Restrictions on indoor and outdoor NO₂ emissions to reduce disease burden for pediatric asthma in China: A modeling study

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Summary

Background Epidemiological studies have reported the associations between nitrogen dioxide (NO₂) and pediatric asthma incidence, but unable to ascertain indoor NO₂ sources. We estimated the pediatric asthma incidence and corresponding economic losses attributable to NO₂ from indoor and outdoor sources in urban areas in China.

Methods Exposure to NO₂ from indoor and outdoor sources in 2019 were estimated separately with a source-specific model validated by measurements from different studies, and NO₂ exposure after restricting emissions indoor (from cooking or second-hand smoking) and outdoor (to meet WHO interim targets and air quality guideline) were projected. Disease burden of NO₂-attributable new-onset pediatric asthma were estimated based on NO₂ exposure, concentration-response function from a meta-analysis, and number of pediatric asthma populations. Economic impacts were estimated based on the costs of pediatric asthma in China.

Findings In China, NO₂ is associated with an estimated 637,000 (95% uncertainty interval 358,000–851,000) new pediatric asthma cases and 1,358 million (674–2145) RMB economic losses in urban areas in 2019. 296,000 (222,000–523,000) new pediatric asthma cases would be prevented each year by restricting NO₂ emissions indoor, i.e., switching from using gas stoves to electric stoves for cooking. 393,000 (119,000–463,000) new pediatric asthma cases would be prevented each year when outdoor air meets the air quality guideline for NO₂ (< 10 µg/m³).

Interpretation Restricting both indoor and outdoor NO₂ emissions are necessary to reduce pediatric asthma incidence in urban areas. NO₂ restrictions may be achieved through clean energy transition and adoption of climate change mitigation activities.

Introduction Air pollution is one of the top five risk factors for disease burden around the world according to the latest estimates from the Global Burden of Diseases, Injuries, and Risk Factors Study. Reducing disease burden attributed to air pollution is also a key indicator of the United Nations Sustainable Development Goal 3, to ensure healthy lives and promote well-being for all at all ages, as well as Goal 11 for sustainable cities and communities. Long-term exposure to high levels of air pollutions would lead to a variety of non-communicable diseases, particularly for children. Asthma is the most common chronic disease among children worldwide, with rising incidences in developing economies. While air pollution control measures have been haphazardly effective in controlling particulate matter exposures, anthropogenic sources of NO₂ mainly derived from on-road and non-road transportation tailpipe emissions may not correlate with particulate matter control measures. There are recent advancements in our understanding of NO₂ and onset of allergic diseases. Epidemiological studies have provided evidences of the associations between air pollutants and new-onset
...disease burden attributable to exposure to NO2 from indoor and outdoor sources separately; and comparing the health benefits of restricting indoor and outdoor NO2 emissions. We focused on urban areas in China, where facing serious air pollution of NO2 both indoor and outdoor. NO2 is estimated to attribute to hundreds of thousands of pediatric asthma cases in Chinese urban areas in 2019, with significantly contributions of NO2 from both indoor and outdoor sources. The cost associated with asthma of each child with asthma is equivalent to about 5% per capita disposable income in China. The reduction of pediatric asthma cases by restricting indoor NO2 emissions, i.e., switching from using gas stoves to electric stoves for cooking, is comparable to the burden reduction when outdoor air meets WHO air quality guideline issued in 2021.

Implications of the available evidence

This study demonstrates the importance of restricting indoor and outdoor NO2 emissions to reduce the disease burden attributable to NO2, typically in pediatric asthma incidence. The measurements to restrict indoor and outdoor NO2 emissions, i.e., switching from using gas stoves to electric stoves for cooking and switching the traditional fossil energy vehicles to new energy vehicles, reflect the demand to adjust the energy consumption structure. These actions may be a win–win opportunity for countries facing both climate change and air pollution challenges.

asthma in children. The evidence for other air pollutants (e.g., fine particulate matter) is mixed except for nitrogen dioxide (NO2). Epidemiological studies in Europe, North America, Japan, China, Korea have consistently shown a significant positive association between NO2 and pediatric asthma incidence. Achakulwisut et al. have linked NO2 with about 4.0 million annual number of new pediatric asthma cases in 194 countries. And China has been estimated to have the most considerable national burdens of NO2-attributable pediatric asthma, with 760,000 new cases per year and more than 50% of the cases occurring in urban areas.

The World Health Organization (WHO) issued new Air Quality Guidelines (AQG) on Sept 22, 2021 (WHO AQG 2021), setting AQG for NO2 of annual averaged concentration of 10 μg/m3 and applied for both indoor and outdoor air. NO2 is usually thought of as a proxy of traffic-related air pollution. Whereas there are also evident sources of NO2 indoor, i.e., NO2 produced during combustion processes indoors, such as cooking (i.e., gas combustion) and smoking (i.e., tobacco combustion), even in areas without using solid fuels and kerosene. Urban areas are typical areas with heavy traffic and do not use solid fuels and kerosene, especially in urban China where the population density is extremely high. Our latest study figured out indoor sources contribute ~33% to human exposure to NO2 in Chinese urban. Despite the importance of indoor sources in NO2 exposure, to the best of our knowledge, no studies focus on the disease burden of NO2 from indoor sources, let alone the policies to restrict NO2 emitted indoors. This is unique compared with those previous studies focused on outdoor NO2. The formulation of policies to restrict the NO2 produced indoor, such as implementing a smoking ban and using electric stoves for cooking, may well be an essential initiative to reduce the disease burden attributable to NO2 exposure.

