Robust association between short-term ambient $PM_{2.5}$ exposure and COVID prevalence in India

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Abstract

Novel coronavirus (COVID) outbreak is the deadliest pandemic in our lifetime. The COVID prevalence risk may be enhanced due to comorbidity from other health risk factors like air pollution. However, such evidence is still lacking in India. Using daily confirmed cases, ambient $PM_{2.5}$ (fine particulate matter) exposure and meteorological parameters from 28 major states of India between March 14-June 9, 2020, in a generalized additive model, we estimate the association between short-term $PM_{2.5}$ exposure and daily COVID confirmed cases. We find that a 10 mg m^{-3} increase in ambient $PM_{2.5}$ exposure (with a lag of 0-14 days) is significantly associated with an increased COVID incidence [relative risk (*RR*) of 1.135 (95% uncertainty interval: 1.091-1.180)] after adjusting for the meteorological factors. A non-linear association between $PM_{2.5}$ (lag 0-14) and COVID infection predicts an *RR* of 4.482 (3.357-5.983) for exposure at 60 mg m^{-3} relative to 25 mg m^{-3}. Our results indicate a significant positive association between ambient $PM_{2.5}$ exposure and COVID prevalence in India. As India is easing lockdown measures, higher outdoor air pollution may have implications on COVID transmission, information which can be helpful for general public and policymakers alike.

Introduction

Novel coronavirus (COVID) outbreak in Wuhan, China in December 2019 and its subsequent spread across the world has been declared as an international public health emergency by the World Health Organization (WHO). The scale of the COVID–19 impact both on morbidity and mortality is unprecedented in our lifetime and is expected to have a momentous socio-economic impact on the global population. The disease has been spreading in almost every country through infected individuals coming in direct or indirect contacts with others[1]. To stop the spread of the disease further, either partial or complete lockdown with strict vigilance of social distancing has been adopted by the affected countries.

Early studies[2,3] have pointed out that patients with any comorbidity are more vulnerable to COVID. Particularly the non-communicable diseases such as hypertension, chronic obstructive pulmonary disease, cerebrovascular disease and diabetes are identified as major risk factors for COVID patients[4]. Besides, a high level of air pollution exposure has been identified as an important risk factor for COVID patients[5,6]. In a study in China[7], a positive association has been observed between COVID cases and major criteria pollutants ($PM_{2.5}$, PM_{10}, NO_2,O_3 and CO) except SO_2. A similar positive association between COVID cases and $PM_{2.5}$ exposure was obtained from Italy[8]. While these studies examined the association between COVID cases and short-term exposure to air pollution, chronic exposure to air pollution is also being considered as a risk of COVID outbreak[9].

In response to COVID pandemic, India was one of the few countries to implement a nationwide lockdown (from March 25 to April 14, 2020) at an early stage and announced the extension of the lockdown till May 30, 2020, with partial relaxation after April 21, 2020. The first COVID case was diagnosed in India on January 30, 2020, and it took 59 days to reach 1,000 cases. In our analysis period the cases steadily rose

from 81 cases as of March 14 to 267,261 cases as of June 9, 136,176 people recovered (50% recovery rate) and 7798 people died. The extent of the success for the early implementation of lockdown in reducing the spread of the disease in India can only be known in future. However, India has a large burden of non-communicable diseases[10] and is one of the most polluted nations in the world[11]. In 2017, 99% of the Indian population was exposed to ambient $PM_{2.5}$ level higher than the WHO air quality guideline[12]. This suggests that the Indian population is likely to be vulnerable to COVID and hence, it is important to examine if the positive association between air pollution and COVID cases found in the recent literature stands true for India too.

In this study, we examine the association of short-term exposure to ambient $PM_{2.5}$ (lag 0–7, 0–14 and 0–21 days) with COVID prevalence in India (Fig. 1) using a generalized additive model (GAM) (see Methods). Due to the paucity in ground-based measurements in India[13], we use satellite-$PM_{2.5}$ data that is calibrated and evaluated against reference-grade monitors (Fig. 2). We analyze COVID prevalence data in place of death because the total number of COVID–19 deaths (fortunately) is not large enough for statistical analysis. We perform additional six sensitivity tests to confirm the robustness of our results—(1) analysis with exclusion of Maharashtra where one-third of the COVID cases in India is registered; (2) inclusion of the total number of testing in the model; (3) altering the period of analysis; (4) exploring the non-linearity in the association; (5) analysis at the district level and (6) use of a mixed-effect quasi-Poisson model.

Results

Association between short-term $PM_{2.5}$ exposure and confirmed COVID cases. In Table 1, we present summary statistics for daily confirmed COVID case count, ambient $PM_{2.5}$ exposure and meteorological data. The 28 states in our study included over 2,67,000 COVID cases during our analysis period. The mean $PM_{2.5}$ for our sample is 60 μg m^{-3} and the average daily number of confirmed cases is 108.5 (with a standard deviation of 311.6, this large standard deviation points towards the disease heterogeneity at the state level). The average daily temperature and humidity were 302.3 K and 0.0124 kg/kg respectively.

Table 1. Summary statistics of daily confirmed new cases, the concentration of air pollution, and meteorological variables across all states and days.

