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Long-term trends in mortality risk associated with short-term exposure to air pollution in 10 Japanese cities between 1977 and 2015

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ABSTRACT

Background and aim: Short-term associations between air pollution and mortality have been well reported in Japan, but the historical changes in mortality risk remain unknown. We examined temporal changes in the mortality risks associated with short-term exposure to four criteria air pollutants in selected Japanese cities.
Methods: We collected daily mortality data for non-accidental causes (n = 5,748,206), cardiovascular (n = 1,938,743) and respiratory diseases (n = 777,266), and air pollutants (sulfur dioxide [SO_2], nitrogen dioxide [NO_2], suspended particulate matter [SPM], and oxidants [Ox]) in 10 cities from 1977 to 2015. We performed two-stage analysis with 5-year stratification to estimate the relative risk (RR) of mortality per 10-unit increase in the 2-day moving average of air pollutant concentrations. In the first stage, city-specific associations were assessed using a quasi-Poisson generalized linear regression model. In the second stage, city-specific estimates were pooled using a random-effects meta-analysis. Linear trend and ratio of relative risks (RRR) were computed to examine temporal changes.
Results: When stratifying the analysis by every 5 years, average concentrations in each sub-period decreased for SO_2, NO_2, and SPM (14.2–2.3 ppb, 29.4–17.5 ppb, 52.1–20.6 μg/m^3, respectively) but increased for Ox (29.1–39.1 ppb) over the study period. We found evidence of a negative linear trend in the risk of cardiovascular mortality associated with SPM across sub-periods. However, the risks of non-accidental and respiratory mortality per 10-unit increase in SPM concentration were significantly higher in the most recent period than in the earliest period. Other gaseous pollutants did not show such temporal risk change. The risks posed by these pollutants were slightly to moderately heterogeneous in the different cities.
Conclusions: The mortality risks associated with short-term exposure to SPM changed, with different trends by cause of death, in 10 cities over 39 years whereas the risks for other gaseous pollutants were relatively stable.

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1. Introduction

The short-term association between ambient air pollution and daily mortality has been widely studied, and evidence suggests that air pollution disproportionately affects the health of different populations to different extents (Analitis et al., 2006; Brunekreef and Holgate, 2002; Wong et al., 2008; Zanobetti et al., 2003). Temporal variability in the short-term effects of air pollution on mortality has also been studied (Dominici et al., 2007; Fischer et al., 2011; Perez et al., 2015; Renzi et al., 2017; Xue et al., 2018). Environmental policies that affect particulate emissions and temporal changes in emission sources may change the chemical compositions and toxicities of particles of different sizes (Health Effects Institute, 2019; Perez et al., 2015; Phosri et al., 2020; Renzi et al., 2017). However, evidence on temporal trends in the health risks posed by pollutants in ambient air is still lacking. Most of the conclusions drawn in previous studies are focused on particulate matter (PM) and are not applicable to gaseous pollutants; moreover, the temporal changes in estimated mortality risks associated with air pollution over multiple decades have not been investigated in depth.

It is important to assess temporal changes in the health effects of air pollution, taking into account the increasing vulnerability of aging populations to air pollution and climate change (Chen et al., 2021) because population aging can potentially amplify the health impacts of ambient air pollution and climate change in the long-term (Yin et al., 2021; Xu et al., 2021). Advances in medical treatments, increasing awareness about the health risks of air pollution, and socioeconomic development may also affect the health impacts of air pollution over time (Sofia et al., 2020). Therefore, more research is needed on this topic in Japan given the different air pollution statuses and changes in emission or population characteristics over time.

Assessing changes in health risks related to air pollution in Japan over the past decades would improve our understanding of the effects on health of people living in major Japanese cities, where the levels of air pollution range from high to low. In Japan, rapid industrialization, economic growth, and urbanization caused serious air pollution between the 1950s and 1970s. Ambient air quality has improved since then because the Air Pollution Control Act, implemented in 1968, led to a decrease in pollutant emissions from fixed and mobile sources while photochemical air pollution level remains high (Japan International Cooperation Agency, 2005; Ministry of the Environment, 2014; 2020). During this period, as a consequence of high life expectancy and a low fertility rate, the proportion of Japanese people aged 65 and older has become the largest in the world, accounting for more than one-quarter of the total Japanese population in 2015 (Cabinet Office Japan, 2020; D'Ambrogio E., 2020).

We hypothesized that daily mortality risks associated with exposure to air pollution have changed over time and that different changes have occurred for different pollutants and causes of death. We aimed to investigate temporal changes in the risks of mortality from non-accidental causes, cardiovascular diseases, and respiratory diseases with short-term exposure to four air pollutants: sulfur dioxide (SO_2), nitrogen dioxide (NO_2), suspended particulate matter (SPM), and oxidants (Ox).

