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Potential Cardiovascular and Total Mortality Benefits of Air Pollution Control in Urban China

Running Title: *Huang et al; Health Benefits of Air Pollution Control in China*

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Abstract

Background**—**Outdoor air pollution ranks fourth among preventable causes of China's burden of disease. We hypothesized that the magnitude of health gains from air quality improvement in urban China could compare with achieving recommended blood pressure or smoking control goals.

Methods**—**The Cardiovascular Disease Policy Model-China projected coronary heart disease, stroke, and all-cause deaths in urban Chinese adults aged 35-84 years from 2017 to 2030 if recent air quality (particulate matter with aerodynamic diameter ≤ 2.5 µm, $PM_{2.5}$) and traditional cardiovascular risk factor trends continue. We projected life years gained if urban China were to reach one of three air quality goals: Beijing Olympic Games level (mean $PM_{2.5}$, 55 µg/m^3), China Class II standard (35 µg/m^3), or World Health Organization (WHO) standard (10 µg/m^3). We compared projected air pollution reduction control benefits with potential benefits of reaching WHO hypertension and tobacco control goals.

Results**—**Mean $PM_{2.5}$ reduction to Beijing Olympic levels by 2030 would gain about 241,000 (95% uncertainty interval, 189,000-293,000) life-years annually. Achieving either the China Class II standard or WHO $PM_{2.5}$ standard would yield greater health benefits [992,000 (95% uncertainty interval, 790,000-1,180,000) or 1,827,000 (95% uncertainty interval, 1,481,000-2,129,000) annual life years gained, respectively] than WHO-recommended goals of 25% improvement in systolic hypertension control and 30% reduction in smoking combined [928,000 (95% uncertainty interval, 830,000-1,033,000) life years].

Conclusions**—**Air quality improvement at different scenarios could lead to graded health benefits ranging from 241,000 life-years gained to much greater benefits are equal to or greater than the combined benefits of 25% improvement in systolic hypertension control and 30% smoking reduction.

Key Words: China; air pollution; cardiovascular disease; health benefits, computer modeling

Clinical Perspective

What is new?

- It is the first forecast that averted cardiovascular disease (CVD) deaths and life years gained from reducing national mean $PM_{2.5}$ in 2017 to 2008 Beijing Olympic Game level would be greater than benefits gained from 30% reduction in tobacco use among urban Chinese adults.
- Achieving the China Class II standard of 35 $\mu g/m^3$ or a more aggressive WHO target of 10 $\mu g/m^3$ for $PM_{2.5}$ control would yield greater CVD deaths reduction and life-year gains than the combined benefits of WHO-recommended 25% systolic hypertension control and 30% smoking reduction in urban China.

What are the clinical implications?

- The findings suggested that small risk reductions from air pollution control across the entire urban population yield health benefits similar to control for systolic hypertension and smoking in a high risk segment of the urban Chinese population.
- Air quality improvement in China will call for joint efforts of the whole society, including development of green transportation, reduction of industrial emission, implementation of governmental control measures, and other collaborative actions in air pollution control.

In urban China, especially in northern cities, hazardous outdoor air pollution has become a major environmental problem. Annual population-weighted mean level of particulate matter with aerodynamic diameter ≤ 2.5μm ($PM_{2.5}$) in all of China rose from 39 μg/m^3 in 1990 to 54 μg/m^3 by 2013.[1] Among 161 selected Chinese cities, mean $PM_{2.5}$ was 62 μg/m^3 in 2014,[2] 90% of cities were in excess of the China Class II air quality standard limit of 35 μg/m^3,[2] and all were above the World Health Organization (WHO) recommended level of 10 μg/m^3.[3] The highest annual average $PM_{2.5}$ level among these cities peaked at 130 μg/m^3, nearly 4-fold higher than the national limit.[2] During the period of 2008 Beijing Olympic Games, a government program of aggressive air quality controls reduced the mean $PM_{2.5}$ by about 30 μg/m^3.[4]

Outdoor air pollution is associated with increased population risk for cardiopulmonary diseases.[5] In 2010, ambient air pollution led to 3.3 million premature deaths per year globally, and most of these avoidable deaths occurred in Asia.[6] The global fractions of adult mortality attributable to the man-made component of $PM_{2.5}$ are 8.0% for cardio-pulmonary disease and 9.4% for ischemic heart disease.[7] Following dietary risks (51.7 million disability-adjusted life years [DALYs]), high blood pressure (37.9 million DALYs) and tobacco smoking (30.0 million DALYs), ambient particulate matter pollution was the 4th leading preventable risk factor responsible for China's avoidable disease burden in 2010 (25.2 million DALYs).[8] Natural experiments associated a 10 μg/m^3 reduction in $PM_{2.5}$ with a 31% reduced in cardiovascular mortality over eight years of follow up.[9]

A long-term interventional trial with large sample size will be optimal to illustrate health benefits gained from air pollution control. However, it seems not feasible to carry out such a trial with enough intervention time to observe cardiovascular health benefits currently. As an initial step, we conducted a computer simulation experiment to explore the potential cardiovascular and non-cardiovascular health benefits of achieving three air quality targets and further compared the scale of predicted health benefits with active tobacco smoking and systolic hypertension controls in urban China.

Methods

Cardiovascular Disease Policy Model-China Overview

The Cardiovascular Disease (CVD) Policy Model-China is a computer-simulation, state-transition (Markov cohort) mathematical model of coronary heart disease (CHD) and stroke incidence, prevalence, mortality, non-cardiovascular deaths, and costs of health care in Chinese population aged 35-84 years old (**Table 1** and **Figure 1**). This model has been used for CVD epidemiological projections and effectiveness analysis of specific policy interventions.[19] The urban-wide population for the years 2017-2030 was estimated using the projected total China population and urban-rural ratio from the *World Urbanization Prospects* (**Supplemental Table S1**).[11, 12] Means and proportions of CVD risk factors in urban Chinese adults aged 35 to 84 years were estimated from the China Cardiovascular Health Study and the China Multi-center Collaborative Study of Cardiovascular Epidemiology (ChinaMUCA).[15, 16] CHD and stroke incidence and non-cardiovascular mortality risk were predicted among individuals without CVD, stratified by age, sex, systolic blood pressure (SBP), body mass index (BMI), low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, smoking status, and diabetes. Multivariable adjusted hazard ratios of SBP, LDL, HDL, BMI, smoking and diabetes for CHD, stroke, and non-cardiovascular (non-CHD, non-stroke) deaths by age and sex were estimated from the China Multi-provincial Cohort Study (CMCS)[18] using a competing risk Cox proportional hazard model for each outcome (**Supplemental Table S2**). Future traditional non-communicable disease (NCD) risk factor trends were projected forward from 2017 to 2030 using China Health Nutrition Surveys (CHNS) study (**Supplemental Table S3**).[17] An annual population-weighted average $PM_{2.5}$ level during the period of 2014-2015 was extracted and assumed as starting national $PM_{2.5}$ level in 2017.[13] Effects of long term $PM_{2.5}$ exposure on CHD and stroke deaths based on a meta-analysis were incorporated into the model (**Supplemental Table S4** and **Figure S1-S3**).[14] Finally, starting with CHD and stroke case fatality obtained from the Sino-MONICA Beijing study,[20] the CVD Policy Model-China mortality projections were calibrated to fit with age-specific and overall CHD and stroke mortality numbers for the years 2010-2011 based on mortality surveillance data from the China Center for Disease Control (CDC).[21] After CHD and stroke mortality were calibrated, age and sex specific non-cardiovascular death rates were also calibrated so that the total of cardiovascular and non-cardiovascular deaths fitted within the envelope of all-cause mortality reported by the China CDC (**Supplemental Tables S5-8**).[21]

The modeling study was approved by the Institutional Review Board at Fuwai Hospital in Beijing. All the preceding original studies included in the secondary analyses obtained written informed consent from each participant before data collection.

Projected population of urban China, 2017-2030

Population estimates for the urban China population were obtained from the 2010 6th China census.[10] The urban population for the years 2017-2030 was estimated by projecting population growth and aging trends from 2017-2030, then multiplying the whole population estimate by the expected urbanization rate (**Supplemental Table S1**).[11, 12]

$PM_{2.5}$ exposure and effect on mortality

The Chinese Ministry of Environmental Protection (MEP) started to measure $PM_{2.5}$ concentrations since 2012. An annual population-weighted average $PM_{2.5}$ level during the period of 2014-2015 was extracted in 190 cities with over 950 monitoring sites and assumed as starting national $PM_{2.5}$ level in 2017.[13] We started with the population-weighted mean 2014-2015 $PM_{2.5}$ of 61 μg/m^3 in urban China, and projected it forward to 2030 as the *status quo* case.[13] In order to quantify the relative impacts of air pollution control, the $PM_{2.5}$ levels for the selected cities (Beiijng, 79.8 μg/m^3, and Baoding, 118.8 μg/m^3) were also obtained.[13] For the 2008 Beijing Olympic Games air quality goal, due to lack of reliable $PM_{2.5}$ level measurement at the city-wide level in Beijing at that time, we based on mean $PM_{2.5}$ levels recorded by the United States embassy in Beijing, located northeast of central Beijing.[22] Relative risks of CHD, stroke and all-cause mortality associated with long term $PM_{2.5}$ exposure were estimated in a meta-analysis of cohort studies using random effects model via the DerSimonian-Laird method (**Supplemental Table S4** and **Figure S1-S3**).[14] Because these studies included in the meta-analysis did not report effects of long term $PM_{2.5}$ exposure on health stratified by age or sex, we assumed a uniform relative risk effect of $PM_{2.5}$ on all urban adults. As our CVD Policy Model-China was not originally designed for pulmonary disease, we could not directly predict pulmonary deaths. Thus, prevented pulmonary deaths were estimated by taking a fixed proportion of prevented non-cardiovascular deaths, based on cause-specific mortality surveillance data from China CDC.[21]

Traditional non-communicable disease risk factor trend projections (2017-2030)

Future traditional NCD risk factor trends were projected forward from 2017 to 2030 based on recent temporal trends from 1990 to 2009 (**Supplemental Table S3**). Temporal trend estimations were based on repeated CHNS from 1991 to 2009.[17] Temporal SBP, BMI, and active smoking trends were estimated using CHNS data and age-adjusted mixed linear random effects model with 10-year age groups. Age-time interactions observed in trends for SBP, BMI, or active smoking were incorporated into age-specific risk factor trend projections. Because serum lipid data were available only for 2009, HDL and LDL trends were assumed to be mediated by the BMI trend.[23] In this model analyses, diabetes was defined as a having a past diagnosis of diabetes, taking anti-diabetes medications, or a fasting glucose ≥126 mg/dL. Diabetes prevalence recorded in the CHNS before 2009 might be underestimated without fasting glucose data. Therefore, we assumed diabetes awareness rate (the proportion of self-reported diabetes among participants defined as diabetes) gradually increased over time. The number of diabetes before 2009 was estimated using the following formula: the number of diabetes = self-reported diabetes/diabetes awareness rate. Self-reported diabetes information was obtained from the CHNS, while diabetes awareness data were from the China Cardiovascular Health Study and the ChinaMUCA. Then the prevalence of diabetes could be obtained as the proportion of the estimated number of diabetes over the total number of subjects in CHNS. Based on the calculated diabetes prevalence, we projected diabetes trend accordingly (**Supplemental Table S3)**.

