Long-term trends in urban NO_2 concentrations and associated paediatric asthma incidence: estimates from global datasets

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Summary

Background Combustion-related nitrogen dioxide (NO_2) air pollution is associated with paediatric asthma incidence. We aimed to estimate global surface NO_2 concentrations consistent with the Global Burden of Disease study for 1990–2019 at a 1 km resolution, and the concentrations and attributable paediatric asthma incidence trends in 13 189 cities from 2000 to 2019.

Methods We scaled an existing annual average NO_2 concentration dataset for 2010–12 from a land use regression model (based on 5220 NO_2 monitors in 58 countries and land use variables) to other years using NO_2 column densities from satellite and reanalysis datasets. We applied these concentrations in an epidemiologically derived concentration–response function with population and baseline asthma rates to estimate NO_2-attributable paediatric asthma incidence.

Findings We estimated that 1·85 million (95% uncertainty interval [UI] 0·93–2·80 million) new paediatric asthma cases were attributable to NO_2 globally in 2019, two thirds of which occurred in urban areas (1·22 million cases; 95% UI 0·60–1·8 million). The proportion of paediatric asthma incidence that is attributable to NO_2 in urban areas declined from 19·8% (1·22 million attributable cases of 6·14 million total cases) in 2000 to 16·0% (1·24 million attributable cases of 7·73 million total cases) in 2019. Urban attributable fractions dropped in high-income countries (–41%), Latin America and the Caribbean (–16%), central Europe, eastern Europe, and central Asia (–13%), and southeast Asia, east Asia, and Oceania (–6%), and rose in south Asia (+23%), sub-Saharan Africa (+11%), and north Africa and the Middle East (+5%). The contribution of NO_2 concentrations, paediatric population size, and asthma incidence rates to the change in NO_2-attributable paediatric asthma incidence differed regionally.

Interpretation Despite improvements in some regions, combustion-related NO_2 pollution continues to be an important contributor to paediatric asthma incidence globally, particularly in cities. Mitigating air pollution should be a crucial element of public health strategies for children.

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Introduction

Nitrogen dioxide (NO_2), a component of nitrogen oxides, is a pervasive air pollutant that is a precursor to ground-level ozone and fine particulate matter ($PM_{2·5}$), the leading contributors to air pollution-related mortality.[1] Major anthropogenic NO_2 sources include on-road and non-road transportation tailpipe emissions (including heavy, medium, and light duty vehicles, shipping, and aviation), power plants, industrial manufacturing, and agriculture.[2–5] NO_2 is an effective tracer for anthropogenic fuel combustion generally and traffic specifically, especially in urban areas.[6–9] NO_2 concentration trends can be used to evaluate the effectiveness of air pollution regulations, as well as the effects of abrupt emission changes (eg, power plant closures, new oil and gas fields, and COVID-19 lockdowns).[10–14]

Beyond its role in $PM_{2·5}$ and ozone formation, NO_2 itself has been associated with adverse health outcomes including asthma exacerbation.[15,16] Epidemiological studies have also found associations between transportation-related air pollutants and new onset asthma in children.[17,18] Toxicological and gene environment research indicates that transportation-related air pollutants cause airway inflammation and remodelling due to oxidative stress, resulting in asthma development in some individuals.[19] Epidemiological studies are generally consistent in their finding that NO_2 is significantly associated with paediatric asthma incidence, whereas the evidence for other transportation-related air pollutants (eg, $PM_{2·5}$) is more mixed.[17,18] Although the putative agent causing asthma in the traffic-related air pollution mixture is unknown, NO_2 could serve as a surrogate for other pollutants causing observed health effects. Previous health impact assessments have linked NO_2 with approximately 13% of the global paediatric asthma burden, and up to approximately 50% in the most populated 250 cities worldwide.[19,20]

Emission of nitrogen oxides and NO_2 concentrations have changed substantially in response to socioeconomic

Research in context

Evidence before this study

We searched PubMed and Google Scholar databases for studies published in English from the database inception until March 11, 2021, using the search terms ("NO_2" OR "nitrogen dioxide") AND "asthma" AND "trends". Previous studies have reported epidemiological analyses linking changes in asthma incidence to changes in nitrogen dioxide (NO_2) or have assessed long-term trends in NO_2 concentrations in some countries or world regions. However, these studies provide little information about how NO_2 concentrations are changing in urban areas all around the world, and the influence those changes have on paediatric asthma incidence. An earlier study published in 2019 showed that more than 4 million new paediatric asthma cases, representing approximately 13% of all paediatric asthma incidence worldwide in 2015, could be attributed to NO_2 pollution. Understanding temporal trends in NO_2-attributable paediatric asthma incidence could help to inform asthma and air pollution mitigation strategies.

Added value of this study

We show that urban areas have higher NO_2 concentrations and disease burdens compared with rural areas, with 16·4% of paediatric asthma incidence in urban areas in 2019 estimated to be attributable to NO_2 pollution. We also find that the proportion of paediatric asthma incidence that is attributable to NO_2 declined in the high-income countries, Latin America and the Caribbean, and central Europe, eastern Europe, and central Asia from 2000 to 2019, and increased in the rest of the world, particularly in south Asia and sub-Saharan Africa. In doing this study, we produced the most spatially resolved (1 km × 1 km) long-term (1990–2019) dataset of surface NO_2 concentrations, which is compatible with the 2019 Global Burden of Disease Study and is now publicly available. Our study also shows the usefulness of satellite remote sensing for environmental and public health surveillance in urban areas worldwide.

