The burden of disease attributable to indoor air pollutants in China from 2000 to 2017

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Summary

Background High-level exposure to indoor air pollutants (IAPs) and their corresponding adverse health effects have become a public concern in China in the past 10 years. However, neither national nor provincial level burden of disease attributable to multiple IAPs has been reported for China. This is the first study to estimate and rank the annual burden of disease and the financial costs attributable to targeted residential IAPs at the national and provincial level in China from 2000 to 2017.

Methods We first did a systematic review and meta-analysis of 117 articles from 37 231 articles identified in major databases, and obtained exposure–response relationships for the candidate IAPs. The exposure levels to these IAPs were then collected by another systematic review of 1864 articles selected from 52 351 articles. After the systematic review, ten IAPs with significant and robust exposure–response relationships and sufficient exposure data were finally targeted: $PM_{2\cdot5}$, nitrogen dioxide, sulphur dioxide, ozone, carbon monoxide, radon, formaldehyde, benzene, toluene, and p-dichlorobenzene. The annual exposure levels in residences were then evaluated in all 31 provinces in mainland China continuously from 2000 to 2017, using the spatiotemporal Gaussian process regression model to analyse indoor originating IAPs, and the infiltration factor method to analyse outdoor originating IAPs. The disability-adjusted life-years (DALYs) attributable to the targeted IAPs were estimated at both national and provincial levels in China, using the population attributable fraction method. Financial costs were estimated by an adapted human capital approach.

Findings From 2000 to 2017, annual DALYs attributable to the ten IAPs in mainland China decreased from 4620 (95% CI 4070–5040) to 3700 (3210–4090) per 100 000. Nevertheless, in 2017, IAPs still ranked third among all risk factors, and their DALYs and financial costs accounted for 14·1% (95% CI 12·3–15·6) of total DALYs and 3·45% (3·01–3·82) of the gross domestic product. Specifically, the rank of ten targeted IAPs in order of their contribution to DALYs in 2017 was $PM_{2\cdot5}$, carbon monoxide, radon, benzene, nitrogen dioxide, ozone, sulphur dioxide, formaldehyde, toluene, and p-dichlorobenzene. The DALYs attributable to IAPs were 9·50% higher than those attributable to outdoor air pollution in 2017. For the leading IAP, $PM_{2\cdot5}$, the DALYs attributable to indoor origins are 18·3% higher than those of outdoor origins.

Interpretation DALYs attributed to IAPs in China have decreased by 20·0% over the past two decades. Even so, they are still much higher than those in the USA and European countries. This study can provide a basis for determining which IAPs to target in various indoor air quality standards and for estimating the health and economic benefits of various indoor air quality control approaches, which will help to reduce the adverse health effects of IAPs in China.

Funding The National Key Research and Development Program of China and the National Natural Science Foundation of China.

Lancet Planet Health 2023; 7: e900–11

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Introduction

In China, with rapid urbanisation and economic growth in the past two decades, air pollution of both outdoor and indoor origins has become a great concern.[1] The Global Burden of Diseases Study (GBD) 2019[2] has identified that, in China in 2019, air pollution was the fourth leading risk factor for disability-adjusted life years (DALYs). Considering that people spend over 80% of their time indoors, with younger (<18 years) and older (>80 years) people being indoors over 90% of their time,[3,4] the health effects of exposure to indoor air pollutants (IAPs) are particularly important.

In the past decade, China has made considerable progress towards achieving clean outdoor air. In 2013, China issued the Air Pollution Prevention and Control Action Plan.[5] Since then, outdoor air pollution in China has been reduced by strict controls of emissions, monitoring pollution concentrations, and financial penalty

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Research in context

Evidence before this study

People spend over 80% of their time indoors, and air inhalation is over 75% of their total mass intake through air, food, and water. Indoor air pollution has become a major health risk in mainland China with the rapid economic growth in the past two decades. However, the burden of disease attributable to exposure to indoor air pollutants (IAPs) in mainland China remains unclear. We searched Web of Science, PubMed, and the China National Knowledge Infrastructure for studies in English or Chinese published from Jan 1, 2000, to Dec 31, 2019, using the search terms ((“burden of disease”) OR (“disease burden”)) AND ((“household air”) OR (“indoor air”)) AND (China). Most studies, including the Global Burden of Diseases (GBD) study, focused on the burden of disease attributable to indoor particulate matter caused by household solid fuel use for cooking or heating. Additionally, the GBD study estimated the burden of disease attributable to indoor exposure to radon in China. For the burden of disease attributable to other IAPs in China, there was only one study, which estimated the burden of disease of children’s indoor formaldehyde exposure in Shanghai, China. To our knowledge, there has been no comprehensive evaluation at the national or provincial levels of burden of disease attributable to IAPs listed in the China Indoor Air Quality Standard (GB/T 18883).

Added value of this study

To the best of our knowledge, this study is the first to estimate the burden of disease caused by several targeted IAPs at both national and provincial levels in all 31 provinces in mainland China from 2000 to 2017. In 2017, the top five IAPs were fine particulate matter ($PM_{2·5}$), carbon monoxide, radon, benzene, and nitrogen dioxide. The DALYs attributable to ten targeted IAPs in China in 2017 were 3700 per 100 000, which was 3·85 to 6·01 times greater than for European countries (reference year: 2004) and 1·84 times greater than for the USA (2010). Although this attributable burden has been reduced by 20·0% compared with what it was in 2000, it still ranked third among all risk factors (after tobacco and high blood pressure) and accounted for 14·1% of the total burden in China. In addition, the attributable financial costs reached about 3·45% of the total gross domestic product in China in 2017. These results suggest that the adverse health effects of indoor air pollution in China require urgent attention. This study also provides provincial-level DALYs for the ten targeted IAPs. In many provinces, the top five IAPs include ozone, formaldehyde, and sulphur dioxide. These findings are essential both for determining the IAPs to be targeted in national-level or provincial-level standards of indoor air quality in China, and for estimating the health and economic benefits of the corresponding control approaches.

Implications of all the available evidence

The DALYs attributable to indoor air pollution in China are five times greater than those for European countries and twice those for the USA. These findings provide a foundation for (1) determining the concentration thresholds for IAPs in indoor air quality standards in China, (2) estimating the health and economic benefits of reducing IAP exposures, and (3) determining the priority for controlling specific IAPs in different provinces in China. In addition, this study shows that it is necessary to refine the exposure–response relationships for IAPs in addition to $PM_{2·5}$.

policies. Huang and colleagues[6] found that the attributable number of deaths due to outdoor $PM_{2·5}$ pollution decreased by 13·1% from 2013 to 2017. However, indoor air pollution as a major component of air pollution in China has received less attention, and thus its related burden of disease is unclear. In fact, compared with outdoor air pollutants, IAPs are often at higher concentrations and with more complex components, due to multiple indoor sources and poor ventilation.[7,8] Moreover, one World Bank report pointed out that “in China, indoor concentrations of known harmful substances are typically higher than in other countries”,[11] which is consistent with several studies.[9–12] Therefore, the health effects of IAPs in China need to be evaluated.