In this study, we estimated the number of pediatric asthma cases and corresponding economic losses attributable to exposure to NO2 from indoor and outdoor sources in Chinese urban areas in 2019. We further projected and compared the health benefits and corresponding economic benefits of policies on restricting the NO2 emissions indoor and outdoor.

Methods

Overview

We first generated the concentration of children exposure to NO2 from indoor and outdoor sources in urban areas in China in 2019 from a previous modeling study (boys and girls in 6 age groups, i.e., 0–0·5 y, 0·5–1 y, 1·2 y, 3–6 y, 7–11 y, 12–17 y, from 330 Chinese cities). We estimated the NO2 exposure after restricting NO2 emissions from indoor and outdoor sources. We then explored pediatric asthma incidence attributable to NO2 from indoor and outdoor sources for urban areas in China in 2019. We projected the reduction of pediatric asthma incidence after restrictions on NO2 emissions. We also estimated the economic burden associated with NO2-attributable pediatric asthma incidence with the
cost of illness methods. The methodology framework is shown in Figure 1. The uncertainty interval (UI) of the results was obtained by Monte Carlo method.

Exposure to NO₂ from different sources in 2019

For human exposure to outdoor sources, it is the sum of exposure to outdoor originated NO₂ indoor when people stay indoors and exposure to outdoor NO₂ directly when people stay outdoor. Human exposure to indoor sources is the exposure to NO₂ emitted from gas combustion during cooking and tobacco combustion during smoking. The concentration of NO₂ exposure is defined as the average concentration of NO₂ in the air people breathe during the studied period, reporting in μg/m³. We estimated the concentration of human exposure to NO₂ from indoor and outdoor sources in Chinese urban areas in 2019 based on a validated source-specific model in our previous study. The model and its validation were detailed in the appendix (Note S1 and Figure S1).

The annual average concentration of human exposure to NO₂ from indoor and outdoor sources for children of 6 age groups (i.e., 0−0.5, 0.5−1, 1-2, 3−6, 7−11, 12−17 years old) and two genders (boys and girls) and exposure to second-hand smoke or not (from smoking households) in urban areas in 330 Chinese cities in 2019 were calculated with the following equations:

\[ C_{\text{ambient}} = \frac{C_{\text{cooking}} + C_{\text{ambient}} + P_{\text{SHS}} \times C_{\text{SHS}}}{1 + P_{\text{SHS}} \times C_{\text{SHS}}} \] (2)

\[ P_{\text{ambient}} = \frac{C_{\text{ambient}}}{C_{\text{cooking}} + C_{\text{ambient}} + P_{\text{SHS}} \times C_{\text{SHS}}} \] (3)

\[ P_{\text{SHS}} = \frac{P_{\text{SHS}} \times C_{\text{SHS}}}{C_{\text{cooking}} + C_{\text{ambient}} + P_{\text{SHS}} \times C_{\text{SHS}}} \] (4)

PS is the proportion of the contribution of different sources in NO₂ exposure, the subscripts ambient, cooking and SHS of PS are the outdoor sources, cooking, and second-hand smoke. \( C_{\text{ambient}}, C_{\text{cooking}}, \) and \( C_{\text{SHS}} \) are the mean of \( C_{\text{ambient}}, C_{\text{cooking}}, \) and \( C_{\text{SHS}} \), respectively. \( P_{\text{SHS}} \) is the proportion of the population exposed to second-hand smoke. The details of calculation of \( P_{\text{SHS}} \) were provided in the appendix (Note S2). The value of PS in 2019 were shown in appendix (Table S1).

NO₂ exposure after restrictions

The restrictions on indoor and outdoor NO₂ emissions included a smoking ban, switching from using a gas stove to electric stove for cooking, and reducing NO₂ emitted outdoor. To see the scope for health benefits from these policies, we projected the scenarios where these policies were 100% achieved (Table S1 in appendix):

- Smoking ban (SB): no people smoking, to reduce the NO₂ produced by tobacco combustion during smoking (\( P_{\text{SHS}}=0; C_{\text{cooking}} \) and \( C_{\text{ambient}} \) were equal to that in 2019);
- Switching from using a gas stove to electric stove for cooking (EC): all residents using electric stove for cooking in Chinese urban areas, to reduce the NO₂ produced by gas combustion during cooking (\( C_{\text{cooking}}=0; C_{\text{smoking}} \) and \( C_{\text{ambient}} \) were equal to that in 2019);
- Reducing NO₂ emitted outdoor: the outdoor air meets the WHO interim targets (IT) and AQG for annual NO₂ concentration issued in 2021 (\( C_{\text{cooking}} \) and \( C_{\text{smoking}} \) were equal to that in 2019). The \( C_{\text{ambient}} \) when IT1, IT2, IT3 and AQG were calculated by

\[ C_{\text{ambient}} = \left\{ \begin{array}{ll}
C_{\text{ambient}} \text{ in 2019} & \text{for Outdoor concentration in 2019 ≤ Target} \\
\text{Target} \times f_{\text{exp}} & \text{for Outdoor concentration in 2019 > Target}
\end{array} \right. \]