Implications of all the available evidence

Current concentrations of NO_2 contribute substantially to paediatric asthma incidence, particularly in cities. Mitigating air pollution should be a crucial element of children's public health strategies.

changes and regulation, even before the large-scale activity changes during the COVID-19 pandemic.[21–25] In the USA, average NO_2 concentrations dropped by approximately 50% from the 1980s to the 2010s,[26] with larger drops near major roadways[26] and point sources.[10] In the last two decades, nitrogen oxide emissions in the USA fell by 3–6% per year as vehicles became more fuel efficient and cleaner and power plants shifted from coal to relatively cleaner fuels (eg, natural gas).[11,27,28] NO_2 concentrations have also decreased in Europe, although more slowly.[29,30] In contrast, NO_2 has increased in India,[31] the Middle East,[32] and eastern Europe.[23] In China, nitrogen oxide emissions peaked around 2011 and 2012 and subsequently declined.[33–35]

NO_2 pollution is a paediatric health challenge in cities, driven by higher population growth, particularly in Asia and Africa where NO_2 concentrations have risen since 2000, and where there are higher asthma rates in cities compared with national averages.[36] Previous research on NO_2 temporal trends has focused on small subsets of cities and not considered its effects on health, precluding globally consistent comparisons of trends in NO_2 concentrations and the associated health burdens. The global coverage and the long continuous record of satellite remote sensing since the 1990s makes it possible to track NO_2 concentrations globally.[37–40] Additionally, the high spatial resolution of current satellites can capture NO_2 variation at urban and intra-urban scales,[41,42] although instrument performance has degraded by 3–8% between 2005 and 2016.[43]

Here we aimed to investigate the long-term trends of annual average NO_2 concentrations and associated paediatric asthma burdens in 13 189 urban areas over the past two decades globally.

Methods

Overview

We first generated a new dataset of the annual average NO_2 concentration of the gridded global surface from 1990 to 2019 that is compatible with the spatiotemporal coverage of the Global Burden of Disease (GBD) 2019 study.[1] We then explored trends in NO_2 concentrations and attributable paediatric asthma incidence for urban areas from 2000 to 2019, for which the estimated concentrations have a greater certainty because of available ground monitoring. Finally, we deconstructed the drivers of these trends to explore the influence of NO_2 concentrations versus demographic changes. We integrated global environmental and demographic datasets from different sources to generate new estimates of surface NO_2 concentrations globally and NO_2-attributable paediatric asthma incidence in cities. The analysis was done in Python (version 3.6.7).

Globally gridded NO_2 concentrations

We generated a new dataset of surface annual average NO_2 concentrations at 0·0083° (~1 km^2) resolution in 5-year increments from 1990 to 2010 and annually from 2010 to 2019, consistent with the years used in the unpublished GBD 2020 analysis. We used an existing global NO_2 concentration dataset (2010–12 average) at a 100 m resolution from a land use regression (LUR) model described by Larkin and colleagues[44] and made adjustments to correct for a high bias in rural areas and

to scale concentrations to additional years (appendix p 8). A full description of the methods and data sources used to construct the concentration dataset is in the appendix (pp 1–3).

For the base year 2011, we used the Larkin and colleagues[44] LUR estimates directly in all grid cells categorised as urban according to the Global Human Settlement Model grid[45] or that included major roadways. The LUR used annual measurements from 5220 air monitors in 58 countries (mostly in urban areas of Europe, North America, and Asia) with inputs from road networks, other land use variables, and satellite NO_2 column observations. Globally, the model captured 54% of NO_2 variation, with a mean absolute error of 3·7 parts per billion (ppb). Model performance differed regionally: the coefficient of determination (R^2) varied from 0·42 in Africa to 0·67 in South America. In North America, Europe, and Asia, the R^2 (0·52 for each region) approximately matched the global average (0·54). For rural areas, we found that the Larkin and colleagues[44] dataset had NO_2 concentrations that were biased high, and therefore we adjusted concentrations using surface NO_2 concentrations derived from the Ozone Monitoring Instrument satellite NO_2 columns (appendix p 8). After adjusting the 2011 rural NO_2 concentration estimates, we scaled all 2011 grid cell concentrations to the GBD 2020 analysis period (1990–2019) using the Modern-Era Retrospective analysis for Research and Applications (version 2) reanalysis product[46] for 1990, 1995, and 2000, and the Ozone Monitoring Instrument NO_2 column densities for 2005–19 (appendix p 9).

Because Larkin and colleagues[44] showed that their NO_2 concentrations agreed well with the urban ground observations, we added evaluations of the changes made in this study. Firstly, we compared our 2011 rural NO_2 concentration estimates to the European Monitoring and Evaluation Programme ground monitoring dataset,[47] which has a large number of stations in rural areas, whereas rural monitors in other ground monitoring networks are often located directly downwind from urban areas. Secondly, we compared our 2019 NO_2 concentration estimates in urban and rural areas against 4348 monitors in the USA, Canada, and Europe.

Although we created this spatially (all urban and rural areas globally) and temporally (1990–2019) complete concentration dataset for compatibility with the GBD 2020 study, we focused our trend analysis on urban areas over the last two decades (2000–19), for which estimated concentrations have a greater certainty than previous decades because of available ground monitoring.

NO_2-attributable paediatric asthma incidence

We estimated the NO_2-attributable cases of paediatric asthma incidence using a log linear concentration–response function that was epidemiologically derived, following on from previous studies, using the equation:[19,20]

$$\text{Burden}_{k,a} = \sum_{\substack{\text{Grid cells}\\ \text{in } k}} \text{Inc}_{c,a} \times \text{Pop}_{i,j,a} \times (1 - e^{-\beta X_{i,j}})$$

where Burden is the NO_2-attributable asthma incidence in city k for age group a, Inc is the baseline asthma incidence rate for age group a and country c, Pop is the population in grid cell i,j for age group a, β is the concentration response factor relating the NO_2 concentration with increased risk of paediatric asthma incidence, and X is the annual average NO_2 concentration in grid cell i,j. We re-gridded all datasets to a 1 km resolution and estimated the NO_2-attributable asthma incidence in each grid cell. We previously found that this resolution balances accuracy with computational efficiency in estimating city-level NO_2-attributable disease burdens.[20] We summed up the results across all grid cells within each city for a city-level total.

