Effects of smoking and solid-fuel use on COPD, lung cancer, and tuberculosis in China: a time-based, multiple risk factor, modelling study

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Summary

Background Chronic obstructive pulmonary disease (COPD), lung cancer, and tuberculosis are three leading causes of death in China, where prevalences of smoking and solid-fuel use are also high. We aimed to predict the effects of risk-factor trends on COPD, lung cancer, and tuberculosis.

Methods We used representative data sources to estimate past trends in smoking and household solid-fuel use and to construct a range of future scenarios. We obtained the aetiological effects of risk factors on diseases from meta-analyses of epidemiological studies and from large studies in China. We modelled future COPD and lung cancer mortality and tuberculosis incidence, taking into account the accumulation of hazardous effects of risk factors on COPD and lung cancer over time, and dependency of the risk of tuberculosis infection on the prevalence of disease. We quantified the sensitivity of our results to methods and data choices.

Findings If smoking and solid-fuel use remain at current levels between 2003 and 2033, 65 million deaths from COPD and 18 million deaths from lung cancer are predicted in China; 82% of COPD deaths and 75% of lung cancer deaths will be attributable to the combined effects of smoking and solid-fuel use. Complete gradual cessation of smoking and solid-fuel use by 2033 could avoid 26 million deaths from COPD and 6·3 million deaths from lung cancer; interventions of intermediate magnitude would reduce deaths by 6–31% (COPD) and 8–26% (lung cancer). Complete cessation of smoking and solid-fuel use by 2033 would reduce the projected annual tuberculosis incidence in 2033 by 14–52% if 80% DOTS coverage is sustained, 27–62% if 50% coverage is sustained, or 33–71% if 20% coverage is sustained.

Interpretation Reducing smoking and solid-fuel use can substantially lower predictions of COPD and lung cancer burden and would contribute to effective tuberculosis control in China.

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Introduction

Chronic obstructive pulmonary disease (COPD), lung cancer, and tuberculosis are the second, sixth, and eighth leading causes of death in China, accounting for almost 2 million deaths in 2002 (20·5% of all deaths in China).[1] A half of Chinese men smoke and more than 70% of Chinese households use solid fuels, such as wood, crop residues, and coal for heating and cooking.[2] Tobacco smoking and indoor air pollution from solid-fuel use are the most important global risk factors for COPD and lung cancer and account for a significant proportion of deaths from these diseases in developing countries.[3,4] Without interventions, the annual numbers of COPD and lung cancer deaths in China are predicted to double over the next 30 years.[1] Systematic reviews have concluded that smoking is also an independent risk factor for tuberculosis[5–7] and suggested a positive association between indoor air pollution and the disease.[5]

Integrated programmes that incorporate multiple risk factor and therapeutic interventions are a potentially effective way to target the cluster of respiratory diseases that share common risks.[8] Planning integrated programmes for respiratory diseases and risk factors requires quantitative estimates of how future COPD, lung cancer, and tuberculosis will be affected by trends in smoking and indoor air pollution. Estimating the effects of smoking and indoor air pollution on COPD and lung cancer requires incorporation of how fast risk accumulates after initiation, or reverses after cessation. Smoking and indoor air pollution also influence the dynamics of tuberculosis, both via direct effect in exposed individuals, and indirect effect in unexposed individuals through infectious source cases.

We provide a systematic assessment of the future trends of these three leading communicable and non-communicable respiratory diseases in China that share smoking and indoor air pollution as risk factors. These results quantify the potential benefits of programmes that target one or more of these risk factors or disease outcomes.

Methods

Analytical models

To estimate the proportional effects of future smoking and solid-fuel use on projected lung cancer and COPD mortality, we used a generalised version of the population attributable fraction (PAF) relationship:

$$PAF_t=\frac{\sum_{i=1}^{n}P_{t,i}RR_{t,i}-\sum_{i=1}^{n}P'_{t,i}RR_{t,i}}{\sum_{i=1}^{n}P_{t,i}RR_{t,i}}$$

$P_{t,i}$=proportion of population in the i^{th} exposure category at time t in one future exposure scenario. We used the scenario of constant exposure as the baseline to which all other scenarios were compared.
$P'_{t,i}$=proportion of population in the i^{th} exposure category at time t in an alternative future scenario.
$RR_{t,i}$=relative risk of disease-specific mortality for the i^{th} exposure category at time t.
n=number of exposure categories. The exposure categories include continuously exposed, non-exposed, as well as those whose exposure began or stopped at different times during the analysis.

PAF estimates the proportional reduction in disease or death that would occur if the observed exposure to a risk factor (P) were modified to an alternative exposure scenario (P').[9] The generalised version of the PAF relationship allows both exposure and relative risk to vary over time. Relative risk at time (t) depends on time since exposure initiation or cessation, because the effects of smoking and indoor air pollution accumulate gradually after exposure begins (eg, smoking initiation) and reverse gradually after exposure stops (eg, smoking cessation).[10,11]