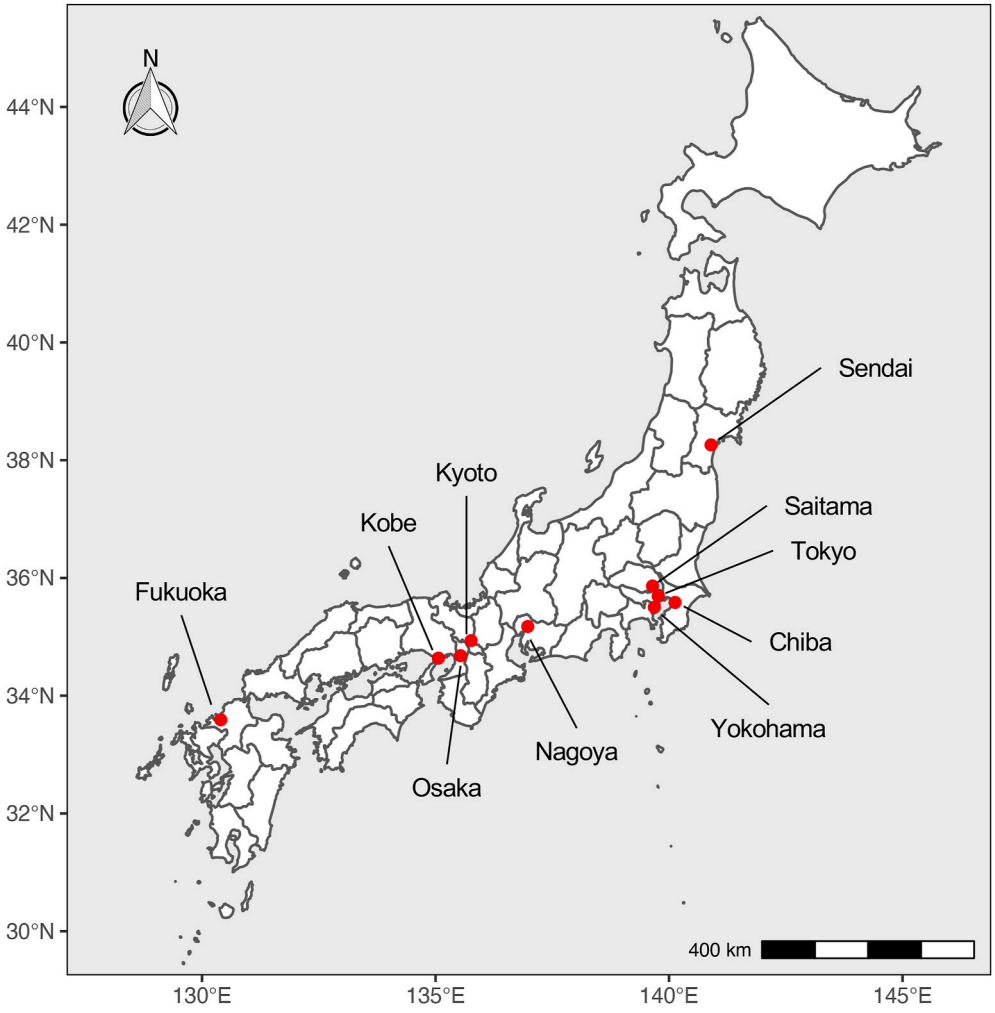

Fig. 1. Locations of the 10 selected cities.

2. Materials and methods

2.1. Study sites and period

To maximize the study period, we focused on 10 major cities in Japan: Fukuoka, Kobe, Osaka, Kyoto, Nagoya, Yokohama, Chiba, Tokyo 23 special wards, Saitama, and Sendai, in order of latitude of the cities. These cities have relatively larger populations than other cities and together accounted for 20.3% of the Japanese population in 2015 (Statistics Bureau, 2016). The study period was 39 years, from January 1, 1977 to December 31, 2015, owing to data availability. The locations of the included cities are shown in Fig. 1.

2.2. Data sources

Daily data for mortality, air pollutant concentrations in ambient air, and meteorological variables were obtained from the Ministry of Health, Labour and Welfare, each municipal government, and the National Institute for Environmental Studies and Japan Meteorological Agency, respectively. The data were processed by the Japan Air Pollution and Health Research (JAPHER) network to yield city-specific datasets (**Method S1**).

2.3. Data description

2.3.1. Mortality data

City-specific daily numbers of deaths were determined using three mortality categories defined in the International Classification of Diseases Eight Revision (ICD-8) for 1972–1978, Ninth Revision (ICD-9) for 1979–1994, and Tenth Revision (ICD-10) since 1995. The mortality categories were non-accidental causes (ICD-8 001–796, ICD-9 001–799, and ICD-10 A00-R99), cardiovascular diseases (ICD-8 390–458, ICD-9 390–459, and ICD-10 I00-I99), and respiratory diseases (ICD-8 460–519, ICD-9 460–519, and ICD-10 J00-J99). We defined each city according to 2020 administrative boundaries. We compiled the death counts for the same geographical areas within the 2020 city boundaries in case a boundary change occurred during the study period.

2.3.2. Air pollution data

PM and photochemical air pollution indices (SPM and Ox concentrations) were used because these are the criteria air pollutants, defined in the Japanese National Ambient Air Quality Standard (NAAQS) "Environmental Quality Standard (EQS)," which was established in 1973 after the occurrence of numerous episodes of severe air pollution. SPM was defined as airborne particles with a diameter $\leq$10 μm, assuming 100% efficiency cut-off at a 10 μm (Ministry of the Environment, 1973). However, at 50% efficiency, SPM in Japan is approximately particles with 7 μm or less diameter (PM_7). Ox was defined as oxidizing substances produced mainly through photochemical reactions. In Japan, before 1996, Ox was monitored based on the potassium iodide (KI) method, a wet chemical method that responds to photochemical oxidants, primarily ozone (O_3) ($\geq$90%), followed by others such as peroxyacetyl nitrate (PAN), hydrogen peroxide (H_2O_2) and organic hydroperoxides. Based on field measurement, local authority has decided to equate ozone levels with Ox levels in 1996 (Fukunaga et al., 2021). Over time, Japan has gradually transitioned to the newer UV absorption method (NIST SRP35), which is the widely used method to monitor O_3 (Akimoto, 2017; World Health Organization, 2021).