Air pollution, smoking, and systolic hypertension control scenarios

In 2013, the Chinese government released the first National Action Plan on Air Pollution Prevention and Control (2013-2017), setting air pollution improvement goals for different areas with 15% to 25% reductions in $PM_{2.5}$ by 2017.[24] The Beijing municipal government also announced a plan to improve air quality to the China Class II standard of 35 μg/m^3 by 2030. Additional health benefits could be gained by lowering $PM_{2.5}$ level to the WHO recommendation of 10 μg/m^3. We assumed health effects of controlled $PM_{2.5}$ levels on CHD and stroke mortality were roughly linear over the range 10 to 65 μg/m^3.[25] A status quo simulation projected cumulative CHD, stroke, and all-cause mortality events for Chinese adults over the years 2017–2030, projecting forward background traditional risk factor secular trends but no change from status quo level of $PM_{2.5}$. Life-years were tabulated without discounting. Annual CHD, stroke and all-cause mortality and life-years were averaged over the simulation period. We simulated three air quality improvement scenarios, with a linear decrease in $PM_{2.5}$ to the following targets by 2030: 1) the Beijing Olympic Games $PM_{2.5}$ level of 55 μg/m^3, 2) the China Class II air quality standard level of 35 μg/m^3, or 3) the WHO recommended level of 10 μg/m^3.

In 2013, the WHO developed a global monitoring framework aimed at reducing global mortality from four major NCDs of which CVD is the main contributor.[26] The framework comprises nine voluntary global NCD targets for 2025, including a 25% reduction in hypertension and a 30% reduction in tobacco use. Although reducing air pollution level was not listed as one of priorities in this framework, to better understand the magnitude of health gains possible of air pollution improvement with control of traditional NCD risk factors, we further projected the effects of a gradual control of systolic hypertension (from ≥140 mmHg to less than 140 mmHg) in 25% of patients with uncontrolled systolic hypertension, and a gradual 30% reduction in tobacco use over 2017-2030, both individually and in combination. Furthermore, we titrated the effect size of simulated blood pressure and tobacco smoking prevalence reductions until the numbers of life years gained matched the projected number of life years gained with the 2008 Beijing Olympic $PM_{2.5}$ improvement.

Statistical Analysis

Projected deaths and life years under different hypothetical scenarios were estimated using the CVD Policy Model-China, which incorporated urban China population projections, $PM_{2.5}$ effect on CVD incidence and CVD and non-CVD mortality, and traditional non-communicable disease risk factor trend projections. Annual numbers of CVD events were deterministically predicted from hazard ratios estimated by Cox proportional hazard models for each simulated outcome (**Supplemental Table S2**). Life years were tabulated for the population alive in each model cycle. Further, deaths averted and life years gained were compared between status quo and projected scenarios. We also performed multivariable probabilistic sensitivity (Markov Monte Carlo) analyses in order to estimate a range of uncertainty surrounding the results of projected air quality improvement and traditional risk factor intervention scenarios. We assumed that the beta coefficient distributions measuring the effect sizes for associations of SBP, smoking and $PM_{2.5}$ with CVD mortality were normally distributed. We performed 1,000 Markov simulations in which the three beta coefficient distributions were randomly and simultaneously sampled in each simulation. The 95% uncertainty intervals (95% UIs) reported in **Table 2** and the figures reflected the lower 2.5^{th} and upper 97.5^{th} percentiles of the 1,000 results for each outcome.

In addition, several sensitivity analyses were conducted to make the results more interpretable. First, considering potential reduced trend of $PM_{2.5}$ in China, health benefits were estimated with a graded reduction of $PM_{2.5}$ over 2017-2030 as alternative status quo scenario. Second, a linear $PM_{2.5}$-CVD morality relationship assumption might overestimate the health benefits, thus 10% and 20% attenuated $PM_{2.5}$-CVD health effects were used to quantify the impact of attenuated relative risk on health benefits. Details could be found in the **Supplemental Methods**.

Results

Because of population growth, aging, and rural-to-urban migration, the urban Chinese population aged 35 to 84 years was projected to grow from 421 million in 2017 to 602 million in 2030 (**Supplemental Table S1**). In the *status quo* simulation holding the $PM_{2.5}$ constant at 61 μg/m^3 and extending traditional risk factor trends forward, about 7,900,000 (95% UI, 7,741,000-8,076,000) CHD deaths [annual average 564,000 (95% UI, 553,000-577,000)] and 11,061,000 (95% UI, 10,408,000-11,617,000) stroke deaths (annual average 790,000 (95% UI, 743,000-830,000)] were projected in urban China from 2017 to 2030 (**Table 2**).

Reduction in mean $PM_{2.5}$ level to the 2008 Beijing Olympics level would prevent about 439,000 (95% UI, 233,000-643,000) CHD deaths [5.6% (95% UI, 3.0-8.1) reduction; annual average −31,000 (95% UI, −46,000-−17,000)], about 237,000 (95% UI, 109,000-357,000) stroke deaths [2.1% (95% UI, 1.0-3.2) reduction; annual average −17,000 (95% UI, −25,000—8,000)], and about 397,000 (95% UI, 386,000-409,000) non-cardiovascular deaths [1.3% (95% UI, 1.2-1.4) reduction; annual average −28,000 (95% UI, −29,000-−27,000)], including about 79,000 (95% UI, 77,000-82,000) pulmonary disease deaths [annual average −5,700 (95% UI, −5,800-−5,500)] and would gain about 3,379,000 (95% UI, 2,645,000-4,109,000) [annual average +241,000 (95% UI, 189,000-293,000)] life years in urban China. We projected that reaching air quality to 2008 Beijing Olympic Games goal (55 μg/m^3), about 43.4% (95% UI, 25.8-53.9) of CHD deaths, 20.7% (95% UI, 9.6-29.7) of stroke deaths and 12.8% (95% UI, 12.1-13.6) pulmonary deaths would be avoided in the highest $PM_{2.5}$ level city (Baoding, $PM_{2.5}$ 118.8 μg/m^3) and 20.8% (95% UI, 10.6-30.0) of CHD deaths, 8.7% (95% UI, 2.1-15.2) of stroke deaths and 5.3% (95% UI, 4.7-6.0) of pulmonary deaths would be avoided in a contrast city (Beijing, $PM_{2.5}$ 79.8 μg/m^3).

The life-years gained from reducing national mean $PM_{2.5}$ to the 2008 Beijing Olympic Games level were fewer than controlling 25% of systolic hypertension but greater than 30% reduction in tobacco use (**Figure 2**). Reaching the Beijing Games air quality goal was projected to yield health gains comparable in magnitude to the life-years gained by controlling 1.8% of systolic hypertension or a 40% reduction in tobacco use over the same time period. For instance, gradually lowering tobacco use by 30% of the 2017 prevalence proportion would prevent 412,000 (95% UI, 268,000-553,000) CHD deaths and 116,000 (95% UI, 9,000-241,000) stroke deaths and gain about 3,094,000 (95% UI, 2,439,000-3,763,000) life years over 2017-2030 [annual averages of −29,000 (95% UI, −40,000-−19,000), −8,000 (95% UI, −17,000-−1,000), and +221,000 (95% UI, 174,000-269,000), respectively]. Controlling 25% of systolic BP to less than 140 mmHg among systolic hypertensive patients was projected to avert 724,000 (95% UI, 577,000-889,000) CHD deaths and 1,268,000 (95% UI, 905,000-1,663,000) stroke deaths and gain 10,066,000 (95% UI, 8,889,000-11,439,000) life years [annual averages of −52,000 (95% UI, −63,000-−41,000), −91,000 (95% UI, −119,000-−65,000), and +719,000 (95% UI, 635,000-817,000), respectively], much larger health benefits than projected for the 2008 Beijing Olympics air quality goal (**Table 2** and **Figure 2**).

Achieving the China Class II standard of 35 $\mu g/m^3$ or the more aggressive WHO target in urban China would achieve much larger CVD mortality reductions and life year gains (**Table 2** and **Figure 2**). For example, during 2017-2030, 13,883,000 (95% UI, 11,061,000-16,514,000) [annual average +992,000 (95% UI, 790,000-1,180,000)] life years and 25,576,000 (95% UI, 20,731,000-29,802,000) [annual average +1,827,000 (95% UI, 1,481,000-2,129,000)] life years will be gained when achieving the goal of the China Class II standard and the WHO target, respectively. Reaching either goal would yield health gains greater than both 30% smoking and

25% systolic hypertension control combined [12,986,000 (95% UI, 11,614,000-14,468,000) life years gained over 2017-2030, annual average +928,000 (95% UI, 830,000-1,033,000) life years].

In the sensitivity analysis, averted CVD deaths and life years gained tended to be less when using a graded reduction of $PM_{2.5}$ over 2017-2030 as an alternative status quo. About 1,115,000 (95% UI, 1,281,000-1,950,000), 11,620,000 (95% UI, 9,738,000-14,355,000) and 23,313,000 (95% UI, 19,526,000-27,682,000) life years could gain from reaching Beijing Olympic Game air quality level, China Class II and WHO goal, respectively (**Supplemental Table S9**). As shown in **Supplemental Table S10-S11**, reaching Beijing Olympic Game level would gain 3,177,000 (95%UI, 2,629,000-3,822,000) and 2,967,000 (95%UI, 2,128,000-3,803,000) life years over 2017-2030 in 10% attenuated and 20% attenuated health effect scenarios, respectively.

Discussion

Despite abundant evidence linking short and long term exposure to high $PM_{2.5}$ levels to increased cardiopulmonary disease risk, the air pollution level in most Chinese cities remains high. Our urban China population simulations projected that considerable health benefits could be gained from the modest $PM_{2.5}$ improvement achieved for the duration of the 2008 Beijing Olympic Games. The potential health benefits of $PM_{2.5}$ reductions to China Class II or WHO goals would be greater in magnitude than the benefits from both 30% reductions in smoking and 25% reduction in uncontrolled systolic hypertension combined.