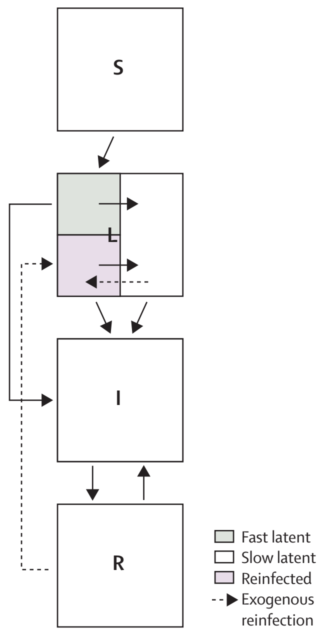

Figure 1: Compartmental susceptible–latent–infectious–recovered (SLIR) model of tuberculosis infection
When susceptible (S) individuals are infected, they enter a state of fast latency (L) from which they may experience primary progression to the infectious (I) state. If not progressed within 5 years of infection, patients enter slow latency, where they may progress to the infectious state via endogenous reactivation at a greatly reduced rate. Individuals in the infectious state can be treated and enter the recovered (R) state from which they remain at risk of relapse to active disease. Individuals in the slowly progressive latent state or the recovered state are at risk of reinfection, although prior infection confers partial immunity. Individuals in any state can die, and new individuals enter the system via the susceptible compartment.

See Online for webappendix 1

We did separate analyses for lung cancer and COPD and for men and women, because they have different relative risks. For both lung cancer and COPD, we first computed PAFs separately for smoking and solid-fuel use. COPD and lung cancer are caused by multiple risk factors acting simultaneously, and hence a proportion of deaths might be prevented by reducing exposure to either factor.[9,12,13] For example, some COPD deaths among smokers who cook with solid fuels may be prevented by smoking prevention or by use of clean fuels. As a result of multicausality, the PAFs for multiple risk factors overlap, and cannot be combined by simple addition. We estimated the PAFs for the combined effects of smoking and solid fuel, accounting for multicausality and avoiding double-counting the overlap of multiple risk factors:[9,12–14]

$$PAF=1-\prod_{i=1}^{n}(1-PAF_i)$$

PAF_i=PAF of the i^{th} risk factor
n=number of risk factors

Three conditions must hold when using the above equation. First, exposures to risks should be uncorrelated. The cross-province correlation coefficient between solid-fuel use and smoking, from the data sources described in webappendix 1, was 0·04 (95% CI –0·32 to 0·40, p=0·82) for men and –0·11 (–0·45 to 0·26, p=0·56) for women, indicating small and non-significant correlation. We also examined individual-level correlation with the 2006 panel from The China Health and Nutrition Survey (a multistage, random cluster survey, including 9788 adults in nine provinces throughout China with significant variation in socioeconomic and health status).[15] 61% of men and 4% of women had ever smoked in homes that did not use solid fuels and 63% of men and 4% of women had ever smoked in homes that did. The odds ratios for smoking, comparing solid-fuel users to non-users, was 1·07 (0·95–1·20) for men and 1·02 (0·76–1·36) for women, showing uncorrelated exposures. The second condition is that the hazardous effects of one risk are not mediated through other risks. Smoking and solid-fuel combustion are both sources of respirable pollutants, but the effects of pollutants from one source are not mediated through exposure to the other. The third condition is that the proportional effects of one risk do not depend on exposure to the other risk factor. The proportional mortality study of smoking in China showed that the relative risks of lung cancer and respiratory-disease mortality among Chinese smokers were not modified by background disease levels,[16]

	Definition	Reasons for scenario use
Men		
Unchanged	Male smoking prevalence remains at its 2003 level in each province	Because tobacco smoking has peaked in Chinese men, possibly with slight decline in the past decade, stabilisation at current prevalence represents the upper bound for male smoking
Moderate control	Male smoking prevalence declines slowly between 2003 and 2033, reaching 30% in each province in 2033	Smoking prevalence in Chinese men has recently declined;[33] many high-income and some middle-income countries (eg, South Africa, Poland, Thailand) have reduced tobacco smoking from its peak through a combination of taxation, regulation (eg, public smoking or advertising ban), and health education;[34–37] the final smoking prevalence of 30% is selected to be slightly higher than those in high-income countries, such as the UK and the USA, where more effective tobacco control policies and programmes have been implemented[38]
Aggressive control	Male smoking prevalence declines more rapidly between 2003 and 2033, reaching 15% in each province in 2033	Nationally, Singapore, Australia, and Canada have successfully reduced smoking prevalence to below 20% through effective tobacco control policies and interventions;[38–40] below 20% prevalence was also achieved through the Massachusetts Tobacco Control Program;[41] a prevalence of 15% is therefore feasible through effective tobacco control mechanisms
To zero	Male smoking prevalence declines to zero in 2033	This is an ideal scenario, included to provide a theoretical upper-bound on the benefits of gradual smoking reduction over the projection period
Women		
Large rise	Female smoking prevalence rises to reach 30% in each province in 2033	The worst-case scenario for female smoking, in which the female smoking epidemic succeeds that of males, as seen in high-income, central European, and Latin American countries,[37,38] where female smoking prevalence typically peaked at levels lower that of men,[37,38] hence set to 30%
Moderate rise	Female smoking prevalence rises to reach 15% in each province in 2033	Similar to large rise in female smoking with a lower peak, as seen for example in Japan;[38] a lower peak than in other populations may result from sociocultural factors
Unchanged	Female smoking prevalence remains at its 2003 low level in each province	Sociocultural factors might prevent female smoking prevalence to rise further with economic development, as evidenced by relative long-term stability of female smoking
To zero	Female smoking prevalence declines to zero in 2033	This is an ideal scenario, included to provide a theoretical upper-bound on the benefits of gradual smoking reduction over the projection period

See webfigure 2 for prevalence over time.

Table 1: **Smoking scenarios**

which is consistent with no effect modification of relative risks between these two risks.