Hourly measurements of the SO_2, NO_2, SPM, and Ox concentrations were modified by following the steps described here. First, station-specific data were extracted from the data for residential stations called "general environment air monitoring stations" in each city. Second, for each city, the station-specific data for each air pollutant were averaged and daily (24-h) mean SO_2, NO_2, and SPM concentrations and daily maximum 8-h moving average Ox concentrations were calculated. For missing values, we first included all stations that had at least 29 days of data; the daily mean was set to "not available" if a station had more than five missing values each day (given an 80% hourly data capture requirement) (Ministry of the Environment, 2010). Data were also set to not available if a station had missing data for >28 consecutive days in a year (this was the annual data capture requirement for a station). Finally, a single station with the longest monitoring coverage was selected for each air pollutant and each city. The percentages of missing SO_2, NO_2, SPM, and Ox concentrations collected over 39 years in the 10 cities were 7.2%, 7.5%, 12.5%, and 12.6%, respectively. All 10 cities were included in each sub-period for SO_2 and NO_2. However, only five cities were eligible in the first sub-period for SPM and Ox. SPM still lacked data for one city (Sendai) in the second sub-period (**Method S1**).

2.3.3. Meteorological data

Hourly measurements of the meteorological variables (including temperature in °C and relative humidity in %) measured at a single monitoring station (the local meteorological observatory) in each of the 10 cities were used to obtain daily averages. If data from a weather monitoring station in a city were not available for the whole study period, we used data from another station closest to that city and in the same prefecture.

2.4. Statistical analysis

Associations between concentrations of SO_2, NO_2, SPM, and Ox and daily death counts from non-accidental causes, cardiovascular diseases, and respiratory diseases for each city were assessed and then pooled in two stages, following the analytic framework used in previous multi-location studies for different air pollutants (Liu et al., 2019; Meng et al., 2021; Vicedo-Cabrera et al., 2020). The main model for each air pollutant was established using the 2-day moving average concentration (lag 0–1), which was the average of the concentrations on the day of interest and the previous day (lag 0 and lag 1, respectively); this was because most pollutants exhibited the largest effects within this period in preliminary analysis, as suggested in previous studies (Orellano et al., 2020, 2021). The analysis was done with the aim to gain an overview of temporal changes in daily mortality risks related to pollutant concentrations over multiple decades; therefore, we stratified the full study period into half decades (i.e., every 5-year sub-period from 1977 to 2015, although the first sub-period contained only 4 years).

In the first stage, temporal variations in city-specific associations were identified using a quasi-Poisson generalized linear regression model with 5-year stratification (Wu et al., 2018). The equation used for each sub-period was:

$$\begin{aligned}\log[E(Y_t)] = \beta_0 + \beta_1 AP_{01} + ns(temp_{01} \times I[temp_{01} > MMT], df = 3) \\ + ns(temp_{16} \times I[temp_{16} < MMT], df = 2) + dow_t + holiday_t \\ + \log[pop_t] + ns(time, df = 7)\end{aligned} \quad (1)$$

where t is the calendar day of the observation; $E(Y_t)$ is the number of deaths in each mortality category on day t; β_0 is the intercept; β_1 is the regression coefficients for air pollutant exposure during a specific sub-period; AP_{01} is the 2-day moving average concentration of the air pollutant (AP_{01}); $ns(\,)$ indicates the natural cubic spline; $temp_{01}$ and $temp_{16}$ are the average of temperatures on the current and previous day (lag 0–1), and the previous 6 days (lag 1–6), respectively, representing high and low temperatures; $I[temp_{01} > MMT]$ and $I[temp_{16} < MMT]$ are indicator functions for the minimum mortality temperature (MMT) using a value of 1 when the condition is true, or 0 otherwise; df is the degrees of freedom; dow_t and $holiday_t$ are indicator variables for the day of the week and holidays, respectively; $\log[pop_t]$ is the prefecture-level population per year in log scale, used as a temporal adjustment of changes in the population; and $ns(time)$ is the natural cubic spline of the calendar time with seven degrees of freedom per year, accounting for seasonality and the long-term mortality trend.

High and low temperatures were adjusted separately to the number of days above or below 26 °C based on our preliminary analysis of MMT for the 10 cities and the published literature (Gasparrini et al., 2015). The natural cubic spline with three and two degrees of freedom were used to account for immediate heat effects (lag 0–1) and prolonged cold effects (lag 1–6) on mortality, respectively (Stafoggia et al., 2013; Tobías and Stafoggia, 2020). The relative risk (RR) of mortality and the 95% confidence interval (CI) were calculated and expressed per 10-unit increases in 2-day moving average air pollutant concentrations. In the second stage, we combined the city-specific estimates to give a pooled estimate using a random-effects meta-analysis with a restricted maximum likelihood method, where the inverse of within- and between-city variances was used as a weight to accommodate heterogeneity (Braga et al., 2002). This process was applied to each sub-period to account for temporal variations.

The linear trend of mortality risk was tested using an interaction term between a continuous variable representing the sub-periods and each air pollutant. We also examined the overall temporal trend in a pooled risk estimates by computing the ratio of relative risks (RRRs) comparing each sub-period to the first (Altman and Bland, 2003). Each time-period was regarded as independent. Thus, they were used to check the difference between the two estimates. Potential heterogeneity in between-city and between-period differences for each pollutant–mortality association was assessed using Cochran Q tests and I^2 statistics with pooled RRs from the 10 cities for the entire study period, and pooled RRRs from each sub-period, respectively.

