Estimates, trends, and drivers of the global burden of type 2 diabetes attributable to PM$_{2.5}$ air pollution, 1990–2019: an analysis of data from the Global Burden of Disease Study 2019

GBD 2019 Diabetes and Air Pollution Collaborators*

Summary

Background Experimental and epidemiological studies indicate an association between exposure to particulate matter (PM) air pollution and increased risk of type 2 diabetes. In view of the high and increasing prevalence of diabetes, we aimed to quantify the burden of type 2 diabetes attributable to PM$_{2.5}$, originating from ambient and household air pollution.

Methods We systematically compiled all relevant cohort and case-control studies assessing the effect of exposure to household and ambient fine particulate matter (PM$_{2.5}$) air pollution on type 2 diabetes incidence and mortality. We derived an exposure–response curve from the extracted relative risk estimates using the MR-BRT (meta-regression—Bayesian, regularised, trimmed) tool. The estimated curve was linked to ambient and household PM$_{2.5}$ exposures from the Global Burden of Diseases, Injuries, and Risk Factors Study 2019, and estimates of the attributable burden (population attributable fractions and rates per 100,000 population of deaths and disability-adjusted life-years) for 204 countries from 1990 to 2019 were calculated. We also assessed the role of changes in exposure, population size, age, and type 2 diabetes incidence in the observed trend in PM$_{2.5}$-attributable type 2 diabetes burden. All estimates are presented with 95% uncertainty intervals.

Findings In 2019, approximately a fifth of the global burden of type 2 diabetes was attributable to PM$_{2.5}$ exposure, with an estimated 3.78 (95% uncertainty interval 2.68–4.83) deaths per 100,000 population and 167 (117–223) disability-adjusted life-years (DALYs) per 100,000 population. Approximately 13.4% (9.49–17.5) of deaths and 13.6% (9.73–17.9) of DALYs due to type 2 diabetes were caused by ambient PM$_{2.5}$, and 6.5% (4.22–9.53) of deaths and 5.92% (3.81–8.64) of DALYs by household air pollution. High burdens, in terms of numbers as well as rates, were estimated in Asia, sub-Saharan Africa, and South America. Since 1990, the attributable burden has increased by 50%, driven largely by population growth and ageing. Globally, the impact of reductions in household air pollution was largely offset by increased ambient PM$_{2.5}$.

Interpretation Air pollution is a major risk factor for diabetes. We estimated that about a fifth of the global burden of type 2 diabetes is attributable PM$_{2.5}$ pollution. Air pollution mitigation therefore might have an essential role in reducing the global disease burden resulting from type 2 diabetes.

Funding Bill & Melinda Gates Foundation.

Introduction Diabetes has been highlighted as a major global health threat by WHO. The disease is characterised by hyperglycaemia resulting from dysfunctional insulin secretion or action. Long-term consequences can be dysfunction and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Type 2 diabetes accounts for 90–99% of diabetes cases globally and contributed to approximately 94% of disability-adjusted life-years (DALYs) and 96% of years lived with disability (YLDs) due to diabetes. In total, the global burden of diabetes was estimated at 1.55 million excess deaths, with 34 million years of life lost (YLLs) and 37 million YLDs in 2019. Since the 1990s, global age-standardised death rates increased by 8–6%, all-age death rates increased by 62%, and the burden of disease has approximately doubled. Recent projections predict a further increase in diabetes-related mortality rates of approximately 75% by 2040. Metabolic and behavioural risk factors, such as obesity, smoking, diet, and physical inactivity, have been highlighted as major contributors to the burden of type 2 diabetes. In the past 15 years, studies have indicated an important role of factors that promote inflammatory responses, such as air pollution. A meta-analysis that included five cross-sectional and five prospective cohort studies showed an increased risk of type 2 diabetes due to exposure to particulate matter (PM) or nitrogen dioxide air pollution.
Experimental studies indicate the role of air pollution in diabetes and cardiovascular disease. Ongoing resistance and systemic inflammation and increased visceral adiposity in obese study animals. Ongoing resistance and systemic inflammation and increased visceral adiposity in obese study animals. Given the relationship between exposure to air pollution and cardiovascular disease and similarities in biological pathways between diabetes and cardiovascular disease, air pollution has been posited to have a causal role in diabetes. Experimental studies indicate the role of inflammation in biological mechanisms linking exposure to PM with diabetes. In a mouse model, exposure to high concentrations of PM2.5 induced insulin resistance and systemic inflammation and increased visceral adiposity in obese study animals. Ongoing exposure led to impaired glucose tolerance, lower circulating concentrations of adipokines (adiponectin and leptin), and mitochondrial alteration in the same mice. This and other evidence generated from experimental studies has led to epidemiological studies assessing the relationship between diabetes risk and air pollution. We aimed to assess the burden of type 2 diabetes attributable to ambient and household PM2.5 air pollution using estimates derived from epidemiological studies. We also aimed to evaluate the relative roles of changes in exposure, population size, age, and diabetes incidence in the observed trend in PM2.5-attributable diabetes burden. This manuscript was produced as part of the GlobalBurden of Diseases, Injuries, and Risk Factors Study (GBD) Collaborator Network and in accordance with the GBD Protocol.