With its dramatic economic growth during the past three decades, China has become the second largest economy in the world. However, China's accelerating economic engine increased energy consumption and resulted in harmful air pollution levels in most of urban China.

Agricultural activities, motor vehicle exhaust, coal-powered winter heating and biogenic emissions have all contributed to the problem. Special occasions like the 2008 Beijing Olympic Games or the 2014 Asia-Pacific Economic Cooperation (APEC) conference demonstrated that systematic air pollution emission control measures can result in substantial declines in air pollution, albeit these improvements were temporary. Indeed, air pollution rebounded to its prior level soon after the Olympics and APEC emission control measures ended.[27, 28] Practical and integrated air quality improvement policies are crucial for achieving sustained air quality improvement. Regulations established in the United States and other countries resulted in substantial reductions in particulate matter and other pollutant levels over the past several decades.[29] Los Angeles, London and Mexico City, once well-known for poor air quality, all improved air quality through policy actions. In England, black smoke levels dropped from 42.7 μg/m^3 in 1971 to 11.8 μg/m^3 in 2001.[30] London's annual mean $PM_{2.5}$ has held at an around 20 μg/m^3. Recent average $PM_{2.5}$ levels in Los Angeles are near the WHO goal at 10 μg/m^3.[31] Mean $PM_{2.5}$ level in Mexico City decreased from 35 μg/m^3 during 2000-2002 to 25 μg/m^3 in 2011,[32, 33] indicating air pollution control is also achievable in middle-income country cities. The Chinese government has already set ambitious air quality goals for the year 2030. A cost-benefit analysis of the Air Pollution Prevention and Control Action Plan promulgated by Chinese government found that a combination of policy measures would be cost-effective during the period 2013 to 2017,[34] especially when taking into account joint regional air pollution measures.[35] In response to the framework proposed by WHO aiming to lower global NCDs mortality by 2025, our comparison of health gains from air pollution improvement with traditional NCDs risk factors control has important implications. Traditional NCD risk factors convey a higher magnitude of individual risk than air pollution, but these risk factors affect only segments of the population.

Though air pollution risk is small at the individual level, the entire population is exposed to poor air quality, so that our projected health benefits from more aggressive air pollution control policies were comparable in magnitude with control of 30% active smoking or 25% of systolic hypertension. Therefore, our findings suggested that China has a specific opportunity to prioritize air pollution control over some other measures to achieve NCD control goal set by the WHO.

Several past modeling studies projected health benefits from planned air quality control policies in China.[4, 9, 36-39] However, most of these studies were conducted in a single city with projected health impact of reduction in PM_{10},[9, 38, 39] or converted to $PM_{2.5}$ from a fixed proportion of PM_{10}.[36] The Benefits Mapping and Analysis Program (BenMAP) projected an annual reduction of between 39 and 1,400 all-cause deaths annually with air pollution control in Shanghai.[36] Another study showed that approximately 4% (1-7%) of all-cause deaths in China can be avoided by implementing emission control policies.[37] Madaniyazi projected that a 20.4 $\mu g/m^3$ decrease in mean $PM_{2.5}$ in East China between 2005 and 2030 under the "maximum technically feasible reduction" scenario would prevent 230,000 deaths.[40] However, aforementioned studies did not model the air pollution effects on health in the context of simultaneous trends in traditional disease risk factors, population aging and growth, and rural-to-urban migration. The Global Burden of Disease (GBD) Study estimated air pollution effects on disease burden from 1990 to 2015 at global, regional, and country levels. Deaths attributed to ambient $PM_{2.5}$ pollution increased from 3.5 million to 4.2 million worldwide, and China experienced the world's largest air pollution-related disease burden in absolute numbers in 2015.[41] About 1.1 million total deaths among adults aged 25-80 years in urban and rural China were attributed to harmful levels of ambient $PM_{2.5}$ pollution ($PM_{2.5} > 7.5$ $\mu g/m^3$).[41] Furthermore, given forecasted demographic and epidemiological trends, China's average $PM_{2.5}$ level would need to decline by 29% over 2015-2030 merely to hold per-capita mortality attributable to $PM_{2.5}$ constant at year-2010 level.[42] In this study, we projected an average reduction of about 0.6 million annual total deaths over 2017-2030 if air quality could be gradually improved to WHO recommended concentration level (10 $\mu g/m^3$) among adults aged 35-84 years in urban China alone. Thus, substantial reduction in disease burden can be achieved for entire populations by controlling air pollution mainly via legislation, government policy and joint initiatives at the national level.

Our study has several limitations. We based our *status quo* exposure scenario on mean $PM_{2.5}$ levels in all urban areas combined. Therefore, we did not assess variable impact of $PM_{2.5}$ exposure by season or city. Though we calculated a mean $PM_{2.5}$ for urban China weighted according to city population size, we did not account for differences in population density among Chinese cities nor specify our analysis to city-level. Due to the CVD Policy Model-China's characteristics, the relative risk of $PM_{2.5}$-CVD was not stratified by age. Considering non-linear exposure-risk relationship, we may have overestimated the health effects changes for cities in urban China. Our results from sensitivity analysis using attenuated health effects estimation provided further information to understand the health benefits from air pollution control. We modeled $PM_{2.5}$ as pollutant representative of multiple component pollutants. Integrated air pollution control of component sources of pollution might yield even greater benefits. Our study did not account for the cumulative effects of past air pollution exposures, which may be refractory to current air quality improvements. Our model is also limited in capturing the total health impact of air pollution control because it was specifically designed for CVD. We therefore likely underestimated pulmonary disease burden averted by improved air quality and did not capture non-cardiovascular health benefits of near-term smoking control that extend beyond the year 2030. Finally, the health gains from tobacco use reduction were likely underestimated because associated reductions in secondhand smoking were not included.

Air pollution is a leading cardiovascular cause of preventable disease burden in urban China. Our simulation modeling study results suggest that modestly controlling air pollution to the Beijing Olympics Games level, which still would be twice as high as current Mexico City, could prevent about 439,000 CHD deaths and 237,000 stroke deaths, and gain 3,379,000 life years in urban China by 2030. Our findings indicated that more health benefits could be gained with more aggressive reductions in $PM_{2.5}$ levels. Aggressive air pollution controls policies would result in health benefits on the same order of magnitude as the combined benefits of 25% improvement in hypertension control and 30% smoking reduction. Our results suggest that air quality improvement should be among the highest priority goals for preventing non-communicable disease deaths and disability in China.

Disclosures

None.

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Author Contributions

CH, AEM and DG designed the study. CH, AEM, PGC, JH, LG, DZ and DG designed and programmed the CVD Policy Model-China. XY, FL and JC updated cardiovascular risk factor levels for the urban Chinese population. CH and AEM designed the model calibration and ran all model simulations and prepared the results. CH, AEM, XY, FL, KC, MW, LG, PK and DG interpreted the data. CH prepared the first draft of the manuscript. All authors contributed to writing and reviewing the manuscript. All authors had approved of this manuscript and confirmed they met ICMJE criteria for authorship.

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Table 1. Main inputs for cardiovascular benefits projections from improved air pollution among urban Chinese population aged 35-84 years old

Inputs	Definition	Source
Population	Population aged 35-84 years old in urban China	The 6th population census of China in 2010[10]
	Impact of growth, aging and urbanization on population	Projections from United Nation Population Division[11, 12]
Air Pollution	An annual population-weighted average level of $PM_{2.5}$ level during 2014-2015 in 190 cities	Zhang Y, et al. 2015[13]
	Main estimates and standard deviations of risk coefficients of long term exposure to $PM_{2.5}$ for CHD, stroke and all-cause mortality with 1 μg/m^3 increase in $PM_{2.5}$	Based on a Meta-analysis by Hoek et al. 2013[14]
Traditional cardiovascular risk factors	Baseline levels of traditional cardiovascular risk factors were analyzed, including SBP, BMI, HDL, LDL, status of smoking and diabetes	China Cardiovascular Health Study, ChinaMUCA[15, 16]
	Trend estimations of risk factors were projected forward over year 2017 to 2030	CHNS study, China Cardiovascular Health Study, ChinaMUCA[15-17]
	Main estimates and standard deviations of risk coefficients of traditional cardiovascular risk factor on CHD, stroke and all-cause mortality were estimated	CMCS study[18]

Abbreviations: CHD, coronary heart disease; SBP, systolic blood pressure; BMI, body mass index; HDL, high density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol; ChinaMUCA, the China Multi-center Collaborative Study of Cardiovascular Epidemiology; CHNS study, China Health and Nutrition Survey study; CMCS study, Chinese Multi-Provincial Cohort Study

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Table 2. Projected CHD and stroke deaths averted with hypothetical air pollution controls in urban Chinese population aged 35-84 years over 2017-2030, the Cardiovascular Disease Policy Model-China

	Annual $PM_{2.5}$ level (μg/m^3)	CHD Deaths (thousands, 95% UI)	Averted CHD Deaths (thousands, 95% UI)	Stroke Deaths (thousands, 95% UI)	Averted Stroke Deaths (thousands, 95% UI)
Status quo case (remain current $PM_{2.5}$ level)	61	7,900 (7,741-8,076)	-	11,061 (10,408-11,617)	-
$PM_{2.5}$ improvement scenarios*					
Target 1: Beijing Olympic Games	55	7,461 (7,184-7,778)	439 (233-643)	10,824 (10,181-11,391)	237 (109-357)
Target 2: China Class II standard limit	35	6,216 (5,524-7,040)	1,684 (947-2,339)	10,080 (9,335-10,797)	981 (466-1,438)
Target 3: WHO recommended level	10	5,031 (4,109-6,255)	2,870 (1,717-3,760)	9,240 (8,292-10,212)	1,821 (896-2,592)
Comparison scenarios*					
25% reduction in uncontrolled systolic hypertension (to <140 mmHg)	61	7,177 (7,097-7,242)	724 (577-889)	9,793 (9,299-10,204)	1,268 (905-1,663)
30% reduction in tobacco use	61	7,489 (7,229-7,720)	412 (268-553)	10,944 (10,183-11,591)	116 (9-241)
25% reduction in uncontrolled systolic hypertension (to <140 mmHg) plus 30% reduction in tobacco use	61	6,806 (6,607-6,967)	1,094 (890-1,282)	9,693 (9,083-10,200)	1,368 (1,003-1,764)

*Each scenario is compared with the status quo case. Ninety-five percent uncertainty intervals were calculated from the results of 1,000 probabilistic simulations.