We applied a relative risk of 1·26 (95% uncertainty interval [UI] 1·1–1·37) per 10 ppb annual average NO_2 concentration increase from a large epidemiological meta-analysis of 20 studies from Europe, 11 from North America, five from Japan, one from South Korea, and one from Taiwan. No regional heterogeneity was apparent in this meta-analysis, despite some variation in the relative risks reported in the underlying studies. We calculated the uncertainty in NO_2-attributable paediatric asthma incidence using the statistical error in this relative risk estimate.[17] Because relative risk error is static over time, it does not influence temporal trends. We used a low concentration threshold of a less than 2 ppb annual average NO_2 concentration, the 5th percentile of the minimum concentrations reported by the studies in the meta-analysis. Alternative low concentration thresholds would not substantially affect the estimated trends in NO_2-attributable asthma incidence, because thresholds were applied uniformly across all grid cells and only 3% of year-specific urban concentrations were less than 2 ppb.

We used population estimates from WorldPop[48] from 2000 to 2019 for ages 1–4, 5–9, 10–14, and 15–18 years at an approximately 1 km resolution, and summed up the results across age groups for total NO_2-attributable paediatric asthma incidence. National baseline annual asthma incidence rates from 2000 to 2019 were obtained from the GBD 2019 study.[1] Urban area boundaries were obtained from the Global Human Settlement–Settlement Model grid Urban Centre dataset for 2015 (the latest year with available data at the time of analysis, applied here to all years).[45] We considered grid cells and in situ monitors (used to evaluate the concentration dataset) to be part of an urban cluster if they were located in urban and suburban areas in the Global Human Settlement–Settlement Model grid dataset (using a majority rule for grid cells), defined as areas with more than 300 people per km^2 that are part of clusters with more than 5000 people. All other grid

See Online for appendix

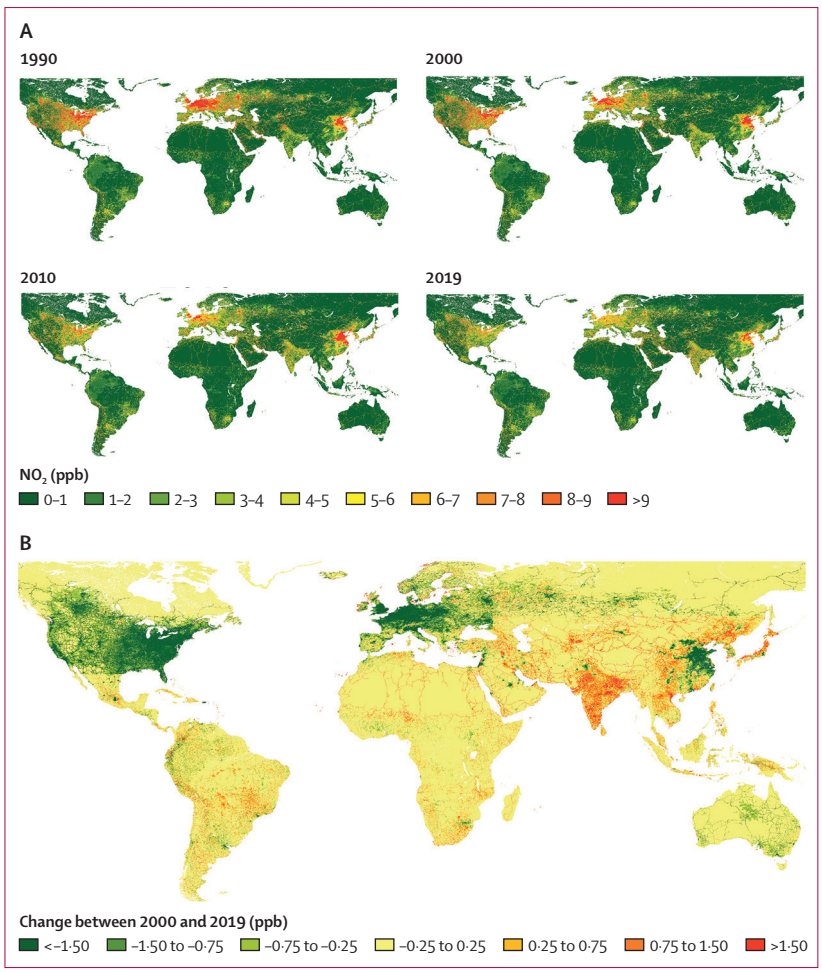

Figure 1: **Annual average NO_2 concentrations at a 1 km × 1 km resolution**
Annual average NO_2 concentrations shown in 1990, 2000, 2010, and 2019 (A) and the difference in these concentrations between 2000 and 2019 (B). NO_2=nitrogen dioxide. ppb=parts per billion.

cells and monitors were considered rural. World regions definitions were obtained from the GBD 2019 study (appendix pp 6, 10).[1]

Drivers of change

To disentangle the drivers of temporal trends in NO_2-attributable paediatric asthma incidence, we isolated the contribution of exposure, population size, and baseline asthma rates using the core results with annually varying data inputs, and three sets of simulations in which we reverted one contributing variable back to 2000 (appendix). Cohen and colleagues[49] used a similar approach for disentangling the drivers of national $PM_{2·5}$ disease burdens. We ignored interactions between the contributing factors (eg, the influence of changing NO_2 concentrations on baseline asthma rates), because we considered them to be minor relative to many other influences on these multi-factorial variables (eg, the effects of health-care advances on baseline asthma rates).