	Mean	Std. Dev	Min	Max
$PM_{2.5}$ (mg/m^3)	60.1	24.5	1.6	161.2
Humidity (kg/kg)	0.0124	0.0042	0.0016	0.0212
Temperature (K)	302.3	3.8	289.1	313.3
Daily confirmed COVID Cases	108.5	311.6	0.0	3041.0

We plot the moving average lag effect of short-term ambient $PM_{2.5}$ exposure with lag 0–7, lag 0–14, lag 0–21 in Fig. 3. We find that a 10 μg m^{-3} increase in ambient $PM_{2.5}$ exposure is associated with an RR of 1.084 (95% uncertainty interval, UI: 1.055—1.115), 1.135 (1.091—1.180) and 1.072 (1.025—1.125) for lag 0–7, lag 0–14 and lag 0–21 respectively.

The sensitivity of the association to various cases for robustness check. Our first sensitivity analysis involves dropping the state of Maharashtra from our analysis (Fig. 4a). We find that a 10 μg m^{-3} increase in ambient $PM_{2.5}$ exposure is associated with an *RR* of 1.013 (0.982– 1.045), 1.048 (1.002—1.096) and 1.014 (0.962– 1.069) for lag 0–7, lag 0–14 and lag 0–21 respectively. The result implies that the relationship between COVID confirmed cases and short-term exposure to ambient $PM_{2.5}$ is still present after the exclusion of the state of Maharashtra. In our next sensitivity analysis, we introduce explicit control for the number of tests conducted (Fig. 4b). The association remains significant and the magnitude of the effects increased as demonstrated by *RR* of 1.190 (1.136–1.247) for lag 0–14 after controlling for testing in each state. Another robustness check involves limiting the analysis to post lockdown period (*i.e.* after March 25, 2020). The result of this analysis (Fig. 4c) reveals that the estimates retain their significance with almost similar magnitudes.

Our fourth sensitivity analysis involves exploring a possible non-linear association between pollution exposure and COVID cases. A quadratic B-spline is introduced for the exposure variable which is centered at 25 μg m^{-3}—the WHO standard for 24-hour $PM_{2.5}$. The exposure-response relationship (depicted in Fig. 5) predicted by this analysis shows the average *RR* between different levels of $PM_{2.5}$ versus the centering point that is 25 μg m^{-3}. The effect of higher pollution level (60 μg m^{-3}) is found to raise the risk of infection. The *RR* at 60 μg m^{-3} versus 25 μg m^{-3} is found to be 2.271 (1.906—2.707), 4.482 (3.357–5.983) and 5.379 (3.598– 8.042) for lag 0–7 (Fig. 5a), lag 0–14 (Fig. 5b) and lag 0–21 (Fig. 5c), respectively.

Analysis using district-level data and meta-analysis reveals similar results as before (Fig. 6). Our estimates from these analyses are similar in magnitude, however, these sensitivity analyses show that estimates for lag 0–21 no longer remains significant. This implies that our results are robust to the alternate unit of analysis (district) and alternate choice of estimation model (meta-analysis with the state as the random variable) as well.

Discussion And Conclusions

Using a GAM, we find that short-term exposure to air pollution as represented by ambient $PM_{2.5}$ is positively associated with daily confirmed COVID cases in 28 states of India. Our results are found to be robust to multiple sensitivity checks. For a country like India with an average $PM_{2.5}$ amongst the highest

in the world, our analysis shows that short-term exposure to $PM_{2.5}$ can be an additional risk factor in COVID infection and transmission.

Previous literature has established associations between exposure to air pollution and spread of measles[14,15] and spread of respiratory diseases[16,17]. Specifically, in case of COVID, studies from China[7] and Italy[8,9] have shown air pollution to be an important factor in disease transmission and mortality. Our study provides evidence from India which is currently witnessing a rapid rise in COVID cases and has a significant proportion of its population residing in areas with poorest air quality in the world.

Our study has important policy implications. Air quality has improved significantly in India during lockdown due to cease of economic activity nationwide[18]. However, since India is currently easing the lockdown, it is expected to increase the pollution level. Pollution mitigation strategies should be adopted by the public and prescribed by policymakers to prevent further spread of the infection, especially in the polluted place like the Indo-Gangetic Plain in Northern India where 24-hr ambient $PM_{2.5}$ remains higher than the national standard most of the time. Such areas should receive special attention as pollution might exacerbate the spread of COVID infection.

We note that our study should be interpreted keeping in mind the following points. First, the unit of analysis is a big geographical unit that is a state. The daily data on COVID infection is released consistently only at this level by the government; hence we conduct our analysis at the state level. Since the association remains significant at a district level, we feel the results to hold good at a finer spatial scale. Future studies can explore pollution-infection association at a city level as more data becomes available. Second, due to the absence of a ground-based monitoring network in India that has adequate regional coverage, we rely on satellite data for $PM_{2.5}$ only. Although most other pollutants are found to be highly correlated with $PM_{2.5}$[7], precise single pollutant models for other pollutants like SO_2, NO_2, PM_{10}, CO and O_3 are not considered in this study due to paucity of representative stations in most of the states. Third, due to the unavailability of other relevant confounding factors like daily mobility or migration data, and age and gender of patients, we could not perform detailed heterogeneity analysis for various subgroups. Lastly, these estimates are not causal, but only highlight the association of air pollution with COVID confirmed cases similar to studies following similar empirical design[3,7]. Our robust association calls for focused cohort studies to establish causality and understand the biological mechanism.

We conclude that a significant positive association between short-term exposure to ambient $PM_{2.5}$ and COVID infection in India suggests that air pollution can be an additional risk factor in disease transmission and therefore, the air pollution mitigation programs need to be implemented with more efficiency.