There have been three main studies of the burden of disease attributable to IAPs. GBD 2019[2] focused on the disease burden of 87 risk factors before 2019 for 204 countries and territories with a systematic framework based on population attributable fraction (PAF). However, only two IAPs were included for residential settings: household $PM_{2·5}$ due to solid fuel combustion and radon. Benzene and formaldehyde were considered for occupational exposure. A study on the environmental burden of disease in Europe[13] was initiated in 2009 and included nine risk factors in six European countries, among which the IAPs were benzene, dioxins, second-hand smoke, formaldehyde, and radon. This study[13] was further extended by the HealthVent study[14] in 26 European countries in 2016, and indoor $PM_{2·5}$, carbon monoxide, and dampness were added. Additionally, Lawrence Berkeley National Laboratory researchers estimated the chronic health effects of 69 IAPs in US residences in 2012.[15] However, in the study,[15] even though the health effects of $PM_{2·5}$, carbon monoxide, nitrogen dioxide, ozone, and sulphur dioxide were estimated using exposure–response relationships from epidemiological evidence of outdoor air pollution, toxicological data from animal tests were used to estimate the attributable burden of the other more than 60 IAPs.[16] Although these studies did not concentrate on the disease burden of IAPs or had some limitation, they provided useful evaluation tools to help deepen the knowledge of the health effects of IAPs in China.

The Chinese Burden of Disease Attributable to Indoor Air Pollutants (CBD–IAP) project was initiated in 2017. It aimed to comprehensively estimate both national-level and provincial-level burden of disease attributable to various residential IAPs from 2000 to 2017 in China. By evaluating and characterising the spatial and temporal distribution of burden of disease attributable to different IAPs, this study helps to identify which IAPs should be targeted in priority in the near future to improve indoor air quality and thereby benefit public health in China. In addition, it provides a basis to estimate health and economic benefits derived from reducing indoor air pollution by using various controlling approaches.

Methods

Overview

The CBD–IAP study used the methods of the GBD 2019 study.[2] It was divided into four steps: (1) selection of the candidate IAPs in China; (2) estimation of relative risks for risk–outcome pairs of each IAP; (3) estimation of exposure levels for targeted IAPs; and (4) estimation of PAF and attributable burden of disease in China.

Selection of the candidate IAPs in China

Candidate IAPs in China were selected using four criteria: (1) the Chinese standard of indoor air quality published in 2002;[17] (2) the WHO global air quality guidelines and guidelines for indoor air quality;[18,19] (3) cancer risk assessment for IAPs in China;[20] and (4) a list recommended by experts in the CBD–IAP workgroup. Over 30 IAPs were selected and classified into five groups: fine particulate matter ($PM_{2\cdot5}$); inorganic air pollutants, namely sulphur dioxide, nitrogen dioxide, ozone, carbon monoxide, radon, and ammonia; volatile organic compounds (VOCs), namely formaldehyde, benzene, toluene, xylenes, acetaldehyde, p-dichlorobenzene, butadiene, trichloroethylene, and tetrachloroethylene; semivolatile organic compounds, namely five phthalates and eight polycyclic aromatic hydrocarbons; and microbial pollutants, namely bacteria and fungi.

Estimating relative risks for included risk–outcome pairs

The relative risks of health outcomes for $PM_{2\cdot5}$ exposure were estimated using the integrated exposure–response (IER) model from GBD 2019[2] for six health outcomes: ischaemic heart disease, stroke, chronic obstructive pulmonary disease (COPD), lung cancer, lower respiratory infection, and diabetes. The IER model describes the increase of relative risk with increasing $PM_{2\cdot5}$ concentration with several shapes, with the following form:[21]

$$RR=\begin{cases}1, C\leq C_{cf}\\ 1+\alpha\left\{1-\exp\left[-\gamma\left(C-C_{cf}\right)^{\delta}\right]\right\}, C>C_{cf}\end{cases}$$

where α is the scale parameter, γ and δ are shape parameters, and C_{cf} is the counterfactual exposure level below which we assume there is no additional risk. We also used an exposure–response relationship between ozone and COPD as described in the GBD study.[2]

Exposure–response relationships for other IAPs have not been extensively reported, and published results are inconsistent. Hence, we did a systematic review and meta-analyses of 37 231 articles to obtain exposure–response relationships for each selected IAP (appendix 1 pp 9–21).[22–26] As in the GBD study, reported exposure–response relationships were collected globally and not limited to China. For use in the evaluation of burden of disease, risk–outcome pairs of IAPs were required to satisfy the following criteria: significant associations in the meta-analysis of epidemiological evidence (cohort studies, case-control studies, and cross-sectional studies), robustness in the sensitivity analysis, and no publication bias detected by Egger's test. The included health outcomes should also be included in the list of outcomes in the GBD study so that the total burden of outcomes would be available.[2] 11 IAPs met these criteria and are used in the present study: $PM_{2\cdot5}$, nitrogen dioxide, sulphur dioxide, ozone, radon, carbon monoxide, formaldehyde, benzene, toluene, p-dichlorobenzene, and butadiene. These IAPs were used in connection with 23 risk–outcome pairs (appendix 1 p 4).

See Online for appendix 1

Based on IAP exposure–response relationships, relative risks for health outcomes can be estimated. The theoretical minimum risk exposure level (TMREL) is the risk exposure that minimises risk in the exposed population. The relative risk for TMREL can be regarded as 1 for the reference.[2] For $PM_{2\cdot5}$, TMREL is expressed as C_{cf} in equation 1 for the IER model, whereas the TMREL for other IAPs was assumed to be 0.[2,18,27,28] When the evaluated exposure levels were higher than the maximum level reported in the literature, rather than extrapolate, we used the maximum relative risk of the curve. Therefore, the relative risk can be calculated as

$$RR=\begin{cases}RR_0^{\frac{C}{C_0}}, C\leq C_{\max}\\ RR_0^{\frac{C_{\max}}{C_0}}, C>C_{\max}\end{cases}$$

where RR is the relative risk, RR_0 is the relative risk per unit increase of exposure to specific IAPs, C is the evaluated exposure level of an IAP, C_0 is the unit increase of exposure used in the exposure–response relationship, and $C_{\max}$ is the maximum level of the exposure–response curve reported in the literature (appendix 1 p 4).

Estimated exposure levels for targeted IAPs

In this study, exposure levels to the 11 IAPs were estimated for residences only, as people spent the longest time per day in residences in China from 2000 to 2017, and concentration data in previous systematic reviews for other indoor environments, such as offices and schools, were insufficient to yield reliable estimates.

