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Spatial-Temporal Distribution of Disability-Adjusted Life-Years of Lung Cancer Attributable to Ambient $PM_{2.5}$ in Guangzhou, China, 2010 ~ 2013: A Population-Based Study

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ABSTRACT. The authors describe district-specific disability-adjusted life-year (DALY) of lung cancer attributable to ambient particulate matter < 2.5 μm in diameter ($PM_{2.5}$) for Guangzhou city in China, so as to help prioritizing environmental health action from geospatial perspective. Comparative risk assessment and satellite-derived $PM_{2.5}$ concentrations were used to investigate the spatial-temporal distribution of DALY attributable to ambient $PM_{2.5}$ for lung cancer. Integrated exposure-response model and kriging model were constructed based on estimated relative risk (RR) from risk assessment. Annual mean $PM_{2.5}$ increased by 25.9% from 2010 (71.1 μg/m^3) to 2013 (89.5 μg/m^3). Estimated RRs ranged from 1.37 (95% uncertainty interval [UI]: 1.04 ~ 1.86) to 1.99 (95% UI: 1.12 ~ 3.19) among the districts. For lung cancer, DALY attributable to $PM_{2.5}$ increased by 26.8% from 2010 to 2013, reaching 4,3352.7 DALYs (95% UI: 8,157.9 ~ 6,2371.7) in 2013. The paper showed that population residing in highly-polluted and aged districts might suffer a higher relative risk for developing lung cancer. Our validated analysis framework also showed that population suffered from a higher loss of lung cancer DALYs, partly due to the higher $PM_{2.5}$ exposure in some subareas within the city. We reveal that ambient $PM_{2.5}$ pollution contributed substantially to lung cancer burden, both locally and sub-locally. These results suggest the need for enhanced environmental health policies in the city.

Keywords: $PM_{2.5}$, spatial analysis, disability-adjusted life-years, comparative risk assessment, lung cancer

1. Introduction

Emission of ambient particulate matter with aerodynamic diameter < 2.5 μm ($PM_{2.5}$) is arousing persistent concern in China, since a great proportion of mainland cities have reported high levels of ambient $PM_{2.5}$ pollution for the past few years (Rohde and Muller, 2015; CMEP, 2018). The 2017 China environmental report (CMEP, 2018) suggested that over 97% of the 338 mainland cities exceeded the Chinese Ambient Air Quality Standard of 15 μg/m^3 (GB 3095-2012, 2012) for annual mean $PM_{2.5}$ concentrations, during 2012 ~ 2017. For instance, the 6-year running average of annual mean $PM_{2.5}$ concentration was 43.8 μg/m^3 in Guangzhou, China, for the corresponding period (GZEPB, 2018). Specifically, Guangzhou is undergoing rapid industrialization, urbanization, and expanding use of vehicles (Chen et al., 2017; Lin et al., 2018a), all of which contribute as primary sources of $PM_{2.5}$ (Chen et al., 2017). The Pearl River Delta industrial region and constant airflow of particles also exacerbate the air pollution issues in Guangzhou (Wang et al., 2015). Indeed, Guangzhou city has been dealing with the severe $PM_{2.5}$ pollution in the past years.

Exposure to ambient $PM_{2.5}$ increases mortality and morbidity, and greatly shortens life expectancy in population (Pope et al., 2002; Cohen et al., 2017; Hay et al., 2017). As revealed by the Global Burden of Disease (GBD) Study (Gakidou et al., 2017), ambient $PM_{2.5}$ exposure is the second leading risk factor for lung cancer, a malignant neoplasm being one of the principal causes of death and morbidity worldwide. In 2016, it was estimated by the GBD study that, for lung cancer, ambient $PM_{2.5}$ exposure caused over 6.15 (95% uncertainty interval [UI]: 3.83 ~ 8.80) million global disability-adjusted life-years (DALY, a comprehensive indicator measuring premature mortality, morbidity and non-fatal health outcomes in GBD studies (Hay et al., 2017)). In China, a total of 3.26 (95% UI: 2.09 ~ 4.49) million DALYs of lung cancer were estimated to be attributable to ambient $PM_{2.5}$ exposure (Gakidou et al., 2017).