Methods

Overview

GBD is the most comprehensive global epidemiological study. It estimates the burden of disease from 286 causes of death, 369 diseases and injuries, and 87 risk factors in 204 countries and territories. Risk factors include metabolic, behavioural and environmental factors, such as air pollution.

Literature review and study extraction

To compile all relevant studies, we followed a two-stage search strategy. In stage 1, we searched PubMed on June 1, 2017, and in 2019 for the most recent meta-analysis or systematic review of studies investigating the effect of ambient air pollution, household air pollution, or...
second-hand smoke on diabetes. We defined a search string consisting of “diabetes”, “meta-analysis”, or “review” and the exposure indicator (eg, “particulate matter”, “household air pollution”, “indoor air pollution”, or “cooking fuel”). The exact search strings are provided in the appendix p 2). In stage 2, we included additional studies that were identified through other sources, such as those referenced in another study or published and unpublished work sent to us by members of the GBD Collaborator Network.

The primary outcome of interest was type 2 diabetes in adults aged 18 years or older. As some studies did not differentiate between type 1 and type 2, we assumed that cases were dominated by type 2.24 We included studies that assessed morbidity (ie, incidence) and mortality. We limited our results to case-control and cohort studies and articles written in English. Studies were excluded if the full text could not be obtained, if exposure to PM$_{2.5}$ was short term (eg, several days), or if exposure to active tobacco smoking was not measured in terms of cigarettes per day. Studies that assessed type 1 or gestational diabetes were also excluded. Information from each of the individual studies that were identified, including effect estimates and additional study-specific information, was extracted and used in the meta-regression.

**Exposure assessment**
For estimation of ambient air pollution exposure, we used the Data Integration Model for Air Quality (DIMAQ2). This model integrates data from satellite-based measurements of aerosol optical depth, ground measurements from 9960 PM monitoring stations across 108 countries, and chemical transport model simulations.16 Global values of PM$_{2.5}$, provided at a 0·1°×0·1° resolution, were population-weighted to generate mean exposure for each location. Methods and data sources are described in more detail in the appendix (pp 2–5) and have been published elsewhere.6

Exposure modelling for household air pollution from solid fuels comprised two components. The first component, the so-called proportional model, estimated the proportion of households using solid cooking fuels, relying on data extracted from multiple national-level and other surveys and the WHO Energy Database.7 The second component, the mapping model, estimated the exposure concentration of PM$_{2.5}$ corresponding to solid-fuel use, measured in µg per cubic metre of air (µg/m$^3$) for a given location and year based on the Socio-demographic Index. Further information is provided in the appendix (pp 3–4).