We calculated the annual number of lung cancer and COPD deaths avoidable by reducing exposure to smoking and solid fuels, individually as well as combined, by multiplying the corresponding PAF by the projected total disease-specific deaths for the year of analysis.

The incidence of tuberculosis depends on risk-factor exposure and population prevalence of infectious cases. We used a dynamic tuberculosis transmission model, specifically the deterministic compartmental susceptible–latent–infectious–recovered model (figure 1), described in detail elsewhere.[17,18]

The susceptible–latent–infectious–recovered model parameters were based on previous epidemiological studies on the natural history of tuberculosis and risk factors, China-specific demographic parameters, and calibration to epidemiology in China (webtable 1). We introduced smoking and indoor air pollution into the model by stratifying the model population into the four possible combinations of exposure to these risk factors, proportional to their actual (time-varying) prevalence in each province. We fitted a time-varying transmission parameter, defined as the rate at which infectious individuals are able to infect people who are susceptible. Available data and previous modelling suggested that the transmission parameter declined almost linearly in England and Wales from about 20 in 1900 to about 1 at the end of the 20th century.[19] We set the value of the transmission parameter to 20 in 1900, and it declined linearly to an empirically-fitted lower bound; the rate of decline and the lower bound were fitted to minimise the root mean square of the differences between the modelled and observed tuberculosis prevalence by province. The fitted lower bound, which determines tuberculosis incidence after 2000, was not sensitive to the initial transmission parameter in 1900. Model fitting also considered that chemotherapy was unavailable before 1960[20] and that the mean duration of disease is 2 years without treatment, 0·8 years under effective DOTS (directly observed treatment, short course), and 1·5 years for programmes other than effective DOTS.[21] We applied the calibrated model to estimate future tuberculosis incidence under different scenarios of smoking, solid-fuel use, and DOTS coverage.

To account for heterogeneity across provinces, we did tuberculsosis analyses at the provincial level. We present results for provinces that span a range of characteristics: Jiangsu, a province with moderate historical prevalence of tuberculosis and representative historical trend in prevalence compared to other provinces and Guizhou and Shanghai which have prevalences and trends that differ from other provinces (webfigure 1).

See Online for webtable 1

See Online for webfigure 1

Risk-factor exposure and DOTS data sources and scenarios

We detail the methods and sources for estimating past trends in smoking,[22,23,24] household solid-fuel use,[2,25] and tuberculosis[26–30] prevalence by province in webappendix 1.

For **China Data Online** see http://chinadataonline.org/

For the **Population Division** see http://esa.un.org/unpp/

See **Online** for webfigure 2

We used China Data Online[31] for data on provincial populations. The future projections of the national population came from the Population Division of the Department of Economic and Social Affairs of the UN Secretariat[32] and those of the disease-specific mortality from the global burden of disease study conducted by the WHO. Global burden of disease forecasts disease-specific mortality on the basis of projections of economic and social development, smoking, obesity, and selected other disease determinants.[1]

We constructed scenarios that represent the range of policies and programmes that can reduce smoking and solid-fuel use on the basis of experiences and trends in other countries and some parts of China (tables 1 and 2 and webfigure 2). All scenarios covered a period of 30 years (2003–33). We constructed prevalence of risk factors over time in the scenarios for each province with a linear time trend, and aggregated the provincial prevalences to the national level. More than 99% of the tobacco market share in China is controlled by the Chinese National Tobacco Corporation. Tobacco prices and taxes are low and there are only a few tobacco control measures in place.[38] However, China ratified the Framework Convention on Tobacco Control in October 2005, which came into effect in January, 2006. Future smoking prevalence will largely depend on the extent to which economic and regulatory approaches to tobacco control are pursued. Although male and female smoking prevalences probably have common policy determinants, the analyses of lung cancer and chronic disease mortality were done separately for men and women and included all sex-specific scenarios. The analysis for tuberculosis was done for men and women combined because relative risks were for both sexes combined and because there are indirect effects of smoking on tuberculosis between sexes. National adult smoking prevalence was 49·6% for men and 3·0% for women in 2003 according to the National Health Service Survey. Another National Tobacco Prevalence Survey in 2002 reported current smoking prevalence of 57·4% for men and 2·6% for women. The two surveys had slightly different definitions of current smoking.[22,33] Tobacco consumption per person in China peaked around 1990 and has declined slowly since then.[38] Data from three National Health Service Surveys (1993, 1998, 2003) show that smoking prevalence declined from 60·3% to 49·6% among men (standardised to the 2003 population); smoking in women declined from 4·7% to 3·0% in this period.

Solid fuels comprise biomass (wood, crop residues, animal dung, and charcoal) and coal and are used for cooking and heating. Only coal smoke raises the risk of lung cancer in epidemiological studies although wood smoke contains small amounts of carcinogens.[47] Non-solid fuels, which have substantially lower emissions of health-damaging pollutants, include liquid and gaseous fuels and electricity.[47] Solid-fuel scenarios only encompass fuel changes and did not take into account alternative stoves. China has implemented an ambitious programme to disseminate improved cooking stoves,[54,55] primarily to improve efficiency and reduce fuel use. The