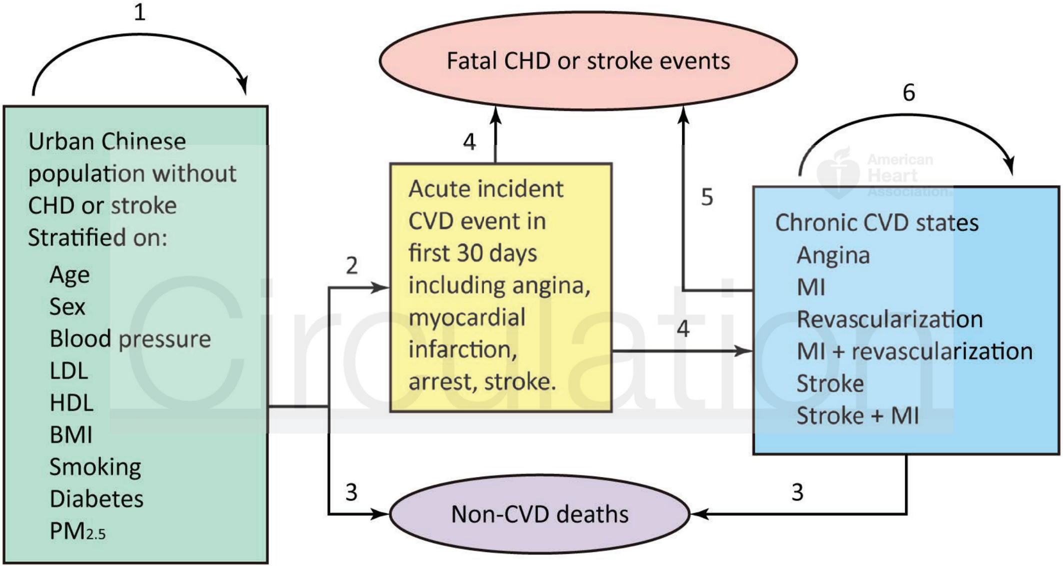
Figure Legends

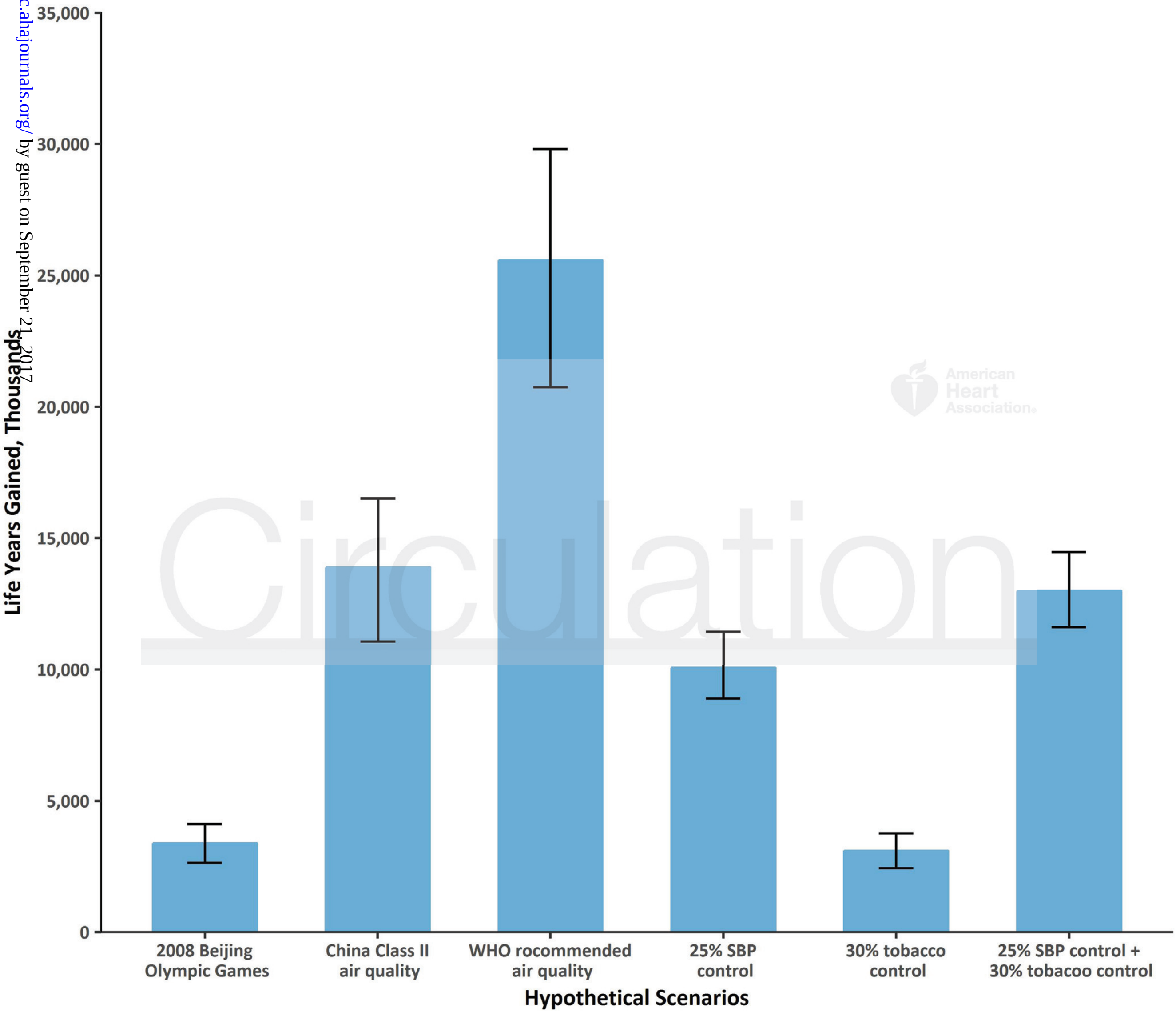
Figure 1. The CVD Policy Model-China structure

Transition 1 = remain in CVD-free state. Transition 2 = incident CVD. Transition 3 = non-CVD death. Transitions 4 and 5 = survival or case-fatality. Transition 6 = survival with or without repeat CVD event in chronic CVD patients.

LDL, low density lipoprotein cholesterol; HDL, high density lipoprotein cholesterol; BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; MI, myocardial infarction.

Figure 2. Projected life years gained in hypothetical scenarios in urban Chinese population aged 35-84 years over 2017-2030


1
Urban Chinese population without CHD or stroke Stratified on:
Age
Sex
Blood pressure
LDL
HDL
BMI
Smoking
Diabetes
PM2.5
2
3
Fatal CHD or stroke events
4
Acute incident CVD event in first 30 days including angina, myocardial infarction, arrest, stroke.
4
5
6
Chronic CVD states
Angina
MI
Revascularization
MI + revascularization
Stroke
Stroke + MI
3
Non-CVD deaths



35,000
30,000
25,000
20,000
15,000
10,000
5,000
0
Life Years Gained, Thousands
2008 Beijing Olympic Games
China Class II air quality
WHO rocommended air quality
25% SBP control
30% tobacco control
25% SBP control + 30% tobacoo control
Hypothetical Scenarios

Circulation

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Potential Cardiovascular and Total Mortality Benefits of Air Pollution Control in Urban China

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SUPPLEMENTAL MATERIAL

(1) Supplemental Methods

(2) Supplemental Tables

Supplemental Table S7. Pre-calibration and post-calibration CHD incidence and 28 day case-fatality inputs

Supplemental Table S8. Pre-calibration and post-calibration stroke incidence and 28 day case-fatality inputs

Supplemental Table S9. Sensitivity analysis for projected CHD and stroke deaths averted with hypothetical air pollution controls in urban Chinese population aged 35-84 years over 2017-2030 with a graded reduction of $PM_{2.5}$ as alternative status quo case

Supplemental Table S10. Sensitivity analysis for projected CHD and stroke deaths averted with hypothetical air pollution controls in urban Chinese population aged 35-84 years over 2017-2030 with 10% attenuated $PM_{2.5}$-CVD health effects

Supplemental Table S11. Sensitivity analysis for projected CHD and stroke deaths averted with hypothetical air pollution controls in urban Chinese population aged 35-84 years over 2017-2030 with 20% attenuated $PM_{2.5}$-CVD health effects

(3) Supplemental Figures and Figure Legends

Supplemental Figure S1. Relative risks for each 10 $\mu g/m^3$ increment in long term $PM_{2.5}$ exposure and risk of all-cause mortality.

Supplemental Figure S2. Relative risks for each 10 $\mu g/m^3$ increment in long term $PM_{2.5}$ exposure and risk of coronary heart disease mortality.

Supplemental Figure S3. Relative risks for each 10 $\mu g/m^3$ increment in long term $PM_{2.5}$ exposure and risk of stroke mortality.

(4) Supplemental Reference

Supplemental Methods

General overview of the Cardiovascular Disease Policy Model-China

The Cardiovascular Disease (CVD) Policy Model-China is a computer-simulation, state-transition (Markov cohort) mathematical model of coronary heart disease (CHD) and stroke incidence, prevalence, mortality, non-cardiovascular deaths, and costs of health care in Chinese population aged 35-84 years old. This model has been used for CVD epidemiologic projections and effectiveness analysis of specific policy interventions.[1-4] Because air pollution was much severer in urban areas and no reliable $PM_{2.5}$ data was available for rural areas, we created an urban China version of the model with updated levels of traditional cardiovascular risk factors for projections. The model start year is 2010 and the model cycle length is one year. Simulations are at the sub-national population level. The standard model simulates a dynamic national population, adding waves of 35-year adults with each successive cycle.

The CVD Policy Model consists of three sub-models: the Demographic-Epidemiological model, the Bridge model and the Disease History model. The Demographic-Epidemiological model predicts CHD and stroke incidence and non-CVD mortality among subjects without CVD, stratified by age, sex, systolic blood pressure (SBP, <140, 140-159.9, ≥160 mmHg), body mass index (BMI, <25, 25-29.9, ≥30 kg/m^2), low density lipoprotein (LDL) cholesterol (<100, 100-129.9, ≥130 mg/dL) and high density lipoprotein (HDL) cholesterol levels (<40, 40-59.9, ≥60 mg/dL), and status of smoking (active smoker, non-smoker with exposure to environmental tobacco smoke, non-smoker without environmental exposure), diabetes (yes or no) and $PM_{2.5}$ exposures (yes or no) in urban Chinese population in ten-year age categories among those aged 35-84 years. Means and proportions of CVD risk factors were estimated from the China Cardiovascular Health Study and the China Multicenter Collaborative Study of Cardiovascular

Epidemiology (ChinaMUCA) for urban adults in 10-year age categories aged 35 to 84 years.[5, 6] An annual population-weighted average $PM_{2.5}$ level during the period of 2014-2015 was extracted in 190 cities with over 950 monitoring sites and was assumed as national $PM_{2.5}$ level in 2017.[7] All individuals were assigned the mean $PM_{2.5}$ exposure for urban China. Multivariable adjusted hazard ratios of SBP, LDL, HDL, BMI, smoking and diabetes for CHD, stroke, and non-CVD (non-CHD, non-stroke) death by age and sex were estimated from the China Multi-provincial Cohort Study (CMCS)[8] using a competing risk Cox proportional hazard model for each outcome.