**Exposure-response curve**
Several studies have derived relative risks over various exposure ranges. These risks differ in magnitude, and the exposure range over which they are assessed varies. Furthermore, at the upper end of the global ambient air pollution exposure range, reliable estimates are not available, due to a scarcity of studies in highly polluted areas. Another challenge in meta-regressing risk estimations from different studies lies in differing study designs and varying adjustment for potential confounders. To account for between-study heterogeneity and to develop a relative risk function that covered the entire global exposure range, we combined risk estimates from all available studies using the newly developed regression tool, MR-BRT (meta-regression—Bayesian, regularised, trimmed).26

Risk estimates from studies assessing the impact of ambient air pollution, household air pollution, and second-hand smoke on type 2 diabetes were used to fit a spline, with each risk estimate informing the curve along the study-specific exposure range. Various model settings and priors were tested for fitting the MR-BRT splines. The final models used third-order splines with two interior knots and a constraint on the right-most segment, forcing the fit to be linear rather than cubic at the upper end. We used an ensemble approach to knot placement, wherein 100 different models were run with randomly placed knots and then combined by weighting based on a measure of fit that penalises excessive changes in the third derivative of the curve. Knots were free to be placed anywhere within the 5th and 95th percentile of the data, as long as a minimum width of 10% of that domain existed between them. We included shape constraints so that the risk curves were concave down and monotonically increasing—the most biologically plausible shape for the PM$_{2.5}$ risk curve. On the non-linear segments, we included a Gaussian prior on the third derivative of mean 0 and variance 0·01 to prevent overfitting; on the linear segment, a stronger prior of mean 0 and variance 1×10$^{-6}$ was used to ensure that the risk curves did not continue to increase beyond the range of the data.

In addition, we extracted a set of study-specific covariates to explain between-study heterogeneity in risk estimates. We considered whether the study assessed the overall population or a subpopulation using a binary variable; two binary variables indicated whether exposure was measured at the population or individual level and whether exposure was measured at the beginning of the study versus at multiple timepoints during the study period. We also included binary variables indicating whether the exposure or the outcome was self-reported and a variable indicating whether the assessment was blind to exposure. We also accounted for the degree to which study participants were lost to follow-up. Finally, we accounted for control of confounding within each study by creating two covariates. First, we created a binary variable indicating whether the study was randomised. As no studies were randomised, this variable was not included in the meta-regression. In addition, we created a categorical variable indicating the degree of statistical control for potential confounding. This covariate had three levels: the first level indicated that the study had controlled for major confounders—specifically, age, sex,
education, income, and smoking status—measured at either the individual or the community level. The next level indicated that the study had controlled for age, sex, and smoking only. The third level indicated that the study controlled only for age and sex but no other confounders. The appendix (pp 9–11) gives a detailed overview over all covariates included in the meta-regression. As none of these covariates was significant in the model, the final model was fitted without them.

**PAF calculation and burden estimation**

The population attributable fraction (PAF) quantifies the proportion of cases that can be attributed to the risk factor. That is, PAFs represent the fraction of cases that would be avoided if exposure were reduced to the theoretical minimum risk exposure level. As individuals who are exposed to household sources of PM$_{2.5}$ are also exposed to ambient sources, we used a proportional approach to calculate PAFs for each risk factor. Using the mean annual ambient PM$_{2.5}$ exposure, the proportion of individuals exposed to PM from household solid fuel use, and the value derived from the household PM$_{2.5}$ mapping function for each location and year, we calculated a corresponding relative risk from the exposure–response curve for each 0.1° × 0.1° grid cell. This relative risk was converted to a PAF using the following formula: PAF = (RR – 1)/RR, where RR is the relative risk. This PAF, which was initially determined for both sources of PM$_{2.5}$, and was then proportionally attributed to ambient and household. We then aggregated up to the location level (country or administrative unit), weighting by grid cell-level population. By using this strategy, the total PAF is the sum of the ambient and household PAFs, and we assume that both exposures are evenly distributed across different slopes of the exposure–response curve. More details about these calculations can be found in the appendix (p 4). Eventually, the type 2 diabetes burden was determined by multiplying age-specific, sex-specific, year-specific, and location-specific PAFs with deaths, YLLs, YLDs, and DALYs for 204 countries and territories from 1990 to 2019. Over this period, we decomposed the trend in the attributable burden to evaluate the relative roles of changes in exposure, population size, age, and type 2 diabetes incidence. To account for uncertainties in our modelling, we produced 1000 draws of all estimates and intermediate steps. We present estimates (with 95% uncertainty intervals [UIs]) of PAFs and rates per 100,000 population of type 2 diabetes deaths, DALYs, YLDs, and YLLs attributable to PM$_{2.5}$ pollution. We also calculated the PM$_{2.5}$ pollution-deleted DALY rate, which is the expected rate if air pollution were reduced to the theoretical minimum risk exposure level and captures changes in other risk factors or treatment practices.