	Definition	Reason for scenario use
Total solid fuels		
Unchanged	Proportion of households using solid fuels remains at its 2003 level in every province	Evidence indicates that few households revert back to solid fuels once they have transitioned to cleaner fuels, with the possible exception of the poorest countries (eg, some in sub-Saharan Africa) during international or national energy or economic crises;[42] therefore, stabilisation at current prevalence is the likely upper bound for household solid fuel use
Half current	Percent of households using solid fuels declines to one half of its 2003 level in each province in 2033	In China, rapid economic growth has contributed to near-universal access to electricity for lighting and for services such as television, but solid-fuel use for cooking and heating has persisted, with 72% of Chinese households continuing to use solid fuels according the 2000 National Census;[43–46] this scenario is based on the experience of middle-income countries (eg, those in Latin America) that have reduced household solid-fuel use through active policy interventions[47–49]
Urban–rural	Percent of households using solid fuels declines to zero in urban populations and to one half of its 2003 level in rural populations in each province in 2033	This scenario modifies the previous scenario of “decline to half the current level” to acknowledge that there are better-developed supply chains in urban populations, even at the same income level;[8,42,50] in China, increased attention to urban air quality may also motivate faster and more extensive transitions in urban areas as has been done in other cities[51–53]
To zero	Percent of households using solid fuels declines to zero in 2033	This is an ideal scenario which provides an upper-bound on the benefits of clean fuels over the projection period
Share of solid fuels from coal		
All biomass converted to coal	The coal share of solid fuel increases to 100% in each province by 2033	Although until the 1980s and 1990s biomass was the dominant source of household energy in China, deforestation and policies to reduce and reverse it have compelled many rural residents to switch to from biomass to coal[43,54]
Unchanged coal share of solid fuels	The coal share of solid fuel remains at its 2003 level	Given the past trends in biomass to coal conversion, and its policy drivers, this is the lowest bound for coal share of solid fuels

See webfigure 2 for fuel-use over time.

Table 2: **Scenarios of household solid-fuel use**

design and performance of the new stoves vary enormously, with many of the stoves lacking flues or other characteristics needed to reduce indoor air pollution.[54] If alternative stove designs reduce exposure significantly, they can be treated as equivalent to fuel change; partial exposure reduction can be modelled with effect sizes between those for solid fuels and clean fuels.

The same solid-fuel scenarios were used for men and women but the relative risk is higher for women (table 3),[47] possibly because they spend more time near the stove. The latest fuel data were from the national census for the year 2000. To be consistent with the smoking and tuberculosis data, we used the 2000 data for 2003, the first year of analysis. The proportion of China's population in urban areas is increasing. To incorporate this effect in the solid-fuel scenarios, we used the current and projected urban and rural population share from the Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat.[32] The national change in relative proportion of urban and rural population over time was applied to all provinces. The proportion of different categories of solid-fuel use in future scenarios were calculated such that transitions from coal and biomass to clean fuels in any year were proportional to their prevalence in the year of transition.

China made significant progress in DOTS expansion between 1990 and 2000 in 13 provinces, municipalities, and autonomous regions. After the outbreak of severe acute respiratory syndrome, China further expanded DOTS coverage so that nationally an estimated 80% of smear-positive cases of tuberculosis were detected and treated in 2005.[56] We used time-varying treatment coverage in each province and municipality based on province-specific implementation before 2002 and a range of possible scenarios from 2003 (webtable 2).

Data sources for risk-factor effect sizes

We used relative risks for the effects of smoking on lung cancer and COPD from the retrospective proportional mortality study of smoking in China[16] (table 3), and from meta-analyses of Chinese cohort studies in a sensitivity analysis (webappendix 2). The relations between smoking or indoor air pollution from solid-fuel use and chronic diseases have a dose–response relationship; therefore risks might differ for men and women.

Because the deaths in the proportional mortality study occurred in 1986–88, around the peak of the smoking epidemic in China,[16,38] relative risks for COPD and lung cancer were substantially lower than in populations in Europe and the USA, which have smoked longer. Low relative risks have also been observed in other Asian populations, which likewise began smoking late.[57] Studies in European and American cohorts at different stages of the tobacco epidemic have shown that relative risks for chronic diseases rise for decades after the peak of the smoking epidemic.[10,58] To account for the accumulation of risk, we allowed COPD and lung cancer relative risks from the proportional mortality study to increase to those from the American Cancer Society Cancer Prevention Study, phase II (CPS-II), which was done primarily in lifelong smokers.[58] In sensitivity analyses, we allowed relative risks to remain at their 1986–88 levels over the complete analysis period, representing the possibility that smoking may be associated with smaller relative risks in Asian populations than among others.

	COPD (n)	Lung cancer	Tuberculosis (latent infection)	Tuberculosis (progression to active disease)
Smoking			1·9 (1·6–2·3)	1·5
Male	5·7/17·9* (15·2–21·0)	7·2/22·0* (19·7–24·5)		
Female	7·1/18·1* (16·0–20·4)	7·1/14·8* (13·7–16·1)		
Solid-fuel use			1·4	1·1
Male	1·8 (1·0–3·2)	1·5 (1·0–2·5)		
Female	3·2 (2·3–4·8)	1·9 (1·1–3·5)		

*The two numbers show relative risks for the beginning and end of analysis period in the main analysis to account for the delayed smoking epidemic in China. We used the same relative risks for the current and future effects of smoking on tuberculosis, because the studies used in the meta-analysis were from populations with various durations of past exposure and because risk accumulation may be different from chronic diseases like COPD and lung cancer.