Methods

COVID data. We use a daily number of COVID confirmed cases for states (and union territories, UTs) of India from a crowdsourced platform (covid19india.org), which collates data from official state bulletins

among other sources. The data on this platform is updated on a real-time basis with information from the official state press bulletins, official (Chief Minister, Health Minister) handles, Press Information Bureau, Press Trust of India, ANI reports. We use data on confirmed COVID cases from March 14 to June 9, 2020. The total number of confirmed COVID cases in India as of June 9th was 267,261 of which 28 major states (and UTs) had more than 100 cases and accounted for 99.9% of all cases (Fig. 1). We include data from Ladakh (a new UT) in the erstwhile state of Jammu and Kashmir in our analysis. We also used data on the number of tests conducted from the same source (i.e. covid19india.org).

Ambient $PM_{2.5}$ exposure data. Inadequate in-situ data of ambient $PM_{2.5}$ in India[13] propels us to utilize satellite-based ambient $PM_{2.5}$ exposure. We derive surface $PM_{2.5}$ from satellite aerosol optical depth (AOD) product following our previous works[19,20]. For this study, we analyze AOD retrieved by Moderate Resolution Imaging Spectroradiometer (MODIS) using MAIAC (Multi-Angle Implementation of Atmospheric Correction) algorithm at 1 km 1 km resolution. We convert daily MAIAC AOD to $PM_{2.5}$ using a dynamic scaling factor derived from MERRA–2 (Modern-Era Retrospective analysis for Research and Applications, version 2) reanalysis data and calibrate the satellite-$PM_{2.5}$ using the coincident in-situ measurements of $PM_{2.5}$ by a ground-based network that is maintained and quality-controlled by the Central Pollution Control Board (CPCB). We have used a percentile-based regression technique to develop region-specific correction factors and tuned the satellite-$PM_{2.5}$ closer to the ground-based measurements[20]. Since the satellite-$PM_{2.5}$ represents satellite overpass time (10 am to 2 pm), we have applied a diurnal scaling factor from MERRA–2 reanalysis data to estimate 24-hr $PM_{2.5}$ from the retrieved $PM_{2.5}$. Comparison of 24-hr satellite-derived calibrated $PM_{2.5}$ with CPCB measurements (Fig. 2) reveals an excellent correlation (R = 0.98) and a reasonable root mean square error (24.2 g/m^3)attesting to the quality of the satellite data product given the large spatial data gaps in ground-based observations.

Meteorological data. We analyze the temperature and specific humidity data from ERA5 reanalysis. ERA5 is an updated and improved version of the ERA-Interim datasets[21]. We use the hourly data at the lowest level averaged over the diurnal scale in our analysis. We note that the surface pressure can be lower than 1000 hPa in a high-altitude grid for which the ERA5 reanalysis extrapolates the values from the level above in the post-processing.

Modeling framework. The ambient $PM_{2.5}$ exposure-COVID relationship has been examined by GAM, which uses daily data on the count of confirmed COVID cases, 24-hr average $PM_{2.5}$ exposure and weather data on humidity and temperature for the 28 major states of India. We estimate daily state-level $PM_{2.5}$ and meteorological parameters by averaging all the grids lying within the state boundary. For the grids that partially belong to a particular state, the area-weighted average is considered in Arc-GIS using the state-level shapefiles. The population-weighted daily exposure estimates allow us to minimize exposure misclassification as the urban areas (where the COVID cases are higher) have a larger population (and hence larger weight) than the rural areas in a state/union territory (UT).

The dependent variable—daily number of confirmed COVID cases is a count variable; hence, we use GAM with a quasi-Poisson family for over-dispersed data[14,22,23]. The median incubation period for COVID cases in China has been estimated to be 5.1 days, with 97.5% of cases developing symptoms within 11.5 days[24,25]. Thus, in this study, we model short-term exposure to ambient $PM_{2.5}$ (lag 0–7, lag 0–14, lag 0–21) as a moving-average[7,22]. Our basic GAM is defined as follows:

$$g(y_{it}) = \alpha + \beta PM_{il} + ns(temp_{il}, 3) + ns(hum_{il}, 3) + y_{i,t-1} + state_i + day_t \qquad (1).$$

In this model, gyit is a log link function of the expectation yit ≡EYit, where Yit is the series of the count of daily confirmed COVID cases in a state. *t* denotes the day of observation and α is the intercept. PMil represents the linear term for *l*+1 day moving average of $PM_{2.5}$ in state *i.* Our main coefficient of interest is β which captures the association between short-term exposure to $PM_{2.5}$ and COVID confirmed cases. The delayed effect of meteorological factors—temperature and humidity are also controlled for the same period.

To capture the possible non-linear relationship between the meteorological factors and COVID incidence, we use a natural cubic spline (*ns ()*) function with three degrees of freedom. The choice of degrees of freedom is based on previous studies[3,7,26,27]. yi,t−1 denotes previous day count of daily confirmed COVID cases in state *i,* to account for serial correlation in our data[7,26,27]. We also introduce state fixed effects, statei, to account for unobserved time-invariant characteristics of states like population density, availability of health infrastructure and total population. Lastly, time fixed effects, dayt, are added to the model to capture unobserved factors at the day level, they account for shocks like national lockdown, lifting of movement restrictions[7]. These fixed effects (state and time) help us in exploiting the temporal and spatial variation in our data.