in which Target is the target concentration of NO₂ outdoor, and it is 40 μg/m³ (IT1), 30 μg/m³ (IT2), 20 μg/m³ (IT3), or 10 μg/m³ (AQG) in this study. \( f_{\text{exp}} \) is the exposure factor. When outdoor NO₂ enters the indoor environment, some of the NO₂ will be removed by indoor surfaces due to deposition or chemical reaction, resulting in a lower concentration of outdoor-originated NO₂ in indoor environment compared with the concentration of NO₂ outdoor. Besides, there exist variations of outdoor
Figure 1. Methodology framework.
activities, respiratory rate, building ventilation and indoor activities between different populations. $f_{exp}$ is a parameter to modify human exposure to ambient NO$_2$ considering building ventilation, air exchange rate between indoor and outdoor environments, indoor surface removal due to deposition or chemical reaction, duration of outdoor activities and respiratory rate for different populations. $f_{exp}$ is used in this study and they were estimated and verified in our previous study (Table S3 in appendix).

In Eq. (5), we assumed the concentration of ambient NO$_2$ will remain the same as that in 2019 for areas where outdoor concentration in 2019 could meet the target. The study by Shi et al. indicate the rural-to-urban migration may increase the emissions of NO$_2$ outdoor in urban areas in China, resulting in extra environmental pressure. Considering the combining effect of other anthropogenic emission reductions, we think those areas may be some insensitive and thus our assumption is reasonable.

Concentration-response relationships

The risks of pediatric asthma associated with long-term exposure to NO$_2$ have been described using concentration-response relationships. Khreis et al. reviewed 41 studies published between 1999 and 2016 (20 studies from Europe, 11 from North America, five from Japan, three from China, one from South Korea, and one from Taiwan) to identify meta-analyses of epidemiological studies on ambient NO$_2$ and pediatric asthma. Following their approach, relative risks ($RR$) of pediatric asthma incidence attributable to ambient NO$_2$ were determined using the following equation:

$$RR = \begin{cases} \frac{1}{C - LC} & \text{for } C \leq LC \\ \frac{RR_c}{\Delta C} & \text{for } C > LC \end{cases}$$

(6)

where $RR$ is the relative risk, representing the ratio of the probability of developing asthma for children exposed to NO$_2$ to the probability of developing pediatric asthma for children in a comparison group. A comparison group was the group exposed to NO$_2$ at the low-concentration threshold ($LC$), below which there is no risk of pediatric asthma development. $RR_c$ represents the change in relative risk for per unit concentration increase ($\Delta C$). $C$ is the concentration of ambient NO$_2$. Khreis and colleagues reported an RR of 1.26 per 10 ppb ambient NO$_2$ (95% uncertainty interval [UI] 1.10–1.37) and assumed LC at 2 ppb (0–5) (ppb NO$_2$ = 0.487 μg/m$^3$ NO$_2$).

Theoretically, $RR$ should be related to the NO$_2$ exposure, i.e., the concentration of exposure to NO$_2$ from both indoor and outdoor sources, as opposed to ambient concentration. So we multiply the reciprocal of the exposure factor ($1/f_{exp}$) by the annual average concentration of human exposure to NO$_2$ ($C_{exp}$) to obtain the equivalent ambient concentration. Therefore, we related $RR$ to the concentrations of NO$_2$ exposure using the following equation:

$$RR = \begin{cases} \frac{1}{C_{exp}/f_{exp} - LC} & \text{for } C \leq LC \\ \frac{RR_c}{\Delta C} & \text{for } C > LC \end{cases}$$

(7)

$NO_2$-attributable pediatric asthma incidence

We estimated the number of new-onset pediatric asthma cases attributable to long-term exposure to NO$_2$ from outdoor source, cooking and second-hand smoke in Chinese urban areas in 2019, and we further projected the reduction of the number of new pediatric asthma cases in the scenarios after restricting NO$_2$ emissions.

The number of new pediatric asthma cases attributable to human exposure to NO$_2$ from specific sources ($AN_s$) was determined by the proportion of contribution of specific sources in NO$_2$ exposure ($PS_s$), the population attributable fraction of NO$_2$ exposure and incidences of pediatric asthma ($PAF_s$), the incidence of pediatric asthma ($IR_s$), and the population of children ($N_s$). $PAF_s$ refers to the proportion of incidence in a population that can be attributed to a certain risk factor, i.e., NO$_2$ exposure in this study. The new pediatric asthma cases attributable to NO$_2$ exposure from specific sources in Chinese urban areas were calculated with the following equation as that applied in the Global Burden of Diseases, Injuries, and Risk Factors Study in 2019:

$$AN_s = \sum_g (PS_s \times PAF_g \times IR_g \times N_g)$$

(8)

where the subscript $s$ represents the source of PM$_{2.5}$ and it is ambient, cooking, or SHS in this study; the subscript $g$ represents the population with specific age and sex in specific city. The group-specific population size of children ($N$) in Chinese urban areas in 2019 was calculated based on the urban population of each city in 2019 (Table S4 in appendix) and the age and gender composition of children of the population of each province (Table S5 in appendix). The age-, sex- and province-specific incidence of pediatric asthma ($IR$) for residents in Chinese urban areas in 2019 (Table S4 in appendix) was calculated using the age- and sex-specific incidence of pediatric asthma in China in 2019 and the ratio of provincial and regional incidence of pediatric asthma. PAF for the population $g$ was calculated by:

$$PAF_g = \frac{RR_g - 1}{RR_g}$$

(9)

$$RR_g = (1 - P_{SHSg}) \times RR_{g,non\text{-}smoking\ household} + P_{SHSg} \times RR_{g,smoking\ household}$$