Table 3: **Relative risks of smoking and solid-fuel use on COPD, lung cancer, and tuberculosis**

We used relative risks for the effects of indoor air pollution from solid-fuel use on COPD (all solid fuels) and lung cancer (coal only) from a recent systematic review and meta-analysis of cohort, case–control, and cross-sectional studies.[47] Because the Chinese population and those in the epidemiological studies have used solid fuels for a long time, relative risks are expected to be at their peak. The relative risks for the effects of smoking and solid-fuel use on tuberculosis were from a recent meta-analysis.[5]

See Online for webtable 2

The relative risks of smoking and indoor air pollution for COPD and lung cancer decline gradually after exposure stops. We used the change after exposure cessation estimated with data from CPS-II (webfigure 3). The CPS-II findings are consistent with studies on how indoor air pollution interventions reduce the COPD and lung cancer relative risks over time[59,60] but provide data in finer time intervals. We used a symmetric pattern for the increase in relative risk after exposure begins.

See Online webfigure 3

See Online webappendix 2

Smoking might increase the risk of latent tuberculosis infection or the risk of progression to active disease from latent infection. For smoking and latent infection, we used the pooled estimate from a recent meta-analysis,[5] which had relative risks for disease similar to other published meta-analyses.[6,7] The relative risk for progression to active tuberculosis was obtained by dividing that for smoking and active tuberculosis from the only cohort study (2·87)[61] by the pooled estimate for smoking and latent infection (1·90). The estimated relative risk of 1·5 (table 3) is within the 95% CI of the

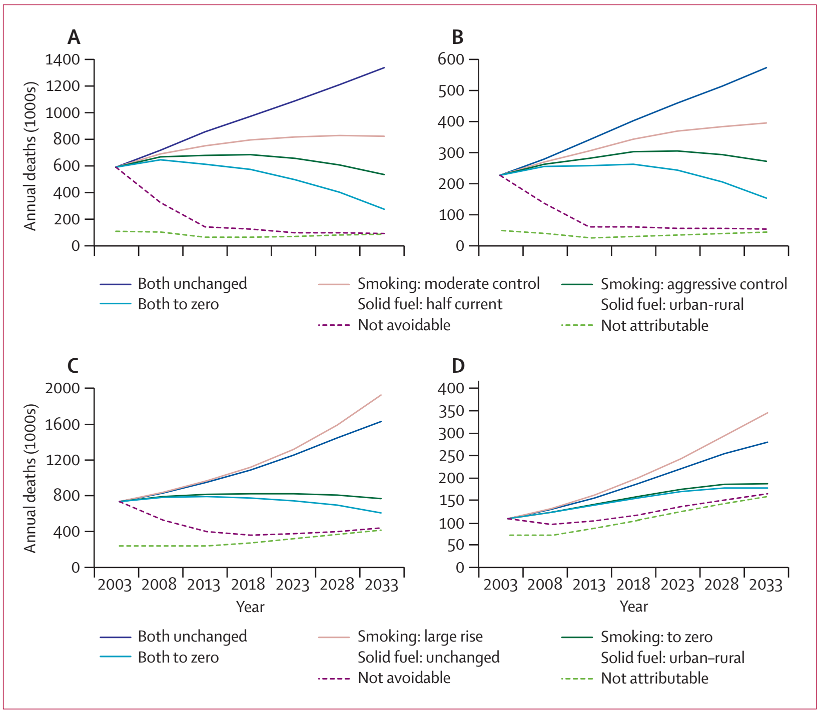

Figure 2: **Annual mortality in men from COPD (A) and lung cancer (B) and in women from COPD (C) and lung cancer (D) under combined scenarios of smoking and solid fuel use**

Not avoidable deaths are those if risk-factor exposures were reduced to zero in 2003. See webfigures 4 and 5 for separate results for smoking and solid fuel use.

See Online for webfigure 4

relative risk in the only study of smoking and active disease among people who were latently infected.[62] We separated the relative risk for the effects of solid-fuel use on active tuberculosis into the effects on latent infection and progression to active diseases using the same proportions as for smoking.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation or writing of the report. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

See Online for webfigure 5

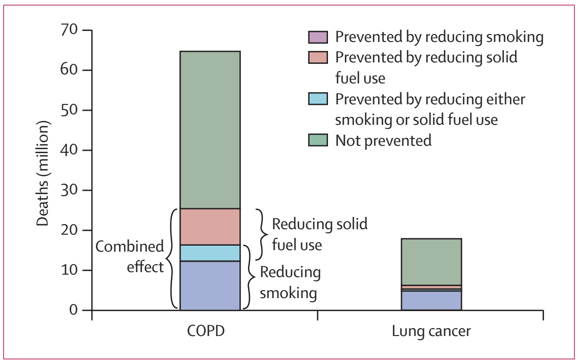

Figure 3: **Sum of annual deaths 2003–33 for both sexes if exposure for both sexes to smoking and solid fuel use are reduced to zero by 2033**

Results

If tobacco smoking and solid-fuel use remain at their current levels, between 2003 and 2033 an estimated 65 million people will die of COPD and 18 million of lung cancer in China, accounting for 19% and 5%, respectively, of all deaths over this period.[1] 82% of the COPD deaths (53 million) and 75% of lung cancer deaths (14 million) will be attributable to the combined effects of smoking and solid-fuel use (figure 2). 52% of COPD deaths and 82% of lung cancer deaths attributable to these risks will be among men. Of the 67 million COPD and lung cancer deaths attributable to smoking and solid-fuel use, over 10 million (8·1 million from COPD and 2·0 million from lung cancer) are unavoidable, even if all smokers had quit and all households had begun to use clean fuels in 2003, because the effect of the exposures on chronic diseases persist even after exposure ends.

