Review

Systematic review of Chinese studies of short-term exposure to air pollution and daily mortality ☆

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ARTICLE INFO

ABSTRACT

Health effects attributable to air pollution exposure in Chinese population have been least understood. The authors conducted a meta-analysis on 33 time-series and case-crossover studies conducted in China to assess mortality effects of short-term exposure to particulate matter with aerodynamic diameters less than 10 and 2.5 μm (PM_{10} and $PM_{2.5}$), sulfur dioxide (SO_2), nitrogen dioxide (NO_2), ozone (O_3) and carbon monoxide (CO). Significant associations between air pollution exposure and increased mortality risks were observed in the pooled estimates for all pollutants of interest. In specific, each 10 μg/m³ increase in $PM_{2.5}$ was associated with a 0.38% (95% Confidence Interval, CI: 0.31, 0.45) increase in total mortality, a 0.51% (95% CI: 0.30, 0.73) in respiratory mortality, and a 0.44% (95% CI: 0.33, 0.54) in cardiovascular mortality. When current annual $PM_{2.5}$ levels in mega-Chinese cities to be reduced to the WHO Air Quality Guideline (AQG) of 10 μg/m³, mortality attributable to short-term exposure to $PM_{2.5}$ could be reduced by 2.7%, 1.7%, 2.3%, and 6.2% in Beijing, Shanghai, Guangzhou and Xi'an, respectively. The authors recommend future studies on the nature of air pollution concentration and health effect relationships in Chinese population to support setting stringent air quality standards to improve public health.

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Contents

1. Introduction

Associations between exposure to air pollution and cardiopulmonary mortality and morbidity are observed in epidemiological studies worldwide (Brunekreef and Holgate, 2002; He et al., 2011; Hwang and Lee, 2010). Based on the health and toxic impact assessments, worldwide air quality guidelines and standards have been established to limit the air pollution levels for public health protection. Commonly in the developed countries, the standard selection and settings for air pollutants are based on the estimates obtained in cohort studies of long-term exposure, as well as quantitative reviews (i.e. meta-analysis) of epidemiologic studies of short-term exposure. For example, the WHO reported the combined relative risk of total mortality of 1.006 (95% CI: 1.004–1.008) and 1.003 (95% CI: 1.001–1.004), per each 10 $\mu g/m^3$ increase in short-term PM_{10} and ozone exposure, respectively, estimated in a meta-analysis of European studies (WHO, 2004). The National Ambient Air Quality Standards (NAAQS) for PM_{10} set by the United States Environmental Protection Agency (USEPA) was also mainly supported by a meta-analysis of time-series analysis nested in the National Morbidity Mortality Air Pollution Study (NMMAPS), which reported the combined estimate of a 0.21% (95% CI: 0.09–0.33) increase in total mortality across 90 US cities, per each 10 $\mu g/m^3$ increase in PM_{10} (USEPA, 2004). In the air quality guidelines released by the World Health Organization (WHO) in 2006 (WHO, 2006), the staged annual mean levels of $PM_{2.5}$ were mainly based on the estimates of exposure–mortality risk derived in long-term follow-up cohort studies (Dockery et al., 1993; HEI, 2000; Jerrett et al., 2005; Pope et al., 1995, 2002); whereas the 24-hour concentration guidelines were based on the pooled estimates of risk coefficients derived from multi-center studies and meta-analyses (Cohen et al., 2004; Katsouyanni et al., 2001; Samet et al., 2000).

Asia has experienced rapid industrialization, urbanization, and transportation development in the past decades. As a result, air pollution levels in many Asian cities remain well above the WHO guideline values (HEI, 2010; WHO, 2006). As one of the fast developing countries with dense population, the air pollution levels in China are at the higher end of the world air pollution level (Gao et al., 2011), and air pollution

associated with health impacts have become a growing concern (Lin et al., 2011; Zhang et al., 2010b). The average annual levels of PM_{10} in 31 provincial capitals in China, has been significantly reduced from 2003 to 2010 (Fig. 1); however, they are still at the higher end of the world. In 2010, the annual concentrations of PM_{10} were 121 $\mu g/m^3$ in Beijing, 79 $\mu g/m^3$ in Shanghai, 69 $\mu g/m^3$ in Guangzhou, and 126 $\mu g/m^3$ in Xi'an, respectively (China Statistic Yearbook, 2011). Yang reported that the annual levels of $PM_{2.5}$ in Beijing (2005–2006), Chongqing (2005–2006), Shanghai (1999–2000) and Guangzhou (2008–2009) were at 118.5, 129.0, 67.6, and 81.7 $\mu g/m^3$, respectively (Yang et al., 2011), which are well above the highest acceptable annual level of $PM_{2.5}$ of 35 $\mu g/m^3$ in Chinese NAAQS (MEPPRC, 2012). Although the ground-level of O_3 has not been routinely monitored in Chinese cities, studies reported that the 8-hour concentrations of O_3 in Shanghai, Guangzhou and Wuhan ranged in 60 to 80 $\mu g/m^3$ between 2001 and 2008 (Shao et al., 2009; Wong et al., 2008b).

Compared to increasing number of air quality studies conducted in China, the air pollution epidemiologic study on $PM_{2.5}$ and O_3 in Chinese population is still very limited. W. Huang et al. (2012) reported that increases of 2.29% (95% CI: 0.83, 3.76) for total mortality and 3.08% (95% CI: 0.94, 5.26) for cardiovascular mortality were associated with an interquartile range (IQR) increase of 103.0 $\mu g/m^3$ in lagged 1–2 day $PM_{2.5}$ exposure in Xi'an. Yang et al. (2012a) reported the increase of 0.9% (95% CI: 0.55, 1.26) in total mortality in Guangzhou, per 10 $\mu g/m^3$ increase in $PM_{2.5}$. A few studies also reported significantly increased mortality risk associated with O_3 exposure in Chinese population (Tao et al., 2012; Zhang et al., 2006).

The quantitative review focusing on the mortality effects of criteria air pollutants in Chinese population is also limited (Atkinson et al., 2011; Aunan and Pan, 2004; HEI, 2010), and none has included studies published in Chinese literature, which has been missed in the published reviews. However, since the exposure level, chemical components and the subsequent toxic characteristics of ambient $PM_{2.5}$ in China differ significantly from those in developed countries, the exposure–response coefficients observed in the western studies could not simply be applied in assessing $PM_{2.5}$ associated with health effects in the populations in the developing world (HEI, 2010). Recently, B. Chen et al. (2011) published a descriptive review on PM_{10}, SO_2 and NO_2 pollution associated with health effect studies in China. Nevertheless, the health effects of $PM_{2.5}$ and O_3 observed in Chinese population have not been systematically reviewed. The aim of present study is to assess the exposure–mortality relationship of acute exposure to criteria pollutants in Chinese population based on the literature published in both English and Chinese. The impact of potential reductions in premature death under different $PM_{2.5}$ reduction scenarios, with reductions from current levels to air quality standard levels, were further assessed for representative mega-Chinese cities.

2. Methods

2.1. Literature search and data extraction

A systematic literature search was conducted for epidemiological studies conducted in China that examined health effects and/or risk in associations with exposure to particulate pollutants (PM_{10}, $PM_{2.5}$) and gaseous pollutants (SO_2, NO_2, O_3, and CO), which were published between January 1990 and July 2012 in peer-reviewed English and Chinese journals.

The on-line electronic databases included both English databases of the Pub-Med (National Library of Medicine, Bethesda, MD, US),
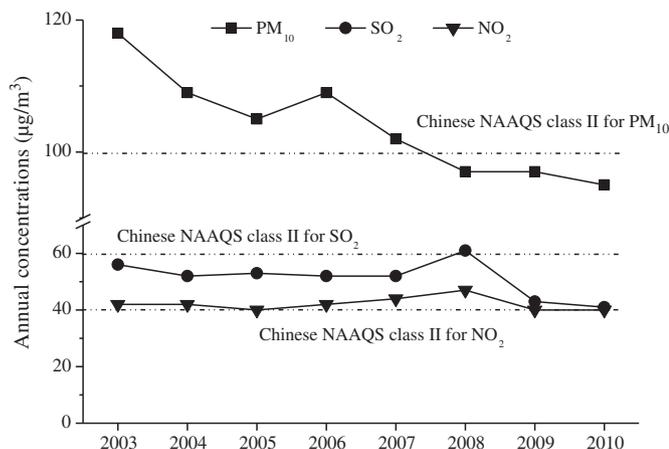
Fig. 1. The average annual levels of PM_{10}, SO_2 and NO_2 in 31 provincial capitals of China 2003–2010. The dotted line indicates the annual level of the Chinese NAAQS class II. Data source: China Statistic Yearbook 2004–2011.