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

Our new NO_2 concentration dataset reduces the rural high concentrations bias from the 2010–12 Larkin and colleagues[44] dataset (mean bias reduced from 2·4 to 1·0 ppb; appendix pp 5, 11) and captures the observed surface-level concentrations in both urban and rural areas in 2019 (mean bias 3·3 in Canada, 1·7 in the USA, and 2·3 in Europe; appendix p 12). See the appendix for further evaluation descriptions and results. Estimated NO_2 concentrations were highest in the most populated regions of the world, including North America, Europe, and south and east Asia throughout the time period (1990–2019; figure 1). The ten cities with the highest NO_2 concentrations in 2019 were located in the Middle East (Lebanon, Iraq, and Iran), China, and Russia (appendix p 13).

We estimated that the average annual mean NO_2 concentration, weighted by the global population, was 6·6 ppb (~12·4 μ/m³ assuming a 1 standard atmosphere ambient pressure at 25° C) in 2019, leading to 1·85 million (95% UI 0·93–2·80 million) new asthma cases among children worldwide that year, or 8·5% (95% UI 4·3–12·8%; 1·85 million attributable cases of 21·78 million total cases) of all paediatric asthma incidence (figure 2). Approximately two thirds of NO_2-attributable paediatric asthma incidence occurred in the 13 189 urban areas (1·22 million cases; 95% UI 0·60–1·79 million). Compared with rural areas, urban areas had 2–4 times higher population-weighted NO_2 concentrations (10·6 ppb in urban areas *vs* 4·2 ppb in rural areas), NO_2-attributable asthma cases (1·22 million [95% CI 0·60–1·79 million] in urban areas *vs* 0·63 million [0·33–0·99 million] in rural areas), NO_2-attributable asthma cases per 100 000 people (156 [77–228] in urban areas *vs* 40 [21–63] in rural areas), and attributable proportions (16·4% in urban areas *vs* 4·5% in rural areas) in 2019.

Focusing on urban areas in the last two decades (2000–19), we found that annual average NO_2 concentrations decreased by 13%, from 12·2 ppb in 2000 to 10·6 ppb in 2019, with a steady decline from 2011 to 2019 after rising from 2000 to 2011 (figure 2). NO_2 concentrations in high-income cities exceeded the global average throughout the time period, despite declining 38% from 17·6 ppb in 2000 to 11·0 ppb in 2019 (figure 3). Contrastingly, concentrations rose by 18% (from 8·6 to 10·1 ppb) in south Asia and 11% (from 6·4 to 7·1 ppb) in sub-Saharan Africa, but were lower than the global urban average throughout the time period. These large regional groupings of cities obscure contrasting trends between sub-regions in some cases (appendix p 14).

We estimated that approximately 1·2 million paediatric asthma cases in urban areas globally were

attributable to NO_2 pollution in both 2000 and 2019, although the rate per 100 000 children declined by 11% from 176 to 156 per 100 000 children as the urban paediatric population grew by 14% (from 679 million to 774 million; figure 2). High-income cities had the most NO_2-attributable asthma incidence in 2019, with 340 900 cases or 28% of the global urban total, despite having only 14% (110 million of 774 million) of the global urban paediatric population (figure 4; appendix p 7). Although the majority of the total NO_2-attributable paediatric asthma cases were in the most populated cities in the world (appendix p 15), all ten highest attributable rates were in US cities (appendix p 16). Contrastingly, cities in south Asia, with approximately a quarter of the global paediatric population, only accounted for 7% (90 400 cases) of global urban NO_2-attributable paediatric asthma incidence. NO_2-attributable paediatric asthma incidence rates were also highest in the high-income region (310 attributable cases per 100 000 children; figure 3 and appendix p 7) and were an order of magnitude lower in south Asia (50 attributable cases in south Asia).

The proportion of paediatric asthma incidence that were estimated to be attributable to NO_2 across all urban areas globally dropped from 19·8% (1·22 million attributable cases of 6·14 million total cases) in 2000 to 16·0% (1·24 million attributable cases of 7·73 million total cases) in 2019 (figure 2). Urban attributable fractions dropped between 2000 and 2019 in high-income countries (–41%), Latin America and the Caribbean (–16%), central Europe, eastern Europe, and central Asia (–13%), and southeast Asia, east Asia, and Oceania (–6%), and rose in south Asia (+23%), sub-Saharan Africa (+11%), and north Africa and the Middle East (+5%; figure 3 and appendix p 7). The large decrease in high-income countries is partly driven by even larger drops in North America (–52%; appendix p 14). The 13% decrease in central Europe, eastern Europe, and central Asia was driven by a 24% increase in central Asia, balanced by a 32% decrease in central Europe and a 16% decrease in eastern Europe. In 2019, the regional urban average attributable fractions ranged from 10% (102 900 attributable cases of 1·05 million total cases) in sub-Saharan Africa to 20% (54 900 attributable cases of 277 800 total cases) in central Europe, eastern Europe, and central Asia, and north Africa and the Middle East. As for concentrations, the ten highest attributable fractions were located in Lebanon, Iraq, Iran, China, and Russia (appendix p 17).

Estimated temporal trends in urban NO_2-attributable paediatric asthma incidence are driven by simultaneous and often competing changes in NO_2 concentrations, paediatric population, and asthma incidence rates (figure 5). Australasia and high-income Asia-Pacific were the only regions where declining concentrations, paediatric population size, and asthma rates all contributed to overall drops in NO_2-attributable paediatric asthma incidence. The