Men who stop smoking in 2003 are expected to lower their absolute risks of COPD by 56% and lung cancer by 60% after 5 years relative to those who continue smoking (the reductions for women are 63% for COPD and 75% for lung cancer; webfigure 3). Risks will be lowered by 83–84% (COPD) and 83–86% (lung cancer) after 10 years and 91–92% (COPD) and 88–91% (lung cancer) after 20 years (webfigure 3). At the population level, with moderate tobacco control, the sum of the annual avoided COPD and lung cancer deaths among men would be an estimated 4·6 and 1·9 million, respectively, 15% of all projected deaths of men from these diseases (webfigure 4). If tobacco control is aggressive, with smoking in men declining to 15% by 2033, 8·0 million COPD deaths and 3·3 million lung cancer deaths would be averted.

If female smoking gradually declines to zero by 2033, the sum of the annual avoided COPD and lung cancer deaths would be 4·9 and 0·76 million, averting 14% and 13% all projected female deaths from these diseases (webfigure 4). Conversely, if female smoking rises to 30% by 2033, an additional 2·2 million COPD deaths and 0·60 million lung cancer deaths are expected among Chinese women. This asymmetry of benefits and harms occurs because the relative risks seem to rise slowly among new smokers but fall steeply in former smokers (webfigure 3).

Halving solid-fuel use by 2033 would lower the sum of the annual number of COPD and lung cancer deaths, respectively, by 2·2 million and 0·30 million in men (7% and 2% of deaths from these causes) and by 4·3 million and 0·27 million in women (12% and 5% of deaths from these causes; webfigure 5). Proportionally, more deaths are prevented among women because they are closer to the pollution source during cooking, have higher exposure to pollutants, and hence higher relative risks. The benefits would be twice as large with a complete transition to clean fuels.

After accounting for the overlap between the effects of the two risk factors, if smoking and solid-fuel use are

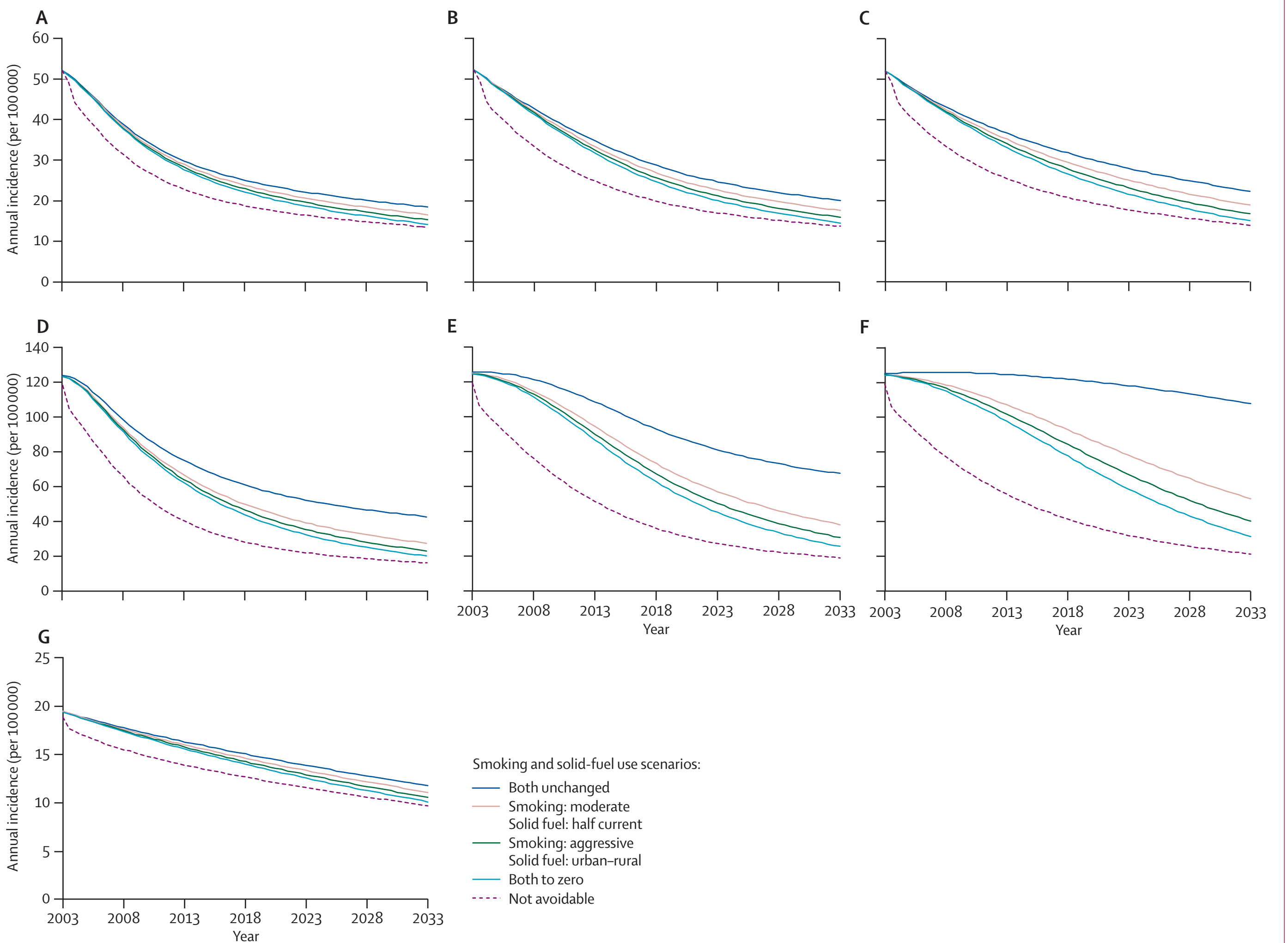

Figure 4: **Annual incidence of infectious tuberculosis under combined effects of smoking and indoor air pollution scenarios by municipality and DOTS effectiveness**
Decreases in incidence with optimum, moderate, or minimum DOTS in Jiangsu (A, B, C, respectively) and Guizhou (D, E, F) and for Shanghai (G), which already has effective DOTS so non-optimum scenarios not shown.