For individuals in whom CVD develops, the Bridge Sub-model characterizes the initial CHD or stroke event (cardiac arrest, myocardial infarction, or angina) and its sequelae for 30 days. Then, the Disease History Sub-model predicts subsequent CVD events, coronary revascularization procedures, CVD mortality, and non-CVD mortality among patients with CVD, stratified by age, sex, and history of events. The general chronic CVD categories include CHD only, stroke only, and combined prior CHD and prior stroke. Each state and event has an annual probability of a recurrent event and/or transition to a different CVD state. The model assumes survivors persist in a chronic disease state without remission.

Stroke incidence[9, 10], mortality[11] and case-fatality[9] were obtained from other studies. The main outcomes predicted were CHD events (nonfatal and nonfatal first-ever and repeat episodes of stable and unstable angina, myocardial infarction, or cardiac arrest) and stroke events (nonfatal and fatal ischemic and hemorrhagic strokes). The CVD Policy Model-China defined CHD as myocardial infarction (ICD-9 410, 412 or ICD-10 I21, I22), angina and other CHD (ICD-9 411, 413 and 414, or ICD-10 I20, I23-I25), and a fixed proportion of “ill-defined” CVD coded events and deaths (ICD-9 codes 427.1, 427.4, 427.5, 428, 429.0, 429.1, 429.2, 429.9, 440.9 or ICD-10 I47.2, I49.0, I46, I50, I51.4, I51,5, I51.9, and I70.9).[12]

Stroke was defined by ICD-9 codes 430-438 (excluding transient ischemic attack) or ICD-10 I60-I69. Finally, starting with CHD and stroke case fatality obtained from the Beijing Sino-MONICA study.[9] The CVD Policy Model-China mortality projections were calibrated to fit with age-specific and overall CHD and stroke mortality numbers for the years 2010-2011 estimated by the China Center for Disease Control (CDC).[13]

Urban China population estimates

Estimates for the urban China population aged 35-84 years old by age and sex were based on the 6th China census conducted in 2010.[14] The impact of aging and growth on population were estimated based on by *World Population Prospects* by United Nation Population Division. Population projections by age and sex started in 2010 were based on historical estimates of population by age and sex using probabilistic projections up to 2100 of total fertility and life expectancy at birth by sex.[15]

Urban-rural ratio was estimated by *World Urbanization Prospects* by United Nation Population Division[16] using an established and robust extrapolation method. Last two empirical data points from two censuses were used to calculate the urban-rural ratio. The average annual rate of change in the urban-rural ratio between the last two data points was calculated and then extrapolated, assuming that the proportion urban follows a logistic path. Then empirical urban-rural growth differences from 148 countries with 2 million or more inhabitants were combined in a regression equation. The fitted regression line was used to calculate a hypothetical urban-rural growth difference for each level of an initial observed percentage urban. Starting from the most recent urban-rural growth difference of a particular country, the hypothetical urban-rural growth difference of all countries over a period of 25 years was converged. In China, urban was defined as cities and towns, excluding villages according to China census protocol.[14] The urban-rural ratio of China was 49.2% in 2010 and projected to increase from 55.6% in 2015 to 68.7% in 2030. Then urban population for year 2017-2030 was estimated by multiplying the projected total China population by urban-rural ratio (**Supplemental Table S1**).

Effects of traditional non-communicable disease (NCD) risk factors

For the standard CVD Policy Model-China, annual probability of first CVD events and non-CVD deaths conditioned on demographic and risk factors were estimated by analyzing the CMCS. The CMCS was a cohort study of 30,121 male and female participants aged 35-64 years and with no CVD at baseline in 1992-1993. Details could be found elsewhere.[8] These participants were recruited from 16 centers in 11 Chinese provinces using a multistage sampling method. Majority of participants (80.3%) were in urban areas and the remainder were in rural areas. Overall baseline participation rate was 82%. Baseline measurement of risk factors followed a standard protocol (WHO-MONICA protocol) and blood samples were processed at a central laboratory. Case-finding of new CHD and stroke events and non-cardiovascular deaths was first done by face-to-face interview. Events were ascertained by 1) detailed interview of participants or family members, 2) review of hospital records. These events were later adjudicated by investigators at the Beijing Institute for Heart, Lung, and Blood Vessel Diseases. After 1996, six centers ceased follow up because of completion of that national research project, but the remaining 10 centers (16,552 participants) were followed up through the end of 2002. Follow up rate was 86% for the centers followed all of 1992-2002, and 65% of the original cohort of 16 centers. Multivariable Cox proportional hazard ratios for SBP, diabetes, LDL, HDL, BMI, and active smoking were estimated from baseline measurements and ischemic and hemorrhagic events occurring over 159,400 person-years of observation in CMCS participants aged 35-74 years (**Supplemental Table S2**).[8] Significant ($P< 0.05$) age*risk factor coefficient interactions (higher risk at higher ages) were found for smoking in CMCS multivariable CHD models, SBP, and smoking in total stroke models, and smoking and diabetes in non-cardiovascular mortality models, so these were incorporated in age-specific risk coefficients.

Traditional NCD risk trend estimations (2017-2030)

Future traditional NCD risk factors trends for population aged 35-84 years were projected forward from 2017 to 2030 based on recent temporal trends from 1990 to 2009. Temporal trend estimations were based on repeated China Health and Nutrition Surveys (CHNS) from 1991 to 2009. The CHNS is repeated household survey which initiated in 1989 using a multistage, random cluster process to draw a sample of over 30,000 individuals in 15 provinces and municipal cities across China. Follow-ups were conducted continuously every two to four years to obtain repeated measures on health and nutrition, including traditional NCD risk factors. Data are available at http://www.cpc.unc.edu/projects/china.

After the participants have seated for at least 5 minutes, blood pressure (BP) was measured on the right arm by trained research staff. BP was measured three times at each survey visit using a standard mercury sphygmomanometer. Then SBP was calculated as the mean of the second two measurements. Weight and height was measured at each survey year for BMI calculation. Weight was measured to the nearest 0.01 kg with a balance-beam scale, and height to the nearest 0.10 cm using a stadiometer. BMI was calculated as weight in kilograms divided by the square of height in meters. Active smoking was defined as self-report of current smoking cigarettes.

Temporal SBP, BMI and active smoking trends were estimated using age-adjusted mixed linear random effects model with 10-year age groups. Due to limited participants aged over 75 years in CHNS, we combined the last two age groups together for trend estimates. Age-time interactions observed in trends for SBP, BMI, or active smoking were incorporated into age-specific risk factor trend projections. Both SBP and BMI were projected to increase over time except for SBP in the oldest age group. While linear declining trends of active smoking prevalence were observed for both male and female. Since the active smoking prevalence among female is relatively low. It was decided a priori that we assumed zero active smoking prevalence among female if the estimated coming active smoking prevalence would be lower than zero.

HDL and LDL trend analysis was not estimated from CHNS because serum lipid data were only available for year 2009. We assumed HDL and LDL changes would be mediated by the BMI trend.[1, 17] An increase of 1 kg/m^2 in BMI was associated with 2.75 mg/dL increase in LDL and 1.55 mg/dL decrease in HDL among male and 2.24 mg/dL increase in LDL and 0.77 mg/dL decrease in HDL among female, respectively. In this model analyses, diabetes was defined as a having a past diagnosis of diabetes, taking anti-diabetes medications, or a fasting glucose ≥126 mg/dL. Since blood sample was collected ever since 2009 in CHNS, diabetes prevalence recorded in the CHNS before 2009 might be underestimated without fasting glucose data. In order to address this issue, we assumed diabetes awareness (the proportion of self-reported diabetes among participants defined as diabetes) gradually increased over time. The number of diabetes before 2009 was estimated using the following formula: the number of diabetes = self-reported diabetes/diabetes awareness. Self-reported diabetes information was obtained from the CHNS, while diabetes awareness data were from the China Cardiovascular Health Study and the ChinaMUCA study, which defined diabetes in the same way as the CVD Policy Model. Then the prevalence of diabetes could be obtained as the proportion of the estimated number of diabetes over the total number of subjects in CHNS. Based on the calculated diabetes prevalence, we projected diabetes trend accordingly. The age-adjusted prevalence of diabetes from the China Cardiovascular Health study was 5.98% in 2000 and 8.33% from the China Cardiovascular Health Study and the ChinaMUCA in 2008. The awareness rate of diabetes grew from 36.1% to 59.8%. We assumed similar awareness change in the CHNS and then estimated diabetes prevalence using linear regression. The diabetes prevalence was projected to increase yearly by 0.187% in male and 0.125% in female (**Supplemental Table S3**).

Effects of long term $PM_{2.5}$ exposure

Reduction in $PM_{2.5}$ air pollution levels was associated with decreased cardiovascular event rates.[18] However, no previous studies were conducted in China to explore the relationship between long term $PM_{2.5}$ exposure and health outcomes. Therefore, relative risks of CHD, stroke and all-cause mortality associated with long term $PM_{2.5}$ exposure were obtained from a meta-analysis of cohort studies.[18, 19] Published studies addressing long term $PM_{2.5}$ exposure with CHD, stroke and all-cause mortality as outcomes were identified (**Supplemental Table S4**).[20-36] If multiple data derived from the same study, the study with the most incident cases was included. Relative risks (RRs) or hazard ratios (HRs) and their 95% confidence intervals (CIs) were extracted and uniformly standardized as 10 $\mu g/m^3$ increment of $PM_{2.5}$. The overall RRs and 95% CIs were pooled using a random-effects model via the DerSimonian-Laird method. The RRs (95% CIs) for a 10 $\mu g/m^3$ increase in long term $PM_{2.5}$ exposure were 1.06 (1.03-1.08) for all-cause mortality, 1.19 (1.10-1.30) for CHD mortality and 1.07 (1.01-1.13) for stroke mortality (**Supplemental Figure S1-S3**). These estimates were further incorporated into the model. Though an integrated-exposure function[37] developed for Global Burden Disease Study showed a non-linear $PM_{2.5}$-CVD relationship by age, due to limitation of model's characteristics, we assumed a uniform relative risk effect of $PM_{2.5}$ on all urban adults across age. It was likely to over-estimate the effect sizes among those at the highest levels of air pollution exposure using the linear function.

