## **SUPPLEMENTAL MATERIAL**

## **(1) Supplemental Methods**

General overview of the Cardiovascular Disease Policy Model-China

Urban China Population estimates

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

Traditional NCD risk trend estimations (2017-2030)

Effects of long term  $PM_{2.5}$  exposure

Epidemiologic input parameters and calibration

Monte Carlo Simulations

Sensitivity Analysis

## **(2) Supplemental Tables**

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.

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

Carlo simulation.

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

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

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

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

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

Supplemental Table S8. Pre-calibration and post-calibration stroke incidence and 28 day casefatality 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  $PM<sub>2.5</sub>$  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<sup>3</sup> increment in long term PM<sub>2.5</sub> exposure and risk of all-cause mortality.

Supplemental Figure S2. Relative risks for each 10  $\mu$ g/m<sup>3</sup> increment in long term PM<sub>2.5</sub> exposure and risk of coronary heart disease mortality.

Supplemental Figure S3. Relative risks for each 10  $\mu$ g/m<sup>3</sup> increment in long term PM<sub>2.5</sub> 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 7 and effectiveness analysis of specific policy interventions.<sup>[1-4](#page-25-0)</sup> Because air pollution was much 8 severer in urban areas and no reliable  $PM<sub>2.5</sub>$  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, 16 stratified by age, sex, systolic blood pressure (SBP, <140, 140-159.9,  $\geq$ 160 mmHg), body mass 17 index (BMI, <25, 25-29.9,  $\geq$ 30 kg/m<sup>2</sup>), 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 20 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 22 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



 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.

17 Stroke incidence<sup>[9,](#page-25-5) [10](#page-25-6)</sup>, mortality<sup>[11](#page-25-7)</sup> and case-fatalit[y](#page-25-5)<sup>9</sup> 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 2 I47.2, I49.0, I46, I50, I51.4, I51,5, I51.9, and I70.9).<sup>[12](#page-26-0)</sup>

 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-5 MONICA study[.](#page-25-5)<sup>9</sup> 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 7 by the China Center for Disease Control (CDC).<sup>[13](#page-26-1)</sup>

**Urban China population estimates**

 Estimates for the urban China population aged 35-84 years old by age and sex were based on the  $6<sup>th</sup> China census conducted in 2010.<sup>14</sup> The impact of aging and growth on population were$  $6<sup>th</sup> China census conducted in 2010.<sup>14</sup> The impact of aging and growth on population were$  $6<sup>th</sup> China census conducted in 2010.<sup>14</sup> The impact of aging and growth on population were$  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 14 expectancy at birth by sex.<sup>[15](#page-26-3)</sup>

 Urban-rural ratio was estimated by *World Urbanization Prospects* by United Nation Population Division<sup>16</sup> 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 3 as cities and towns, excluding villages according to China census protocol.<sup>[14](#page-26-2)</sup> 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 11 and with no CVD at baseline in 1992-1993. Details could be found elsewhere.<sup>[8](#page-25-4)</sup> 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**)[.](#page-25-4)<sup>8</sup> 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.](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 21 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.



 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 PM2.5 exposure**

10 Reduction in PM<sub>2.5</sub> air pollution levels was associated with decreased cardiovascular event 11 rates.<sup>[18](#page-26-6)</sup> However, no previous studies were conducted in China to explore the relationship 12 between long term  $PM<sub>2.5</sub>$  exposure and health outcomes. Therefore, relative risks of CHD, stroke 13 and all-cause mortality associated with long term  $PM_{2.5}$  exposure were obtained from a meta-14 analysis of cohort studies.<sup>[18,](#page-26-6) [19](#page-26-7)</sup> Published studies addressing long term  $PM_{2.5}$  exposure with CHD, 15 stroke and all-cause mortality as outcomes were identified (**Supplemental Table S4**). <sup>20-36</sup> 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 18 extracted and uniformly standardized as 10  $\mu$ g/m<sup>3</sup> increment of PM<sub>2.5</sub>. The overall RRs and 95% CIs were pooled using a random-effects model via the DerSimonian-Laird method. The RRs 20 (95% CIs) for a 10  $\mu$ g/m<sup>3</sup> increase in long term PM<sub>2.5</sub> 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. 23 Though an integrated-exposure function<sup>37</sup> developed for Global Burden Disease Study showed a

1 non-linear  $PM_{2.5}$ -CVD relationship by age, due to limitation of model's characteristics, we 2 assumed a uniform relative risk effect of  $PM<sub>2.5</sub>$  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 8 Epidemiology Follow Up Study (CHEFS)<sup>[10](#page-25-6)</sup> and calibrated to fit with CHD mortality and case-9 fatality assumptions. Incident stroke rates were also identified from the CHEFS.<sup>[10](#page-25-6)</sup> 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 18 CHD mortality estimates for ages 35-84 years were obtained from the China CDC.<sup>[13](#page-26-1)</sup> 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 4 mortality based on China CDC data.<sup>[13](#page-26-1)</sup>

# 5 **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 8 assumed that the beta coefficient distributions of SBP, smoking and  $PM<sub>2.5</sub>$  on CHD deaths and stroke deaths were normally distributed. Standard deviations for the SBP and smoking beta 10 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 12 coefficient distributions for SBP, smoking, and  $PM<sub>2.5</sub>$  were randomly and simultaneously sampled 1,000 times in the Monte Carlo simulations.

## 14 **Sensitivity Analysis**

15 In the main analysis, no PM<sub>2.5</sub> change in 2017-2030 was assumed as status quo case. However, 16 the Global Burden of Disease – Major Air Pollution Sources (GBD MAPS) project has estimated 17 that PM<sub>2.5</sub> in China would modestly reduce by 4  $\mu$ g/m<sup>3</sup> from 2013 to 2030 under the business as 18 usual scenario (current legislation and implementation status as of end of 2012 and twelfth five-19 year plan for environmental protection).<sup>38</sup> Thus a sensitivity analysis was conducted assuming a 20 graded reduction trend over 2017-2030 as the base case. The starting level of  $PM_{2.5}$  remained 61 21  $\mu$ g/m<sup>3</sup> in 2017, and it will slowly reduce to 57.9  $\mu$ g/m<sup>3</sup> in 2030, with an average annual decrease 22 of 0.24  $\mu$ g/m<sup>3</sup> estimated from GBD MAPS project.



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**.



**Supplemental Table S2. Beta coefficients for CHD and stroke estimated from China Multi-provincial Cohort Study (CMCS) and standard deviations for SBP, smoking and PM2.5 for Monte Carlo simulation.** 



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



**Supplemental Table S4. Prospective studies exploring risk of long term PM2.5 exposure and CHD, stroke and all-cause mortality.**

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**

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



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

\*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**



\*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**



\*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**



† Alternative status quo case scenario (PM<sub>2.5</sub> remained 61 μg/m<sup>3</sup> in 2017, and it will slowly reduce to 57.9 μg/m<sup>3</sup> 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 PM2.5-CVD health effects**



\*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 PM2.5-CVD health effects**



\*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<sup>3</sup> increment in long term PM2.5 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<sup>3</sup> increment in long term PM2.5 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<sup>3</sup> increment in long term PM2.5 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<sup>3</sup> increment in long term PM2.5 exposure and risk of all-cause mortality**



**Supplemental Figure S2. Relative risks for each 10 μg/m<sup>3</sup> increment in long term PM2.5 exposure and risk of coronary heart disease mortality**



**Supplemental Figure S3. Relative risks for each 10 μg/m<sup>3</sup> increment in long term PM2.5 exposure and risk of stroke mortality**



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