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A previous burden of disease study (Yu et al., 2017) estimated that ambient $PM_{2.5}$ exposure led to over 16489.3 (95% UI: 10902.8 ~ 21228.8) DALYs for lung cancer in Guangzhou, in 2013. Lung cancer burden in Guangzhou is indeed severe because it remains one of the leading causes of death and morbidity ever since the last two decades (Zhang, 2014), especially among the middle-aged and the elderly (Lin et al., 2018b). However, burden of disease study concerning ambient particulate matter exposure in Guangzhou is scattered (Yang et al., 2016; Yu et al., 2017; Lin et al., 2018a, 2018b), with none focusing on the city district-level DALYs attributable to $PM_{2.5}$ for lung cancer.

Investigating district-level burden of disease may help the local government to prioritize air pollution issues from a more refined environmental health perspective (Cohen et al., 2017), and spatial interpolation analysis may be useful for more accurate and precise decision-making (Lam, 1983; Oliver and Webster, 1990; Chang, 2006). In the past, most burden of disease studies (Yang et al., 2016; Lin et al., 2018b) with a city-level focus implemented ground-based monitoring stations that recorded various pollutants including $PM_{2.5}$, particulate matter with aerodynamic diameter < 10 μm (PM_{10}), nitrogen dioxide, etc., for continuous time points. However, ground-based sites are often limited in number and scales (Chen et al., 2018). Specifically, there are only 11 officially-established ground monitoring stations in Guangzhou (Wang et al., 2013; Lin et al., 2018a), all of which are distributed non-uniformly across the city. Therefore, ground-based $PM_{2.5}$ monitoring data may lead to potential biases in spatial interpolation analysis, due to non-coverage of all areas of the city. Fortunately, remote sensing images can be implemented to overcome the drawback of ground-level sites. Particularly, satellite-derived aerosol optical depth (AOD), which is a measure of light scattering between ground surface and the remote sensing satellite (De Sherbinin et al., 2014), can help to fill in the spatial gaps. Previous studies (Weber et al., 2010) have proven the strong correlation between AOD and $PM_{2.5}$ concentrations. By implementing chemical transport models and statistical regression models (Chen et al., 2018), van Donkelaar and colleagues (van Donkelaar et al., 2018) were able to derive $PM_{2.5}$ concentrations from several satellite instruments including the Moderate Resolution Imaging Spectro radiometer (MODIS), the Multi-Angle Imaging Spectro radiometer (MISR), and the Sea-Viewing Wide Field-of-View Sensor (SeaWiFS) satellite images. Even though a previous burden of disease study in Guangzhou has attempted to implement the remote sensing data regarding $PM_{2.5}$ exposure (Yu et al., 2017), it fails to investigate the district-level DALY attributable to $PM_{2.5}$ for lung cancer on a higher resolution and more detailed scale.

In the present study, we presented an analysis framework to study the spatial-temporal distribution of DALY attributable to $PM_{2.5}$ for lung cancer in Guangzhou, based on lung cancer registry data, and global annual $PM_{2.5}$ data extracting from MODIS, MISR and SeaWiFS satellites (BMI and CIESIN, 2018). We also aimed to update burden of disease evidence on attributable DALY with a higher spatial resolution, using the spatial kriging interpolation technique (Lam, 1983; Oliver and Webster, 1990). The estimated results may provide the authorities with important public health implications for the control of lung cancer burden attributable to $PM_{2.5}$ exposure in Guangzhou. This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement.

2. Methods

2.1. Study Area and Population

The study was conducted in Guangzhou, China, where the total number of permanent registered residents have reached over 8 million by 2013 (see Table S1). Guangzhou, a port city on the edge of the Pearl River Delta, lies in southern China. It contained 12 administrative districts in 2010 ~ 2013, taking up a total area of 7,434 km^2. Besides, grid-level population counts estimated at 1/8 × 1/8º (or approximately 14 km^2 at the equator) resolution were collected in the study. They were obtained from the Global Population Projection Grids (Jones and O Neill, 2016) and provided a continuous surface of population counts covering the 12 districts of Guangzhou. Detailed information and validation of the population estimates can be extracted from elsewhere (Jones and O Neill, 2016).