(10)

where $RR_g$ is the average relative risk for the population $g$ in 2019, and $RR_{g,smoking\ household}$ and $RR_{g,non\text{-}smoking\ household}$ are the average $RR$ for
people from smoking and non-smoking households in the population $g$, $RR_{g,\text{smoking household}}$ in 2019 was calculated based on the annual average concentration of exposure to NO$_2$ ($C_{exp}$) for people from smoking households in 2019 and concentration-response relationship of long-term NO$_2$ exposure and incident of pediatric asthma (Eq. (7)). $RR_{g,\text{non-smoking household}}$ in 2019 was calculated based on $C_{exp}$ for people from non-smoking households in 2019 and Eq. (7). The value of $RR$ in 2019 were shown in appendix (Table S9).

The reductions of new pediatric asthma cases attributable to human exposure to NO$_2$ from specific sources ($RAN_{po}$) were calculated with the following equations:

$$RAN_{po} = \sum_{g} (PIF_{po,g} \times IR_{g} \times N_{g})$$  \hspace{1cm} (11)

$$PIF_{po,g} = \frac{RR_{g} - PIF_{po} \times RR_{g}}{1}$$  \hspace{1cm} (12)

where $PIF$ is potential impact fraction, referring to the proportion reduction in the incidence in a population when a certain risk factor change, i.e., human exposure to NO$_2$ in this study. $RR_{g}$ is the average relative risk for the population $g$ under the scenarios $po$ after restrictions on NO$_2$ emissions and $po$ is SB, EC, IT1, IT2, IT3 or AQG in this study. $RAN_{po,g}$ were calculated based on NO$_2$ exposure ($C_{exp}$) after restrictions and concentration-response relationships of long-term exposure to NO$_2$ and asthma incidence in children (Eq. (7)). The value of $RAN_{po}$ were provided in appendix (Table S9).

**Economic losses**

In this study, the cost of illness methods was applied to monetize the health effects of NO$_2$ from direct and indirect costs.$^{16}$ Direct costs include the direct costs of treatment and hospitalization related to pediatric asthma. Indirect costs include the reduction in the income due to absence from work for childcare. The total cost in 2019 or reduction of total cost after restrictions on NO$_2$ emissions ($Cost$) is defined as:

$$Cost = (Cost_d + GDP_p \times T) \times (ANorRAN)$$  \hspace{1cm} (13)

where $Cost_d$ is the per capita direct costs, $GDP_p$ is a daily average of per capita Gross Domestic Product, and $T$ is the per capita treatment and hospitalization days. The age- and sex-specific per capita directs cost and the per capita treatment and hospitalization days was from the China Medical Insurance Research Association database (Table S6 in appendix). The GDP$_p$ in 330 Chinese cities was from the China city statistical year book-2020 (Table S2 in appendix).

**Uncertainty analysis**

We applied a two-stage Monte Carlo simulation$^{20}$ to obtain the mean and 95% uncertainty interval (95% UI) of the new pediatric asthma cases attributable to NO$_2$ exposure and corresponding economic loss or benefits. The two stages reflected the intra-population variability distribution (human exposure to NO$_2$), and the uncertainty distribution (the concentration-response function, baseline pediatric asthma incidence, direct cost, and the treatment and hospitalization days), respectively. We first performed 2000 iterations at variability stage (i.e., human exposure to NO$_2$) and 1000 iterations at uncertainty stages (i.e., the concentration-response function) to obtain $2000 \times 1000$ RRs for each population, respectively. We averaged the variability stage to obtain 1000 population-level RRs, and further calculated 1000 population-level $PAF$ and $PIF$. We further performed 1000 iterations for other uncertainties (i.e., base line pediatric asthma incidence, directs cost, and the treatment and hospitalization days) to obtain new pediatric asthma cases attributable to NO$_2$ and corresponding economic loss or benefits, and reported their mean and 95% UI, i.e., the 2.5th–97.5th percentile of their values in the 1000 uncertainty runs. Finally, we tested the robustness of the model by performing 250 times of Monte Carlo simulations and calculating the error of those 250 simulations. The result showed that the error was within 5%, indicating $2000 \times 1000$ runs were sufficient to quantify the uncertainty of the projected results.

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

**Results**

**The pediatric asthma incidence attributable to NO$_2$ exposure in 2019**

Long-term exposure to NO$_2$ is associated with 637 thousand (95% UI 338–851) new pediatric asthma cases in Chinese urban areas in 2019, equating to 360 (202–482) per 100 000 children (less than 18 years old). NO$_2$ from indoor and outdoor sources is associated with 166 thousand (91–223) and 471 thousand (266–628) new pediatric asthma cases in urban areas in China in 2019, respectively, accounting for 74% and 26% of pediatric asthma cases attributable to NO$_2$ exposure (Figure 2a). Cooking is the most important indoor source of NO$_2$ in urban areas, accounting for 25% (161 thousand (88–216) cases) of pediatric asthma cases attributable to NO$_2$ exposure.