Web of Science (Thompson Scientific, Philadelphia, PA, US), and Chinese database of China National Knowledge Infrastructure (CNKI). The combinations of following key words were used in our literature search: (1) air pollution, ambient particulate matter, particles, sulfur dioxide or SO_2, nitrogen dioxide or NO_2, ozone or O_3, carbon monoxide or CO, PM_{10}, or $PM_{2.5}$, (2) mortality, death or health effects, (3) China, Chinese or Hong Kong, and (4) timeseries, time series, time-series or case-crossover. We also searched the reference lists of identified papers for additional publications. Study identification steps are summarized in Fig. 2.

In this analysis, we focused on time-series and case-crossover studies that reported excessive mortality risk in associations with acute exposure to ambient air pollutants. Among the identified publications, the studies included in meta-analysis were those of full-length time-series or case-crossover study articles reporting the increased mortality risk associated increases in air pollutant concentrations. The statistic methods applied in these identified studies are either generalized additive model (GAM) or Poisson regression models, whereas temperature and relative humidity are controlled for potential meteorological effects. The conference abstracts which are published similar to full publication version and with study details were also included. We excluded the duplicate publications reporting identical results or using similar approaches from a single analysis, conference abstracts without study details, government reports, and occupational and indoor exposures. When both time-series and case-crossover study articles were published for the same city, period and air pollution data, time-series study was included in the meta-analysis. Two pairs of case-crossover and time-series studies were conducted in Shanghai and Anshan,
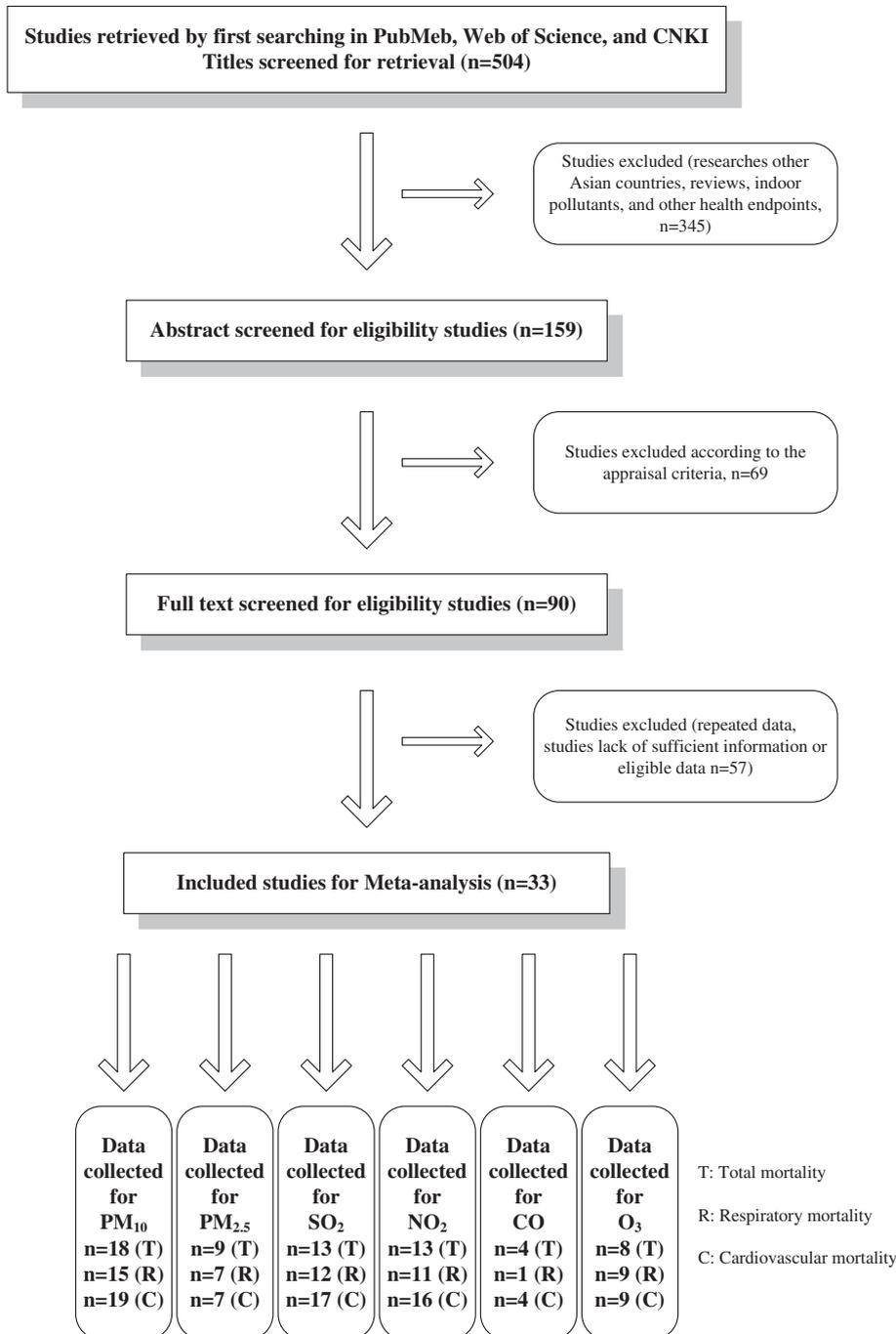
Fig. 2. Flow chart for study retrieval and selection process.

respectively; due to the result redundancy, we only included the time-series studies in the present meta-analysis. Three multi-city based time-series articles reporting the combined estimate of PM_{10} (16 cities), SO_2 (17 cities) and NO_2 (17 cities) in the China Air Pollution and Health Effects Study (CAPES) were identified in our literature search (Chen et al., 2012a, 2012b, 2012c); however, some of individual CAPES study city results have been identified separately and included in the meta-analysis, and no city-specific result in CAPES study was reported in these three publications, we did not include the overall combined estimates of CAPES study into the present meta-analysis.

For each selected study, the information on study location, duration, population, pollutants and health endpoints of interest, and primary exposure and effects estimates were extracted and entered into the database prepared in Microsoft Access (version 2007 Microsoft Corp, WA, US). Air pollution mortality effects were often assessed over the past few days (multiple lags). In the present study, we selected the lags following the rules summarized previously by Atkinson et al. (2011). Briefly, if only one lag estimate was presented, this estimate was recorded; if multiple lags were presented, we selected the one for meta-analysis based on the criteria: (1) the lag that the author focused on or stated as a priori; (2) the lag that was of the most statistically significance

(positive or negative) and (3) the lag with the largest effect estimate (positive or negative) (Atkinson et al., 2011).