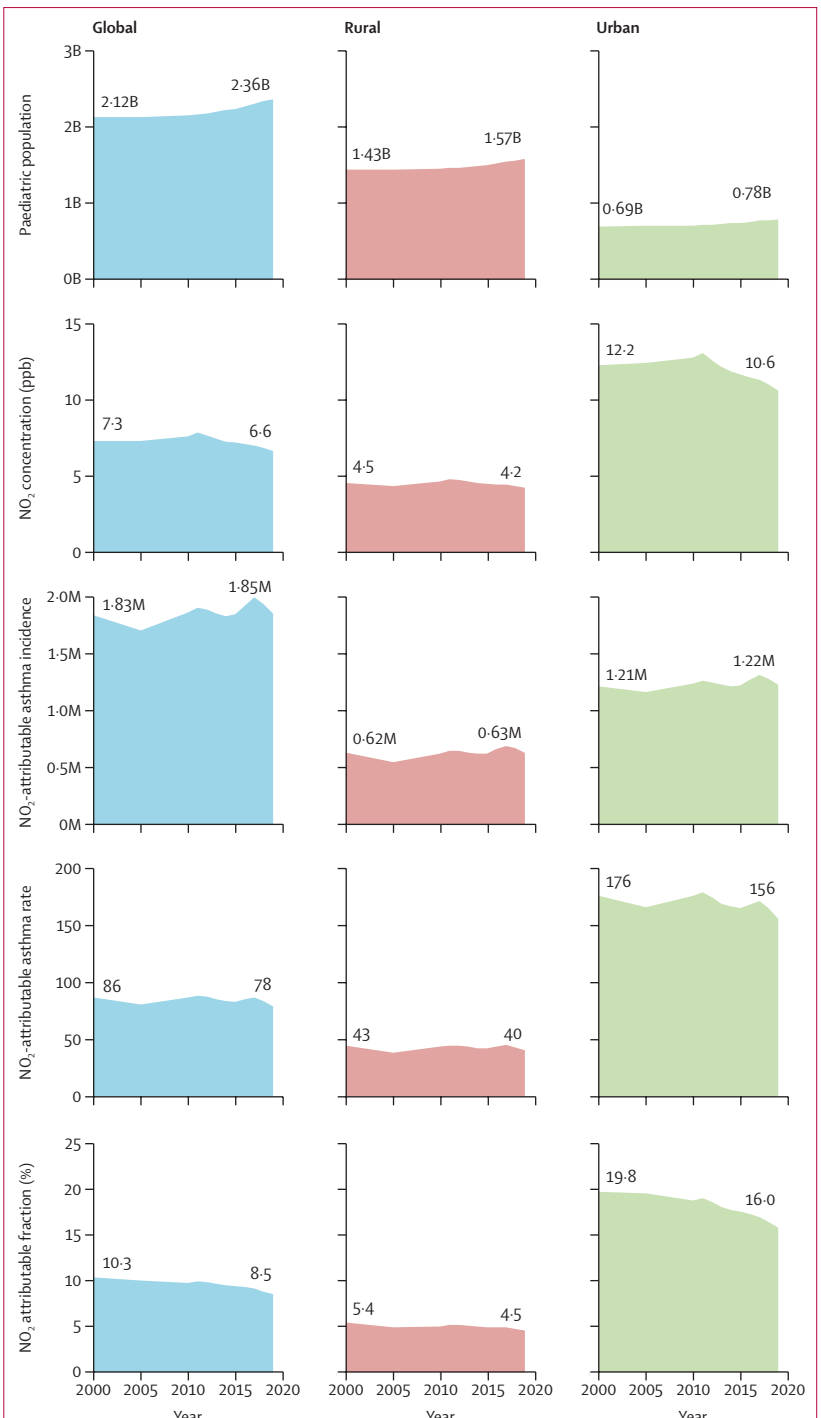

Figure 2: **Trends between 2000 and 2019 globally and in urban and rural areas**
The paediatric population, the population-weighted annual average NO_2 concentrations (ppb), NO_2-attributable paediatric asthma incidence (number of cases), NO_2-attributable paediatric asthma incidence rate (per 100 000 children), and NO_2 attributable fraction (% of all paediatric asthma incidence) globally, in all rural areas, and in 13 189 urban areas are shown. The uncertainty intervals for NO_2-attributable paediatric asthma incidence are not shown since they are based on error in the relative risk estimate, which is constant over time. B=billion. M=million. NO_2=nitrogen dioxide. ppb=parts per billion.