Indoor $PM_{2\cdot5}$, nitrogen dioxide, sulphur dioxide, ozone, and carbon monoxide originate both outdoors and indoors. The contribution of outdoor origin to indoor concentrations was estimated by the infiltration factor method, which used the outdoor concentration data and an infiltration factor (appendix 1 pp 22–33).[29–33] The outdoor concentrations of $PM_{2\cdot5}$ and ozone were obtained from global model estimates,[34,35] whereas the other three IAP concentrations were obtained from fixed-site atmospheric monitoring stations.[36] The infiltration factor describes the relationship between outdoor and indoor concentrations with air exchange rate, penetration coefficient, removal rate, and window-opening behaviour. For the contribution of indoor originating IAPs, field measurement data from 2000 to 2017 in China have been summarised in a systematic review.[37] With a spatiotemporal Gaussian process regression (ST-GPR) model (appendix 1 pp 22–33), a non-parametric Bayesian regression method for interpolating non-linear trends, we estimated IAP contributions of indoor origins.[2,38] Finally, the indoor concentrations of these five IAPs were calculated as

$$C_{\mathrm{in}}=C_{\mathrm{out}}F_{\mathrm{inf}}+C_{\mathrm{S}}$$

See Online for appendix 2

where C_{in} is the indoor concentration of the IAP, C_{out} is the outdoor concentration of the IAP, F_{inf} is the infiltration factor,[30] and C_{S} is the contribution of indoor originating IAPs estimated by the ST-GPR model. We noted that due to scarce indoor measurements for nitrogen dioxide, sulphur dioxide, and ozone, C_{S} for these three IAPs could not be estimated so only the contributions of outdoor origin were used.

Indoor concentrations of other IAPs (ie, radon, formaldehyde, benzene, toluene, and p-dichlorobenzene) were directly evaluated from systematic reviews of field measurement data in residences,[9,25,39–41] and estimates using ST-GPR models, since the indoor origins of these IAPs are much stronger than outdoor contributions. We note that the indoor concentration of butadiene could not be estimated due to scarce data. This is further clarified in the discussion.

Finally, ten IAPs were targeted for analysis of attributable burden of disease. Consistent with the quantity and precision of available data, we chose province in China as the geographical unit for analysis (appendix 1 p 7). Detailed methods and data sources for each of the ten IAPs are available (appendix 1 pp 22–33).

Estimating PAF and attributable burden of disease

The PAF of health outcome i attributable to pollutant A (denoted as $PAF_{A,i}$) can be calculated as[2,42]

$$PAF_{A,i}=\frac{\int_C p_A(\mathrm{RR}_{A,i}-1)dC}{\int_C p_A(\mathrm{RR}_{A,i}-1)dC+1}=\frac{\overline{RR_{A,i}}-1}{\overline{RR_{A,i}}}$$

where $RR_{A,i}$ is the relative risk of outcome i for C exposure to pollutant A, and p_A is the population fraction for C exposure to pollutant A. Based on the estimated PAF, the attributable burden of disease for pollutant A (denoted as $DALY_A$) can be calculated as[2,13]

$$DALY_A=\sum_i PAF_{A,i}\times DALY_{total,i}$$

where $DALY_{\mathrm{total},i}$ is the total DALYs for outcome i, as derived from the GBD database (appendix 1 p 34).[2,43] Then the IAPs can be ranked according to their relative attributable burden of disease so as to prioritise the urgency of their control.

Then, to evaluate the proportion accounted for by the health effects of IAPs among all risk factors, the total attributable burden of diseases for IAPs (denoted as $DALY_{\mathrm{IAPs}}$) was estimated. The attributable burden of outcome i for all IAPs (denoted as $DALY_i$) is first obtained, and then $DALY_{\mathrm{IAPs}}$ can be expressed by[2,38]

$$DALY_{\mathrm{IAPs}}=\sum_i DALY_i=\sum_i\Big(1-\prod_A(1-PAF_{A,i})\Big)\times \mathrm{DALY}_{\mathrm{total},i}$$

Based on the attributable burden of disease, the IAP-attributable cost can be estimated. An adapted human capital method assumes that one DALY equals gross domestic product (GDP) per capita for each province (appendix 2) because 1 year of life lost to disability or death is equivalent to the loss of the annual economic production value of one person in the population.[44,45] Therefore, the IAP-attributable costs can be estimated by

$$\mathrm{Costs}=DALY_{\mathrm{IAPs}}\times GDP \text{ per capita}$$

Uncertainty analysis

The mean and 95% CI of the attributable DALYs and costs were obtained through the two-stage Monte Carlo simulation.[42,46,47] The first stage describes the IAP concentration distribution due to intrapopulation variability, and the second stage reflects the uncertainty in the exposure–response relationships (appendix 1 pp 35–36).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Median exposure levels of the ten targeted IAPs in all 31 provinces of mainland China in 2000, 2005, 2010, 2015, and 2017 were estimated (appendix 1 p 8). The exposure level of most IAPs decreased from 2000 to 2017 in China, except ozone and radon. Detailed analysis of the spatiotemporal distribution of IAP exposure levels is available (appendix 1 pp 37–38).

National-level DALY numbers and rates attributable to IAPs in China are shown in table 1. Generally, there

	DALYs (thousand)	DALY rate (per 100 000)	Proportion of DALYs	Costs (billion)	Per-capita costs	Proportion of GDP
2000	58 500 (51 600–63 900)	4620 (4070–5040)	15·8% (13·9–17·2)	437 (384–477)	347 (305–379)	4·5% (3·9–4·9)
2005	58 200 (50 900–63 600)	4450 (3890–4860)	16·1% (14·1–17·6)	807 (704–885)	628 (548–688)	4·3% (3·7–4·7)
2010	56 000 (48 800–61 300)	4180 (3640–4570)	15·8% (13·7–17·3)	1630 (1420–1790)	1230 (1070–1350)	3·9% (3·4–4·3)
2015	52 200 (45 200–57 600)	3770 (3270–4170)	14·6% (12·6–16·1)	2460 (2140–2720)	1780 (1550–1970)	3·6% (3·1–3·9)
2017	51 800 (45 000–57 300)	3700 (3210–4090)	14·1% (12·3–15·6)	2880 (2500–3190)	2060 (1790–2280)	3·5% (3·0–3·8)

Data are mean (95% CI). DALYs=disability-adjusted life-years. IAPs=indoor air pollutants. GDP=gross domestic product. Costs are in Chinese yuan.