**Role of the funding source**

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

**Results**

The literature search resulted in 13 studies with 16 effect estimates for ambient air pollution, two sources and effect estimates for household air pollution, and five sources and seven effect estimates for second-hand smoke. Studies assessing the effects of ambient air pollution, second-hand smoke, and household air pollution covered an exposure range of approximately 5–100 µg/m$^3$ (annual average). All ambient air pollution, household air pollution, and second-hand smoke studies revealed an increase in type 2 diabetes risk with increased exposure to PM with varying degrees of precision. The estimated relative risk increases rapidly between a PM$_{2.5}$ exposure concentration of 5 µg/m$^3$ and approximately 50 µg/m$^3$; above this concentration, the curve flattens and shows only minimal increases (figure 1).

In 2019, about a fifth of the total type 2 diabetes burden was attributable to air pollution, with a death rate of 3.78 (95% UI 2.68–4.83) per 100,000 population and a DALY rate of 167 (117–223) per 100,000 population (table). 13.4% (9.49–17.5) of type 2 diabetes deaths were due to ambient air pollution, whereas 6.50% (4.22–9.53) were due to household air pollution. Africa, the Middle East, and south and east Asia exhibited a particularly high PM$_{2.5}$-attributable burden (figure 2A). Noticeably, ambient air pollution contributed to a large extent of this burden in north Africa and the Middle East, whereas in sub-Saharan Africa, most of the air pollution-attributable burden stemmed from household air pollution (figures 2B, 2C). North America, Australia, and Scandinavia showed distinctly low air-pollution-attributable type 2 diabetes burden (figure 2). YLDs showed a greater increase than YLLs; this trend could be observed globally, but especially

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[Figure 1: Exposure–response function for PM$_{2.5}$ exposure and type 2 diabetes for an exposure range of 0–100 µg/m$^3$ (A) and 0–500 µg/m$^3$ (B)]

The solid line shows the central estimate of the exposure–response curve, and the shaded area depicts 95% uncertainty intervals. The relative risk equals 1 for PM$_{2.5}$ concentrations of 0–2.4 µg/m$^3$, which corresponds to the lower bound of the theoretical minimum risk exposure level uncertainty distribution. Each point represents an epidemiological study included in the model. The size of the point reflects the inverse variance used to weight the model. The relative risk axis is on a log scale. PM = particulate matter.
Discussion

The study provides a systematic analysis of the increase of attributable type 2 diabetes DALYs in all super-regions, with a global increase of approximately 140%. GDP drivers—the quantities of population attributable burden. We show most of the increase in population attributable burden is due to increases in household air pollution and air pollution in ambient air pollution and ambient PM2·5 across all regions. An increase of approximately 140%.

In high income countries, central and eastern Europe, and central Asia, income regions, central and eastern Europe, and central Asia, population ageing played a major part, in high income countries, central and eastern European, and central Asian populations. Although population ageing played a major part, in high income countries, central and eastern Europe, and central Asia, population ageing played a major part, in high income countries, central and eastern Europe, and central Asia.

In Latin America and the Caribbean, southeast Asia, east Asia, and Oceania, and south Asia, where observed an increase in DALYs due to ambient PM2·5 attributable risks, whereas in all other regions we observed a decrease in ambient PM2·5 attributable risks. In Latin America and the Caribbean, southeast Asia, east Asia, and Oceania, and south Asia, where observed an increase in DALYs due to ambient PM2·5 attributable risks, whereas in all other regions we observed a decrease in ambient PM2·5 attributable risks.