Sensitivity analysis. We employ six additional sensitivity analysis to check for robustness of our results. First, we exclude the state of Maharashtra which accounts for the largest contribution (one-third) to the total cases in India (as of June 9, 2020) from our analysis to check whether the results hold. Second, we include total tests conducted in each state in our analysis to check whether our results are sensitive to this alternate specification. This variable (total tests conducted) captures how states are ramping up their efforts to detect COVID infections which in turn affects the total confirmed case count in each state. The data on total cases confirmed in each state is not available for every day and hence the inclusion of this variable in our model has reduced our analysis sample considerably. Third, we test for the robustness of our results by altering the choice of the analysis period. We do this by restricting our study only to the post lockdown period, that is from March 25 to June 9, 2020. Fourth, we test whether our findings are sensitive to an alternate non-linear specification for the exposure variable. We replace the linear $PM_{2.5}$ variable with a quadratic B-spline[23]. The quadratic B-spline for the moving average $PM_{2.5}$ is defined by 3 knots placed at 20 μg m^{-3}, 60 μg m^{-3} and 100 μg m^{-3}. All the spline basis variables are centered at 25 μg m^{-3} (which is the WHO air quality guideline for 24-hour $PM_{2.5}$).

Our next sensitivity analysis is to test the impact of exposure misclassification (if any, due to the use of state-level population-weighted $PM_{2.5}$ exposure) on our results. We could not carry out city-level analysis as the COVID cases are not reported systematically at city-level. Instead, we used the second-order geographical and administrative unit (*i.e.* district) as the unit of analysis. On April 30, 2020 Government of India through a circular (available at https://static.mygov.in/rest/s3fs-public/mygov_158831498053877021.pdf) categorized all districts of India (total number of districts in India is 733) into the red zone (hotspots), orange zone (incidence of cases, doubling rate is relatively lower than red zones) and green zone (no confirmed cases in the last 21 days). We note that even the district-level data on COVID confirmed cases is only available from April 21, 2020, and the data is not available for each day for every district (the reason for mainly relying on the state-level analysis). Out of 130 districts categorized as red zone districts, we conducted our analysis on 118 districts which have consistent data.

Our final robustness check comprises of conducting an alternate analysis which used meta-analysis following a two-stage process. In the first stage, state-specific $PM_{2.5}$-COVIDrelationshipsare analyzed using a time series Poisson model which accounted for overdispersion in the data. The first stage model is similar to equation 1 described above, it used a linear control for exposure (moving average), a natural cubic spline with df = 2 for humidity, df = 3 for temperature, df = 4 for time and is also controlled for the previous day-case count to account for serial correlation. In the second stage, these individual state associations are combined using a random-effects meta-analysis to arrive at a national level estimate. The random-effects meta-analysis model was fitted using maximum likelihood estimation.

The analysis has been carried out in R (version 3.5.1) using *glm* command in the *mgcv* package. The meta-analysis was conducted using *mvmeta* command. The estimates of ambient $PM_{2.5}$ exposure is expressed as relative risk (*RR)* with $RR > 1$ representing an increased risk due to unit increases in $PM_{2.5}$ exposure by 10 μg m^{-3} and corresponding 95% confidence intervals have also been provided.

Declarations

Data availability. All data will be made available on request from the first author.

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Author contributions

P. S. and S. D. conceived the study and wrote the initial manuscript. P. S. did the modelling and analysis. B. P. and K. D. analyzed ambient $PM_{2.5}$ exposure and meteorological data. S. C. helped in collating COVID

data. All authors provided comments and contributed to the final version of the manuscript.

Competing interests

The authors declare no competing interests.