Additional analyses based on the main model (**Eq. (1)**) were performed to determine whether a concentration–response function (CRF) changed over time. Because of the different concentration ranges across time periods, pooled CRFs for each pollutant–mortality association were calculated on absolute and relative exposure scales using distributed lag linear models (DLMs) and a multivariate meta-analysis with restricted maximum likelihood method for the first and last sub-periods (i.e., 1977–1980 and 2011–2015). The cross-basis function for the CRF was defined by modeling each pollutant as a linear function and a mean-constrained lag from lag 0 to lag 1, centered on the first percentile of the pollutant concentration for the 10 cities throughout the study period. Possible non-linear associations were assessed by producing non-linear CRFs on absolute and relative scales using distributed lag non-linear models, replacing the main exposure terms in the DLMs by the form of natural cubic spline with three degrees of freedom. The fitnesses of the linear and non-linear CRFs were determined by calculating quasi-Akaike information criteria (QAIC).

Finally, we performed several sensitivity analyses. The sensitivity for the 5-year time window was assessed by shortening the 5-year strata to 1-year strata and lengthening it to a 10-year overlapping moving window. Additional adjustments for the relative humidity and influenza-like illnesses were made. The results were checked against the results for longer lag periods for the air pollutant (i.e., using 3-day and 4-day moving averages) and two-pollutant models. We also examined the younger and older population separately by restricting the death cases and population offset for the different age-groups (i.e., aged below 65, and aged 65 and above). All statistical analyses were performed using R version 4.0.3 statistical software (R Core Team, 2020) with packages for the two-stage analysis (e.g., *tsModel*, *splines*, *Epi*, *meta*, *metafor*), and CRFs (e.g., *dlnm*, *mixmeta*, *splines*).

3. Results

3.1. Descriptive results

A summary of the data for the 10 cities in the first and last sub-periods and the whole study period are shown in Table 1. The average daily mean concentrations of SO_2, NO_2, and SPM in the first and last sub-periods decreased by 83.8% (14.2–2.3 ppb), 40.5% (29.4–17.5 ppb), and 60.5% (52.1–20.6 μg/m^3), respectively. The daily maximum 8-h moving average concentrations of Ox in the first and last sub-periods increased by 34.4% (29.1–39.1 ppb). The ambient temperatures and relative humidities in the 10 cities were between −5.2 °C and 33.7 °C and 18.8% and 100.0%, respectively. Average daily mortality for the 10 cities in the first and last sub-periods were 292 and 555, respectively, i.e., an increase of 90.1%, for non-accidental causes; 128 and 151, respectively, i.e., an increase of 18.0%, for cardiovascular diseases; and 22 and 91, respectively, i.e., an increase of 313.6%, for respiratory diseases. The descriptive summary in each sub-period and city-specific trends for the different variables are shown in the supplementary material (Table S1, Figs. S1–S4).

3.2. Temporal changes in daily mortality risk associated with air pollution

The pooled risk estimates of three mortality categories per 10-unit increase in concentrations of the four air pollutants during the different sub-periods are shown in Fig. 2. The corresponding distributions of the pollutant concentrations are shown in the bottom row.

For non-accidental mortality, the estimated risks (RRs) for SO_2, NO_2 and Ox were generally stable as positive and did not show any clear trend whereas only the RRs for SPM showed a slight increase in the recent periods. Taking a closer look, the RRs for SO_2 decreased slightly

Table 1
Summary of daily air pollutant concentrations, meteorological variable value, and mortality data (for non-accidental causes, cardiovascular diseases, and respiratory diseases) in 10 cities during the first sub-period (1977–1980), last sub-period (2011–2015), and the entire study period (1977–2015).

Variable	First sub-period (1977–1980)			Last sub-period (2011–2015)			Whole period (1977–2015)		
	Mean	SD	IQR	Mean	SD	IQR	Mean	SD	IQR
Air pollutants									
SO_2 (ppb)	14.2	8.0	10.3	2.3	1.9	2.3	6.8	5.7	6.6
NO_2 (ppb)	29.4	13.8	16.9	17.5	8.6	11.4	26.5	13.0	17.5
SPM (μg/m^3)	52.1	39.5	38.7	20.6	12.6	14.5	35.8	25.7	26.4
Ox (ppb)	29.1	16.8	21.8	39.1	16.0	20.6	33.6	17.2	22.6
Meteorological variable									
Temperature (°C)	15.4	8.2	13.8	16.1	8.4	14.7	15.7	8.2	14.0
Relative humidity (%)	66.9	13.5	19.1	66.6	14.3	20.1	67.0	13.8	19.3
Mortality									
Non-accidental causes	292	33	43	555	57	83	404	96	141
Cardiovascular disease	128	21	30	151	28	41	136	25	35
Respiratory disease	22	7	9	91	15	21	55	25	37

Notes: Daily means (24-h averages) for SO_2, NO_2, SPM, temperature, and relative humidity are shown. Daily maximum 8-h moving averages for Ox are shown. Mortality counts represent the sum of the 10 cities.
SD, standard deviation; IQR, interquartile range; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; SPM, suspended particulate matter; Ox, oxidants.