Epidemiologic input parameters and calibration

Prior to calibration (see below), CHD incidence in male and female aged 35-84 years with no prior CHD diagnosis was based on 10-year incidence rates from the China Hypertension Epidemiology Follow Up Study (CHEFS)[10] and calibrated to fit with CHD mortality and case-fatality assumptions. Incident stroke rates were also identified from the CHEFS.[10] Main CVD Policy Model-China 28-day case-fatality assumptions were estimated from pooled Beijing Sino-MONICA Study data from 1993-2004 (personal communication, Dong Zhao, MD, PhD, 2006) and the main age-specific CHD case-fatality rate assumptions were estimated from the overall rates. Self-reported history of a physician-diagnosed myocardial infarction and/or stroke was based on data from CHEFS. In CHEFS, each self-reported case of prevalent CVD was ascertained with chart review by study staff. Final epidemiologic parameter estimates are shown in **Supplemental Tables S5-6.**

In order to evaluate the accuracy of CVD Policy Model predictions over time, China stroke and CHD mortality estimates for ages 35-84 years were obtained from the China CDC.[13] In the calibration procedure, CHD and stroke parameters were calibrated separately. Starting with default incidence, case-fatality, and prevalence assumptions, the simulation model was run forward from year 2010 to 2016. Incidence and case-fatality inputs were iteratively calibrated primarily to match with age-specific mortality numbers in 2010 overall and within ten-year age groups (**Supplemental Tables S7-8**). After CHD and stroke mortality were satisfactorily calibrated, age and sex specific non-cardiovascular death rates were also calibrated so that the totals of cardiovascular and non-cardiovascular deaths fitted within the envelope of all-cause mortality based on China CDC data.[13]

Monte Carlo Simulations

Markov Monte Carlo analyses were performed to estimate a range of uncertainty surrounding the results of projected air quality improvement and traditional risk factor intervention scenarios. We assumed that the beta coefficient distributions of SBP, smoking and $PM_{2.5}$ on CHD deaths and stroke deaths were normally distributed. Standard deviations for the SBP and smoking beta coefficients came from the CMCS study and the standard deviation for the $PM_{2.5}$ beta coefficient came from a meta-analysis of air pollution studies (**Supplemental Table S2**). The beta coefficient distributions for SBP, smoking, and $PM_{2.5}$ were randomly and simultaneously sampled 1,000 times in the Monte Carlo simulations.

Sensitivity Analysis

In the main analysis, no $PM_{2.5}$ change in 2017-2030 was assumed as status quo case. However, the Global Burden of Disease – Major Air Pollution Sources (GBD MAPS) project has estimated that $PM_{2.5}$ in China would modestly reduce by 4 $\mu g/m^3$ from 2013 to 2030 under the business as usual scenario (current legislation and implementation status as of end of 2012 and twelfth five-year plan for environmental protection).[38] Thus a sensitivity analysis was conducted assuming a graded reduction trend over 2017-2030 as the base case. The starting level of $PM_{2.5}$ remained 61 $\mu g/m^3$ in 2017, and it will slowly reduce to 57.9 $\mu g/m^3$ in 2030, with an average annual decrease of 0.24 $\mu g/m^3$ estimated from GBD MAPS project.

A linear $PM_{2.5}$-CVD morality relationship assumption might overestimate the health benefits, thus additional sensitivity analysis was conducted to quantify the impact of attenuated relative risk on health benefits. A 10% and 20% diminished beta-coefficient for the association between $PM_{2.5}$ and CHD and stroke death was recalculated. In recalculation for 10% diminished beta-coefficient, the point estimate of $PM_{2.5}$ for CHD deaths changed from 0.0174 to 0.0157 and stroke deaths changed from 0.0068 to 0.0061, and were further incorporated into the model. We re-run the CVD Policy Model-China (**Supplemental Table S10 and S11**).

Supplemental Table S1. Estimated China urban population aged 35-84 years old during 2017-2030 according to *World Population Prospects* by Population Division, United Nation.

Year	Male	Female	Total
2017	214,357,359	206,957,964	421,315,323
2018	221,214,027	213,805,560	435,019,587
2019	228,483,453	221,030,198	449,513,652
2020	236,269,514	228,703,794	464,973,308
2021	244,183,114	236,467,837	480,650,951
2022	252,549,397	244,626,274	497,175,671
2023	261,167,065	252,978,094	514,145,160
2024	269,637,173	261,153,768	530,790,940
2025	277,640,682	268,853,018	546,493,700
2026	284,503,701	275,452,872	559,956,573
2027	290,753,757	281,438,995	572,192,751
2028	296,427,057	286,839,505	583,266,562
2029	301,588,483	291,731,420	593,319,904
2030	306,302,815	296,167,648	602,470,463

Supplemental Table S2. Beta coefficients for CHD and stroke estimated from China Multi-provincial Cohort Study (CMCS) and standard deviations for SBP, smoking and $PM_{2.5}$ for Monte Carlo simulation.

	SBP (1 mmHg)				Smoking (yes/no)				$PM_{2.5}$(1 μg/m^3)			
	CHD death		Stroke death		CHD death		Stroke death		CHD death		Stroke death	
	Main point estimate	Standard deviations	Main point estimate	Standard deviations	Main point estimate	Standard deviations	Main point estimate	Standard deviations	Main point estimate	Standard deviations	Main point estimate	Standard deviations
Males, years												
35-44	.0338	.0036	.0472	.0048	.5640	.1526	.2550	.1064	.0174	.0041	.0068	.0017
45-54	.0302	.0017	.0422	.0035	.6940	.1526	.2550	.1064	.0174	.0041	.0068	.0017
55-64	.0271	.0013	.0368	.0022	.8240	.1526	.2550	.1064	.0174	.0041	.0068	.0017
65-74	.0221	.0016	.0283	.0041	.9540	.1526	.2550	.1064	.0174	.0041	.0068	.0017
75-84	.0161	.0018	.0162	.0022	1.0840	.1526	.2550	.1064	.0174	.0041	.0068	.0017
Females, years												
35-44	.0319	.0036	.0433	.0048	.5890	.1526	.4450	.2707	.0174	.0041	.0068	.0017
45-54	.0303	.0015	.0420	.0032	.8400	.1526	.4450	.2707	.0174	.0041	.0068	.0017
55-64	.0265	.0013	.0358	.0022	.9200	.1526	.4450	.2707	.0174	.0041	.0068	.0017
65-74	.0216	.0015	.0267	.0021	1.1000	.1526	.4450	.2707	.0174	.0041	.0068	.0017
75-84	.0159	.0017	.0159	.0021	1.1700	.1526	.4450	.2707	.0174	.0041	.0068	.0017

Supplemental Table S3. Annual future changes of traditional NCD risk factors were estimated based on China Health and Nutrition Survey.

	SBP (mmHg)	BMI (kg/m^2)	Smoking (%)	HDL (mg/dL)	LDL (mg/dL)	Diabetes (%)
Male, years						+0.187
35-44	+0.394	+0.121	-1.54	-0.188	+0.333	
45-54	+0.381	+0.117	-0.63	-0.181	+0.322	
55-64	+0.121	+0.092	-0.20	-0.143	+0.530	
65-84	-0.026	+0.088	-0.09	-0.136	+0.242	
Female, years						+0.125
35-44	+0.224	+0.054	-0.12	-0.042	+0.121	
45-54	+0.263	+0.087	-0.19	-0.067	+0.195	
55-64	+0.235	+0.095	-0.32	-0.073	+0.213	
65-84	-0.096	+0.111	-0.12	-0.085	+0.249	

Supplemental Table S4. Prospective studies exploring risk of long term $PM_{2.5}$ exposure and CHD, stroke and all-cause mortality.

Study	Population	Time period	Average $PM_{2.5}$ exposure level ($\mu g/m^3$)	RRs and 95% CIs with 10 $\mu g/m^3$ increment of $PM_{2.5}$		
				All-cause mortality	CHD mortality	Stroke mortality
Harvard six cities[20], 2012	Six cities in US	1974-2009	16	1.14 (1.07-1.22)		
ACS, extended I[21], 2004	Adults in metropolitan areas in US	1982-1998	17			1.02 (0.95-1.10)
ACS, extended II[22], 2009	Adults in metropolitan areas in US	1982-2000	14	1.06 (1.04-1.08)	1.24 (1.20-1.29)	
AHSMOG[23], 2000	Nonsmoking, non-Hispanic whites	1977-1992	NA	1.09 (0.97-1.21)		
VA study I[24], 2006	Hypertensive male veterans in US	1989-1996	19	1.15 (1.05-1.26)		
VA study II[25], 2006	Hypertensive male veterans in US	1997-2001	12	1.06 (0.94-1.22)		
CA CPS[26], 2005	11 counties in California, US	1973-1982	23	1.04 (1.01-1.07)		
CA CPS[26], 2005	11 counties in California, US	1983-2002	23	1.00 (0.98-1.02)		
WHI[27], 2007	Postmenopausal women in 36 US metropolitan areas	1994-2002	14		2.21 (1.17-4.16)	1.83 (1.11-3.00)
HPFS[28], 2011	Health professionals in US	1989-2003	18	0.86 (0.72-1.02)	0.98 (0.70-1.35)	
NHS[29], 2009	Registered nurses in US	1992-2002	14	1.26 (1.02-1.54)	2.02 (1.07-3.78)	
NLCS[30], 2008	Adults in 204 municipalities through Netherlands	1987-1996	28	1.06 (0.97-1.16)		
California Teachers Study[31], 2011	Female public school teachers in California, US	1997-2005	16			1.16 (0.92-1.46)
California Teachers Study[32], 2015	Female public school teachers in California, US	2001-2007	18	1.01 (0.97-1.05)	1.19 (1.08-1.31)	
US trucking industry cohort[33], 2011	Male employed in US trucking industry	1985-2000	14	1.10 (1.03-1.18)		
Canadian national cohort[34], 2012	Nonimmigrant Canadian adults	1991-2001	9	1.10 (1.05-1.15)	1.30 (1.18-1.43)	1.04 (0.93-1.16)
Rome Longitudinal Study[35], 2013	Italian population-based cohort	2001-2010	23	1.04 (1.03-1.05)	1.10 (1.06-1.13)	1.08 (1.04-1.13)
*ESCAPE study[36], 2014	22 cohorts across in Europe	1985-2007	7~31		0.98 (0.74-1.30)	1.21 (0.87-1.69)

US, the United States; ACS, American Cancer Society; AHSMOG, Adventist Health Study of Smog; VA, Veterans cohort; CA CPS, California Cancer Prevention Study; WHI, Women's Health Initiative; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; NLCS, Netherlands Cohort Study on Diet and Cancer; ESCAPE, European Study of Cohorts for Air Pollution Effects.