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Figures

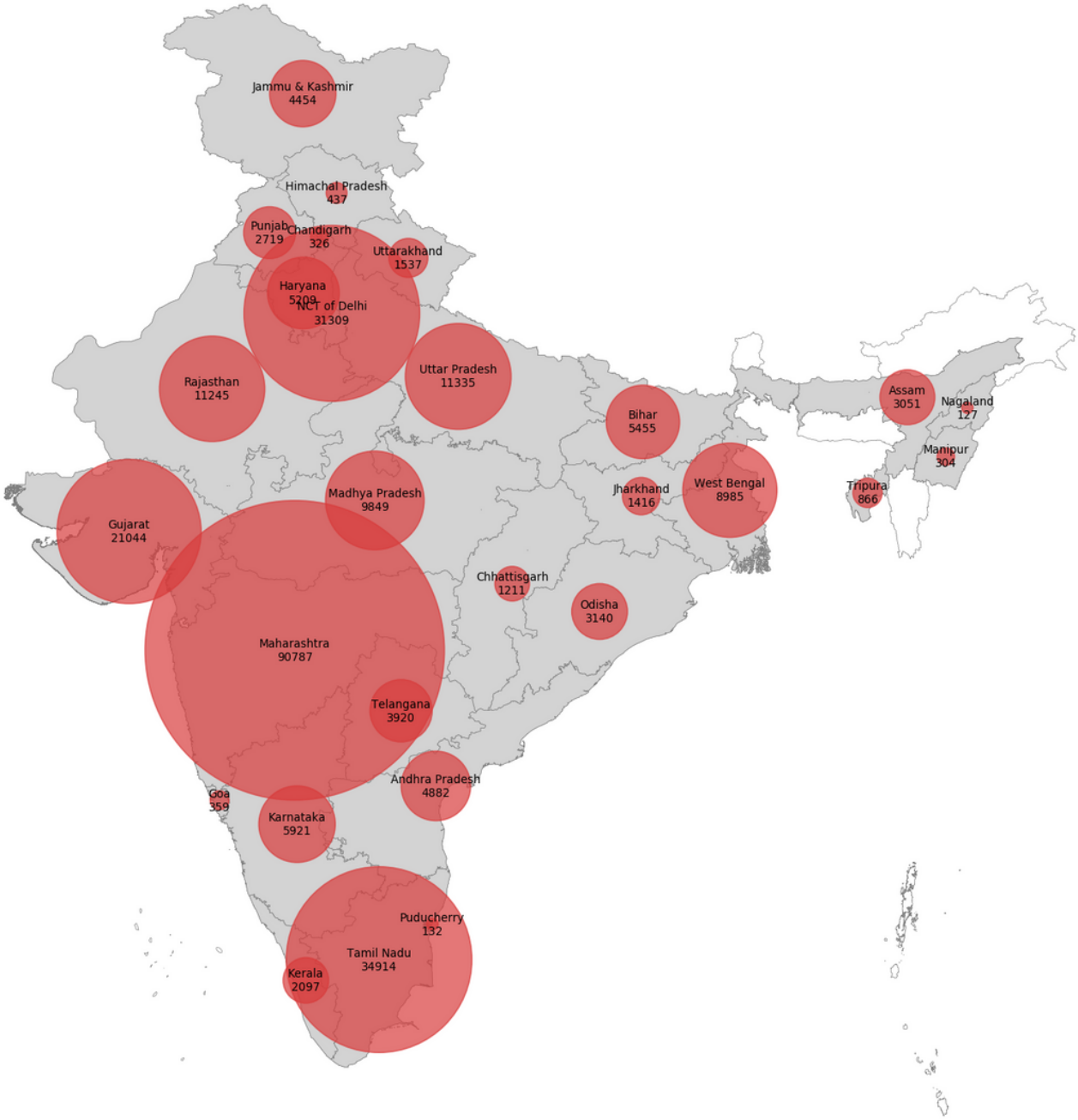

Figure 1

Cumulative confirmed COVID cases in states of India with more than 100 cases (grey shade) as of June 9, 2020. Larger circle implies higher COVID cases.