Regionally, the larger burden of new pediatric asthma cases associated with NO$_2$ is found in areas with higher population density, i.e., cities in eastern China, especially
Figure 2. Estimates of number of new pediatric asthma cases attributable to nitrogen dioxide (NO₂) in urban areas in 2019 (a) number of new pediatric asthma cases from different sources of NO₂ in 2019 (b) number of new pediatric asthma cases in 330 Chinese cities, and (c) percentage of NO₂-attributable pediatric asthma incidence from indoor sources to total NO₂-attributable pediatric asthma incidence in 330 Chinese cities. SHS, second hand smoke.
municipalities and provincial capitals (Figure 2b). Shanghai (a municipality), Chongqing (a municipality), and Zhengzhou (the capital of Henan province) are the top three cities with the greatest number of NO2-attributable pediatric asthma cases, with 26.1 thousand (15.1—36.8), 24.2 thousand (13.8—35.6) and 14.1 thousand (9.1—18.4), respectively. Figure 2c shows the percentage of NO2-attributable pediatric asthma incidence from indoor sources to total NO2-attributable pediatric asthma incidence (hereinafter referred to “the percentage of contribution from indoor sources”) in 330 Chinese cities. The percentage of contribution from indoor sources is higher in cities in the north and northwest of China, where people open their windows less frequently and spend less time outdoors. The top three cities with the highest percentage of contribution from indoor sources are Hegang (67%), Yichun (65%), and Heihe (64%) in Heilongjiang province.

In general, the incidence of pediatric asthma is highest in the youngest age group and decreases with age, and it is higher in boys than girls. Our estimation support this point (Table S10 in appendix), with the largest number of new asthma cases attributable to NO2 exposure in the youngest age group (less than six years old, 386 thousand (220—521) cases) and a higher number of new cases for boys (385 thousand (212—522) cases) than girls (252 thousand (142—388) cases). However, the number of new asthma cases attributable to NO2
exposure is not significantly different between the age groups 7–11 years old and 12–17 years old (7–11 years old, 128 thousand (72–171) cases; 12–17 years old, 123 thousand (62–167) cases). The percentage of contribution from indoor sources is higher for children aged 12–17 years old (31%) than other age groups (less than six years old, 25%; 7–11 years old, 26%), and it is higher for boys (28%) than girls (26).

The health benefits of policies on restricting NO₂ emissions
The reduction of the burden of new pediatric asthma associated with NO₂ after restricting the NO₂ emissions is shown in Figure 3a. Outdoor air meeting the WHO AQG 2021 is projected to be the scenarios with the largest reduction of new pediatric asthma cases, with reductions of 62% (393 thousand (222–463) cases) of new pediatric asthma cases attributable to NO₂ exposure in 2019. The burden reduction of new pediatric asthma cases by switching from using a gas stove to the electric stove for cooking (EC) is on a par with restricting the NO₂ emissions in outdoor air to meet WHO interim targets 3 (IT₃), with reductions of 46% (296 thousand (119–403) cases) and 44% (278 thousand (148–382) cases) of new pediatric asthma cases attributable to NO₂ exposure in 2019. The smoking ban has little effect on the number of pediatric asthma cases attributable to NO₂, with a reduction of 2% (16 thousand (2–44) cases). The percentage of reduction of NO₂-attributable pediatric asthma incidence after restricting the indoor and outdoor NO₂ emissions to total NO₂-attributable pediatric asthma incidence in 2019 in 330 Chinese cities are shown in Figure 3b and 3c, respectively. Pediatric asthma incidences are estimated to be reduced effectively by restrictions on outdoor NO₂ emissions in cities with high population density, such as cities in eastern China. While restrictions on indoor NO₂ emissions effectively reduce pediatric asthma incidences in most areas of China, especially in cities in northern China with more than 80% reductions of new pediatric asthma cases attributable to NO₂ exposure.

The economic losses associated with NO₂-related pediatric asthma
The economic burden of pediatric asthma is 2130 (1380–2870) RMB for each child with asthma, accounting for about 5% of per capita disposable income in China. The per capita cost of pediatric asthma is higher in cities with high per capita Gross Domestic Product, such as Shenzhen (4380 (2630–5060) RMB), Beijing (3620 (2220–4940) RMB), and Shanghai (3510 (2150–4740) RMB) (Figure S4). Pediatric asthma attributable to NO₂ is estimated to cause 1358 million (674–2145) RMB economic losses in Chinese urban areas in 2019. Shanghai was the city with the highest economic losses at 92.7 million (45.1–155.1) RMB. NO₂ from cooking, second-hand smoking, and outdoor source are associated with 323 million (161–513) RMB, 11 million (6–17) RMB, and 1024 million (505–1617) RMB economic losses (Table 1). The restrictions on indoor and outdoor NO₂ emissions in urban China would reduce the economic loss from pediatric asthma by up to 594 million (228–1052) and 867 million (427–1364) RMB, respectively (Table 1). Shanghai would be the city with the most reductions of economic loss from pediatric asthma under both restrictions on indoor and outdoor NO₂ emissions.