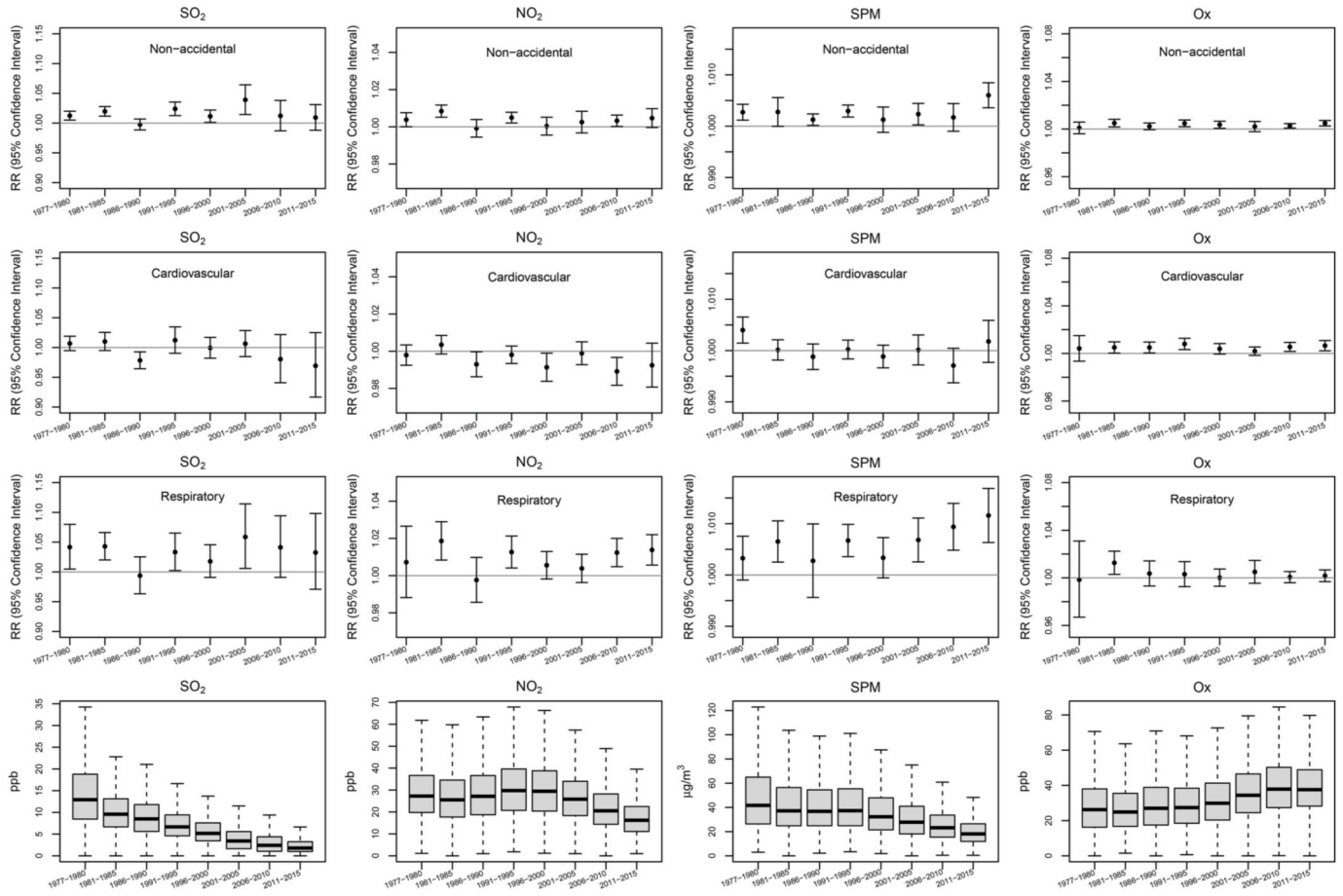

Fig. 2. Pooled estimates expressed as relative risk (RR) and 95% confidence interval for 10-unit increases in the concentrations of four air pollutants (columns) and three mortality categories (top three rows) for 5-year sub-periods (except the first period, which was 4 years) between 1977 and 2015, and boxplots of air pollutant concentration distributions (bottom row).
SD, standard deviation; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; SPM, suspended particulate matter; Ox, oxidants.

in the late 1980s, peaked in the early 2000s, and decreased to non-significant levels in the recent period. The RRs for NO_2 reached a maximum in the early 1980s and then decreased but remained positive for the rest of the study period. The RRs for SPM remained statistically significant for the first two decades and then increased slightly in the last two decades. The RRs for Ox were positive throughout the study period and exhibited statistically significant risks even in the final decade of the study period.

For cause-specific mortality, the RRs for cardiovascular mortality with exposure to SO_2, NO_2, and SPM were mostly non-significant. The RRs for respiratory mortality were generally higher than those for non-accidental mortality, and their changing pattern seemed to be similar. Notably, only the RRs for respiratory mortality with SPM depicted an upward trend over the study period. Conversely, the RRs for cardiovascular mortality with Ox were similar to the RRs for non-accidental mortality whereas the RRs for respiratory mortality were mostly non-significant.

The interval estimates in 95% CI for SO_2 with each outcome were noticeably wider in recent sub-periods than in earlier sub-periods. Conversely, slightly narrower 95% CI in recent sub-periods compared with earlier sub-periods were observed for Ox, especially with cause-specific mortality; such changes were not obvious for NO_2 and SPM. We found RRs below 1 for cardiovascular mortality with SO_2 and NO_2 in certain periods (the late 1980s for SO_2, the late 1990s and late 2000s for NO_2). However, these estimates were not stable in the other periods and were also sensitive to the different lengths of time-window (Fig. S21). The city-specific estimates are separately presented in the supplementary material (Figs. S5–S16).

We found evidence of a negative linear trend for cardiovascular mortality associated with SPM. Other pollutant–mortality associations

Table 2
List of p-values for linear trend of pooled mortality risk among 10 cities and cities with a significantly positive/negative linear trend at city level.

