease?" Journal Article. *Proceedings of the American Thoracic Society* 3 (4): 293–98.

Tobacco Advisory Group of the Royal College of Physicians. 2018. "Hiding in plain sight: Treating tobacco dependency in the NHS." Research report. *Available from: Https://Www.rcplondon.ac.uk/Projects/Outputs/Hiding-Plain-Sight-Treating-Tobacco-Dependency-Nhs.*

Tramacere, Irene, Carlo La Vecchia, and Eva Negri. 2011. "Brief Report: Tobacco Smoking and Esophageal and Gastric Cardia Adenocarcinoma: A Meta-Analysis." Journal Article. *Epidemiology*, 344–49.

Xia, Jia, Lin Wang, Zhiheng Ma, Liping Zhong, Ying Wang, Yachan Gao, Liqun He, and Xiao Su. 2017. "Cigarette Smoking and Chronic Kidney Disease in the General Population: A Systematic Review and Meta-Analysis of Prospective Cohort Studies." Journal Article. *Nephrology Dialysis Transplantation* 32 (3): 475–87.

Ye, Juan, Jinjing He, Changjun Wang, Han Wu, Xin Shi, Huina Zhang, Jiajun Xie, and Sang Yeul Lee. 2012. "Smoking and Risk of Age-Related Cataract: A Meta-Analysis." Journal Article. *Investigative Ophthalmology & Visual Science* 53 (7): 3885–95.

Zhang, Peng, Rui Wang, Zhijun Li, Yuhan Wang, Chunshi Gao, Xin Lv, Yuanyuan Song, and Bo Li. 2016. "The Risk of Smoking on Multiple Sclerosis: A Meta-Analysis Based on 20,626 Cases from Case-Control and Cohort Studies." Journal Article. *PeerJ* 4: e1797.

Zhong, Guochao, Yi Wang, Yong Zhang, Jeff Jianfei Guo, and Yong Zhao. 2015. "Smoking Is Associated with an Increased Risk of Dementia: A Meta-Analysis of Prospective Cohort Studies with Investigation of Potential Effect Modifiers." Journal Article. *PLoS One* 10 (3): e0118333.

Zuo, Jing-Jing, Ze-Zhang Tao, Chen Chen, Zhang-Wei Hu, Ye-Xing Xu, An-Yuan Zheng, and Yi Guo. 2017. "Characteristics of Cigarette Smoking Without Alcohol Consumption and Laryngeal Cancer: Overall and Time-Risk Relation. A Meta-Analysis of Observational Studies." Journal Article. *European Archives of Oto-Rhino-Laryngology* 274 (3): 1617–31.