Discussion
Our results show that a large number of pediatric asthma cases in Chinese urban areas in 2019 were attributable to NO₂, with significant contributions from both indoor and outdoor sources. The cost of each child with asthma is equivalent to about 5% of per capita disposable income in China. The reduction of pediatric asthma cases and its corresponding economic losses by restricting indoor NO₂ emissions is comparable to the burden reduction when outdoor air meets WHO AQG

### Table 1: The economic losses due to pediatric asthma attributable to NO₂ in Chinese urban areas [mean (95% UI) in million RMB].

| Sources of NO₂ | In 2019 | Reductions after restrictions on NO₂ emissions |
|---------------|---------|-----------------------------------------------|
| **Outdoor**   |         |                                               |
|               | Total   | IT₁<sup>a</sup> | IT₂ | IT₃ | AQG<sup>b</sup> | EC<sup>c</sup> | SB<sup>d</sup> |
|               | 1024 (505, 1617) | 209 (79, 365) | 398 (177, 663) | 629 (297, 1011) | 867 (427, 1364) | 594 (228, 1052) | 42 (1, 114) |
| **Indoor**    |         |                                               |
|               | Total   |                                               |
|               | 1358 (674, 2145) |                                               |

<sup>a</sup> IT, the outdoor air meets the World Health Organization interim target for NO₂, IT₁ = 40 μg/m³, IT₂ = 50 μg/m³, IT₃ = 60 μg/m³;  
<sup>b</sup> AQG, the outdoor air meets the World Health Organization Air Quality Guideline for NO₂, AQG = 10 μg/m³;  
<sup>c</sup> EC, using electric stoves for cooking, under the condition of all residents using electric stoves for cooking in Chinese urban areas;  
<sup>d</sup> SB, smoking ban, under the condition of no people smoking.
2021 (i.e., the annual NO$_2$ concentration lower than 10 µg/m$^3$). The restrictions on indoor and outdoor NO$_2$ emissions are of the essence in reducing pediatric asthma incidence in urban China. The unique approach of this study is estimating the disease burden attributable to exposure to NO$_2$ from indoor and outdoor sources separately, and comparing the health benefits of restricting indoor and outdoor NO$_2$ emissions.

NO$_2$ is an oxidizing gas associated with oxidative stress in asthma morbidity. Studies have identified associations between NO$_2$ and increased airway responsiveness, airway inflammation, and enhanced responses to allergen. Two latest studies have shown NO$_2$-attributable new pediatric asthma cases at 4.0 million in 2015 and 1.9 million in 2019 globally. The incidence of new pediatric asthma associated with NO$_2$ exposure in China in both studies (260 (120–340) per 100 000 children in 2015 and about 129 per 100,000 children in 2019, respectively) are lower than that in our study (360 (202-482) per 100 000 children per year), but similar to the scenario when indoor sources of NO$_2$ were completely restricted in our study (194 (109–260) per 100 000 children per year). The biases between our results and those of previous studies reflects the serious impact of NO$_2$ from indoor source on the assessment of NO$_2$-attributable asthma incidence in children.

Air Pollution Prevention and Control Action Plan was implemented in China in 2013, aiming to reduce the concentration of ambient air pollutants. But the concentration of ambient NO$_2$ has not decreased significantly in recent years, with the annual average concentration only reduced by 7% from 29.3 g m$^{-3}$ in 2015 to 27.7 µg m$^{-3}$ in 2019. Ambient NO$_2$ is traffic-related air pollution associated with the combustion of gasoline and diesel in vehicles. Transportation contributes up to 80% of ambient NO$_2$ in urban areas. Population growth, extensive urbanization, and wealth creation have combined to create ever-increasing traffic volumes in urban areas in China, making it increasingly difficult to reduce ambient NO$_2$ pollution. Studies have shown that replacing the traditional fossil energy vehicles with new energy vehicles would lead to substantial reductions of ambient NO$_2$ (3-7 g/m$^3$) in most of China. General Office of the State Council of the People’s Republic of China issued the Development Plan for New Energy Vehicle Industry (2021–2035) on November 2, 2020, to increase the new energy vehicles quotas in total vehicle production, aiming at peaking fossil fuels consumption of land transport by 2030. This policy would bring benefits in terms of reduce ambient NO$_2$ concentrations in China.

Despite the policies on developing new energy vehicles, it might be decades before the ambient NO$_2$ meet the WHO AQG 2021. Prior to this time point, restricting NO$_2$ from indoor sources would reap health benefits efficiently, especially in reducing pediatric asthma incidence in Chinese urban areas. Switching from using a gas stove to the electric stove for cooking to reduce the NO$_2$ produced by gas combustion is a vital strategy to restrict NO$_2$ emissions indoors. With the popularity of induction cookers and ceramic cooktops in China in recent years, the acceptability of electric stoves in Chinese families has been increasing year by year. However, using gas stoves for cooking is still mainstream in households in Chinese urban areas. It is necessary to encourage the use of electric stoves for cooking in Chinese urban areas. The government may need to provide some preferential policies to increase the utilization rate of electric stoves. The increase in the utilization rate of electric stoves is accompanied by the increase in demand for electricity and a decrease in demand for gas in residence. The urban energy system needs to be adjusted accordingly to meet the new demand for energy.