Table 1: **National-level disease burden and costs attributable to ten targeted IAPs in China in 2000, 2005, 2010, 2015, and 2017**

was a decrease in the $DALY_{IAPs}$, with a slow reduction from 2000 to 2005 but a rapid decline from 2010 to 2015. The annual attributable burden of disease decreased from 4620 (95% CI 4070–5040) DALYs per 100 000 in 2000 to 3700 (3210–4090) DALYs per 100 000 in 2017. The proportion of $DALY_{IAPs}$ in the total DALYs dropped from 15·8% (95% CI 13·9–17·2) in 2000 to 14·1% (12·3–15·6) in 2017, suggesting that a preliminary decrease in health risks from indoor air pollution had been reached.

The GBD database shows that the leading three risk factors in China in 2017 were tobacco, high blood pressure, and dietary risks, and the corresponding DALY rates were 4370, 3750, and 3240 per 100 000, respectively.[2] These DALY rates imply that the health risks of indoor air pollution potentially outweigh the dietary risks, ranking third among all risk factors in 2017. This further suggests that the adverse health effects of indoor air pollution are not negligible.

The total costs, in Chinese yuan (¥), due to exposure to IAPs in China reached ¥437 billion (95% CI 384–477) in 2000 and ¥2880 billion (2500–3190) in 2017, which accounted for 4·45% (95% CI 3·92–4·86) and 3·45% (3·01–3·82) of the total GDP of China, respectively (table 1).

The burden of disease attributable to each specific IAP and the corresponding health outcomes in 2017 were also analysed (figure 1; appendix 3). For the attributable disease burden, the ten targeted IAPs ranked from largest to smallest in 2017 were $PM_{2·5}$, carbon monoxide, radon, benzene, nitrogen dioxide, ozone, sulphur dioxide, formaldehyde, toluene, and p-dichlorobenzene. Among all IAPs, $PM_{2·5}$ contributed 88·5% (95% CI 83·1–94·5) of attributable DALYs, or 3270 (95% CI 2810–3630) per 100 000 in 2017. The results also show that cardiovascular diseases (including ischaemic heart diseases and stroke) and chronic respiratory diseases (including asthma and COPD) were the two most serious health outcomes caused by exposure to IAPs, accounting for 61·4% (56·0–66·3) and 16·6% (13·2–19·8) of the attributable DALYs of IAPs, respectively.

The leading IAPs have varied by year in the past two decades (figure 2). In 2000, the top five IAPs were $PM_{2·5}$, benzene, carbon monoxide, sulphur dioxide, and nitrogen dioxide, which were quite different from those

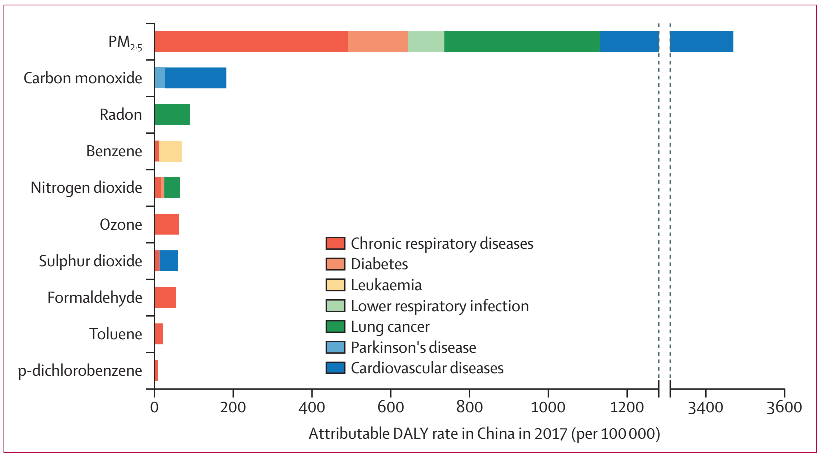

Figure 1: **National-level DALY rates (per 100 000) attributable to ten targeted indoor air pollutants in China in 2017**
DALYs=disability-adjusted life-years.

in 2017 when the top five were $PM_{2·5}$, carbon monoxide, radon, benzene, and nitrogen dioxide. $PM_{2·5}$ has remained the leading risk factor in the past two decades, despite a decrease of approximately 10% every decade in DALYs per 100 000 attributable to $PM_{2·5}$. Nitrogen dioxide and carbon monoxide remained in the top five between 2000 and 2017. The attributable DALYs for nitrogen dioxide and sulphur dioxide have substantially decreased, especially from 2010 to 2017. The rankings of radon increased from ninth in 2000 to third in 2017. Among the compounds emitted from furnishing and decorating materials, benzene declined from second in 2000 to fourth in 2017, a 66·7% (65·6–67·7) reduction of its burden. The disease burden of formaldehyde increased by 30·3% (29·0–31·5) from 2010 to 2017. Based on the available reliable exposure–response relationships, the indoor pollution of fine particulate matter and inorganic chemical pollutants have more negative health effects than other IAPs in China presently.

See Online for appendix 3

The attributable DALY rates of IAPs in 31 provinces in 2000, 2005, 2010, 2015, and 2017 were calculated (figure 3; appendix 3). From the perspective of temporal variation, attributable DALYs per 100 000 decreased by an average of 20·0% in most provinces from 2000 to 2017. More rapid improvement occurred in western China. For example, the $DALY_{IAPs}$ per 100 000 in Tibet

IAP 2000	DALY rate (per 100 000)	Proportion of DALYs	IAP 2010	DALY rate (per 100 000)	Proportion of DALYs	IAP 2017	DALY rate (per 100 000)	Proportion of DALYs
1 $PM_{2·5}$	4010·4	13·8 %	1 $PM_{2·5}$	3679·5	13·9 %	1 $PM_{2·5}$	3271·2	12·3 %
2 Benzene	204·2	0·7 %	2 Carbon monoxide	194·6	0·7 %	2 Carbon monoxide	182·5	0·7 %
3 Carbon monoxide	178·8	0·6 %	3 Benzene	121·6	0·5 %	3 Radon	90·6	0·3 %
4 Sulphur dioxide	166·8	0·6 %	4 Sulphur dioxide	120·3	0·5 %	4 Benzene	68·1	0·3 %
5 Nitrogen dioxide	115·5	0·4 %	5 Nitrogen dioxide	103·4	0·4 %	5 Nitrogen dioxide	64·6	0·2 %
6 Ozone	82·6	0·3 %	6 Ozone	67·5	0·3 %	6 Ozone	61·7	0·2 %
7 Formaldehyde	64·4	0·2 %	7 Radon	59·7	0·2 %	7 Sulphur dioxide	59·9	0·2 %
8 Toluene	43·3	0·1 %	8 Formaldehyde	41·3	0·2 %	8 Formaldehyde	53·8	0·2 %
9 Radon	42·1	0·1 %	9 Toluene	29·8	0·1 %	9 Toluene	21·1	0·1 %
10 p-dichlorobenzene	18·5	0·1 %	10 p-dichlorobenzene	11·3	0·0 %	10 p-dichlorobenzene	8·9	0·0 %

Particulate matter
Inorganic chemical pollutants
Volatile organic compounds

Figure 2: **Leading ten IAPs by attributable DALY rates (per 100 000) in China in 2000, 2010, and 2017**
The dashed line refers to the decreasing ranking for this IAP, whereas the solid line refers to the non-decreasing ranking. DALYs=disability-adjusted life-years. IAP=indoor air pollutants.