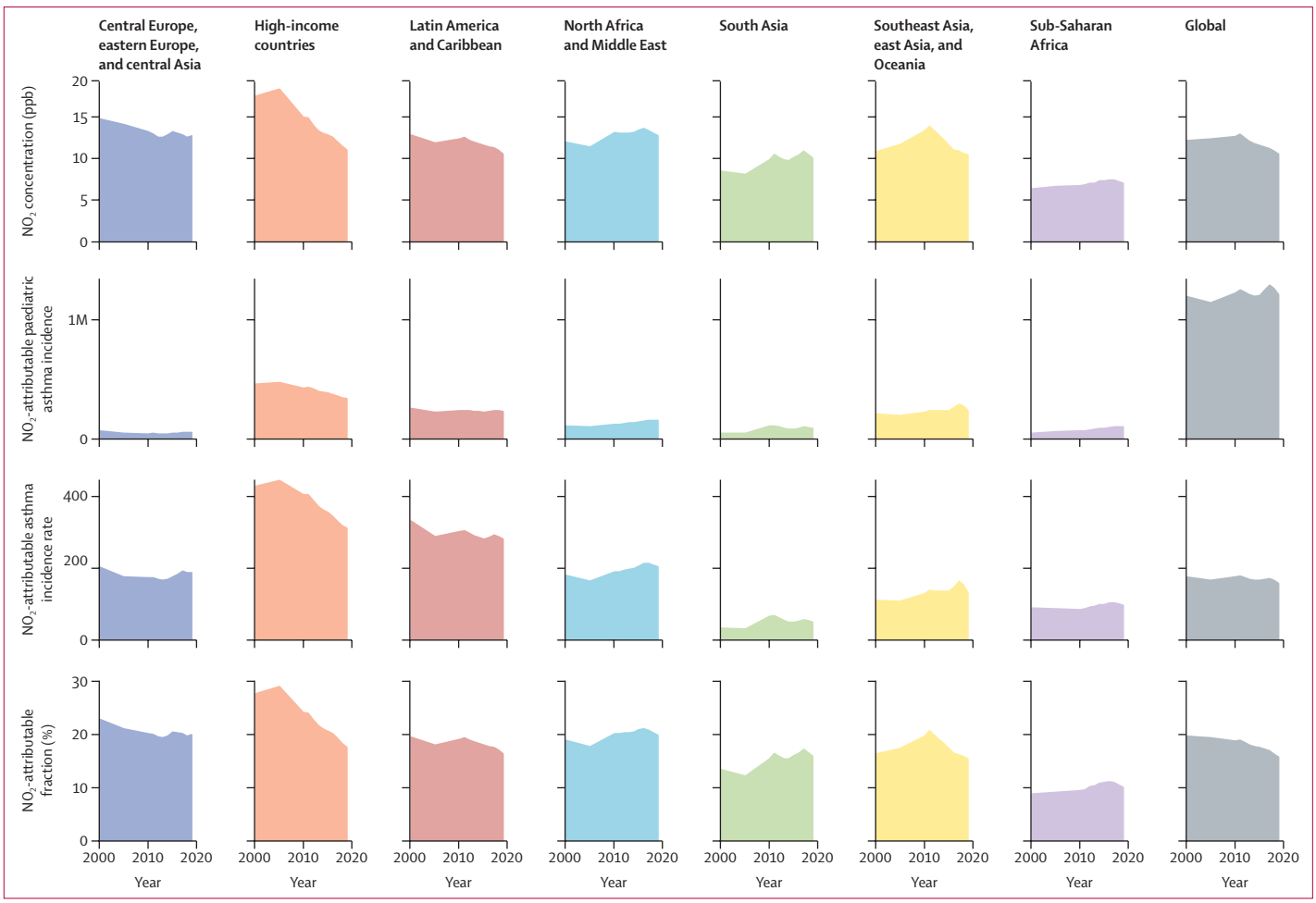

Figure 3: **Trends between 2000 and 2019 in urban areas by region**
Population-weighted annual average NO_2 concentrations (ppb), NO_2-attributable paediatric asthma incidence (number of cases), NO_2-attributable paediatric asthma rates (per 100 000 children), and NO_2 attributable fraction (% of all paediatric asthma incidence) in urban areas in each region are shown. Results for each sub-region within each super-region are shown in the appendix (p 14). Uncertainty intervals for NO_2-attributable paediatric asthma incidence are not shown since they are based on error in the relative risk estimate, which is constant over time. M=million. NO_2=nitrogen dioxide. ppb=parts per billion.

opposite occurred in central, south, and southeast Asia, and in north Africa and the Middle East, where concentrations, paediatric population, and asthma rates all rose. In high-income North America, western, eastern, and central Europe, southern, central, tropical, and Andean Latin America, east Asia, and central sub-Saharan Africa, declining NO_2 concentrations were offset by increases in asthma incidence rates or paediatric population size, or both. These competing influences changed over time, with declining concentrations becoming more influential over time in North America and southern Latin America, and population growth becoming more influential in north Africa and the Middle East and southern sub-Saharan Africa (appendix p 18).

Discussion

We estimated that 1·85 million (95% UI 0·93–2·80 million) paediatric asthma cases globally could be attributable to NO_2 pollution in 2019. Despite having only a third of the global paediatric population, urban areas had two thirds of NO_2-attributable paediatric asthma incidence. The NO_2-attributable fraction of paediatric asthma incidence in urban areas globally declined from 19·8% in 2000 to 16·0% in 2019. Regional trends were inconsistent: urban average attributable fractions dropped in high-income countries, Latin America and the Caribbean, central and eastern Europe, central, southeast, and east Asia, and Oceania, and rose in south Asia, sub-Saharan Africa, and north Africa and the Middle East. The drivers of temporal trends in NO_2 concentrations and paediatric asthma burdens were also inconsistent regionally, with declining NO_2 concentrations in some regions counteracted by increases in paediatric population size and asthma incidence rates.

Our study is consistent with the broader literature showing that NO_2 is largely an urban pollutant.[7,50–52]