In North Africa and the Middle East and in south Asia, we observed marked increases in the rate of increase in DALYs due to ambient PM2·5 attributable risks, whereas in all other regions we observed a decrease in ambient PM2·5 attributable risks.

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<table>
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<th>Rate per 100 000</th>
<th>Percentage change (%)</th>
<th>DALYs (%)</th>
<th>Rate per 100 000</th>
<th>Percentage change (%)</th>
<th>YLDs (%)</th>
<th>Rate per 100 000</th>
<th>Percentage change (%)</th>
<th>YLLs (%)</th>
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<td>117</td>
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<td>(9·4 to 18·1)</td>
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<td>164</td>
<td>(117 to 220)</td>
<td>164%</td>
<td>105</td>
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<td>(44·4 to 117)</td>
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<td>71</td>
<td>(4·2 to 10·8)</td>
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<td>139%</td>
<td>416</td>
<td>(26·5 to 61·2)</td>
<td>149%</td>
<td>134</td>
<td>(7·4 to 21·0)</td>
<td>211%</td>
<td>134</td>
<td>(7·4 to 21·0)</td>
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**Household air pollution from solid fuels**

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<tr>
<th></th>
<th>Deaths (%)</th>
<th>Rate per 100 000</th>
<th>Percentage change (%)</th>
<th>DALYs (%)</th>
<th>Rate per 100 000</th>
<th>Percentage change (%)</th>
<th>YLDs (%)</th>
<th>Rate per 100 000</th>
<th>Percentage change (%)</th>
<th>YLLs (%)</th>
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<td>1·24</td>
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<td>11·5%</td>
<td>507</td>
<td>(31·4 to 75·6)</td>
<td>13·3%</td>
<td>227</td>
<td>(12·1 to 37·6)</td>
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<td>280</td>
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<td>171</td>
<td>(1·7 to 4·5)</td>
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<td>15·0</td>
<td>(1·7 to 4·5)</td>
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<td>(0·289 to 2·1)</td>
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<td>52·3</td>
<td>(0·26 to 4·0)</td>
<td>3·6%</td>
<td>23·1</td>
<td>(1·1 to 4·6)</td>
<td>16·1%</td>
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<td>1·52</td>
<td>(0·7 to 2·4)</td>
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<td>(32·3 to 89·5)</td>
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<td>(52·0 to 12·5)</td>
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<td>15·8%</td>
<td>5·34</td>
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Data in parentheses are 95% uncertainty intervals. Data are presented to three significant figures. DALYs=disability-adjusted life-years. GBD=Global Burden of Diseases, Injuries, and Risk Factors Study. PM=particulate matter. YLDs=years lived with disability. YLLs=years of life lost.
Percentage of type 2 diabetes
DAlYs attributable to PM$_{2.5}$ air pollution

- (0%, 0%)
- (0%, 2.6%)
- (2.6%, 5.6%)
- (5.6%, 8.0%)
- (8.0%, 10.0%)
- (10.0%, 12.0%)
- (12.0%, 15.2%)
- (15.2%, 19.4%)
- (19.4%, 23.0%)
- (23.0%, 31.7%)

Caribbean and central America
Persian Gulf
Balkan Peninsula
Southeast Asia
Northern Europe
Eastern Mediterranean

(Figure 2 continues on next page)
global burden of type 2 diabetes was attributable to air pollution, with 13.4% from ambient PM$_{2.5}$ and 6.5% from household air pollution. At the population level, air pollution was responsible for more attributable burden than either tobacco or physical inactivity. Combining the exposure–response relationship with global location-specific exposure data revealed a geographically explicit pattern. Africa, Asia, and South America in particular showed a high burden attributable to air pollution. In most areas, with the exception of sub-Saharan Africa, this burden was dominated by ambient PM$_{2.5}$, whereas household air pollution played only a minor part. Over the past three decades, absolute DALYs and DALY rates attributable to PM$_{2.5}$ pollution have considerably increased. Our decomposition analysis showed that in most regions, improvements in household air pollution were counterbalanced by increased ambient air pollution. In addition to increased ambient air pollution exposure, population growth and ageing contributed to the large increase in the type 2 diabetes burden attributable to air pollution.