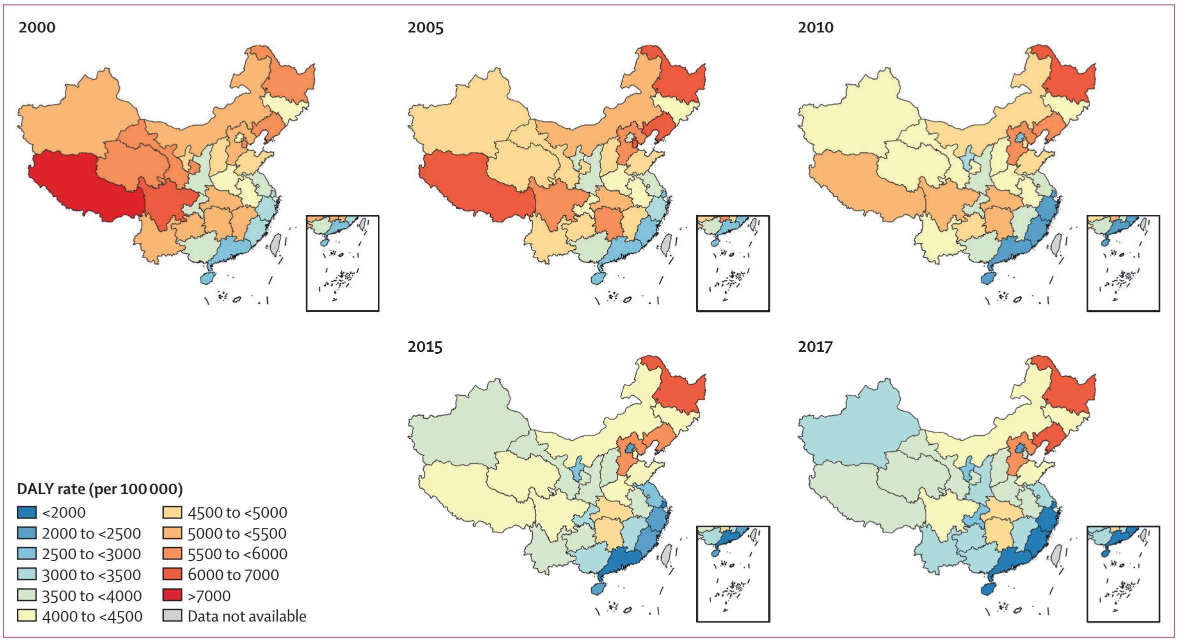

Figure 3: **DALY rates (per 100 000) attributable to ten targeted indoor air pollutants in 31 provinces in China in 2000, 2005, 2010, 2015, and 2017**
DALYs=disability-adjusted life-years.

was reduced by 51·1% (95% CI 50·7–51·4) and in Xinjiang by 36·3% (35·9–36·7). The provinces in the southeast of China consistently had the lowest attributable DALYs per 100 000 in the past two decades, whereas the Hebei province and the northeastern provinces showed an increase. From the perspective of spatial distribution, attributable DALYs per 100 000 in the northern and western provinces were higher than those in the southern and eastern provinces. The Yangtze River Delta and Pearl River Delta, two of the most developed metropolitan regions, had relatively lower attributable burdens than the rest of China. Two provinces in northeastern China, Heilongjiang and Liaoning, had the highest attributable DALYs per 100 000 in 2017.

To clarify the contribution of IAPs to the total burden of disease, proportions of $DALY_{IAPs}$ in the total DALYs were further estimated (figure 4; appendix 3). The temporal trend for all provinces shows a general decline over 17 years. The spatial differences show that people in the northern and central provinces had their health affected from IAP exposure more than those in the western and southeastern provinces. In 2017, the highest proportion of $DALY_{IAPs}$ in the total DALYs was

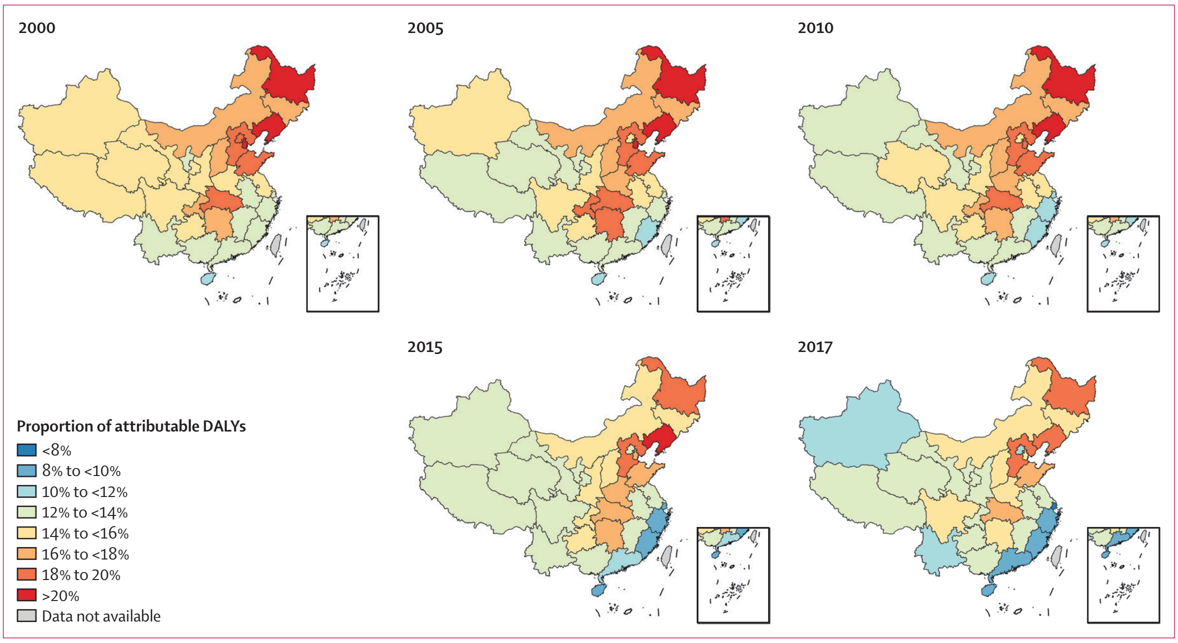

Figure 4: **Proportions of DALYs attributable to ten targeted indoor air pollutants in total DALYs in 31 provinces in China in 2000, 2005, 2010, 2015, and 2017**
DALYs=disability-adjusted life-years.