The measures for restriction on NO$_2$ emissions from indoor and outdoor reflect the demand to adjust the energy consumption structure of residences and transportations in Chinese urban areas, respectively. Traditional energy consumption is accompanied by greenhouse gas emissions. China pledged to achieve the goal of cutting greenhouse gas emissions to net-zero by 2050 at the 2019 Climate Action Summit. Developing new energy and constructing new electrical power systems, including the power systems for transportation and residences, are important measures to achieve this goal. These actions may be a win-win opportunity for not only China but also other developing countries which are facing both climate change and air pollution challenges.

Several limitations exist in our approach. First, we applied the concentration-response function from a meta-analysis of studies in multiple countries around the world to estimate the NO$_2$-attributable burden of pediatric asthma incidence in urban areas. The relative risk from east Asia weighted 22.8% in the meta-analysis. Our sensitivity analysis using the pooled relative risk from studies in east Asia showed a low uncertainty (Figure S3 in appendix). It should be noted that NO$_2$ from indoor cooking is mixed with other air pollutants from burning oil, heating ingredient and stirring ingredient. Applying the coefficient of concentration-response function from ambient NO$_2$ for the indoor part may introduce some uncertainties. However, NO$_2$ is produced from gas combustion during cooking and it can be reduced by changing the type of energy to cook (i.e., switching from gas to electricity), and this is different from those pollutants produced from burning oil, heating ingredient or stirring ingredient. Therefore, other pollutants produced during cooking are not necessarily accompanied by the emission of NO$_2$. As our aim was to analyze the disease burden attributable to NO$_2$ itself, rather than the disease burden associated with all the air pollutants from cooking, the concentration-response function from ambient NO$_2$ is still applicable to this study. Secondly, we estimated exposure to NO$_2$ from two
main indoor sources, i.e., cooking and second-hand smoke. Another indoor source of NO₂, wall-mounted gas boiler, was not considered in this study. The wall-mounted gas boilers are equipped with enclosed combustors and exhaust ducts, which emit negligible NO₂ indoors compared to cooking and smoking. Due to central heating systems in northern China, the wall-mounted gas boilers were mainly used in families in southern China. Studies have shown the low usage of wall-mounted gas boilers in south China.⁵⁹ So the contribution of wall-mounted gas boiler to NO₂ exposure is too low to affect the incidence of NO₂-attributable pediatric asthma incidence in this study. Thirdly, we estimated the incidence of pediatric asthma associated with an annual average exposure of NO₂, while the time period of changes in NO₂ exposure may also influence the incidence and introduce uncertainties. Zhu et al. studied temporal variations of short-term associations between NO₂ concentrations and emergency department visits in Shanghai, China, in 2008–2019. They found the associations of emergency department visits and NO₂ remained stable over the study period.⁶⁰ This evidence means that effects on pediatric asthma incidence for NO₂ may also remain stable over time, and we expect more direct evidence in future studies.

Despite these limitations, our results showed that indoor and outdoor NO₂ emissions are associated with the disease burden of pediatric asthma incidence in households without using solid fuels and kerosene. The implementation of the policies on developing clean and alternative energy vehicles has brought hope for reducing ambient NO₂ pollution in the future. We call on individuals to use the electricity for cooking instead of gas to reduce exposure to NO₂ from indoor sources. The government may need to adjust the energy structure of residences to meet the new demand for energy. These measurements on restrictions of NO₂ emissions, i.e., developing new energy vehicles and switching from gas stove to electric stove, support clean energy consumption and aid in achieving climate change mitigation.

Contributors
Ying Hu designed the study and planned the analysis, performed the model analysis, analyzed the results, interpreted the results, validated and completed all figures, and drafted the manuscript. John S. Ji drafted and commented on the manuscript. Bin Zhao coordinated and supervised the project, designed the study and planned the analysis, analyzed the results, interpreted the results, and drafted the manuscript.

Data sharing statement
Datasets generated and/or analyzed in the present study are available from the corresponding author upon reasonable request.

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Declaration of interests
The authors declare no competing interests.