Mortality	Pollutant	p-value for linear trend	Cities with linear trend (p-value<0.05)
Non-accidental causes	SO_2	0.481 (↑)	
	NO_2	0.671 (↓)	
	SPM	0.802 (↑)	Kyoto (↓), Chiba (↑), Tokyo (↑)
	Ox	0.863 (↑)	
Cardiovascular disease	SO_2	0.118 (↓)	
	NO_2	0.204 (↓)	
	SPM	**0.026** (↓)	
	Ox	0.997 (↓)	Tokyo (↑)
Respiratory disease	SO_2	0.754 (↑)	Kobe (↑), Chiba (↑)
	NO_2	0.615 (↑)	Kobe (↑), Nagoya (↑)
	SPM	0.470 (↑)	Kobe (↑), Kyoto (↓), Chiba (↑)
	Ox	0.105 (↓)	

Notes: Linear trend, p-value for testing of linear trend between pooled or city-specific risk estimates for each pollutant–mortality association and an indicator variable for sub-periods. Up (red) and down (blue) arrows indicate a positive and negative linear trend, respectively.
SD, standard deviation; SO_2, sulfur dioxide; NO_2, nitrogen dioxide; SPM, suspended particulate matter; Ox, oxidants.

did not show a clear trend; p-values and directions (either positive or negative) are summarized in Table 2 and Table S2(a–d). Some city-specific estimates also indicated significant evidence of a linear trend for cities listed in Table 2. These cities are indicated with an asterisk (*) in the supplementary material (Figs. S5–S16).

The overall temporal trend in mortality risks for each sub-period, represented as RRRs relative to the RRs for the first sub-period, is shown in Fig. 3 and Table S3(a–d). For non-accidental mortality, none of the estimated risk changes (RRRs) for SO_2, NO_2, SPM, and Ox showed a clear trend throughout the study period. However, significant risk changes were observed for certain periods only (the late 1980s and early 2000s for SO_2, and the early 2010s for SPM).

For cause-specific mortality, most RRRs for cardiovascular mortality with SPM indicated a significant risk decrease except in the last period (early 2010s); the RRRs for SO_2, NO_2, and Ox indicated a non-significant risk change or significant decrease only for a certain period (late 1980s for SO_2). The RRRs for respiratory mortality with SPM indicated a significant risk increase in the early 2010s (RRR of the latest sub-period to that of the earliest sub-period: 1.008, 95% CI: 1.002–1.015) whereas the RRRs for SO_2, NO_2, and Ox did not show any significant risk change over the study period.

The linear CRFs on an absolute exposure scale for the pollutant–mortality associations in the first and last sub-periods are shown in Fig. S17. For non-accidental mortality, the CRFs for SO_2 and NO_2 in the two periods largely overlapped whereas the CRFs for SPM and Ox indicated slightly steeper slopes in the latter period. The corresponding distributions of the pollutant concentrations in the two periods depicted a substantial decrease for SO_2, NO_2, and SPM but a slight increase for Ox. For cause-specific mortality, the CRFs in the two periods indicated different slopes for the different pollutants as observed for the temporal changes in RRs (Fig. 2).

The linear and non-linear CRFs on absolute and relative scales are shown in Figs. S17–S20. There was no evidence to support the associations being non-linear or the use of the relative scale for the linear associations (Table S5). The QAIC values were lower for the linear CRFs than non-linear CRFs on the absolute scale. Furthermore, the QAIC values for the linear CRFs on the absolute and relative scales were not markedly different.

The spatial heterogeneity in between-city differences of pooled RRs for the whole study period were low to moderate or non-significant for non-accidental and cardiovascular mortality with each pollutant (I^2 11.8%–67.8%) and much smaller for respiratory mortality with each pollutant (I^2 0%); see Table S4(a). The temporal heterogeneity in between-period differences of pooled RRRs from each sub-period for each pollutant–mortality association were low or non-significant (I^2 0%–13.0%); see Table S4(b).

Results from sensitivity analysis of time-window using non-overlapped 1-year stratification showed more variation, and results with an overlapped 10-year moving-window showed a more smoothed trend, close to the results of 5-year stratification (Fig. S21). The RRs did not change markedly when additional adjustments for relative humidity and influenza-like illnesses were made (Table S6). The RRs were slightly different when adjusting for another pollutant in the two-pollutant model (Table S6) as well as extended lag periods for 3-day and 4-day moving averages of each pollutant (Table S7). Results of analysis for the older population were comparable but the results for younger population showed wide 95% CI (Figs. S22–S23).

4. Discussion

To the best of our knowledge, this was the first study to explore the time trend in the short-term association between air pollution and mortality over four decades at the same locations. When stratifying the analysis by every 5 years, average concentrations in each stratified period decreased for SO_2, NO_2, and SPM but increased for Ox over the study period. Among these pollutants, we found evidence of a negative linear trend in the mortality risks of cardiovascular diseases associated with short-term exposure to SPM whereas other pollutant-mortality associations did not show a linear temporal trend. However, the risks of non-accidental and respiratory mortality per 10-unit increase of SPM