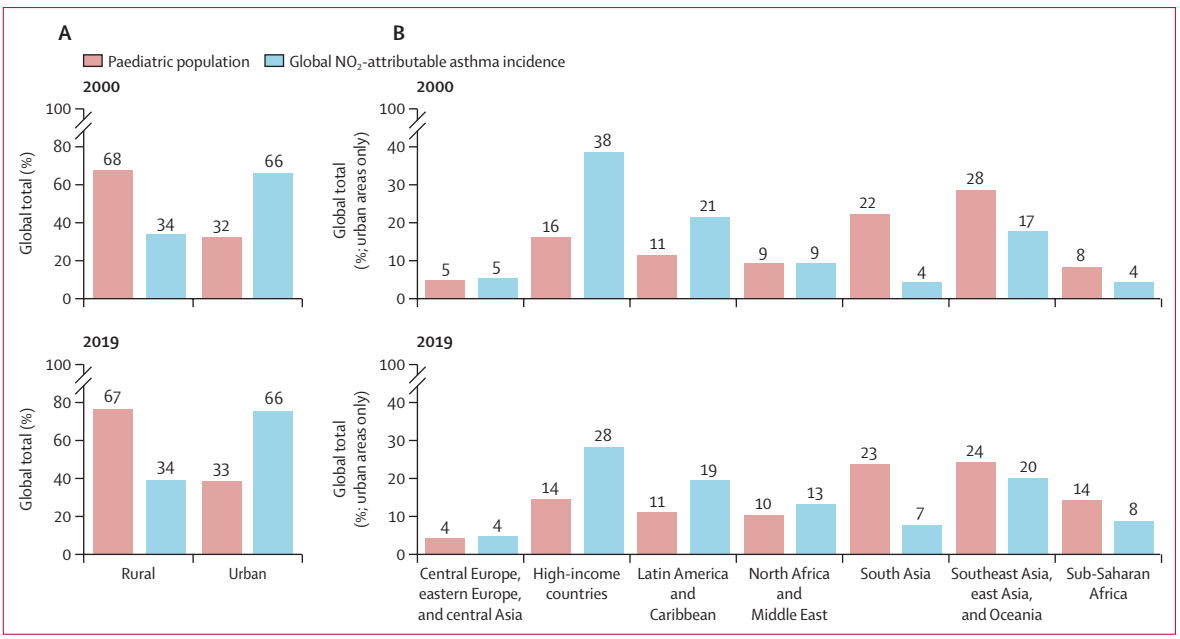

Figure 4: **Percentage of global total paediatric population and NO_2-attributable asthma cases in 2000 and 2019**
Percentage of global total paediatric population and NO_2-attributable asthma cases in all rural areas and 13 189 urban areas globally (A), and urban areas only within each region (B). NO_2=nitrogen dioxide.

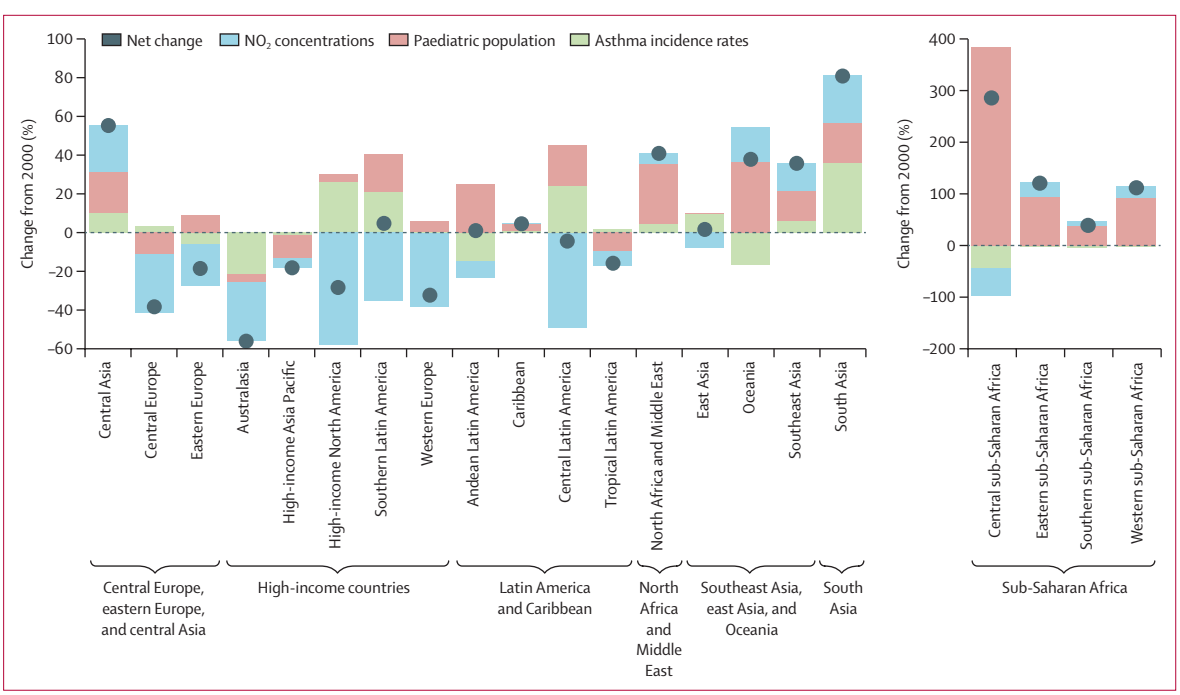

Figure 5: **Contribution of paediatric population, baseline paediatric asthma rates, and NO_2 concentrations to the changes in estimated NO_2-attributable paediatric asthma incidence between 2000 and 2019 for each sub-region**
A different y-axis is used for regions in sub-Saharan Africa, as shown in the figure. Results for the full time period are shown in the appendix (p 18). NO_2=nitrogen dioxide.

Estimated NO_2 concentration trends are consistent with studies using satellite data to investigate NO_2 concentration trends during 2004–18 for the USA, Europe, China, India, and Japan.[23,31,53] For example, Qu and colleagues[54] also showed a similar decrease in US NO_2 concentrations based on ground observations, satellite data, and modelling outputs from 2006 to 2016, and Henneman and colleagues[26] showed a similar decrease using ground

observations from 1980 to 2020. One study focused on biomass burning in the equatorial Africa region found declining concentrations in NO_2 from 2005 to 2017,[55] whereas we found an increase in sub-Saharan Africa from 2000 to 2019. A biomass burning decline in the region might be smaller and offset by anthropogenic emission changes in populated urban areas. A reduced effect on asthma where NO_2 concentrations are declining is consistent with observational studies.[56]

Although our new NO_2 dataset leverages the advantages of having different data sources, the concentrations are still uncertain. Many cities, particularly in low-income and middle-income countries (LMICs), do not have ground NO_2 monitors, challenging the calibration and evaluation of LUR models.[44] Urban NO_2 concentrations are therefore more certain in North America, Europe, and Asia compared with Africa and south America. Rural concentrations are uncertain globally with little ground monitoring outside of urban areas. Scaling the 2010–12 LUR NO_2 concentrations to other years assumes that the land use predictors are static over time. This assumption is likely to be supported by slow changes in road density and volume and urban form, but over the two decades explored here, some land use evolution is probable,[57] particularly in rapidly developing LMICs. The actual relationships between land use variables and NO_2 concentrations probably differ temporally, and holding these variables constant results in greater uncertainties in NO_2 concentrations in areas where land use is changing rapidly. The directional effect of these uncertainties on the results is unknown.