19·8% (SD 1·5%) in Liaoning province, whereas the lowest was 7·15% (SD 0·60%) in Shanghai. It should be noted that IAPs in the western provinces contributed a lower proportion to the total disease burden, although their absolute number of DALYs was higher. This might be related to socioeconomic factors, such as the relative poverty of the western provinces compared with the eastern provinces.

The rankings of IAPs by their contributions to DALYs were different in each province. The ten targeted IAPs are ranked according to their contribution to DALYs in 31 provinces in 2017 (appendix 1 pp 5–6). In some provinces, the top five IAPs were the same as those for the national level (ie, $PM_{2·5}$, carbon monoxide, radon, benzene, and nitrogen dioxide), whereas in many provinces, ozone, formaldehyde, and sulphur dioxide ranked in the top five contributing pollutants. Ozone ranked in the top five in 14 provinces, whereas formaldehyde and sulphur dioxide listed in the top five pollutants in 12 provinces.

Discussion

This study estimates the burden of disease for IAPs in China at both national and provincial levels from 2000 to 2017 for the first time. In 2017, DALYs attributable to ten targeted IAPs were 3700 per 100 000, costing ¥2880 billion (3·45% of GDP). Although the attributable burden had decreased by 20·0% from 2000 to 2017, it still accounted for 14·1% of the total burden of disease and ranked third among all risk factors in 2017, suggesting the severity of the health effects of indoor air pollution. $PM_{2·5}$, carbon monoxide, radon, benzene, and nitrogen dioxide were the top five pollutants in the burden of disease nationwide, whereas ozone, formaldehyde, and sulphur dioxide were in the top five in many provinces.

The attributable burden of IAPs in this study was further compared with those in European countries and the USA for a broader view of our findings (figure 5; appendix 1 pp 39–41).[13–15] To guarantee comparability, the comparison was based on the reported IAPs in common in both countries. Compared with the USA in 2010, DALYs caused by $PM_{2·5}$, benzene, sulphur dioxide, carbon monoxide, and toluene were much higher in China, whereas the burdens due to indoor formaldehyde, nitrogen dioxide, and p-dichlorobenzene in the USA were greater. Altogether, these IAPs contributed to 2200 DALY losses per 100 000 and 7·14% of the total DALYs in the USA in 2010, whereas they caused 4050 DALY losses per 100 000 and 15·0% of the total DALYs in China in 2010, 1·84 times that in the USA. Additionally, attributable DALYs for $PM_{2·5}$ and benzene in China were at least twice as high as in European countries in 2004, whereas the burden for radon exposure in China was much lower. In total, the four reported IAPs in common led to 4160 DALY losses per 100 000 and 14·6% of the total DALY losses in China in 2004, which was 3·85 to 6·01 times those in six European countries. To sum up, the comparisons show that different countries had quite different distributions of burden of disease attributable to indoor air pollution, but the health effects of most IAPs in China were more severe than those in the USA and Europe.

The attributable burden of disease due to IAPs was also compared with that of outdoor air pollution in China.

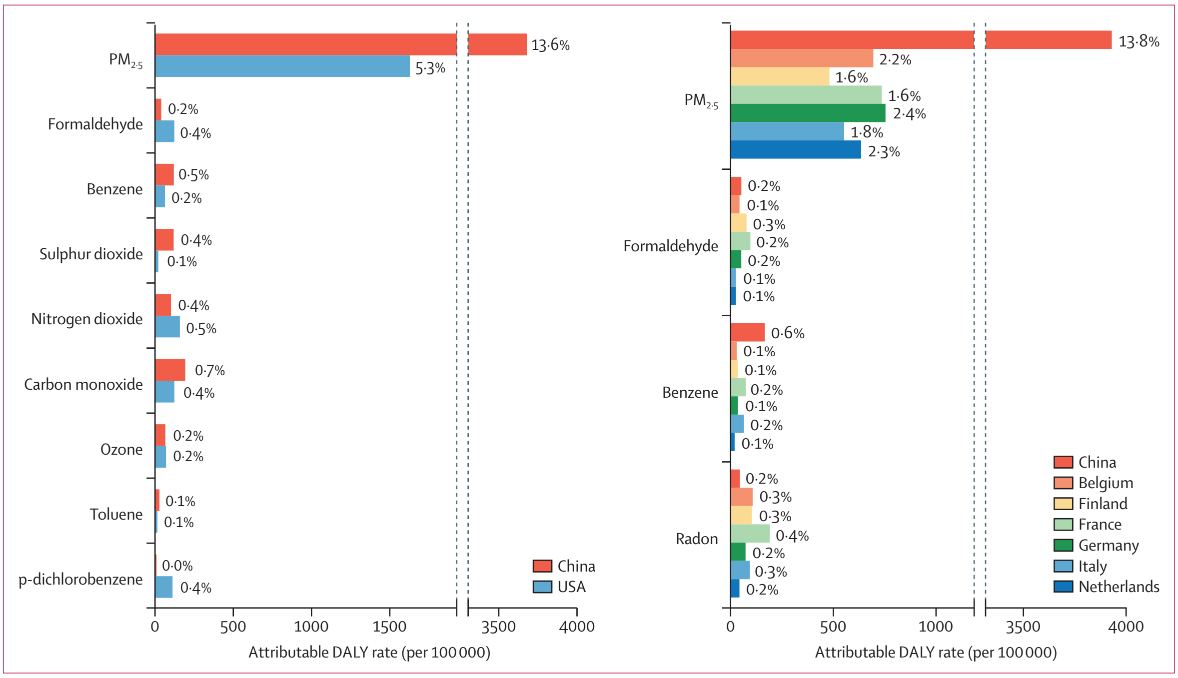

Figure 5: **Comparisons of attributable DALY rate (per 100 000) and proportion of various indoor air pollutants between China and six European countries in 2004, and between China and USA in 2010, respectively.**
DALYs=disability-adjusted life-years.

The outdoor air pollution considered $PM_{2·5}$, nitrogen dioxide, sulphur dioxide, carbon monoxide, ozone, and radon (appendix 1 pp 22–31). The outdoor concentrations of VOCs were assumed to be zero. In China, the attributable DALYs of outdoor air pollution per 100 000 reached 3810 (95% CI 3290–4280) in 2000, 3860 (3320–4340) in 2005, 3810 (3310–4250) in 2010, 3610 (3120–4050) in 2015, and 3370 (2920–3800) in 2017. The attributable DALYs of IAPs were higher by 21·3% in 2000, 15·0% in 2005, 9·71% in 2010, 4·43% in 2015, and 9·50% in 2017 than those of outdoor air pollution (table 1). Although the gap between the burden of IAPs and that of outdoor air pollution has narrowed recently, the health effects of IAPs still outweigh those of outdoor air pollution currently, suggesting the severity of indoor air pollution in China.