Our study relied on an extensive number of studies and effect estimates that were combined and integrated across the exposure ranges. Based on the exposure–response curve, we estimated the attributable burden for ambient air pollution and household air pollution from 1990 to 2019 and did a decomposition analysis. Despite these obvious strengths, there are several limitations, and causality and confounding especially need to be addressed. Although cohort and case-control studies, the two types of epidemiological studies compiled for this research, rank at the upper end of the epidemiological evidence hierarchy, they are by no means proof of causality. Studies assessing the relationship between air pollution and type 2 diabetes consistently revealed increased incidence and prevalence. Most of the studies adjusted for personal-level confounders such as age and sex. Some, but not all, studies adjusted for socioeconomic status (eg, income, education and body-mass index) and behaviour (eg, smoking, alcohol use, and physical activity). Several studies have suggested that the effect of air pollution on type 2 diabetes varied over different groups. Honda and colleagues found increased risk in a cohort of older people (age ≥57 years), and other studies particularly highlighted women as more vulnerable. Park and colleagues emphasised the likelihood of different population groups and ethnicities exhibiting different risks. Similarly, other forms of ambient air pollution not considered in our and other studies, such as gaseous pollutants, might also be relevant. Some evidence suggests that traffic-related air pollution is a higher risk for type 2 diabetes. Several studies have
found a consistent effect of nitrogen dioxide on type 2 diabetes incidence, but this effect is less consistent for PM.\textsuperscript{7,24} However, few studies adjust for nitrogen dioxide or noise, which are often correlated.\textsuperscript{25}

The exposure–response relationship sharply increases from the theoretical minimum risk exposure level to approximately 50 µg/m\textsuperscript{3} and levels off throughout the exposure range. Although the shape fits the data well, the constraints and priors imposed on the fit enable this shape. Specifically, we included shape priors so that the curve would be monotonically increasing and concave. Furthermore, a strong prior on the upper segment prevented the curve from strongly increasing beyond the exposure range for which effect estimates were available. The shape of our derived exposure–response curve, which reflects a strong increase at lower exposures and a levelling off at higher air pollution levels, has been found in other studies, such as the hazard curve developed from the US Veterans Cohort data.\textsuperscript{26} This suggests the possibility of saturation of the mechanism (or mechanisms) driving the biological connection between PM exposure and type 2 diabetes, as has been postulated for cardiovascular mortality.\textsuperscript{27,28} Indeed, the same non-linearity has been reported for cardiovascular mortality in the Canadian Census and cohort studies in males in China.\textsuperscript{24,29} In addition to saturation, changes in the aerosol composition might be driving this shape. The issue of equitoxicity has
frequently been raised within the scientific community. Although differing toxicity is plausible, so far, PM₂·₅ has proved to be the most consistent and robust predictor of mortality in studies of long-term exposure.⁴⁰–⁴⁷

In summary, the relationship between air pollution and type 2 diabetes is highly complex, and effect estimations are strongly affected by study design, cohort characteristics, the degree of covariate adjustment, and exposure assessment. Although our meta-regression framework cannot fully overcome all limitations in the original study designs, the MR-BRT tool allowed us to account for several study-level covariates and remaining between-study heterogeneity. The exposure–response relationship was significant along the entire range of exposures. In conjunction with the biological plausibility of an effect of PM inhalation on type 2 diabetes, we considered the evidence sufficient to include PM₂·₅ and type 2 diabetes as a new risk–outcome pair into the GBD.

Our results highlight the relevance of air pollution as a risk factor for type 2 diabetes. The attributable burden shows strong regional variation and distinct temporal trends: although ambient air pollution contributes a large share globally, in sub-Saharan Africa, a larger part can be attributed to household air pollution. In almost all GBD super-regions, except the high-income region, the burden attributable to ambient air pollution has increased, whereas the burden attributable to household air pollution has decreased globally and in all regions.

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Data sharing

To download the data used in these analyses, please visit the Global Health Data Exchange GBD 2019 results website

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## References