2.2. Meta-analysis

Given that individual study result may not be representative and often present a "no statistically significant" conclusion due to its limited sample size, meta-analysis becomes a useful tool to identify, appraise, synthesize and quantify the results of relevant studies of the same interest to reach the conclusions in a systemic approach in clinical and epidemiologic research (Petitti, 1994). In this meta-analysis, we first examined the heterogeneity of total and cause-specific mortality effects assessed across studies for each individual air pollutant of interest. Based on the significance of effect heterogeneity across studies, we applied either fixed-effect or random-effect models to summarize the pooled estimates of premature death attributable to pollutants of interest. The estimated percent increases in risk of total and cause-specific mortality were presented for each 10 μg/m³ increase in PM_{10}, $PM_{2.5}$, SO_2, NO_2 and O_3 and each 1 mg/m³ increase in CO. Additionally, since the revolutionary improvement in statistical methods applied in time-series analysis after 2002 (Dominici et al., 2002), we only included
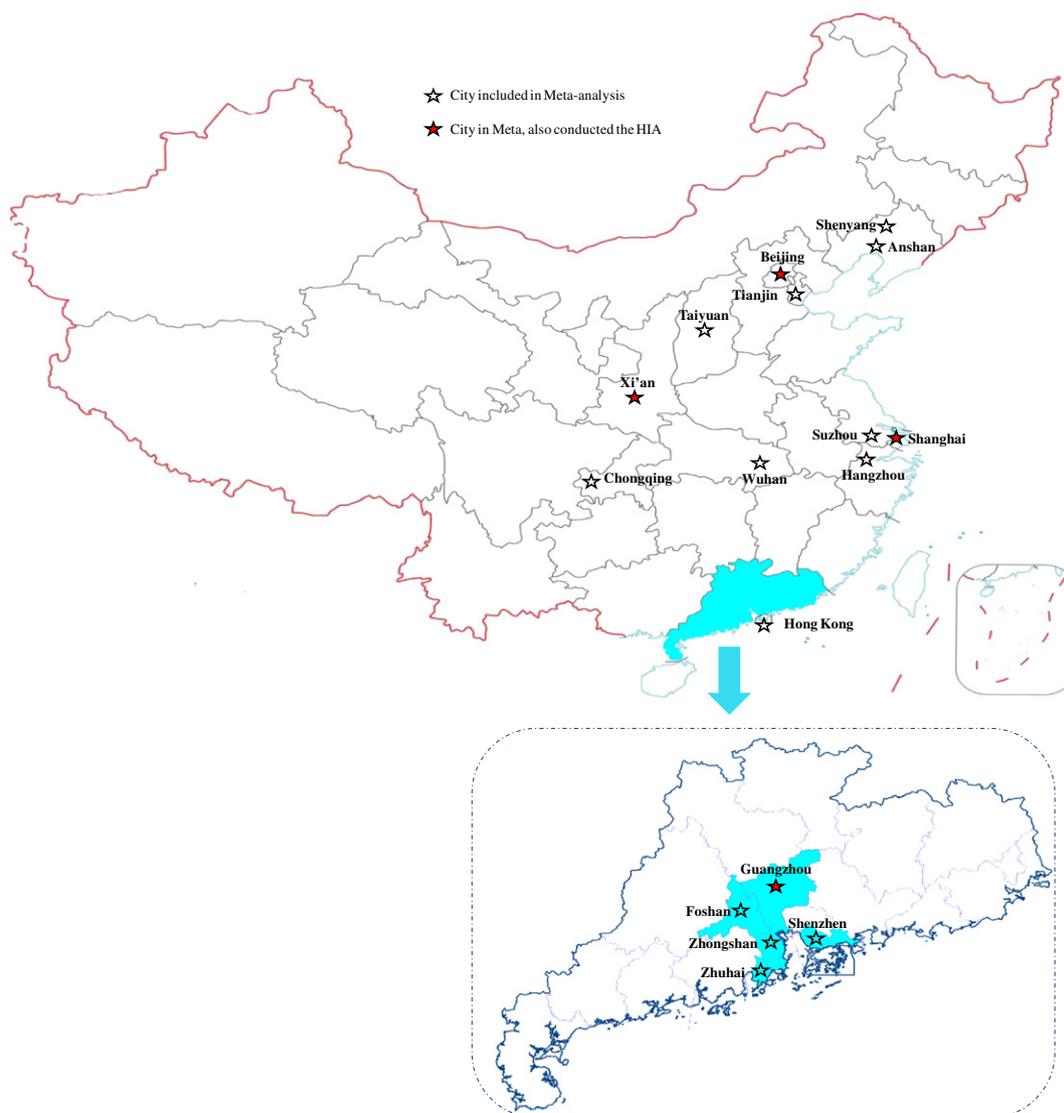
Fig. 3. Cities conducted with the time-series and/or case-crossover studies examining the associations between daily mortality and exposure to ambient particulate and gaseous pollutants in China.

Table 1

The estimated excess risk (ER) of mortality and detailed information for each study included in the meta-analysis. The ER for mortality was assessed for each 10 μg/m^3 increase for PM$_{10}$, PM$_{2.5}$, SO$_2$, NO$_2$ and O$_3$; each 1 mg/m^3 increase for CO.