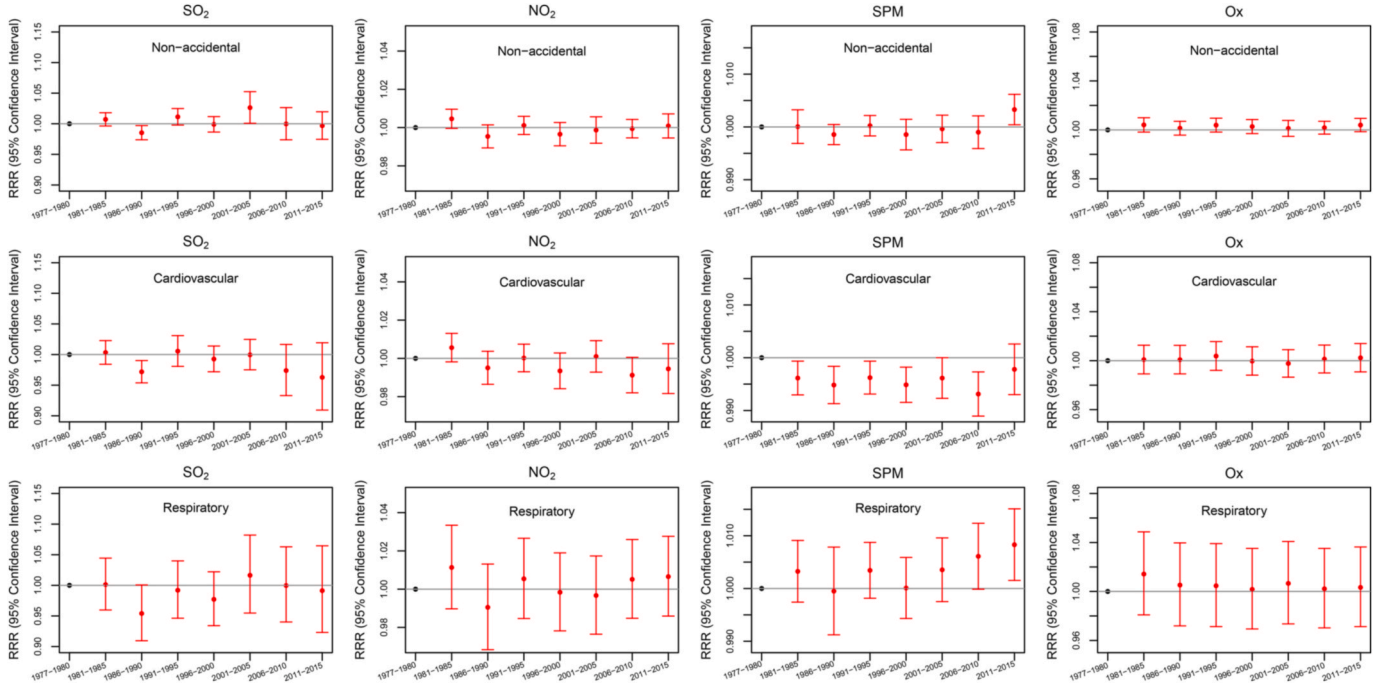

Fig. 3. Temporal trends in the estimated mortality risks (presented as ratio of relative risks (RRR) and 95% confidence interval) from 1977 to 2015 using the first sub-period (1977–1980) as the reference point. The black dot in each plot is the reference value. The red dots are RRRs for the second to the last sub-periods. Plots for the different pollutants and mortality categories are shown in different columns and rows, respectively. SO_2, sulfur dioxide; NO_2, nitrogen dioxide; SPM, suspended particulate matter; Ox, oxidants. . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

concentration were significantly higher in the most recent period, with reference to the earliest part of the study period. Other gaseous pollutants did not show such temporal risk change, suggesting their exposure–response functions remained relatively stable over time. These changing patterns of risk were stable even after restricting the analysis to the older population only. The risks posed by these pollutants were slightly to moderately heterogeneous for the different cities, and their between-period differences were low or non-significant for the stratified periods.

SO_2 emissions in the country decreased because desulfurization techniques and low-sulfur heavy oil began to be used since the 1960s (Ito et al., 2021). Further decreases were achieved by reducing the sulfur content of diesel in the 1990s (Wakamatsu et al., 2013). Several measures have been implemented to reduce the emissions from traffic, including promoting PM filters and catalytic converters, establishing stricter emissions standards, requiring that diesel vehicles use low-sulfur fuel (Ministry of the Environment, 2020; Yorifuji et al., 2011). The regulations aimed to decrease Ox precursors such as nitrogen oxides (NOx) and volatile organic compounds have become stricter. However, decreases in the NOx titration effect and long-range transboundary air pollution may make it difficult to further decrease Ox concentrations (Ministry of the Environment, 2017; Ohara et al., 2020).

Consistent with our findings for SO_2, no clear temporal trends in the mortality risk associated with SO_2 were found in Rome, Italy over 17 years (1998–2014) (Renzi et al., 2017). Owing to SO_2 emissions from Miyakejima volcano erupted in July 2000 (Kazahaya et al., 2004), we observed wider 95% CI in the early 2000s, than in earlier periods (Table S1(a)). We observed that the change patterns in non-accidental mortality risks associated with NO_2 and SPM were not obvious, similar to the findings for NO_2 and either $PM_{2.5}$ or PM_{10} in another study in Switzerland during 2001–2010 (Perez et al., 2015), and in Italy (Renzi et al., 2017). However, our results on the linear trend and risk change in RRRs suggested the risk for cardiovascular mortality associated with SPM decreased significantly over time; temporal changes in respiratory mortality risks for NO_2 and SPM were unclear. The smaller samples for respiratory mortality than for the other two categories might have resulted in less ability to detect a linear trend. For Ox, we did not observe a clear temporal pattern in RRs, similar to a study on O_3 (Fischer et al., 2011) conducted in the Netherlands for 15 years (1992–2006). Besides, the slight increase in Ox concentrations might have contributed to the significance of risk estimates with narrower 95% CI in the recent sub-periods than in the earlier sub-periods.

Notably, our findings on the greater RRs of non-accidental and respiratory mortality associated with SPM in the early 2010s compared with the late 1970s might be related to the concentration ranges substantially decreasing over time. Previous studies have reported that the CRF in non-linear form for $PM_{2.5}$ or PM_{10} and total mortality had a steeper slope at lower concentrations than higher concentrations (e.g., below or above 50 $\mu g/m^3$ for PM_{10}) (Liu et al., 2019). Liu et al. combined data from 652 locations and suggested that the leveling off at higher concentrations was because of the saturation effect, i.e., a smaller effect per fixed unit increment of concentration when the average concentration was higher. In that study, the lower PM range showed a steeper slope, probably because the lower part represented low- and middle-income countries (LMICs) and the higher part represented other high-income countries. This would probably be because other risks of premature death are substantially higher in LMICs, and air pollution-related risk would be relatively small. If this is correct, lower PM concentrations should be related to higher RRs. Thus, a declining pollutant trend would lead to an increasing trend of RRs.