It is a strength of our study that the estimates of indoor concentrations accounted for both pollutants of indoor origin and pollutants of outdoor origin transported indoors. To differentiate the burden of disease of IAP of indoor and outdoor origins, the comparison was done for $PM_{2·5}$, the first IAP in the ranking. The results of DALYs per 100 000 and the proportion of DALYs were also collated (table 2). Due to non-linear exposure–response relationships, the total attributable DALYs of both indoor and outdoor origins are not equal to the sum of those from indoor and outdoor sources. The estimated attributable DALYs per 100 000 for $PM_{2·5}$ of indoor origin were 57·7% (in 2000) and 18·1% (in 2017) higher than those of outdoor origin. Over time, the proportion of DALYs attributable to $PM_{2·5}$ of indoor origin has continuously decreased from 12·6% in 2000 to 9·75% in 2017, whereas those of outdoor origin increased from 7·96% to 9·37% between 2000 and 2010 and then decreased to 8·26% in 2017. Thus, the attributable DALYs for $PM_{2·5}$ of both indoor and outdoor origins have been alleviated, and the declining rate of the proportion for indoor origin is comparable to that for outdoor origin, suggesting that exposure to $PM_{2·5}$ of indoor origin will still be the dominant component of the attributable DALYs for indoor $PM_{2·5}$ in the near future. This finding implies that controlling the indoor origins of IAPs is an efficient pathway to further reduce the health effects of these pollutants, especially given the high costs of improving the atmospheric environment to reduce the outdoor-originated fraction of IAPs. Compared with this study, the GBD study only considered $PM_{2·5}$ generated indoors by solid fuels when estimating exposure levels and attributable DALYs of household air pollution. Moreover, the GBD study applied the difference between indoor concentrations and outdoor concentrations to represent the exposure to indoor $PM_{2·5}$,[2] whereas the present study used the difference between indoor concentrations and the product of outdoor concentrations and infiltration factors, since only 50–70% of outdoor $PM_{2·5}$ moves into the indoor environment. Therefore, the GBD study might have underestimated the health effects of indoor $PM_{2·5}$.

There are several reasons for the decreasing trend of attributable burden of disease for IAPs in China in the past

	DALY rate (per 100 000)			Proportion of DALYs		
	Indoor and outdoor origins	Indoor origin	Outdoor origin	Indoor and outdoor origins	Indoor origin	Outdoor origin
2000	4010 (3490–4380)	3640 (3150–4030)	2310 (1760–2790)	13·8% (12·1–15·1)	12·6% (10·9–13·9)	8·0% (6·1–9·6)
2005	3870 (3330–4230)	3450 (2970–3830)	2340 (1780–2830)	14·0% (12·1–15·3)	12·5% (10·8–13·9)	8·5% (6·5–10·3)
2010	3680 (3170–4030)	3130 (2710–3510)	2490 (1980–2960)	13·9% (11·9–15·2)	11·8% (10·2–13·2)	9·4% (7·4–11·1)
2015	3320 (2850–3650)	2590 (2230–2960)	2330 (1840–2790)	12·6% (10·9–13·9)	9·9% (8·5–11·3)	8·9% (7·0–10·6)
2017	3270 (2810–3630)	2590 (2220–2960)	2190 (1710–2670)	12·3% (10·6–13·7)	9·8% (8·4–11·2)	8·3% (6·4–10·1)

Data are mean (95% CI). DALYs=disability-adjusted life-years.

***Table 2*: National-level burden of disease attributable to $PM_{2·5}$ stratified by indoor and outdoor origins in China in 2000, 2005, 2010, 2015, and 2017**

two decades. As $PM_{2·5}$ contributed over 80% of attributable DALYs among all included IAPs, reducing indoor $PM_{2·5}$ concentrations has had a large role in decreasing the attributable burden of IAPs. In 2012, the Ambient Air Quality Standard (GB 3095) was issued in China, and real-time monitoring of $PM_{2·5}$ and five other outdoor air pollutants began to be published in cities in China. Then, the Air Pollution Prevention and Control Action Plan was launched in China in 2013 and led to improved outdoor air quality.[5] This action plan put forward ten practical measures to effectively reduce the outdoor particulate matter, and set specific concentration goals for $PM_{2·5}$ and PM_{10}. The emphasis on outdoor $PM_{2·5}$ control has led to the significant decrease in outdoor $PM_{2·5}$ concentrations in the past decade, as it decreased the contribution of outdoor origin to indoor $PM_{2·5}$ exposure. Also, in the past two decades, household solid fuels for cooking have been gradually replaced by natural gas or electric stoves. Solid fuels for heating, such as coal in northern China, especially in rural areas, have been gradually replaced by electrical devices, such as electric heat pumps. These improvements reduce the $PM_{2·5}$ of indoor origin. Additionally, indoor exposure to most of the other IAPs has also declined. This decline can date back to 2001, when the State Council of China started to emphasise the importance of indoor air pollution reduction. The Standard for Indoor Environment Pollution Control of Civil Building Engineering (GB 50325) was put forward in 2001 and the Indoor Air Quality Standard (GB/T 18883) in 2002. The 2002 standard has played a fundamental role in indoor air quality control in China, regulating the indoor concentrations of ozone, nitrogen dioxide, sulphur dioxide, carbon monoxide, formaldehyde, benzene, toluene, radon, and other IAPs. Meanwhile, a series of national standards for indoor decorating and refurbishing materials was issued in China in 2001, to control the emissions of IAPs, such as standards for wood-based panels (GB 18580), architectural wall coatings (GB 18582), and wood-based furniture (GB 18584). These standards have also significantly helped reduce IAP exposures.