	Study city/year	Species	Average concentration	ER (%) of total mortality	95% CI	ER (%) of respiratory mortality	95% CI	ER (%) of cardiovascular mortality	95% CI
J. Zhang et al. (2010a) In Chinese	Beijing 2004–08	PM$_{10}$	146.1 ± 91.6	0.25	(0.08, 0.42)	–	–	–	–
		SO$_2$	48.7 ± 49.3	0.47	(0.03, 0.91)	–	–	–	–
		NO$_2$	63.9 ± 26.0	0.55	(−0.02, 1.12)	–	–	–	–
Pan et al. (2008)	Beijing 2003	PM$_{10}$	140.8 ± 79.1	–	–	–	–	0.40	(0.20, 0.60)
		SO$_2$	60.3 ± 56.2	–	–	–	–	0.40	(0.10, 0.80)
		NO$_2$	–	–	–	–	–	1.30	(0.20, 2.40)
Pan et al. (2007)	Beijing 1998–2000	SO$_2$	–	–	–	4.21	(1.85, 6.83)	3.97	(2.44, 5.53)
Huang et al. (2009)	Shanghai 2004–05	PM$_{10}$	107.9 ± 2.3	0.14	(0.02, 0.26)	0.22	(−0.08, 0.52)	0.24	(0.08, 0.40)
		PM$_{2.5}$	56.4 ± 1.3	0.30	(0.06, 0.54)	0.71	(0.05, 1.37)	0.39	(0.12, 0.66)
Kan and Chen (2003)	Shanghai 2000–01	PM$_{10}$	91.1 ± 51.9	0.30	(0.10, 0.50)	–	–	0.30	(0.00, 0.60)
		SO$_2$	42.5 ± 20.2	1.40	(0.80, 2.00)	–	–	1.30	(0.40, 2.20)
		NO$_2$	32.5 ± 14.4	1.50	(0.80, 2.20)	–	–	1.80	(0.70, 2.80)
Kan et al. (2008)	Shanghai 2001–04	PM$_{10}$	102.0 ± 1.7	0.25	(0.14, 0.37)	0.27	(−0.01, 0.56)	0.27	(0.10, 0.44)
		SO$_2$	44.7 ± 0.6	0.95	(0.62, 1.28)	1.37	(0.51, 2.23)	0.91	(0.42, 1.41)
		NO$_2$	66.6 ± 0.7	0.97	(0.66, 1.27)	1.22	(0.42, 2.01)	1.01	(0.55, 1.47)
		O$_3$	63.3 ± 1.0	0.31	(0.04, 0.58)	0.29	(−0.44, 1.03)	0.38	(−0.03, 0.80)
Dai et al. (2004) in Chinese	Shanghai 2002–03	PM$_{10}$	111.9 ± 76	0.53	(0.22, 0.85)	–	–	–	–
		PM$_{2.5}$	68.8 ± 47.9	0.85	(0.32, 1.39)	–	–	–	–
Kan et al. (2007)	Shanghai 2004–05	PM$_{10}$	107.9 ± 2.39	0.16	(0.02, 0.36)	0.33	(−0.08, 0.75)	0.31	(0.10, 0.53)
		PM$_{2.5}$	56.4 ± 1.3	0.36	(0.11, 0.61)	0.95	(0.16, 1.73)	0.41	(0.01, 0.82)
Zhang et al. (2006)	Shanghai 2001–04	O$_3$	63.3 ± 36.7	0.45	(0.16, 0.73)	0.35	(−0.40, 1.09)	0.53	(0.10, 0.96)
Yu et al. (2012)	Guangzhou 2006–09	PM$_{10}$	59.5 ± 24.2	1.26	(0.86, 1.66)	0.05	(0.49, 1.46)	1.79	(1.11, 2.47)
		SO$_2$	43.3 ± 21.2	1.54	(1.03, 2.06)	0.89	(−0.36, 2.16)	2.28	(1.40, 3.16)
		NO$_2$	47.7 ± 26.4	1.42	(1.06, 1.78)	0.95	(0.08, 1.83)	1.81	(1.20, 2.41)
Yang et al. (2012a)	Guangzhou 2007–08	PM$_{2.5}$	70.1 ± 34.6	0.90	(0.55, 1.26)	0.97	(0.16, 1.79)	1.22	(0.63, 1.80)
X. Huang et al. (2012) in Chinese	Guangzhou 2004–08	PM$_{10}$	81.1 ± 44.8	0.94	(0.79, 1.09)	–	–	–	–
		SO$_2$	54.4 ± 35.8	1.09	(0.91, 1.27)	–	–	–	–
		NO$_2$	66.6 ± 30.1	1.55	(1.31, 1.78)	–	–	–	–
Y. Zhang et al. (2010a) in Chinese	Tianjin 2005–07	SO$_2$	68 ± 54	0.56	(0.23, 0.89)	1.03	(−0.06, 2.14)	0.49	(0.06, 0.93)
		NO$_2$	47 ± 18	0.94	(0.17, 1.70)	1.44	(−1.04, 3.98)	1.29	(0.29, 2.30)
Guo et al. (2010)	Tianjin 2005–07	PM$_{10}$	105 ± 57	–	–	–	–	0.48	(0.23, 0.73)
		SO$_2$	68 ± 54	–	–	–	–	0.27	(−0.13, 0.68)
		NO$_2$	47 ± 18	–	–	–	–	1.08	(0.13, 2.04)
Y. Zhang et al. (2010b) in Chinese	Tianjin 2005–07	PM$_{10}$	105 ± 57	0.45	(0.21, 0.69)	0.82	(0.04, 1.61)	0.60	(0.29, 0.91)
Wong et al., 2008a	Hong Kong 1996–2002	PM$_{10}$	51.6 ± 25.3	0.45	(0.19, 0.72)	0.89	(0.36, 1.42)	0.58	(0.14, 1.03)
		SO$_2$	17.8 ± 12.1	0.68	(0.24, 1.12)	1.06	(0.06, 2.06)	1.03	(0.21, 1.85)
		NO$_2$	58.7 ± 20.0	0.79	(0.49, 1.10)	0.92	(0.25, 1.60)	1.17	(0.61, 1.73)
		O$_3$	36.9 ± 23.0	0.27	(0.00, 0.53)	0.36	(−0.21, 0.93)	0.45	(−0.04, 0.94)
Wong et al. (2002)	Hong Kong 1995–1998	PM$_{10}$	51.5 ± 24.8	–	–	0.8	(0.1, 1.4)	0.3	(−0.2, 0.8)
		SO$_2$	16.7 ± 11.6	–	–	1.5	(0.1, 2.9)	0.7	(−0.6, 2.0)
		NO$_2$	56.4 ± 19.2	–	–	1.3	(0.4, 2.2)	0.8	(−0.1, 1.6)
		O$_3$	33.9 ± 23.2	–	–	1.0	(0.4, 1.6)	−0.3	(−0.9, 0.3)
Qian et al. (2007a)	Wuhan 2001–04	PM$_{10}$	141.8	0.36	(0.19, 0.53)	0.71	(0.21, 1.23)	0.51	(0.28, 0.75)
Qian et al. (2006)	Wuhan 2000–04	PM$_{10}$	–	0.28	(0.09, 0.46)	0.73	(0.15, 1.32)	0.42	(0.17, 0.66)
Wong et al. (2008b)	Wuhan 2001–04	PM$_{10}$	141.8 ± 80.2	0.43	(0.24, 0.62)	0.87	(0.34, 1.41)	0.57	(0.31, 0.84)
		SO$_2$	39.2 ± 25.3	1.19	(0.65, 1.74)	2.11	(0.60, 3.65)	1.47	(0.70, 2.25)
		NO$_2$	51.8 ± 24.0	1.97	(1.31, 2.63)	3.68	(1.77, 5.63)	2.12	(1.18, 3.06)
		O$_3$	85.7 ± 67.4	0.29	(−0.05, 0.63)	0.12	(−0.89, 1.15)	−0.07	(−0.53, 0.39)
	Hong Kong 1996–2002	PM$_{10}$	51.6 ± 25.3	0.53	(0.26, 0.81)	0.83	(0.23, 1.44)	0.61	(0.11, 1.10)
		SO$_2$	17.8 ± 12.1	0.87	(0.38, 1.36)	1.28	(0.19, 2.39)	1.19	(0.29, 2.10)
		NO$_2$	58.7 ± 20.0	0.90	(0.58, 1.23)	1.15	(0.42, 1.88)	1.23	(0.64, 1.82)
		O$_3$	36.9 ± 23.0	0.32	(0.01, 0.62)	0.22	(−0.46, 0.91)	0.62	(0.06, 1.19)
Qian et al. (2007b)	Wuhan 2000–04	SO$_2$	44.1 ± 25.3	0.01	(−0.46, 0.47)	1.13	(−0.28, 2.56)	0.20	(−0.45, 0.86)
		NO$_2$	51.8 ± 18.8	1.43	(0.87, 1.99)	2.23	(0.52, 3.96)	1.65	(0.87, 2.45)
		O$_3$	78.0 ± 41.1	0.22	(−0.09, 0.54)	0.64	(−0.39, 1.67)	0.04	(−0.39, 0.47)
Tao et al. (2012)	PRD 2006–08	PM$_{10}$	77.5	0.79	(0.62, 0.96)	1.26	(0.88, 1.65)	0.91	(0.64, 1.19)
		NO$_2$	52.7	1.95	(1.62, 2.29)	3.48	(2.73, 4.23)	2.12	(1.58, 2.65)
		O$_3$	80.0	0.81	(0.63, 1.00)	1.33	(0.89, 1.76)	1.01	(0.71, 1.32)
Tao et al. (2011)	PRD 2006–08	CO	1.37	6.08	(4.36, 7.80)	7.44	(3.42, 11.52)	7.24	(4.40, 10.12)
Hou et al. (2011) in Chinese	Xi'an 2004–08	PM$_{10}$	130.7 ± 55.3	0.35	(0.11, 0.58)	0.32	(−0.42, 1.06)	0.38	(0.04, 0.73)
		SO$_2$	48.2 ± 28.9	0.60	(0.16, 1.05)	1.02	(−0.32, 2.38)	−0.09	(−0.74, 0.57)
		NO$_2$	38.5 ± 15.0	2.42	(1.57, 3.27)	3.71	(1.09, 6.40)	2.06	(0.82, 3.32)
W. Huang et al. (2012)	Xi'an 2004–08	PM$_{2.5}$	177 ± 104	0.20	(0.07, 0.33)	0.19	(−0.20, 0.59)	0.27	(0.08, 0.46)
Chen et al. (2010)	Anshan 2004–06	PM$_{10}$	110.9 ± 60.2	0.24	(−0.03, 0.51)	0.21	(−0.82, 1.24)	0.67	(0.29, 1.04)
		SO$_2$	59.0 ± 74.3	0.27	(−0.05, 0.60)	0.04	(−1.16, 1.24)	0.38	(−0.06, 0.83)
		NO$_2$	25.5 ± 16.3	1.30	(−0.06, 2.67)	−0.18	(−5.39, 5.02)	2.11	(0.22, 4.00)

Table 1 (continued)

	Study city/year	Species	Average concentration	ER (%) of total mortality	95% CI	ER (%) of respiratory mortality	95% CI	ER (%) of cardiovascular mortality	95% CI
Venners et al. (2003)	Chongqing 1995–95	PM$_{2.5}$	146.8	0.00	(−0.70, 0.70)	–	–	–	–
		SO$_2$	213.0	0.40	(0.00, 0.90)	1.10	(0.20, 2.20)	1.00	(0.20, 2.00)
Yang et al. (2012b)	Suzhou 2006–2008	O$_3$	57.7 ± 39.8	2.15	(0.36, 3.93)	−1.85	(−6.91, 3.22)	4.47	(1.43, 7.51)
Ren et al. (2007) in Chinese	Hangzhou 2002–04	PM$_{10}$	113.0	–	–	–	–	0.60	(0.30, 0.90)
		SO$_2$	46.0	–	–	–	–	1.70	(0.70, 2.80)
		NO$_2$	53.0	–	–	–	–	2.00	(0.90, 3.20)
Yang et al. (2010) in Chinese	– 2002–07	SO$_2$	45.5 ± 23.2	–	–	–	–	5.60	(4.90, 6.40)
		NO$_2$	49.5 ± 20.2	–	–	–	–	1.00	(0.20, 1.80)
R. Chen et al. (2011a)	Beijing 2007–08	PM$_{2.5}$	82 ± 52	0.53	(0.37, 0.69)	0.66	(0.21, 1.11)	0.58	(0.35, 0.81)
	Shanghai 2004–08	PM$_{2.5}$	55 ± 30	0.47	(0.22, 0.72)	0.61	(−0.15, 1.37)	0.41	(0.00, 0.81)
	Shenyang 2006–08	PM$_{2.5}$	94 ± 52	0.35	(0.17, 0.53)	0.29	(−0.29, 0.88)	0.46	(0.19, 0.73)
R. Chen et al. (2011b)	Shanghai 2006–08	CO	1.3 ± 0.5	2.41	(0.64, 4.19)	–	–	3.85	(1.29, 6.40)
	Anshan 2004–06	CO	1.1 ± 0.8	1.97	(0.13, 3.81)	–	–	2.83	(0.27, 5.38)
	Taiyuan 2004–08	CO	1.8 ± 1.0	3.90	(2.54, 5.26)	–	–	5.38	(3.28, 7.49)
Zhang et al. (2008)	Beijing Shanghai Guangzhou Tianjin 2005–07	PM$_{10}$	–	0.20	(0.14, 0.27)	0.13	(0.09, 0.35)	0.19	(0.16, 0.22)

– indicates that the data were not reported in the study. The average concentrations for PM$_{10}$/PM$_{2.5}$/SO$_2$/NO$_2$/O$_3$ were 24-h data with mass unit of μg/m^3; that for CO was 8-h average data with mass unit of mg/m^3.

the analyses conducted after 2002 in our meta-analysis. All analyses were conducted using the software of Review Manage 5 (free software downloaded from http://ims.cochrane.org/revman).