2.2. Data Collection

2.2.1. Mortality and Morbidity Data

We obtained district-specific annual mortality and morbidity data in 2010 ~ 2013 from the cancer registry system at the Guangzhou Center for Disease Control and Prevention. Lung cancer mortality and morbidity counts for standard 5-year abridged age groups (from 0-year to ≥ 85 years) and for both genders were extracted, based on the International Classifi cation of Diseases and Related Health Problems 10th Revision (ICD-10), and were coded as ICD-10: C33-C34. Population data were also obtained from the system and classified by broader age group (see Table S1) to demonstrate the age structure (Murray, 1994) in different administrative districts. Detailed description on cancer registry system and data quality control can be extracted elsewhere (Chen et al., 2016; Luo et al., 2019).

2.2.2. Ambient $PM_{2.5}$ Data

Spatial annual mean ground-level $PM_{2.5}$ concentrations for 2010 ~ 2013 were extracted from multiple satellite images, available on the CIESIN website as a ready-to-use data product (BMI and CIESIN, 2018). $PM_{2.5}$ concentrations were derived from AOD via chemical transport model and geographically weighted regression (van Donkelaar et al., 2018). The derived data had a grid cell resolution of 0.01º (or approximately 1 km^2 at the equator), covering Guangzhou from latitude 22°26' to 23°56' North, and from longitude 112°57' to 114°03' East (Figure 1). Besides, based on the geographically weighted regression, the extracted satellite images from the CIESIN website were pre-adjusted by the global ground-based monitoring sites on the grid-cell level, which included the official ground-level monitoring stations in Guangzhou. In the pre-adjustment, influence of surface dust was also removed. Finally, it was reported that the consistent agreement rate between satellite-derived $PM_{2.5}$ estimates and ground-based measurements was over 80% for the CIESIN dataset. All relevant information regarding the modelling and data adjustment can be extracted elsewhere (van Donkelaar et al., 2018).

2.3. DALY of Lung Cancer

In the study, we applied the morbidity-mortality DALY approach (Murray, 1994; Yang et al., 2015) to estimate the district-specific lung cancer burden for Guangzhou in 2010 ~ 2013. DALY estimates early death as years of life lost (YLL), and non-fatal outcomes as years lived with disability (YLD). One DALY refers to one-year of "healthy" life lost (Yang et al., 2015).

To estimate YLL for sex-specific (*s*) outcomes (*c*) that could lead to early death, the age-specific (*a*) fatal cases (*d*) for the outcome (*c*) was multiplied by the remaining life expectancy (*e*) at age $\tilde{a}$ [Equation (1)]. Secondly, incident YLD was derived for sex-specific (*s*) outcomes (*c*) by multiplying the morbidity cases without fatality (*n*), with the duration of the disabling status-quo (*t*), and the disability weight (*w*) [see Equation (2)]. Coale and Demeny West Level-25 (for males) and Level-26 (for females) life tables were employed for calculating YLL, as in some previous studies (Lin et al., 2018a). The durations and disability weights of lung cancer were extracted from the 2015 GBD study (Cohen et al., 2017). City-level estimates were aggregated from the district-specific values:

$$YLL = \sum_{c,a,s} d_c^{(a,s)} \times e_c^{(\tilde{a},s)} \tag{1}$$

$$YLD = \sum_{c,a,s} n_c^{(a,s)} \times t_c^{(\tilde{a},s)} \times w_c^{(\tilde{a},s)} \tag{2}$$