gradually eliminated between 2003 and 2033, an estimated 26 million COPD deaths (40% of all projected COPD deaths) and 6·3 million lung cancer deaths (34% of all projected lung cancer deaths) would be avoided (figures 2 and 3). The intermediate scenarios have the potential to reduce mortality from these diseases by an estimated 17–34% among men and 18–29% among women.

The prevalence of active tuberculosis declined between 1979 and 2000 in most provinces in China (webfigure 1). If there is sustained 80% coverage of effective DOTS (webtable 2), the annual incidence of infectious tuberculosis in the three provinces presented here is estimated to decline after 2003, even if smoking and solid-fuel use remain at their current levels (figure 4). Nonetheless, reducing smoking and solid fuels would further reduce incidence of tuberculosis from projected levels. The estimated reductions in 2033, under different scenarios of smoking and solid-fuel use, range from 10% to 23% of the projected levels in Jiangsu, 35% to 52% in Guizhou (where prevalence has increased), and 5% to 14% in Shanghai (where prevalence has been lowest; figure 4).

Incidence of tuberculosis is projected to decline even when DOTS implementation is less effective. The decline in incidence in these three provinces will be 4–28% less under moderate DOTS than under optimum DOTS, and 11–79% smaller under minimum DOTS. This slower decline in tuberculosis incidence would, in turn, lead to smoking and solid-fuel interventions having larger relative and absolute beneficial effects on trends in tuberculosis (figure 4). For example, in Jiangsu province, the relative reduction in projected incidence in 2033, under different scenarios of smoking and solid-fuel use, would be 10–23% under optimum DOTS, 12–27% under moderate DOTS, and 15–33% under minimum DOTS.

Discussion

Reductions in smoking and solid-fuel use can significantly reduce the burden of COPD and lung cancer. Moderate, aggressive, and complete reduction of these exposures over the next three decades, through mechanisms such as tobacco taxation, advertising ban, and fuel pricing, can lead to 7–38% reduction in deaths from these two diseases, which have few other effective treatments.

See Online for webappendix 3, webfigures 6 and 7, and webtables 3–5

We observed a difference in how risk-factor interventions affect population-level trends in tuberculosis compared with those of COPD and lung cancer: in the absence of new technologies for early detection and treatment, the burden of COPD and lung cancer will remain high as long as smoking and indoor air pollution persist because these two risk factors are the most important causes of chronic respiratory disease incidence and mortality in China. But tuberculosis incidence can decline significantly because treatment reduces the risk of infection through reducing the duration of infectiousness. Nonetheless, smoking and solid-fuel interventions should be components of tuberculosis control for at least three reasons. First, irrespective of coverage and effectiveness of DOTS, risk-factor interventions can further reduce incidence of tuberculosis. The complementary effects of risk-factor interventions occur through reducing the risk of latent infection and progression from latent infection to infectious disease. Second, reducing smoking in patients with tuberculosis might further strengthen DOTS effectiveness because smoking has been associated with delayed response to treatment.[63] Third, reducing smoking may itself lower the risk of drug resistance as recent studies have suggested a link between smoking and drug-resistant tuberculosis.[64,65]

See Online for webfigure 8

Our quantitative analysis of the effects of the two leading environmental and lifestyle sources of respirable pollutants on a common set of infectious and chronic diseases used models that incorporated the aetiological risk factors in disease incidence and mortality over time. Specifically, our models and data sources accounted for the fact that effects on lung cancer and COPD accumulate or reverse gradually after exposure begins or stops and for dependency of tuberculosis incidence on prevalent infectious cases. We used several large sources of data to reconstruct consistent and comparable trends of smoking, solid-fuel use, and tuberculosis in China's provinces. Scenarios were constructed on the basis of policy experiences in China and other countries, and can provide programme targets and benchmarks. Current and projected mortality from COPD and lung cancer from the global burden of disease analysis used Chinese mortality data sources and accounted for demographic and socioeconomic development.[1] The relative risks and how they change over time were based on meta-analyses and large high-quality epidemiological studies in China and elsewhere.

Population-level analyses of mortality effects of risk factors, including ours, may also be affected by some limitations and uncertainties. We quantified selected major sources of uncertainty in sensitivity analyses (webappendices 2 and 3, webfigures 6 and 7, and webtables 3–5). These analyses show that the largest source of uncertainty for COPD and lung cancer is whether the relative risks of smoking related diseases in China will reach those observed in western populations. One recent study in China is consistent with increasing relative risks,[66] but the possibility of ethnic differences cannot be ruled out.[67] Benefits of tobacco control in different scenarios would be 23–81% smaller for men and 84–94% smaller for women if the relative risks for effects of smoking on COPD and lung cancer do not rise significantly after the peak of the smoking epidemic (webfigure 6). The effects of all other sensitivity analyses on the number of averted deaths from COPD and lung cancer were less than 11% for the combined effects of smoking and solid-fuel use, and less than 18% for the effects of individual risk factors.