This study can help identify which IAPs China should prioritise for indoor environments in the near future. From 2000 to 2017, the attributable DALY of $PM_{2·5}$ was at least one order of magnitude higher than that of any other IAP and accounted for more than 80% of the total attributable burden. Although the burden attributable to $PM_{2·5}$ has been reduced by 18·4% during these past 17 years, the control of outdoor and indoor $PM_{2·5}$ to a safer level is still a worthy and valuable target for China in the long term. Carbon monoxide and nitrogen dioxide remain in the top five due to their associations with cardiovascular diseases, lung cancer, and other health outcomes. However, these two IAPs, along with sulphur dioxide and ozone, are commonly monitored in the outdoor air but neglected in the indoor environment because researchers tend to focus more on indoor VOCs caused by decoration and refurbishment. In this study, we did not collect enough data on indoor measurements of some of these compounds. Thus, the indoor origins of nitrogen dioxide, sulphur dioxide, and ozone were not accounted for, so the health effects of these compounds are likely to be underestimated, especially for nitrogen dioxide. Hu and Zhao[48] developed a source-specific exposure model on the basis of the source emission rate and found that indoor origins strongly contribute to indoor exposure to nitrogen dioxide. Contribution from cooking is strong, but contribution from smoking is negligible. More field measurements and more rigorous control of these inorganic IAPs should be done in the future. Radon was the only IAP whose attributable burden of disease increased steadily from 2000 to 2017, and it could become the dominant problem in indoor air quality as the disease burden of other IAPs decrease. Therefore, strategies to reduce radon concentration should be a priority. As for VOCs, benzene remains in the top five, even though the benzene-attributable DALYs have decreased drastically. The attributable DALYs of formaldehyde have slowly increased since 2013 and ranked in the top five in many provinces. As the associations between benzene or formaldehyde and more adverse health outcomes remain unknown, the corresponding attributable burden might also be underestimated due to omission of such potential health effects. Therefore, the rankings of these two VOCs might be higher, and their indoor concentrations should be further reduced. In addition, although indoor butadiene was only measured in Tianjin in 2008 and Shaanxi in 2016,[49,50] our meta-analysis shows its significant association with leukaemia.[23] The attributable burden of disease for butadiene reached 140 DALYs per 100 000 in Tianjin in 2008, ranking fourth, and 130 DALYs per 100 000 in Shaanxi in 2016, ranking third, suggesting that butadiene exposure cannot be overlooked in the future and that measurement of indoor butadiene concentrations should be included in future monitoring surveys in China. Finally, the provincial-level ranking reminds us that different provinces had different priority problems of indoor air pollution, which need to be tackled by different control strategies. Based on the above analyses, some recommendations for future prevention and control of indoor air pollution have been made (appendix 1 p 42).

There are some limitations in this study. First, there is potential bias in the exposure assessment. Compared with Europe and the USA, China has not had systematic and extensive field measurements of IAPs in the past few decades. The currently available field measurements of IAPs in China also do not have the standard guidance or protocol of sampling and testing, so the sample representativeness and comparability might not be optimal. With respect to building types, this study used indoor concentrations only in residences due to a scarcity of data for offices and schools, where the indoor concentrations might be quite different due to different fuel combustion, decoration, ventilation strategies, and other reasons. With respect to regional differences, the available studies mostly focused on urban areas, so the exposure levels for IAPs in rural areas are not well represented. With respect to measurement methods, a large proportion of field studies reported their measurement methods following local sampling standards, but we cannot be sure that all data were generated by the same standard methods. With respect to sampling duration, the annual exposure levels were estimated on the basis of the short-term measurement data (ie, daily or hourly mean concentrations) in different seasons across different years. These data were not equal to the annual levels based on the actual long-term field measurements, which were unlikely to be available for decades since it is time-consuming, expensive, and usually refused by residents. We should cautiously show the estimated data but even so, they provide us valuable references. Future studies can use newly emerging methods to measure exposure (eg, low-cost sensors) for large-scale, long-term exposure monitoring to improve reliability of the estimates.

Second, there are some limitations on the exposure–response relationships. Except for $PM_{2\cdot5}$, exposure–response relationships for most IAPs were based on case-control or cross-sectional studies due to a scarcity of cohort studies, so evidence for causal relationships is scarce. Associations between many health outcomes and IAPs are unknown, especially for VOCs and semivolatile organic compounds, such that their attributable burden of disease is most likely underestimated. The widely-used exposure–response relationships of $PM_{2\cdot5}$ from GBD combined evidence from ambient $PM_{2\cdot5}$ pollution, household use of solid fuels, and second-hand smoke from the perspective of mass concentration. The health effects of indoor originating $PM_{2\cdot5}$ can be different from those of outdoor originating $PM_{2\cdot5}$, due to the difference in chemical components and size distribution of the particles. However, there is an absence of widely agreed exposure–response relationship purely based on particles of indoor sources. Also, this study used the IER model for $PM_{2\cdot5}$ provided by GBD 2019, rather than another favoured meta-regression Bayesian, regularised, trimmed model. Besides, due to a scarcity of data, the exposure–response relationships in the present study relied on non-Chinese global epidemiological studies and cannot evaluate possible ethnic differences. Future studies should include more databases, such as Embase, to enrich related evidence.

Third, current epidemiological studies have not considered IAP coexposures from common sources, which might lead to overestimation of DALYs attributable to a single IAP.

Fourth, as the total DALYs of various health outcomes for different age and gender groups at the province level are not available, the attributable burden of IAPs for different age and gender groups cannot be estimated, nor can susceptible subpopulations be identified. Tackling these problems would help improve and deepen the understanding of the burden of disease for IAPs in China in the future.

In conclusion, despite the improvements from 2000 to 2017, the burden of disease for IAPs in China still ranked third among all risk factors in 2017 and cost 3·45% of the GDP. The attributable burden of IAPs in China is also higher than that of IAPs in USA and European countries, and that of outdoor air pollution in China, suggesting its severity. Attributable burden for $PM_{2\cdot5}$, especially from indoor origins, has contributed the most to burden of disease in China. This study provides a foundation for determining the targeted IAPs in China's indoor air quality standards and estimating the benefits of control approaches.

Contributors

YZ, ZZh, FD, HK, CH, BZ, XZh, YS, HQ, JM, ChaS, XZe, WL[1], CM, and OH designed the framework of the CBD–IAP project in China. NL, WL[1], ZZh, XG, ZB, and YZ further developed the analysis plan. NL, WL[1], YL, XG, LF, ZC, HT, SH, MP, WL[2], XH, KG, FR, WZ, ChuS, ChaS, ZZo, HL, and ZB did the systematic review, meta analysis, and preliminary data analysis. NL and YL applied statistical models for the data analysis of the exposure level and attributable burden of disease. NL wrote the manuscript under the guidance of WL[1], HK, ZZh, and YZ, and editing was done by LBW. All authors reviewed the study findings and the manuscript. NL and YL had full access to and verified all the data. HK, ZZh, and YZ were responsible for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

The main input datasets are available in appendix 2. The main results for the burden of disease and the corresponding financial costs attributable to ten IAPs in 31 provinces in China from 2000 to 2017 are available in appendix 3. The baseline burden of disease is available from http://ghdx.healthdata.org/gbd-results-tool. For more information on study protocols and for other datasets, please contact a corresponding author.

Acknowledgments

This research was funded by the National Key Research and Development Program of China (grant number 2017YFC0702700) and the National Natural Science Foundation of China (grant numbers 51976106 and 92043301). We are also grateful to Chen Wang and Zaiying Zhou from the Department of Industrial Engineering, Tsinghua University, Beijing, China, for their advice in data analysis. LBW is an independent researcher.

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