*ESCAPE study includes 22 European cohorts using a standardized protocol for analysis.

Supplemental Table S5. Coronary Heart Disease (CHD) Inputs used for the CVD Policy Model-China

	CHD incidence rate per 100,000	CHD 28 day case-fatality (proportion)	CHD mortality per 100,000	Prevalence of prior myocardial infarction (proportion)
Males, years				
35-44	130	0.12	10	0.006
45-54	135	0.21	36	0.012
55-64	220	0.29	97	0.034
65-74	500	0.33	243	0.047
75-84	2,010	0.48*	1,104	0.060*
Females, years				
35-44	19	0.18	1	0.004
45-54	49	0.23	20	0.013
55-64	141	0.27	43	0.031
65-74	310	0.43	160	0.040
75-84	1,900	0.51*	1,028	0.060*

*Estimate not available from original source data and imputed using linear interpolation.

Supplemental Table S6. Stroke Inputs used for the CVD Policy Model-China

	Total stroke incidence rate per 100,000	Total stroke 28 day case-fatality (proportion)	Total stroke mortality per 100,000	Prevalence of prior stroke (proportion)
Males, years				
35-44	24	0.25	20	0.013
45-54	145	0.18	62	0.032
55-64	670	0.12	151	0.088
65-74	1,250	0.20	502	0.142
75-84	2,510	0.45*	1,708	0.150*
Females, years				
35-44	23	0.18	10	0.009
45-54	180	0.14	30	0.024
55-64	800	0.15	131	0.060
65-74	1,500	0.20	375	0.100
75-84	2,500	0.45*	1,359	0.120*

*Estimate not available from original source data and imputed using linear interpolation.

Supplemental Table S7. Pre-calibration and post-calibration CHD incidence and 28 day case-fatality inputs

	CHD incidence rate per 100,000		CHD 28 day case-fatality (proportion)	
	Pre-calibration (based on CHEFS, 1991-2000, ICD9 430-438)	Post-calibration (identical CVDPM definition)	Pre-calibration (based on Sino-Monica Beijing)	Post-calibration (identical CVDPM definition)
Males, years				
35-44	54	130	0.12	0.05
45-54	112	135	0.21	0.15
55-64	342	220	0.29	0.18
65-74	540	500	0.33	0.25
75-84	889	2,010	0.48*	0.50
Females, years				
35-44	23	19	0.18	0.14
45-54	96	49	0.23	0.20
55-64	188	141	0.27	0.20
65-74	368	310	0.43	0.46
75-84	752	1,900	0.51*	0.47

*Estimate not available from original source data and imputed using linear interpolation.

Supplemental Table S8. Pre-calibration and post-calibration stroke incidence and 28 day case-fatality inputs

	Stroke incidence rate per 100,000		Stroke 28 day case-fatality (proportion)	
	Pre-calibration (based on CHEFS, 1991-2000, ICD9 410-414)	Post-calibration (identical CVDPM definition)	Pre-calibration (based on Sino-Monica Beijing)	Post-calibration (identical CVDPM definition)
Males, years				
35-44	91	24	0.25	0.19
45-54	240	145	0.18	0.17
55-64	711	670	0.12	0.12
65-74	1,292	1,250	0.20	0.25
75-84	1,904	2,510	0.45*	0.48
Females, years				
35-44	59	23	0.18	0.11
45-54	176	180	0.14	0.11
55-64	424	800	0.15	0.12
65-74	848	1,500	0.20	0.22
75-84	1,500	2,500	0.45*	0.38

*Estimate not available from original source data and imputed using linear interpolation.

Supplemental Table S9. Sensitivity analysis for projected CHD and stroke deaths averted with hypothetical air pollution controls in urban Chinese population aged 35-84 years over 2017-2030 with business as usual scenario as status quo case

	CHD Deaths (thousands)	Averted CHD Deaths (thousands)	Stroke Deaths (thousands)	Averted Stroke Deaths (thousands)	Life years gained (thousands)
Alternative Status quo case†	7,604 (7,450-7,863)	-	10,902 (10,355-11,528)	-	
$PM_{2.5}$ improvement scenarios*					
Target 1: Beijing Olympic Games	7,462 (7,172-7,726)	143 (120-299)	10,824 (10,233-11,451)	78 (58-169)	1,115 (1,281-1,950)
Target 2: China Class II standard limit	6,216 (5,537-6,931)	1,388 (886-1,982)	10,080 (9,385-10,839)	823 (449-1,246)	11,620 (9,738-14,355)
Target 3: WHO recommended level	5,031 (4,122-6,089)	2,574 (1,701-3,403)	9,240 (8,330-10,314)	1,663 (914-2,399)	23,313 (19,526-27,682)
Comparison scenarios*					
25% reduction in uncontrolled systolic hypertension (to <140 mmHg)	6,915 (6,823-7,107)	689 (555-859)	9,657 (9,227-10,112)	1,245 (869-1,674)	9,911 (8,750-11,327)
30% reduction in tobacco use	7,210 (6,984-7,519)	394 (258-542)	10,788 (10,146-11,505)	115 (5-225)	3,034 (2,429-3,708)
25% reduction in uncontrolled systolic hypertension (to <140 mmHg) plus 30% reduction in tobacco use	6,560 (6,369-6,813)	1,044 (866-1,255)	9,559 (9,029-10,110)	1,343 (948-1,781)	12,774 (11,435-14,275)

† Alternative status quo case scenario ($PM_{2.5}$ remained 61 $\mu g/m^3$ in 2017, and it will slowly reduce to 57.9 $\mu g/m^3$ in 2030)
*Each scenario is compared with the status quo case. Ninety-five percent uncertainty intervals were calculated from the results of 1,000 probabilistic simulations.

Supplemental Table S10. Sensitivity analysis for projected CHD and stroke deaths averted with hypothetical air pollution controls in urban Chinese population aged 35-84 years over 2017-2030 with 10% attenuated $PM_{2.5}$-CVD health effects

	CHD Deaths (thousands)	Averted CHD Deaths (thousands)	Stroke Deaths (thousands)	Averted Stroke Deaths (thousands)	Life years gained (thousands)
Status quo case (remain current $PM_{2.5}$ level)	7,910 (7,741-8,094)	-	11,069 (10,219-11,611)	-	
$PM_{2.5}$ improvement scenarios*					
Target 1: Beijing Olympic Games	7,514 (7,291-7,693)	397 (206-616)	10,857 (10,049-11,406)	212 (92-323)	3,177 (2,629-3,822)
Target 2: China Class II standard limit	6,370 (5,672-7,016)	1,540 (845-2,258)	10,187 (9,408-10,814)	882 (392-1,317)	13,114 (11,018-15,467)
Target 3: WHO recommended level	5,253 (4,241-6,332)	2,657 (1,546-3,664)	9,422 (8,658-10,467)	1,647 (758-2,397)	24,280 (20,744-27,809)
Comparison scenarios*					
25% reduction in uncontrolled systolic hypertension (to <140 mmHg)	7,186 (7,117-7,235)	724 (591-905)	9,801 (9,159-10,129)	1,268 (808-1,642)	10,068 (8,929-11,237)
30% reduction in tobacco use	7,498 (7,257-7,704)	412 (306-562)	10,953 (9,955-11,563)	116 (30-273)	3,095 (2,623-3,831)
25% reduction in uncontrolled systolic hypertension (to <140 mmHg) plus 30% reduction in tobacco use	6,815 (6,629-6,899)	1,095 (953-1,265)	9,701 (8,924-10,102)	1,368 (958-1,726)	12,988 (12,036-14,320)

*Each scenario is compared with the status quo case. Ninety-five percent uncertainty intervals were calculated from the results of 1,000 probabilistic simulations.

Supplemental Table S11. Sensitivity analysis for projected CHD and stroke deaths averted with hypothetical air pollution controls in urban Chinese population aged 35-84 years over 2017-2030 with 20% attenuated $PM_{2.5}$-CVD health effects

	CHD Deaths (thousands)	Averted CHD Deaths (thousands)	Stroke Deaths (thousands)	Averted Stroke Deaths (thousands)	Life years gained (thousands)
Status quo case (remain current $PM_{2.5}$ level)	7,922 (7,780-8,066)	-	11,077 (10,547-11,305)	-	
$PM_{2.5}$ improvement scenarios*					
Target 1: Beijing Olympic Games	7,570 (7,265-7,933)	352 (100-551)	10,890 (10,348-11,132)	187 (95-326)	2,967 (2,128-3,803)
Target 2: China Class II standard limit	6,539 (5,718-7,608)	1,383 (422-2,050)	10,295 (9,530-10,727)	782 (409-1,326)	12,303 (8,970-15,437)
Target 3: WHO recommended level	5,504 (4,409-7,227)	2,418 (800-3,377)	9,608 (8,493-10,305)	1,470 (789-2,411)	22,892 (17,011-28,081)
Comparison scenarios*					
25% reduction in uncontrolled systolic hypertension (to <140 mmHg)	7,198 (7,119-7,307)	724 (595-850)	9,809 (9,291-10,135)	1,269 (877-1,490)	10,069 (8,907-10,925)
30% reduction in tobacco use	7,509 (7,323-7,719)	413 (266-508)	10,961 (10,339-11,277)	116 (34-239)	3,097 (2,584-3,666)
25% reduction in uncontrolled systolic hypertension (to <140 mmHg) plus 30% reduction in tobacco use	6,826 (6,683-6,996)	1,096 (926-1,244)	9,709 (9,088-10,106)	1,368 (998-1,618)	12,991 (11,636-13,907)

*Each scenario is compared with the status quo case. Ninety-five percent uncertainty intervals were calculated from the results of 1,000 probabilistic simulations.

Figure Legends

Supplemental Figure S1. Relative risks for each 10 μg/m^3 increment in long term $PM_{2.5}$ exposure and risk of all-cause mortality.

The horizontal lines represent 95% confidence interval and grey squares represent the weights of each study in random effect models.