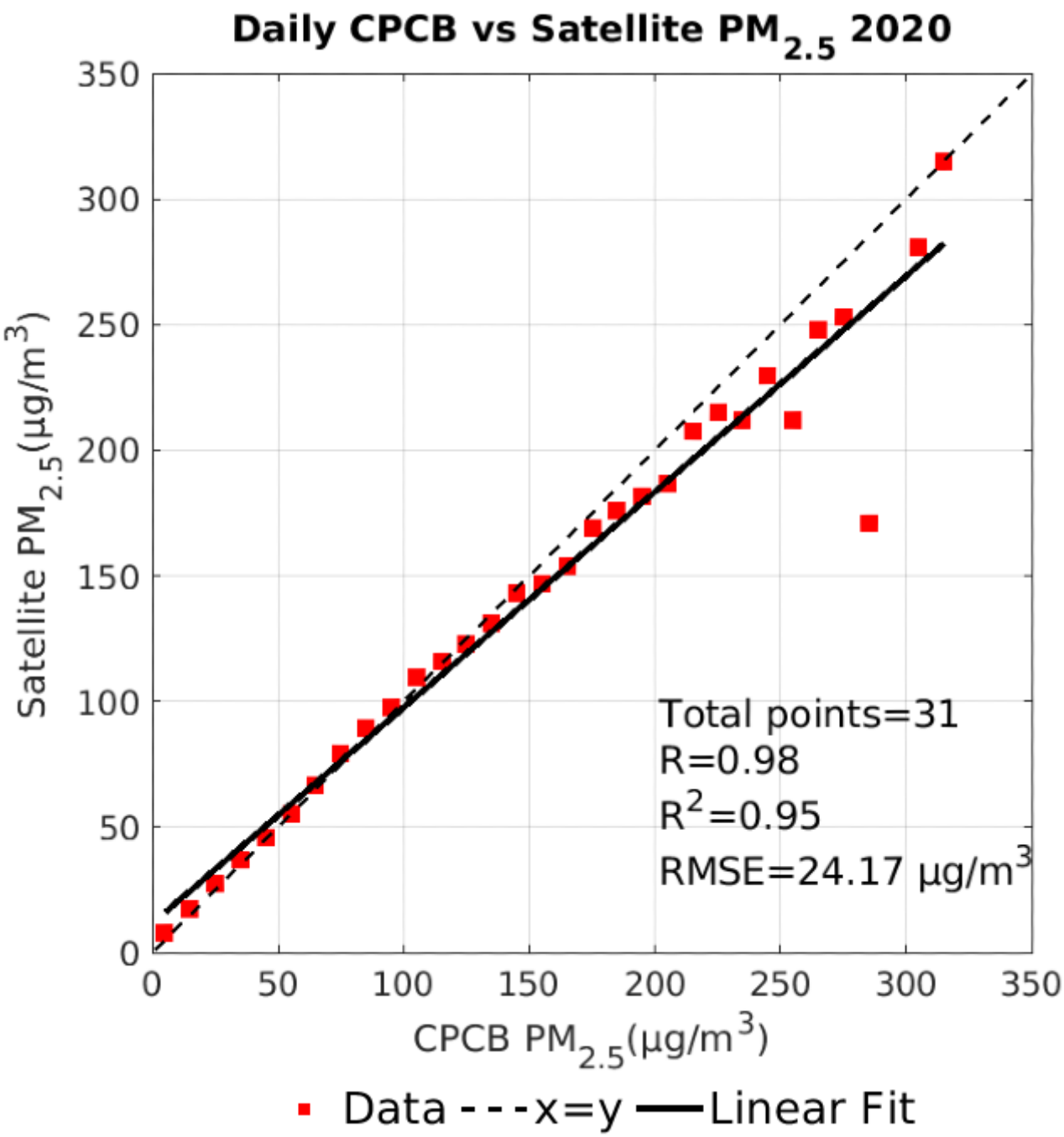

Figure 2

Scatter plot and regression statistics between daily CPCB and satellite-PM2.5 binned at every 10 g m-3 interval across 120 CPCB sites in India.

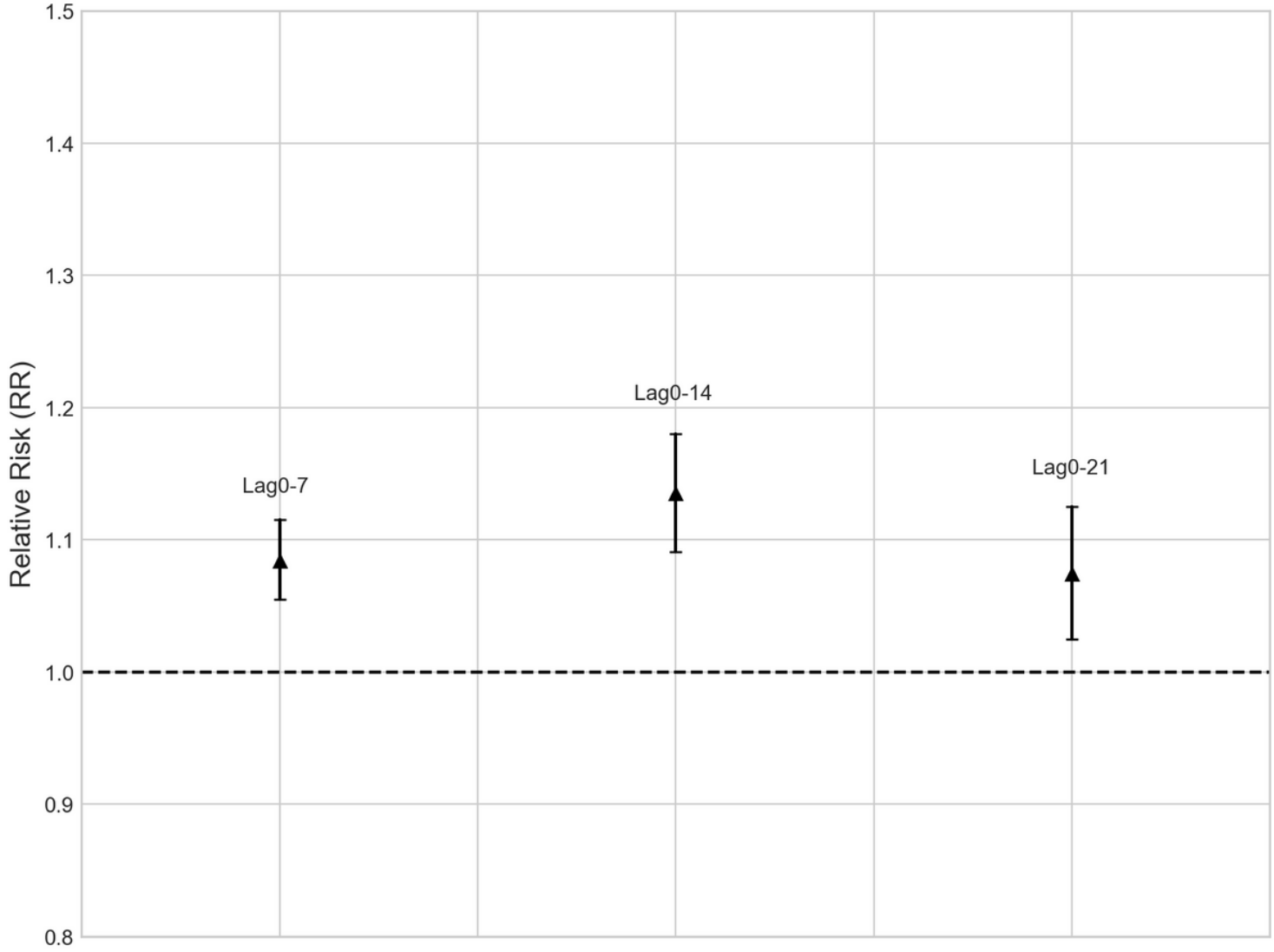

Figure 3

Relative Risk (RR) associated with a 10 μg/m3 increase in PM2.5 exposure with 95% confidence interval.