2.3. Health impact assessment

To assess the health impact of air pollution in Chinese population, we applied the exposure–mortality coefficients derived in the meta-analysis to assess the expected deaths attributable to PM$_{2.5}$. Since PM$_{2.5}$ has not been routinely monitored in China, we collected the PM$_{2.5}$ annual concentrations reported in the identified studies the present meta-analysis. We estimated the potential reductions in number and percentage of death attributable to PM$_{2.5}$ reduction, under reduction scenarios of PM$_{2.5}$ to the WHO interim targets of annual levels of 35, 25, and 15 μg/m^3, and the WHO Air Quality Guidelines (AQG) of 10 μg/m^3. The assessment was made for Beijing, Shanghai, Guangzhou and Xi'an. Consensus data of each city was obtained from local public information websites (http://www.bjstats.gov.cn/; www.stats-sh.gov.cn; http://www.gzstats.gov.cn/; http://www.xatj.gov.cn/).

The expected number (EN) of premature deaths due to PM$_{2.5}$ exposure was calculated as: EN = the total number of deaths in each city × attributable fraction (AF). Assuming all the residents are exposed to the mean concentration in the city, the AF to estimate the impact of exposure variations can be calculated by: AF = (RR − 1)/RR. The relative risks (RR) was calculated as RR = exp [β × ΔC], where β is the regression coefficient derived from our meta-analysis. The value of β represents the excess risk of mortality per each increase in 1 μg/m^3 of PM$_{2.5}$, and ΔC is the difference between annual concentration of PM$_{2.5}$ in each city and projected reduction target levels.

3. Results

3.1. Meta-analysis

After a systematic search and review of English and Chinese literature, thirty time-series and three case-crossover studies assessing acute mortality effects attributable to air pollution exposure and conducted in mainland China and Hong Kong were identified and included in the meta-analysis, which were all published after 2002. Most of the studies were conducted in medium-to-large size cities with dense population and serious air pollution levels in the past decade, including Beijing, Hong Kong, Tianjin, Shanghai, Suzhou, Hangzhou, Wuhan, Xi'an, Chongqing, Anshan, Shenyang, Taiyuan, and the Pearl River Delta (PRD) cities (Fig. 3).

Table 2
The combined estimates for ER (%) and 95% Confidence Intervals (95% CI) for a 10 μg/m^3 increase in PM$_{10}$, PM$_{2.5}$, SO$_2$, NO$_2$ and O$_3$ and 1 mg/m^3 increase in CO for total and cause-specific mortalities.

Mortality	Age	PM$_{10}$	PM$_{2.5}$	CO	SO$_2$	NO$_2$	O$_3$
Total	All aged	0.32 (0.28, 0.35) **18**[*]	0.38 (0.31, 0.45) **9**[*]	3.70 (2.88, 4.51) **4**[*]	0.81 (0.71, 0.91) **13**[*]	1.30 (1.19, 1.41) **13**[*]	0.48 (0.38, 0.58) **8**[*]
Respiratory	All ged	0.32 (0.23, 0.40) **15**[*]	0.51 (0.30, 0.73) **7**	NA	1.18(0.83, 1.52) **12**	1.62 (1.32, 1.92) **11**[*]	0.73 (0.49, 0.97) **9**
Cardiovascular	All aged	0.43 (0.37, 0.49) **19**[*]	0.44 (0.33, 0.54) **7**	4.77 (3.53, 6.00) **4**	0.85 (0.70, 1.00) **17**[*]	1.46 (1.27, 1.64) **16**	0.45 (0.29, 0.60) **9**[*]

Numbers next the percentage are the number of studies included.
NA: insufficient numbers available for meta-analysis (n<2).
[*] If the heterogeneity test on the effects observed across selected studies was significant at (p=0.05 level), random-effect model was applied to obtain the pooled estimates.

The estimates and detailed information reported in the thirty-three identified studies are summarized in Table 1. Among the identified studies, total and cardio-respiratory mortality effects were assessed in association with exposure to six criteria air pollutants, including PM_{10}, $PM_{2.5}$, SO_2, NO_2, CO and O_3. In these studies, the reported 24-hour concentrations of PM_{10}, $PM_{2.5}$, SO_2, NO_2, and CO ranged in 44–172 μg/m³, 55–177 μg/m³, 29–213 μg/m³, 26–70 μg/m³, and 1.10–1.80 mg/m³, and 8-hour O_3 ranged in 56–86 μg/m³. Notably, the reported concentrations of $PM_{2.5}$ often exceeded current Chinese NAAQS for highest acceptable 24-hour and annual level of $PM_{2.5}$ at 75 μg/m³ and 35 μg/m³. Among the individual studies, the estimates for PM_{10} on total mortality ranged in 0.14 and 1.26, with the highest estimate observed in Guangzhou (2006–2009) and the lowest in Shanghai (2004–2005), whereas the estimates in other cities mostly between 0.25 and 0.50. The estimates for $PM_{2.5}$ on total mortality ranged in 0.00 to 0.90, with the highest estimate observed in Guangzhou (2007–2008) and the lowest in Chongqing (1995).

The number of eligible studies and combined estimates derived in present meta-analysis are summarized in Table 2 and Fig. 4. The mortality risk of $PM_{2.5}$ was higher than that of PM_{10} when these two particulate pollutants were studied in the same study, whereas the risks for cardio-respiratory mortality were higher than total mortality. It's worth noting that the overall estimates in cause-specific mortality are largely weighed by the studies recently conducted in Shanghai, Xi'an, Guangzhou, and Beijing.

In specific, per 10 μg/m³ increase in PM_{10} concentrations, total mortality was increased by 0.32% (95% CI: 0.28, 0.35), respiratory mortality by 0.32% (95% CI: 0.23, 0.40), and cardiovascular mortality by 0.43% (95% CI: 0.37, 0.49). Per 10 μg/m³ increase in $PM_{2.5}$, we observed a 0.38% (95% CI: 0.31, 0.45) increase in total mortality, a 0.51% (95% CI: 0.30, 0.73) increase in respiratory mortality, and a 0.44% (95% CI: 0.33, 0.54) increase in cardiovascular mortality.

Per 10 μg/m³ increases in gaseous pollutants SO_2, NO_2, and O_3, the total mortality risk increased by 0.81% (95% CI: 0.71, 0.91), 1.30% (95% CI: 1.19, 1.41), and 0.48% (95% CI: 0.38, 0.58), respectively; the respiratory mortality risk increased by 1.18% (95% CI: 0.83, 1.52), 1.62% (95% CI: 1.32, 1.92), and 0.73% (95% CI: 0.49, 0.97), respectively; the cardiovascular mortality risk increased by 0.85% (95% CI: 0.70, 1.00), 1.46% (95% CI: 1.27, 1.64), and 0.45% (95% CI: 0.29, 0.60), respectively. Whereas per 1 mg/m³ increase in CO, the combined estimated mortality risk increases were 3.70% (95% CI: 2.88, 4.51) in total mortality, and 4.77% (95% CI: 3.53, 6.00) in cardiovascular mortality. However, there were insufficient numbers of studies for meta-analysis on respiratory mortality risk attributable to CO exposure.