Our estimate of the global burden of NO_2 on paediatric asthma incidence in 2019 is less than half of the 4·2 million found by Achakulwisut and colleagues[19] in 2015. Our results for India are also lower than previous estimates, whereas our results for the USA are higher.[17,20] Several factors explain this discrepancy. First, our new NO_2 concentrations correct for a high rural NO_2 bias, leading to lower NO_2-attributable asthma incidence estimates, especially in countries with larger rural populations (eg, India). Second, the GBD 2019 study baseline asthma rates are much lower than in previous versions, except in high-income areas (eg, the USA), because of a change in the case definition used that lowered the estimated rates in most places and raised them for the USA.[58] For example, baseline paediatric asthma incidence rates in 2015 (the year analysed by Mohegh and colleagues[20]) in the GBD 2019 study were 81% of the GBD 2017 study values. Contrastingly, US paediatric asthma incidence rates were 2·2 times higher in the GBD 2019 study versus the GBD 2017 study. Changes in baseline asthma rates approximately proportionally affect estimated NO_2-attributable paediatric asthma incidence. Our NO_2 attributable fraction result in high-income North America in 2019 (17·3%) was similar to a previous estimate for the USA in 2000 (17·9%), although our NO_2 concentrations were lower than the previous study (10·9 ppb in urban areas *vs* 13·2 ppb overall).[50] The different analysis years are important because, as we have shown, NO_2 concentrations trends are changing rapidly.

The health impact assessment method also introduces uncertainties. Baseline paediatric asthma incidence rates might be underestimated in many LMICs, leading to underestimated NO_2-attributable asthma effects. Additionally, although we used national paediatric asthma rates because city-level rates are unavailable globally, asthma prevalence varies within countries.[50] Living in urban areas has been associated with an increased risk of asthma prevalence in LMICs[36] and asthma-related emergency department visits and admissions to hospital in the USA.[59] Similarly, temporal trends in baseline asthma incidence might differ in urban areas compared with national averages, especially in rapidly urbanising LMICs. If asthma prevalence is higher in urban areas compared with national averages, NO_2-attributable asthma incidence might be underestimated. Temporal trends could also be affected by changing population structure, health-care levels, and other factors that we have not attempted to quantify here. In addition, it is currently unknown whether paediatric asthma incidence is directly associated with NO_2, or with the traffic-related air pollution mixture or the broader combustion-related air pollution mixture. Our results could be affected by exposure misclassification, which would tend to lead to bias towards the null and underestimated attributable asthma effects. Similarly, we have not accounted for various factors that influence the ambient NO_2–asthma relationship in the underlying epidemiological studies and meta-analysis from which we drew relative risk estimates (effect modification). These include parental income and educational levels, environmental tobacco smoke, and presence in the home of mildew, water damage, pests, and pets. Since we held urban area boundaries constant over the time period examined, we were not able to associate NO_2-attributable asthma changes with the evolving urban area. Finally, the 1 km resolution of our NO_2 concentration estimates might not capture areas with co-located steep spatial gradients in concentrations and population, potentially leading NO_2-attributable asthma incidence to be underestimated.

Despite these uncertainties and limitations, our results show the important influence of combustion-related air pollution on children's health in cities globally. In places that have effective air quality management programmes (eg, in the USA and Europe), NO_2 concentrations have been trending downward for decades, with benefits for children's respiratory health. Even with these improvements, current NO_2 concentrations contribute substantially to paediatric asthma incidence, highlighting that mitigating air pollution should be a crucial element of public health strategies for children. For cities that have not benefited from strong air quality management programmes at the local or national scale, the experience

of cities that have such programmes shows that addressing combustion-related air pollution can lead to major air quality and public health improvements over short time frames. These air quality improvements can be achieved through either end-of-pipe emission control technologies such as catalytic converters or avoiding the combustion in the first place, which would have additional benefits from reduced greenhouse gas emissions.

Our study shows the value of satellite remote sensing and statistical models for tracking NO_2 pollution and for environmental health surveillance at local, national, and global scales. The combination of methods offers strengths beyond the capabilities of each technique alone: a long and consistent observational record of NO_2 column densities from satellites in combination with the high spatial resolution of surface concentration predictions from LUR models. Future studies might leverage these data sources and others, including new satellite sensors that have higher temporal and spatial resolutions, mobile monitoring, distributed ground sensor networks, and chemical transport models, to further improve the accuracy and spatiotemporal resolution of NO_2 concentration estimates, which can be used in both epidemiological studies and health impact assessments. Further, our study shows the importance of considering demographic changes over time for understanding air pollution health risks. Improved and more widely accessible information about disease rates, and capturing population distribution and movement, will enable more accurate and highly resolved air pollution health impact assessments.

Contributors

SCA, AM, and DLG designed the study. PH, AL, and LL provided data. AM and GHK carried out the calculations. SCA, AM, DLG, KB, MB, PH, AL, and SW contributed input on methods development. SCA and AM wrote the paper. All authors helped interpret the results and reviewed the paper. AM, GHK, and DLG have verified the underlying data. AM, GHK, DLG, and SCA had full access to all data in the study. SCA and AM had final responsibility for the decision to submit for publication.

Declaration of interests

GHK declares a consulting relationship with the Environmental Defense Fund. SCA declares consulting relationships with the Environmental Defense Fund and International Council on Clean Transportation; and unpaid advisory board membership for the American Geophysical Union, US Environmental Protection Agency, WHO, Clean Air Partners, and the National Academies of Sciences, outside the submitted work. All other authors declare no competing interests.

Data sharing

The NO_2 concentrations are available at: https://doi.org/10.6084/m9.figshare.12968114. The estimated NO_2-attributable asthma incidence results are available at: https://blogs.gwu.edu/sanenberg/.

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