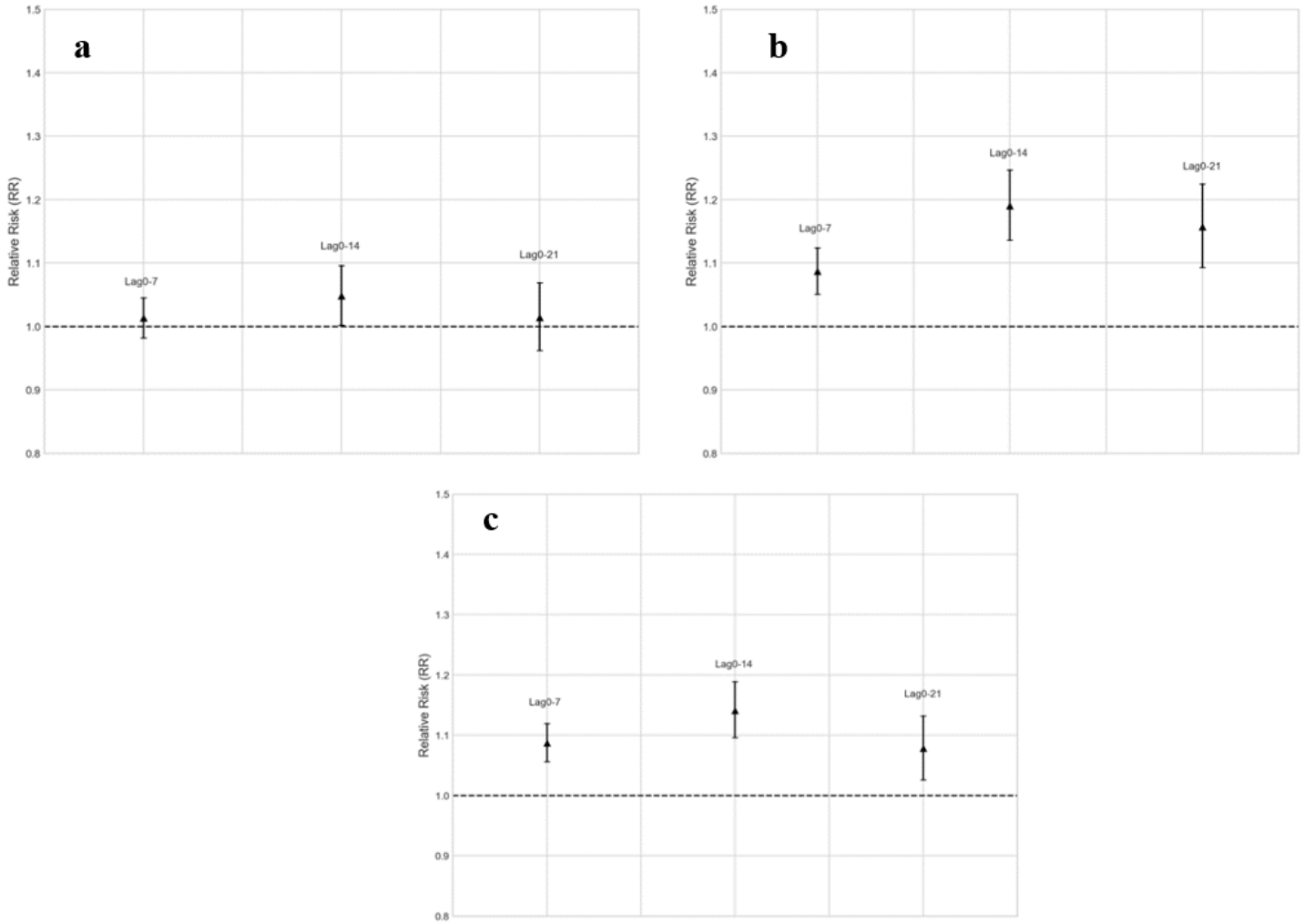

Figure 4

RR associated with a 10 µg m-3 increase in ambient PM2.5 exposure with 95% uncertainty interval with analysis (a) excluding the state of Maharashtra, (b) including the daily number of tests conducted in each state as an additional control and (c) analysis for the post-lockdown period (March 25-June 9, 2020).