In contrast, we observed a substantial risk reduction for cardiovascular mortality associated with SPM. The effects of SPM were greater for cardiovascular mortality than for respiratory mortality in the late 1970s but this was reversed in the early 2010s. The opposite pattern might initially appear suspicious; however, it may support the efforts to reduce SPM emissions in Japan. In terms of the size of SPM (similar to PM_7) and the pathway of inhaled particles via the respiratory system to deep in the lungs and the bloodstream, it is plausible that the reduced SPM concentrations might have contributed to reducing the deleterious effects on the cardiovascular system of the human body, although short-term effects on the respiratory system can still exist. Furthermore, the reduced SO_2 concentration may be related to changes in sulfate particles, as suggested by previous study (Dominici et al., 2007).

More information on temporal changes in the SPM composition or emissions sources may help to better understand these changing patterns and mechanisms. Previous studies in Tokyo and Nagoya suggest that some PM components (e.g., organic and elemental carbon) have decreased with measures to reduce traffic emissions in recent years (Minoura et al., 2006; Yamagami et al., 2021). Additionally, trans-boundary air pollution and forest fires may not a major source of urban air pollution in Japan, except in northern or western parts of the country. Thus, such air pollution mixtures and components might differ from those of other countries where desert dust or forest fires are a major concern.

The selection of 10 cities to maximize the study period might have resulted in similar city characteristics and less heterogeneity in risks. However, some evidence of linear trends in city-specific results imply the need to further investigate potential sources of heterogeneity by incorporating more cities with location-specific information. For example, only Kyoto showed a negative linear trend for non-accidental and respiratory mortality risks with SPM whereas Chiba, Tokyo, and Kobe showed a positive linear trend. Specific aspects in Kyoto, such as restrictions on construction or local industries and an increased number of universities, may have resulted in decreased exposure and population susceptibility.

In our study, the long time-series data over multiple decades provided an important opportunity with ample statistical power to quantify temporal changes in the effects of air pollutants on daily mortality. We stratified the 39 years of data into 5-year sub-periods to identify long-term trends in associations over multiple decades. We then assessed temporal changes in the mortality risks by testing linear trends and by comparing the estimated risks for later sub-periods with those for the earliest sub-period. From a public health perspective, assessing temporal trend of mortality risk is crucial to estimate mortality burden attributable to air pollution over time in addition to their change in concentration level. Also, further investigation on the heterogeneous health effects of air pollution will be needed to identify potential sources of heterogeneity so that they could be targeted to reduce health burden from air pollutant exposures, and for policies on effective risk management.

Our study has several limitations. We used air pollution data collected at a single monitoring station for each pollutant in each city over the study period. Therefore, air pollution exposure measurement errors would have been inevitable. Furthermore, the mortality data potentially include a period of hospitalization before death. Such errors independent of mismeasured observation may have affected the errors in the estimates but not the estimates themselves. Other unmeasured changes, such as in measuring equipment or methods, and changes in local emissions sources might have occurred with such a long study period. Temporal data for the SPM compositions were not available. Uncertainty may also remain in long-term vital statistics owing to changes in ICD codes and diagnostic guidelines, although the effects may have been limited owing to the broad mortality categories used and the reporting of results by sub-periods. The method of pooling effect estimates by sub-periods may not fully account for clustering within city across time, even though influence on the overall findings is likely limited given the homogeneity among the selected Japanese cities.

Further research is needed to better understand the underlying mechanism of increased risk with low-level air pollution exposure, including other time-varying covariates such as age distribution, disease structure, changes in the PM composition, or emissions sources. Elucidating city-specific results by including more cities instead of shortening

the study period will help to identify potential effect modifiers in the variation of RRs and improve our understanding of the results in terms of inter-city variability because location-specific information (e.g., climatic, demographic, and socioeconomic factors, and other public health indicators such as advances in medical treatment) could have been averaged out from the pooled results. Possible lagged effects of covariates or policies could also be an important focus in future investigation.

5. Conclusions

We assessed long-term trends in the mortality risk with short-term exposure to air pollution in 10 Japanese cities from 1977 to 2015. Four air pollutants and three mortality categories were investigated. We found that daily mortality risks associated with SPM have changed with different trends according to cause of death whereas the risks for other gaseous pollutants remained relatively stable over 39 years.

Credit author statement

Hironori Nishikawa: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualization, Funding acquisition. **Xerxes Tesoro Seposo**: Methodology, Software, Investigation, Resources, Data curation, Writing – review & editing, Supervision, Project administration, Funding acquisition. **Lina Madaniyazi**: Writing – review & editing, Supervision. **Yoonhee Kim**: Investigation, Data curation, Writing – review & editing. **Aurelio Tobías**: Validation, Writing – review & editing. **Makiko Yamagami**: Validation, Writing – review & editing. **Satbyul Estella Kim**: Writing – review & editing. **Akinori Takami**: Resources, Data curation, Writing – review & editing. **Seiji Sugata**: Resources, Data curation. **Yasushi Honda**: Resources, Data curation, Writing – review & editing. **Kayo Ueda**: Validation, Resources, Data curation, Writing – review & editing, Project administration, Funding acquisition. **Masahiro Hashizume**: Validation, Resources, Data curation, Writing – review & editing, Supervision, Project administration. **Chris Fook Sheng Ng**: Conceptualization, Methodology, Software, Validation, Investigation, Resources, Data curation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.115108.

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