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Supplementary materials
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References
1. Murray CJL, Aravkin AY, Zheng P, et al. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1233–1424.
2. United Nations. Sustainable Development Goal 3: Ensure Healthy Lives and Promote Well-Being for all at all Ages. United Nations, https://www.un.org/sustainabledevelopment/health/ Accessed 6 January 2022.
3. World Health Organization. Asthma fact sheet. 2021. http://www.who.int/en/news-room/fact-sheets/detail/asthma Accessed 6 January 2022.
4. Khreis H, Kelly C, Tate J, Parshall R, Lucas K, Nieuwenhuijsen M. Exposure to traffic-related air pollution and risk of development of childhood asthma: a systematic review and meta-analysis. Environ Int. 2017;100:1–11.
5. Gazana J, Dillikar D, Mendy A, Forno E, Viesca E. Motor vehicle air pollution and asthma in children: a meta-analysis. Environ Res. 2012;117:46–45.
6. Achakulwisut P, Brauer M, Hystad P, Anenberg SC. Global, national, and urban burdens of paediatric asthma incidence attributable to ambient NO₂ pollution: estimates from global datasets. Lancet Planet Health. 2019;3(4):e166–78.
7. World Health Organization. WHO Global air Quality Guidelines. Particulate Matter (PM2.5 and PM10), Ozone, Nitrogen Dioxide, Sulfur Dioxide and Carbon Monoxide. World Health Organization; 2021. https://apps.who.intiris/bitstream/handle/10665/345259/9789240015442-eng.pdf.
8. Hu Y, Zhao B. Relationship between indoor and outdoor NO₂: a review. Build Environ. 2020;188:106909.
9. Hu Y, Zhao B. Indoor sources strongly contribute to exposure of Chinese urban residents to PM2.5 and NO₂. J Hazard Mater. 2022;416:127929.
10. Hu Y, Yao M, Liu Y, Zhao B. Personal exposure to ambient PM2.5, PM10, O₃, NO₂, and SO₂ for different populations in 31 Chinese provinces. Environ Int. 2020;144:106018.
11. Shi G, Lu X, Zhang H, et al. Air pollutant emissions induced by rural-to-urban migration during China’s urbanization (2005–2015). Environ Sci Ecotechnol. 2022;10:100166.
12. National Bureau of Statistics of China. Tabulation on the 2019 Population Census of the People’s Republic of China (in Chinese). National Bureau of Statistics of China; 2020. http://www.stats.gov.cn/tjsj/rdrk/mzdxgg/202005/tdk_165680.htm. Accessed 16 March 2022.
13. National Bureau of Statistics of China. Tabulation on the 2010 Population Census of the People’s Republic of China (in Chinese). Beijing: China Statistics Press; 2012. http://www.stats.gov.cn/tjsj/pcsj/rfcjk/jrck_left.htm.
14. Institute for Health Metrics and Evaluation. Global Burden of Disease Results Tool. Institute for Health Metrics and Evaluation; 2021. http://ghdx.healthdata.org/gbd-results-tool. Accessed 6 January 2022.
15 The National Cooperative group on Childhood Asthma. Institute of environmental health and related product safety, chinese center for disease control and prevention. Third nationwide survey of childhood asthma in urban areas of China. Chin J Pediatr. 2013;51:10.

16 Wu R, Dai H, Geng Y, et al. Economic impacts from PM2.5 pollution-related health effects: a case study in Shanghai. Environ Sci Technol. 2017;51(9):5035–5042.

17 Wu JT, Jit M, Zheng YM, et al. Routine pediatric enterovirus 71 vaccination in china: a cost-effectiveness analysis. PloS Med. 2016;13(5):e1001975.

18 Li D, Wang JY, Zhang ZY, et al. Effects of air pollution on hospital visits for pneumonia in children: a two-year analysis from China. Environ Sci Pollut Res. 2018;25(01):10049–10057.

19 Editorial board and editorial staff editorial board. China City Statistical Year Book-2020. China Statistics Press; 2020. https://data.cnki.net/yearbook/Single/N2021050059.

20 Zhou B, Zhao B. Population inhalation exposure to polycyclic aromatic hydrocarbons and associated lung cancer risk in Beijing region: contributions of indoor and outdoor sources and exposures. Atmos Environ. 2012;62:472–480.

21 Guarnieri M, Balmes JR. Outdoor air pollution and asthma. Lancet. 2014;383(9928):1581–1592.

22 Anenberg SC, Mohrle A, Goldberg DL, et al. Long-term trends in urban NO2 concentrations and associated paediatric asthma incidence: estimates from global datasets. Lancet Planet Health. 2022;6 (1):e49–e58.

23 Zhou W, Chen C, Lei L, Fu P, Sun Y. Temporal variations and spatial distributions of gaseous and particulate air pollutants and their health risks during 2015–2019 in China. Environ Pollut. 2021;272:116031.

24 Wang L, Chen X, Zhang Y, et al. Switching to electric vehicles can lead to significant reductions of PM2.5 and NO2 across China. One Earth. 2021;4(7):1037–1048.

25 The State Council of China. Guidelines on the Development of New Energy Vehicle Industry (2021–2035). The State Council of China; 2020. http://www.gov.cn/zhengce/content/2020-11/02/content_5556716.htm.

26 Chen KH, Lam KBH, Kurmi OP, et al. Trans-generational changes and rural-urban inequality in household fuel use and cookstove ventilation in China: a multi-region study of 0.5 million adults. Int J Hyg Environ Health. 2017;220(8):1170–1181.

27 Hale T. All hands on deck”: the Paris Agreement and nonstate climate action. Glob Environ Politics. 2016;16(3):12–22.

28 The State Council of China. Implementation scheme of promoting peak carbon dioxide emissions in China. The State Council of China; 2021. http://www.ggi.gov.cn/tzgg/202111/t20211115_335936.htm.

29 Zhang Y. Contrastive analysis of heating modes of residential buildings in southern Jiangsu. Energy Conserv. 2021;08(39):1004–7948.

30 Zhu Y, Peng L, Li H, Pan J, Kan H, Wang W. Temporal variations of short-term associations between PM10 and NO2 concentrations and emergency department visits in Shanghai, China 2008–2019. Ecotoxicol Environ Saf. 2022;229:110587.

24 www.thelancet.com Vol 24 Month July, 2022