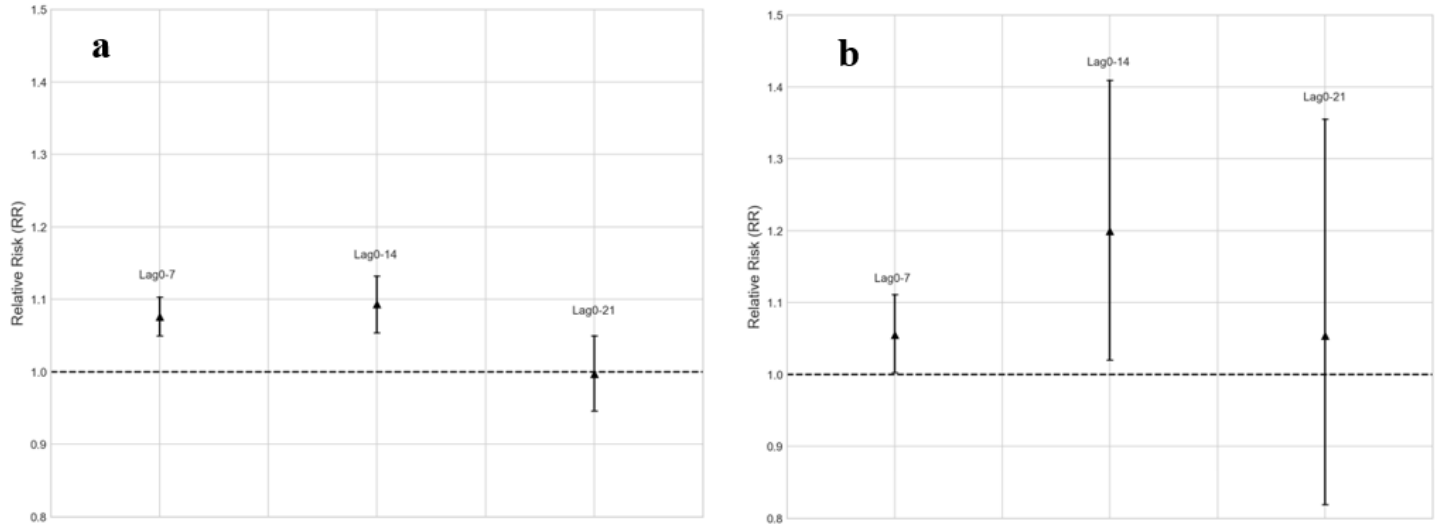

Figure 5

Exposure-response relationship in RR between ambient PM2.5 and daily confirmed COVID cases in 28 states of India for (a) lag 0-7, (b) 0-14 and (c) 0-21. Gray area represents 95% confidence interval. Dots depict the location of knots. Reference is at 25 µg/m3 (WHO 24-hr PM2.5 standard).

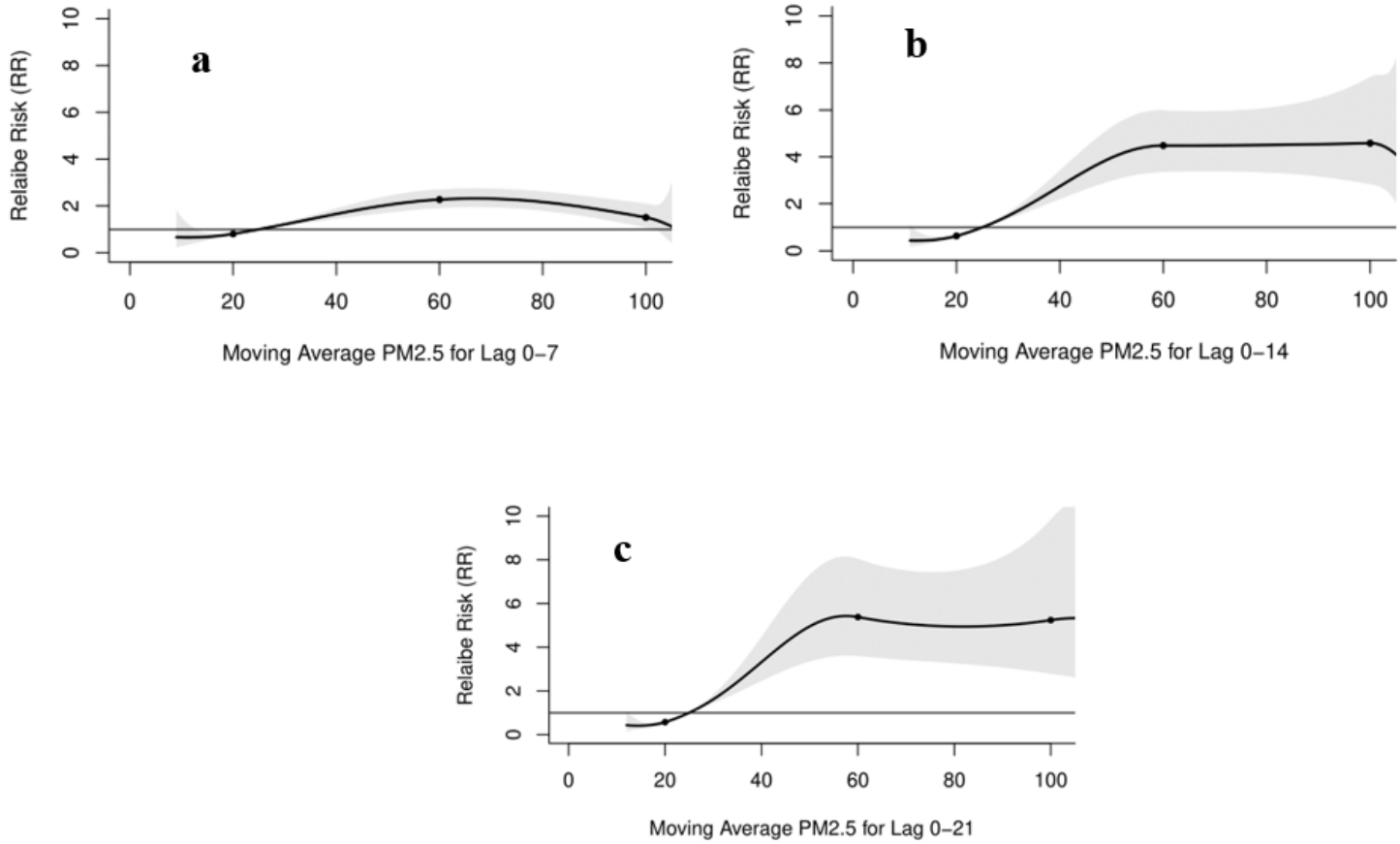

Figure 6

RR associated with a 10 μg m-3 increase in ambient PM2.5 exposure with 95% uncertainty interval with analysis (a) using district as a unit of analysis and (b) estimates from a meta-analysis with the state as the random variable.