The predictions for tuberculsosis are subject to uncertainties of model parameters, including how smoking and indoor air pollution affect the risk of different stages of tuberculosis natural history (latent infection versus progression) and the values of the transmission and progression parameters (webappendix 3, webfigure 8, and webtable 5). These analyses show that the largest source of uncertainty for the tuberculosis model is the future trend of transmission parameter, which depends on how sociodemographic change affects the patterns of contact and other determinants of transmission in China. If factors such as higher population density and increased travel increase the number of contacts that lead to tuberculosis transmission, the transmission parameter might not continue its expected decline. In this case, reducing smoking and indoor air pollution will have an even greater effect on tuberculosis control than estimated. For example, if the transmission parameter in Jiangsu doubles over the next 30 years, the benefits of the different scenarios of smoking, solid-fuel use would be 58–77% greater than the original analysis in figure 4. Multiparameter uncertainty analysis showed the interquartile range of the estimated effects was within 14–33% of its central value in all provinces and in all scenarios of DOTS, smoking, and solid-fuel use. Finally, the causal link between smoking and tuberculosis is based on a larger number of epidemiological studies than that of indoor air pollution from solid-fuel use. If the causal effect on tuberculosis were only from smoking, the benefits of reducing exposure would be smaller than those in figure 4, by 19–37% for different scenarios in Jiangsu, by 23–32% in Guizhou, and by 9–13% in Shanghai.

In addition to the above sources of uncertainty, fundamentally new technologies for early detection and treatment of chronic diseases could significantly affect future burden. Discovery and large-scale use of such technologies over the duration of our analysis are less likely for COPD, but cannot be ruled out for lung cancer and tuberculosis. Finally, relative risks from meta-analyses may not be generalisable to population-level effects; nevertheless, such estimation is necessary and indispensable to inform policy making.

In addition to smoking and solid-fuel use, respiratory diseases are affected by other sources of inhaled pollutants, including passive smoking, air pollution from transport and industrial sources, and occupational exposures. In China, in 2003 passive smoking was responsible for an estimated 17 000 and 7000 deaths from COPD and lung cancer, respectively, among men (compared with 412 000 and 170 000 from direct smoking) and 126 000 and 25 000 deaths among women (compared with 113 000 and 16 000) because substantially more women are non-smokers and exposed to passive smoking[33] (webappendix 2). The quantitative evidence on the effects of passive smoking on tuberculosis is more limited, although a causal effect is likely.[5] Ambient urban air pollution, which in China might be partly due to household solid-fuel use, was responsible for an estimated 32 000 lung cancer deaths and 317 000 cardiopulmonary deaths in the Western Pacific region in 2000 (no independent effects on COPD were estimated for ambient urban air pollution) and selected occupational exposures for an estimated 34 000 lung cancer deaths and 161 000 COPD deaths in the same region.[4] The effect of ambient air pollution on tuberculosis has not been investigated in epidemiological studies.

Infectious and chronic respiratory diseases, smoking, and indoor air pollution are either already concentrated or increasingly prevalent in developing countries. In addition to their disease burden, these diseases have large and inequitable household and societal economic burden associated with health-care costs, reduced labour-market participation, and decreased accumulation of human capital, described in detail elsewhere for China and for other developing countries.[68–72] Our results show that reducing common risk factors could have a substantial effect on future burden of COPD and lung cancer, and be an important contributor to tuberculosis control. Our findings have several potential policy and programme implications at the national, community, household, or individual levels. At the national level, our results on the projected burden of disease from COPD and lung cancer alone reinforce the need for regulatory and economic policies that reduce smoking and promote clean household energy sources in China. Tuberculosis control however cannot rely on risk-factor reduction as its main intervention, and the core of national or regional tuberculosis control programmes should remain interventions that can reduce and eventually interrupt transmission under generalisable circumstances, currently DOTS. Nonetheless, at the community level, some interventions could increase the coverage or community effectiveness of others. For example, case detection and treatment completion under DOTS in China have been constrained by limitations of physical and human infrastructure, financial factors, and compliance, especially in rural areas and marginalised social groups.[73–76] Low-income or marginalised communities could be enrolled in programmes that provide cleaner fuels or stoves and nutritional supplements, conditional on periodic tuberculosis tests and DOTS treatment completion. At the individual level, tobacco cessation can be added to tuberculosis treatment, possibly with financial incentives.[77,78] If multiple interventions are implemented, the management structure of DOTS, including its standardised approach to registration, recording, and reporting of enrolled individuals (or households) and their status in receiving intervention, can strengthen planning and implementation of interventions for indoor air pollution and smoking.[79] Tobacco taxes might also be used to subsidise DOTS, clean energy technology, and nutrition for low-income households that take part in integrated programmes. An important next step would be a policy dialogue between the different economic, energy, and health-sector agencies in China as well as community-based intervention studies that assess the effectiveness of combining risk factor interventions with tuberculosis case finding and treatment under actual conditions of implementation.

Contributors

HHL, MM, and ME designed the study and the analyses. HHL and ME collected data and wrote the report, with input from other authors. HHL conducted data analysis. ME contributed to analysis for chronic diseases. MM, TC, and CC contributed to analysis for TB. All authors reviewed and approved the final report.

Conflict of interest

We declare that we have no conflict of interest.

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