3.2. Health impact assessment

For $PM_{2.5}$ reduction associated with health benefit assessment, the assessment was conducted for the four mega-cities, including Beijing, Shanghai, Guangzhou, and Xi'an, based on population, mortality rate
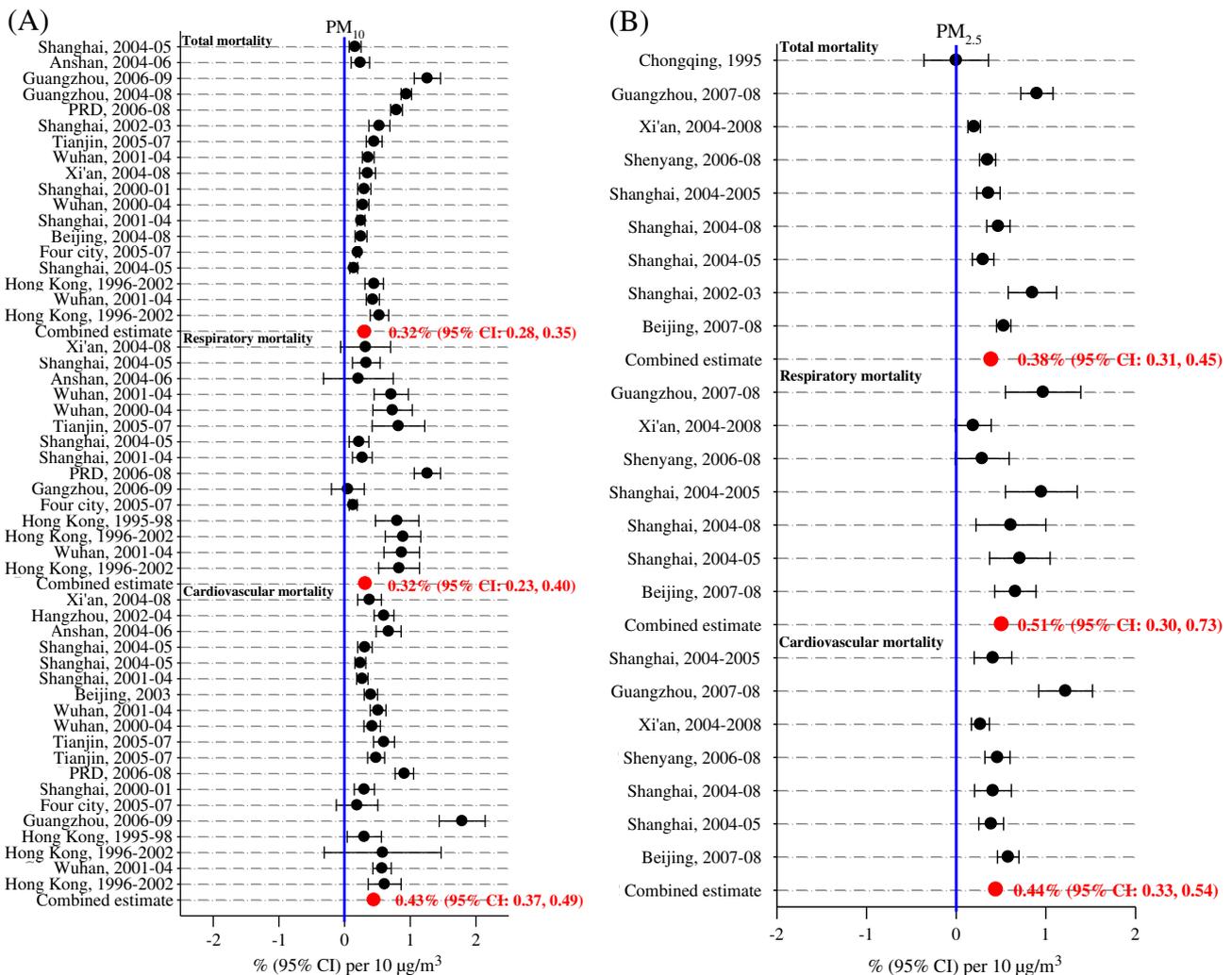
Fig. 4. Forrest plots for each pollutant combined with total and cause-specific mortality, (A): PM_{10}; (B): $PM_{2.5}$; (C): SO_2; (D): NO_2; (E): O_3; and (F): CO. There was insufficient numbers of estimates for meta-analysis in respiratory mortality caused by CO exposure.
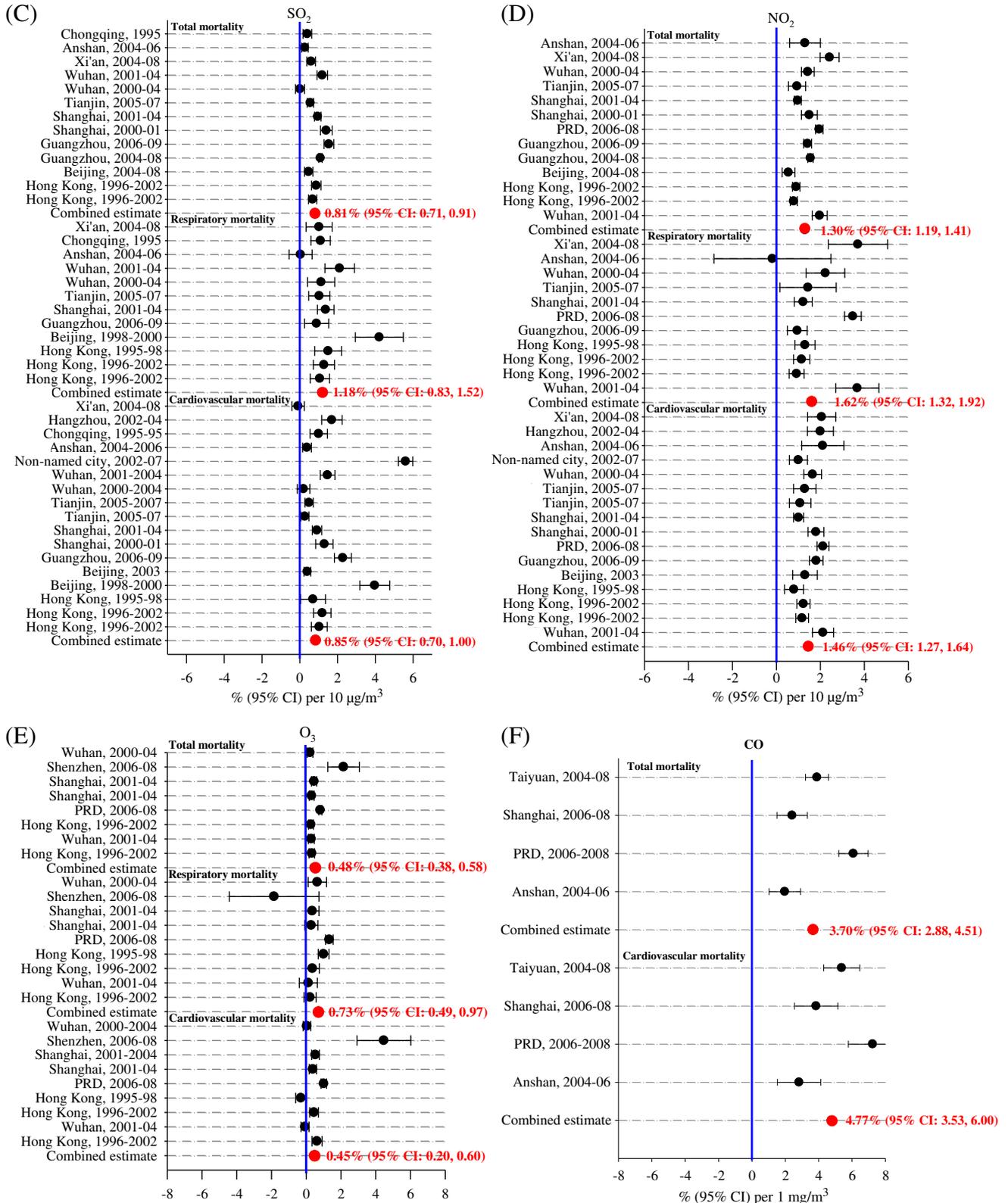
Fig. 4 (*continued*).

and PM$_{2.5}$ levels. The consensus data for each study city in 2008 are summarized in Table 3. The annual levels of PM$_{2.5}$ in each city were extracted from the studies included in the meta-analysis and summarized in Fig. 5A. Fig. 5B presents the estimates of reductions in annual death in these cities using the exposure–mortality coefficient of a 0.38% increase in total mortality per each 10 μg/m^3 increase in

short-term exposure to PM$_{2.5}$, under several PM$_{2.5}$ reduction scenarios from current levels to the WHO AQG and interim target levels. With reductions in PM$_{2.5}$ from its current annual levels to 35 μg/m^3, the numbers of death per 100,000 person would be reduced 7.5 in Beijing, 5.7 in Shanghai, 7.6 in Guangzhou, and 25.2 in Xi'an, with corresponding reduction rates of 1.8%, 0.8%, 1.3% and 4.6% in these mega-cities,

Table 3
Consensus data (2008) of selected cities.

