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Smoking and the risks of adult diseases

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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).

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

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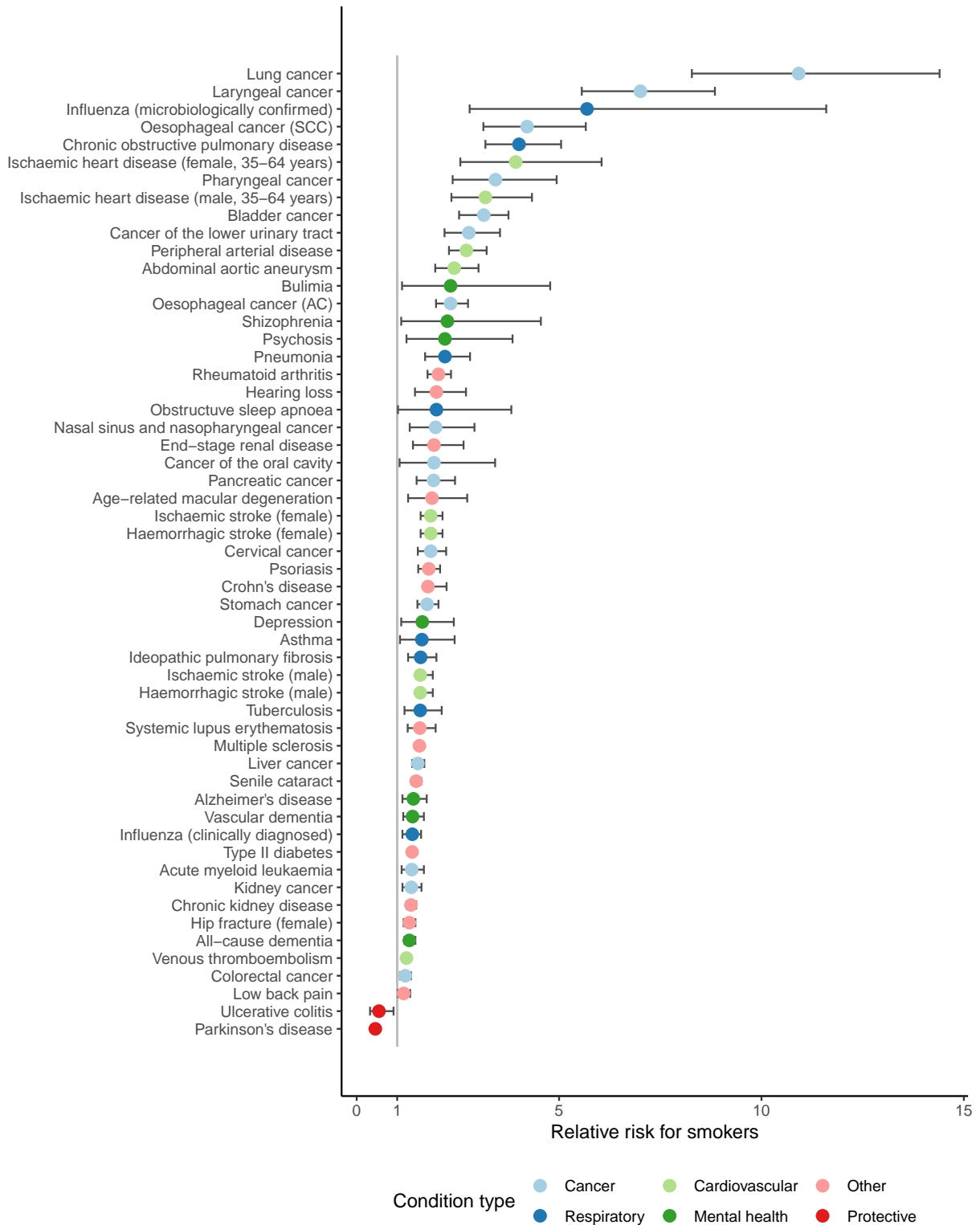
Figure 1: Relative risks and 95 percent confidence intervals in current smokers for 52 conditions attributable to smoking.

3 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).

3.1 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.

3.2 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.

3.3 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.

3.4 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.

3.5 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.

3.6 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.

3.7 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.

3.8 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.

3.9 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).

3.10 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.

3.11 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).

3.12 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.

3.13 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.

3.14 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).

4 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.

5 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).

6 Mental health

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

7 Other adult diseases

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

8 Conditions less common among smokers

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

9 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.
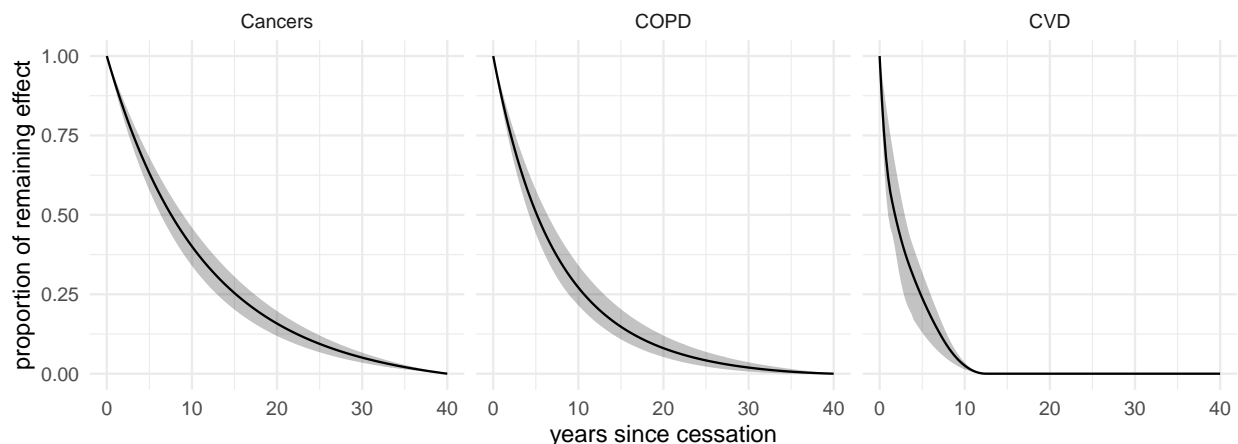
Figure 2: The proportion of remaining risk after quitting.

10   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)		2.32 (1.96–2.75)	(Tramacere, La Vecchia, and Negri 2011)
	Oesophageal (Squamous cell carcinoma)	C15	4.21 (3.13–5.66)	(Prabhu, Obi, and Rubenstein 2013)

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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)

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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)

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