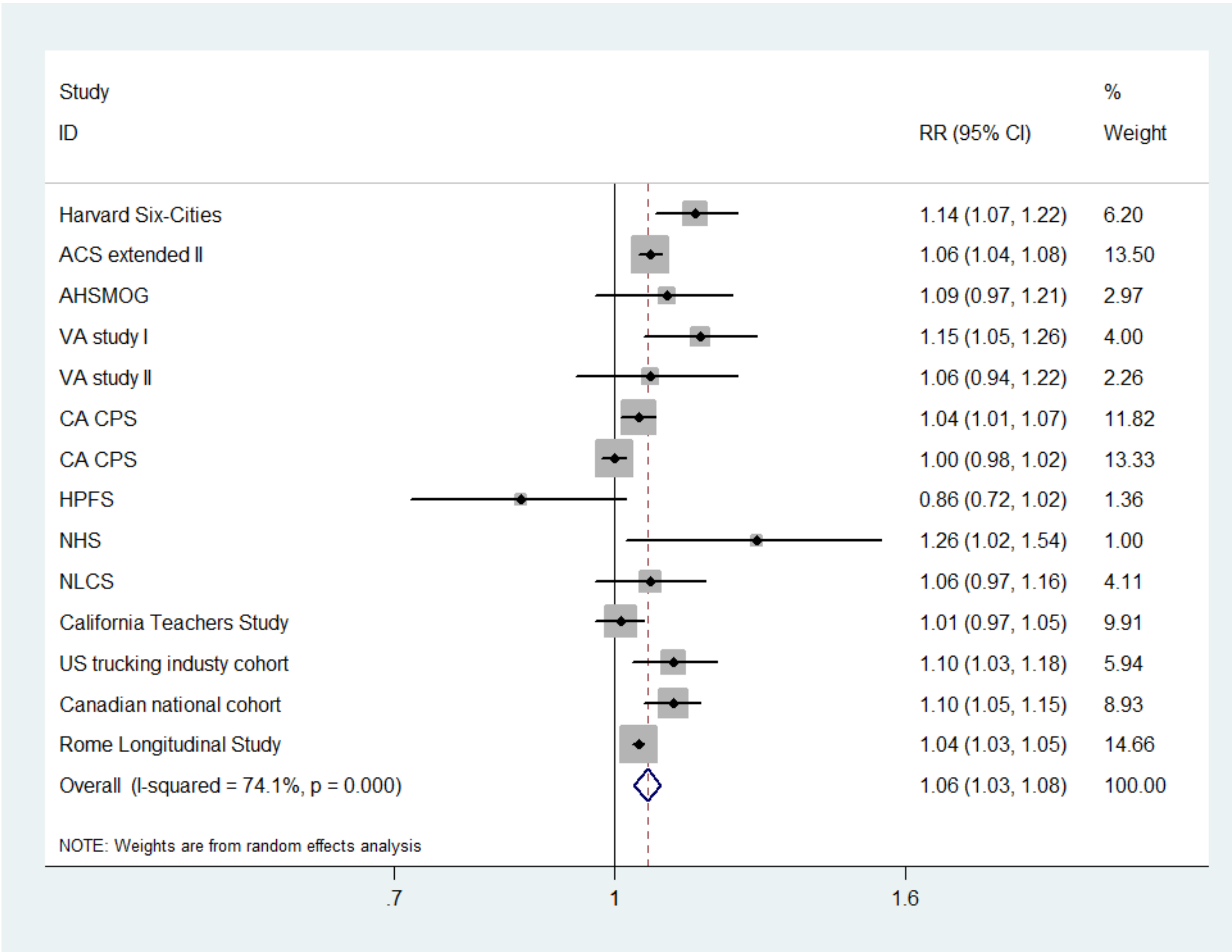
Supplemental Figure S2. Relative risks for each 10 μg/m^3 increment in long term $PM_{2.5}$ exposure and risk of coronary heart disease mortality.

The horizontal lines represent 95% confidence interval and grey squares represent the weights of each study in random effect models.

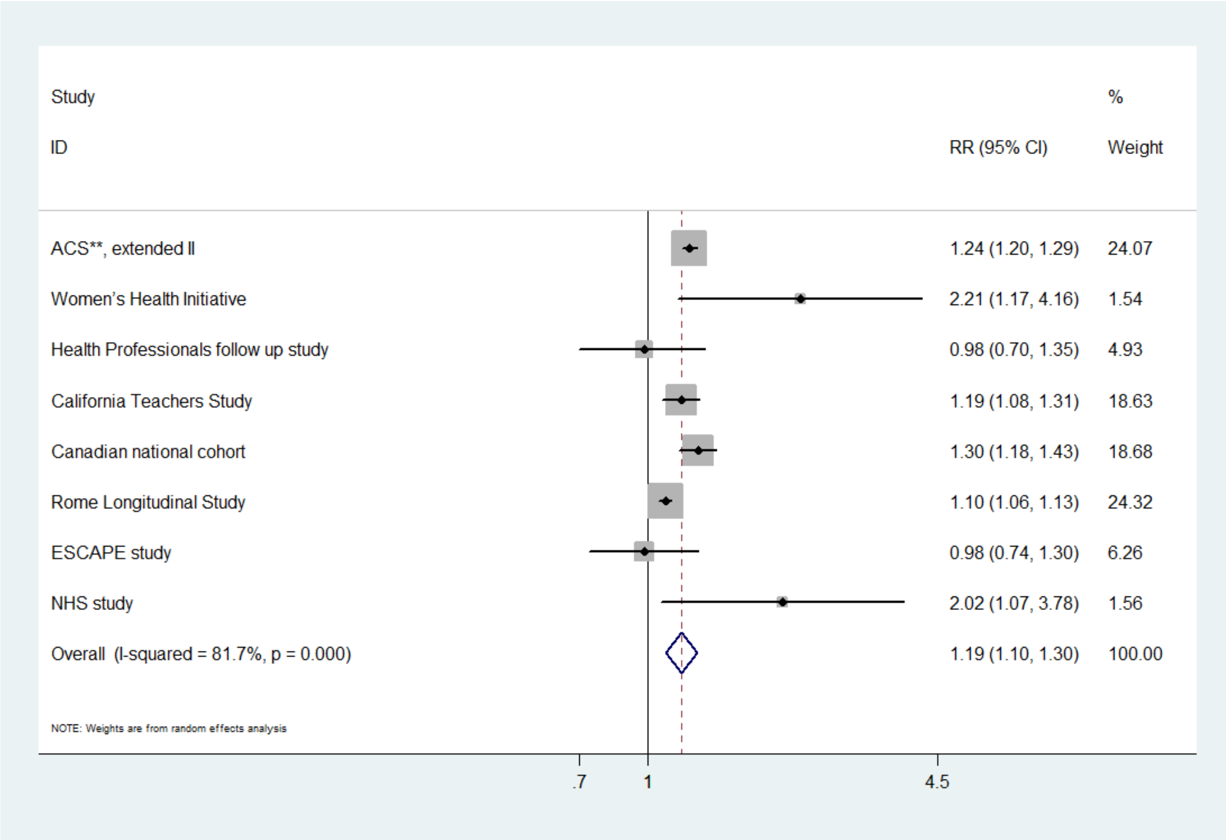
Supplemental Figure S3. Relative risks for each 10 μg/m^3 increment in long term $PM_{2.5}$ exposure and risk of stroke mortality.

The horizontal lines represent 95% confidence interval and grey squares represent the weights of each study in random effect models.

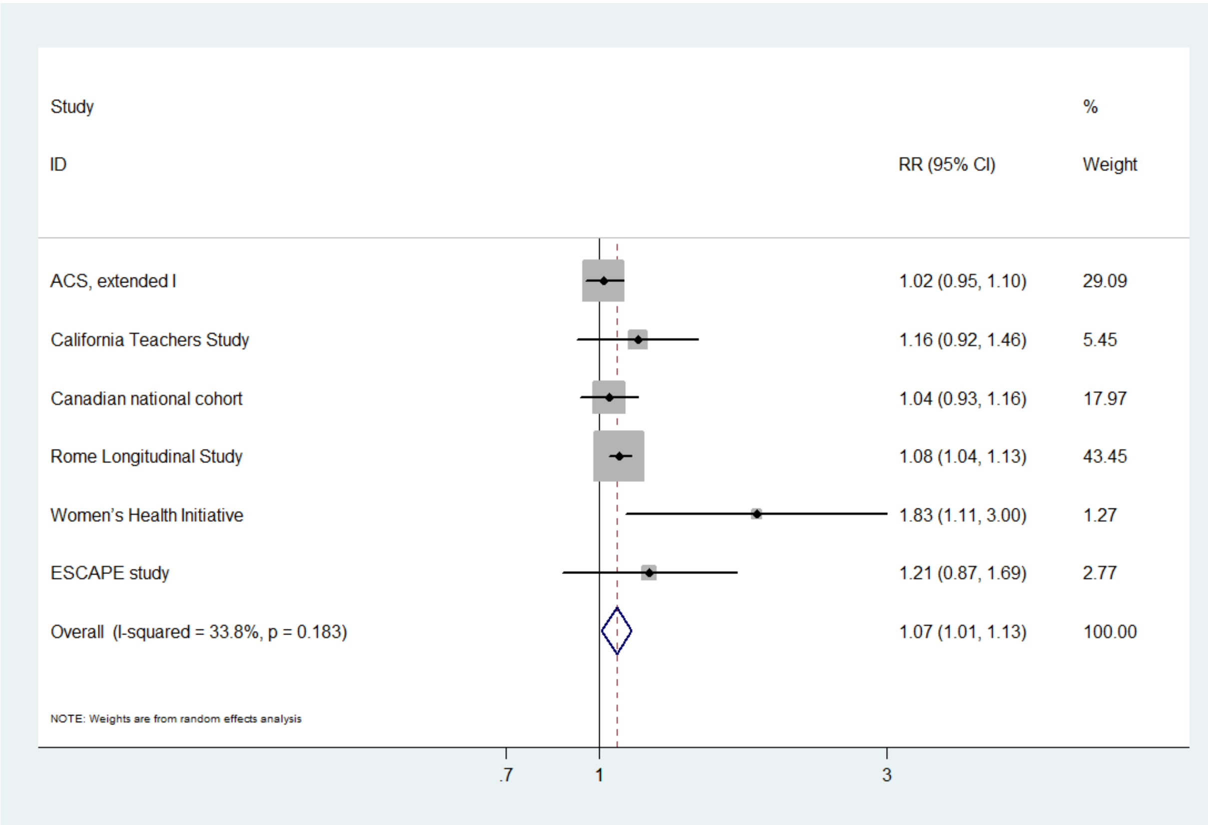
Supplemental Figure S1. Relative risks for each 10 μg/m^3 increment in long term $PM_{2.5}$ exposure and risk of all-cause mortality



Supplemental Figure S2. Relative risks for each 10 μg/m^3 increment in long term $PM_{2.5}$ exposure and risk of coronary heart disease mortality



Supplemental Figure S3. Relative risks for each 10 μg/m^3 increment in long term $PM_{2.5}$ exposure and risk of stroke mortality



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