City	Demographic and mortality data		
	Population ($\times 10,000$)	Death ($\times 10,000$)	Mortality ratio (‰)
Beijing	1229.90	5.13	4.17
Shanghai	1391.04	10.70	7.73
Guangzhou	641.30	3.73	5.82
Xi'an	554.73	3.09	5.57

respectively. For greater reductions of $PM_{2.5}$ to 25, 15 and 10 μg/m³, the $PM_{2.5}$ exposure associated with mortality risk would be further reduced by 2.1%, 2.5%, and 2.7% in Beijing, 1.1%, 1.5% and 1.7% in Shanghai, 1.7%, 2.1%, and 2.3% in Guangzhou, and 5.6%, 6.0%, and 6.2% in Xi'an.

4. Discussion

In this quantitative review of excess mortality risk attributable to air pollution exposure in Chinese population, we identified thirty-three time-series and case-crossover studies reporting mortality effects of acute exposure to six air quality criteria pollutants including PM_{10}, $PM_{2.5}$, SO_2, NO_2, O_3, and CO. In these studies, most of the earlier studies reported the acute effects of exposure to PM_{10}, SO_2, and NO_2, whereas recent studies focused on the acute effects of exposure to $PM_{2.5}$, O_3, and CO. The combined estimates in our meta-analysis showed that exposures to PM_{10}, $PM_{2.5}$, SO_2, NO_2, O_3 and CO are significantly associated with increased all-cause and cardio-respiratory mortality risks in Chinese population.

In specific, we observed increased summary risk of excess total mortality of 0.32% (95% CI: 0.28, 0.35) and 0.38% (95% CI: 0.31, 0.45), per 10 μg/m³ increases in PM_{10} and $PM_{2.5}$. Meanwhile, per 10 μg/m³ increases in PM_{10} and $PM_{2.5}$, the summary risks of excess death increased 0.32% (95% CI: 0.23, 0.40) and 0.51% (95% CI: 0.30, 0.73) in respiratory mortality, and 0.43% (95% CI: 0.37, 0.49) and 0.44% (95% CI: 0.33, 0.54) in cardiovascular mortality. Further, based on the derived exposure–mortality coefficient of a 0.38% (95% CI: 0.31, 0.45) increase in total mortality per 10 μg/m³ increase in short-term exposure to $PM_{2.5}$, we observed substantial reductions in total mortality, in projected $PM_{2.5}$ reduction scenarios. To the best of our knowledge, this is the first systemic review of potential health risk attributable to exposure to criteria pollutants in Chinese population, with quantitative assessment of the impact of air pollution associated with mortality reduction.

Resulted from the unprecedented rapid development in industrialization and urbanization in the past decades, many Chinese cities have air pollution levels well above health-based standards (HEI, 2010). Due to various control measures in places in the last decade, though the levels of PM_{10}, SO_2 and CO have been largely reduced, the annual level of NO_2 remains stable or slightly increased (Fig. 1). For an example, the annual levels of PM_{10}, SO_2 and CO in Beijing decreased to 120 μg/m³, 32 μg/m³ and 1.5 mg/m³ in 2010, whereas the annual level of NO_2 remained at the level of 60 μg/m³ (BEPB, 2011). Until now, very limited data is available on the annual levels of pollutants of $PM_{2.5}$ and O_3 that have been newly included in the revised Chinese NAAQS released in March 2012. Brauer et al. (2012) estimated that the population-weighted annual average levels of $PM_{2.5}$ had increased from 44 to 55 μg/m³ between 1990 and 2005 in eastern Asia. They reported the highest measurement of annual (2005) average concentration of $PM_{2.5}$ of 58 μg/m³ in Beijing, China, and the highest derived $PM_{2.5}$ concentration (calculated from PM_{10} measurements) of 121 μg/m³ in Datong, a coal mining center in Shanxi Province, in China.

The overall effects of PM_{10} observed in our analysis are comparable with those assessed in Chinese or Asian population. Several meta-analysis or multi-city based combined analysis reported the summary or pooled estimates of exposure–response coefficients for health effects associated with acute exposure to air pollution, based on studies conducted in China or in Asia. Aunan and Pan (2004) reported summarized estimates of 0.3% and 0.4% increases in total mortality per 10 μg/m³ increases in PM_{10} and SO_2, based on studies published between 1994 and 2004. The Public Health and Air Pollution in Asia (PAPA) study has assessed the effects of short-term exposure to PM_{10}, SO_2, NO_2 and O_3 on daily mortality in Bangkok, Thailand, and in three Chinese cities: Hong Kong, Shanghai, and Wuhan. In the three Chinese cities, the combined excess total mortality risks were 0.37%, 0.98%, 1.19%, and 0.31%, per 10 μg/m³ increases in PM_{10}, SO_2, NO_2 and O_3 (Wong et al., 2008b). Recently, Chen et al. (2012b) reported combined estimates of a 0.35% (95% CI: 0.18, 0.52) increase in total mortality, a 0.56% (95% CI: 0.31, 0.81) increase in respiratory mortality, and a 0.44% (95% CI: 0.23, 0.64) increase in cardiovascular mortality, per 10 μg/m³ increase in PM_{10} 16 Chinese cities. Further, the authors reported combined estimates of 0.75% (95% CI: 0.45, 1.02) and 1.63% (95% CI: 1.09, 2.17) increases in total mortality, 1.25% (95% CI: 0.78, 1.73) and 2.52% (95% CI, 1.44, 3.59) increases in respiratory mortality, 0.83% (95% CI: 0.47, 1.19) and 1.80% (95% CI, 1.00, 2.59) increases in cardiovascular mortality, respectively, per 10 μg/m³ increases in SO_2 and NO_2, in 17 Chinese cities (Chen et al., 2012a, 2012c). With inclusion of more studies conducted in highly polluted Asian countries, a recent systematic review and meta-analysis of Asian time-series literature reported 0.27% (95% CI, 0.12, 0.42), 0.86% (95% CI, 0.34, 1.39), and 0.36% (95% CI, 0.09, 0.62) increases in total, respiratory, and cardiovascular mortality, per 10 μg/m³ increases in PM_{10} (Atkinson et al., 2011).

However, the combined estimates observed in the developed world tend to be higher per same unit increase in PM_{10} than that observed in Chinese or Asian population. With PM_{10} concentrations observed in the range between 10 and 70 μg/m³, a meta-analysis of time series studies in European cities reported significant increases of 0.6 (95% CI, 0.4, 0.8) in total mortality, 1.3 (95% CI, 0.5, 2.0) in respiratory mortality and 0.9 (95% CI, 0.5, 1.3) in cardiovascular mortality, per 10 μg/m³ increase in PM_{10} (WHO, 2004). In the NMMAPS study conducted in the 20 largest US cities, with PM_{10} concentrations ranged in 27.5 to 42.5 μg/m³ and per 10 μg/m³ increase in PM_{10}, significant increases of 0.51% (95% CI: 0.07, 0.93) in total morality and, 0.68% (95% CI: 0.20, 1.16) in cardio-respiratory mortality were observed (Samet et al., 2000).

$PM_{2.5}$ and O_3 pollution has become an emerging health concern in China. Several studies reported excess mortality risk attributable to acute exposure to $PM_{2.5}$ and O_3 in Chinese population (Tao et al., 2012; W. Huang et al., 2012; Yang et al., 2012a, 2012b); however, no study has quantitatively assessed the acute effects of exposure to $PM_{2.5}$ in Chinese population. Our combined estimates for $PM_{2.5}$ also appeared to be lower than those reported in developed countries. Zanobetti and Schwartz (2009) conducted a multicity time-series analysis reporting the associations between $PM_{2.5}$ and mortality in 112 U.S. cities. Per 10 μg/m³ increase in $PM_{2.5}$, the overall combined excess risk estimates were 0.98% (95% CI: 0.75, 1.22) for total mortality, 1.68% (95% CI: 1.04, 2.33) for respiratory mortality, and 0.85% (95% CI: 0.46, 1.24) for cardio-vascular mortality. In a 27 US city time-series analysis nested in the NMMAPS study, per 10 μg/m³ increase in $PM_{2.5}$, Franklin et al. (2007) reported the combined estimates of 1.2% (95% CI: 0.29, 2.1), 0.94% (95% CI: −0.14, 2.0), 1.8% (95% CI: 0.20, 3.4), and 1.0% (95% CI: 0.02, 2.0) for total, cardiovascular, respiratory, and stroke mortality.

In this meta-analysis, only eight time-series studies were identified examining mortality risk of acute exposure to O_3. With the O_3 concentrations ranged in 56 to 86 μg/m³ in study cities, per 10 μg/m³ increase, we observed combined estimates of 0.48% increase in total mortality attributable to O_3 exposure. Our combined estimate appeared to be higher than that reported by WHO of 0.3% increase in total mortality per same unit increase in O_3, with concentrations ranged in 18 to 68 μg/m³ in study cities (WHO, 2004).

With much higher annual average air pollution concentrations observed in Chinese cities, compared to those in western cities, the exposure–response coefficient derived from western studies cannot be simply applied in assessing the health effects attributable to air
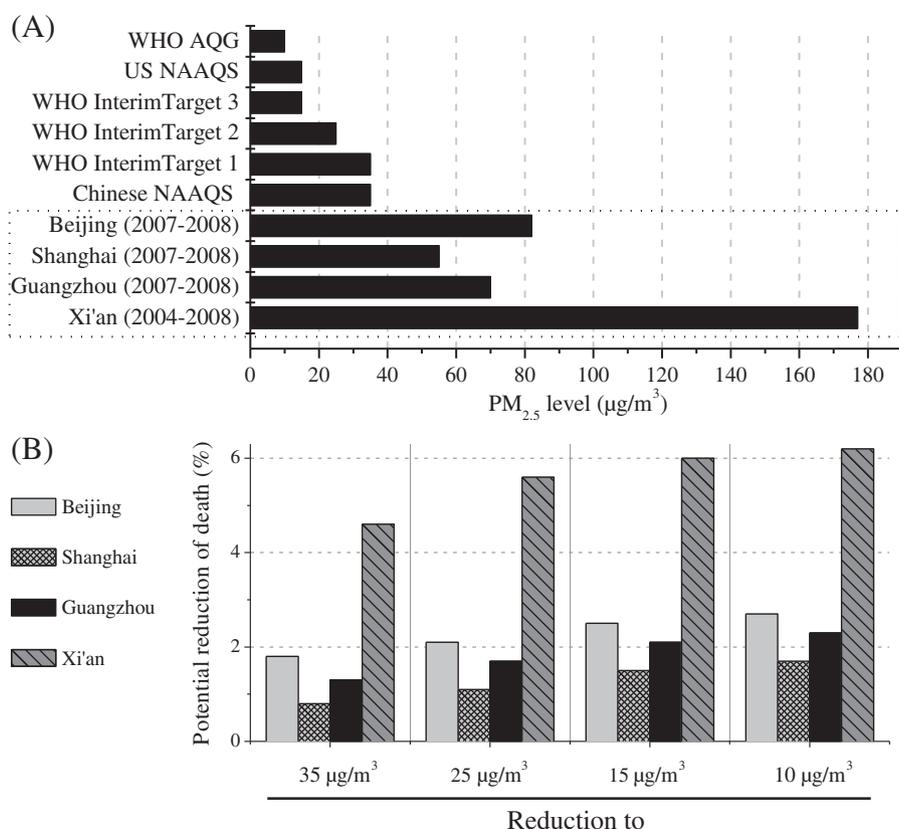
Fig. 5. (A): Comparison of the annual level of $PM_{2.5}$ in Beijing, Shanghai, Guangzhou, Xi'an and the Chinese National/International Air Quality Standards; and (B): Projected mortality reductions in the selected mega-cites in 2008.

pollution exposure in Chinese population. The differences in population size, air pollution levels and sources, and chemical compositions of PM in various study locations can at least partially explain some of the heterogeneity of effect estimates observed in China and developed countries. In addition, the variations in analytic approaches and possible non-linearity in the shape of the exposure–response function can also be the important explanations for the heterogeneity of effect estimates observed across locations.

The quantitative review and assessment of air pollution health effects and impact research have important policy implications. HIA has been one of the important tools to assess the years of healthy life lost due to air pollution, and should be best based on the results presented in cohort studies of long-term exposure (Cohen et al., 2004). However, only one long-term cohort study has been published reporting the mortality risk associated with total suspended particle (TSP), SO_2 and NO_2 exposure in China, up-to-date (Cao et al., 2011). In the present study, by applying the short-term concentration-response coefficients derived in our meta-analysis, the significant reductions in total premature death could be achieved at 2.7% in Beijing, 1.7% in Shanghai, 2.3% in Guangzhou, and 6.2% Xi'an, when $PM_{2.5}$ concentrations in these cities would be reduced from current levels to the WHO AQG level of 10 μg/m³. It should be noted that the mortality impacts attributable to air pollution exposure in Chinese population obtained in this assessment is likely underestimated, as a result of the application of concentration-response coefficients derived from the pooled estimates in short-term effect studies.

A mortality impact assessment of $PM_{2.5}$ in 26 European cities estimated of 0.3% to 9.0% reductions in total mortality would be achieved by reducing $PM_{2.5}$ levels to 10 μg/m³ (Ballester et al., 2008). The benefit for mortality reduction could vary among different reduction projections and across locations, depending on the magnitude of pollution reduction, baseline mortality rate and the exposure–mortality coefficient applied in risk estimate. However, when assuming that the relation between particles and mortality is causal and take no

account of population and exposure levels, the difference likely arise from the selection of the risk estimate. In the HIA study conducted in Europe by Ballester et al. (2008), the relative risk (RR) of 1.04 of long-term exposure to $PM_{2.5}$ was applied in the mortality reduction estimation. The European estimate is approximately ten times greater than the risk estimate derived from short-term exposure effect studies in present analysis with a RR of 1.0038.

In quantitative assessment of published literature, publication bias always arises because there are more rewards for publishing positive or at least statistically significant findings. We assessed possible publication bias in identified literature in present analysis, using funnel plots (Egger et al., 1997). The funnel plots for all pollutant–mortality pairs are summarized in the supplementary file, Fig. S1. Approximately symmetrically shaped funnels for most pollutant–mortality pairs suggested limited publication bias in assessing the identified literature; however, our study results still should be interpreted with cautions because the relatively small number of studies identified and included in the overall assessment. Lag selection is also likely to introduce bias into meta-analysis (Anderson et al., 2005). These sources of biases could be significantly reduced by conducting coordinated multicity studies, in which common analytical protocols are followed by study cities with commitments to publish city-specific and combined estimates.

In summary, significant improvement in ambient air quality has substantial and measurable public health benefits, given current air pollution levels in major Chinese cities are still at the higher end of the world level. However, the concentration–response relationships derived from long-term air pollution exposure studies, which have been largely absent in China, are fundamental in the air quality standard setting and risk estimation. Our results urge future studies on the nature of air pollution concentration and health effect relationships in China that is currently under rapid development and with dense population, and support setting stringent air quality standards to improve public health.

5. Recommendations

Health effects attributable to air pollution exposure in Chinese population has been least understood. Although the levels of ambient PM_{10} and SO_2 have been reduced in the past decade in major Chinese cities, whereas NO_2 is stable or slightly increased; however, the air pollution levels are still much higher compared to those in the developed countries. Besides conventional criteria pollutants, $PM_{2.5}$ and O_3 are being regulated based on the adverse health effects observed in the developed world and in limited Chinese studies. Our systemic review indicates that the air pollution sources and the chemical composition of ambient particles may partially explain the heterogeneity of effect estimates observed in studies across locations and over time. A better understanding of the air pollution sources and ambient particular chemical components that are most harmful to Chinese population would be important to decision-makers in developing more stringent air pollution regulations. In addition, the standard selection and settings for air pollutants should be based on the estimates obtained in air pollution long-term exposure cohort studies, which are largely absent in China. The exposure–response coefficients derived from long-term follow-up of air pollution exposure are urgently needed to support future air quality standard revisions in stages in China.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.envint.2013.01.010.

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