2.4. $PM_{2.5}$ Exposure Assessment

A previous review (Hoek et al., 2013) indicated that, $PM_{2.5}$ is the most robust and consistent predictor of disease burden in long-term exposure studies. In these studies, comparative risk assessment is implemented to quantify long-term $PM_{2.5}$ exposure (Lim et al., 2012), and to estimate attributable burden of disease. In the exposure assessment, we first estimated relative risk (RR) of $PM_{2.5}$ via an integrated exposure-response (IER) model (Burnett et al., 2014; Cohen et al., 2017) [see Equation (3)], so that population exposure to $PM_{2.5}$ could be accounted for. The IER model was widely applied in the GBD study (Burnett et al., 2014; Cohen et al., 2017) and was fitted using logarithm of RRs and standard errors per unit change of $PM_{2.5}$ by type of combustion (namely, outdoor air pollution, second-hand smoke, household air pollution, and active smoking). The complete fitted curve of IER model was then implemented to predict for relative risks corresponding to the observed $PM_{2.5}$ exposure levels in our study. Additional detail, including modeling specifications and covariate-adjustment for the IER model, can be found in the appendix of the GBD study (Burnett et al., 2014; Cohen et al., 2017) and in Table S2. We then estimated population-weighted population attributable fraction (PAF), based on the derived RRs and the collected population grid data. The district-specific and city-specific population-weighted PAF = 1 - 1/WRR_{IER} [Equation (4)], where WRR_{IER} is the population-weighted mean of the RR_{IER} at each $PM_{2.5}$ grid cell. The population grid data were disaggregated and projected to have a resolution of 0.01º, using the bilinear interpolation (Chang, 2006). Lastly, attributable burden was calculated by *Attributable DALY* = *DALY* × *PAF* [Equation (5)]. The estimated attributable DALY also had a spatial resolution of 0.01º:

$$RR_{IER} = \begin{cases} 1 & , C_t < C_0 \\ 1 + \alpha \left[1 - e^{-\beta (C_t - C_0)^{\gamma}} \right] & , C_t \geq C_0 \end{cases} \tag{3}$$

where C_t is the exposure level of $PM_{2.5}$ in each grid cell, and C_0 is the counterfactual exposure level below which no excess risk could be observed theoretically (Cohen et al., 2017). In the study, we restrained the counterfactual level within a uniform distribution of 5.8 ~ 8.8 μg/m^3 for $PM_{2.5}$ (Krewski et al., 2009). The distribution was chosen to account for the uncertainty, which was related to the adverse effects of exposure to low $PM_{2.5}$ concentration. The power of γ for $PM_{2.5}$ was set up to predict the RR over a large range of concentrations. β is the ratio of the RR at low to high $PM_{2.5}$ levels. Finally, $1 + \alpha$ reflects the maximum risk that RR_{IER} is likely to reach, if given a large $PM_{2.5}$ concentration.

2.5. Statistical Analysis

In the exposure assessment, RRs were estimated within a Bayesian framework implementing the STAN fitting algorithm, as described in previous GBD study (Cohen et al., 2017). For the unknown parameters (α, β, γ), we assumed that they each had a gamma-distributed hyper-prior (α, β, γ ~ Gamma (1, 0.001)). To properly estimate the unknown prior parameters, technique of two-step Bayesian fitting was implemented in the study. In the first step, STAN-fitted IER model was run under a random initialization for three times. Parameter information was then extracted from the three IER models and implemented as initial priors in the second step. The fixed-initialized IER model achieved better performance in terms of Watanabe-Akaike information criterion, deviance information criterion and sampling time (see Table S2), and it was implemented in the estimation of RR. Next, the logarithm of RR was assumed to be distributed normally, with mean defined by the RR_{IER} and variance defined by the square of observed standard errors of RR, for the four different combustion sources of $PM_{2.5}$. The IER model was then fitted based on observed ambient $PM_{2.5}$ concentrations. Full description of the IER model, and data on standard errors and source types can be extracted from elsewhere (Burnett et al., 2014). Using the fixed-initialized IER model, standard errors of $PM_{2.5}$, information on source types, and the pre-specified uniform distribution of counterfactual concentration, we derived the model-fitted RRs for the spatially-distributed ambient $PM_{2.5}$ concentrations through an iteration of 12,000 steps of Markov Chain Monte Carlo sampling, 12,000 steps of Markov Chain Monte Carlo sampling, for a for a total of three Markov Chains (where each chain had a burn-in iteration of 6,000, as shown in Table S2). The median of

Table 1. Mortality and Morbidity Rate (per 100,000) of Lung Cancer in Guangzhou during 2010 ~ 2013, by Gender and Administrative District

Administrative district	Male mortality rate		Female mortality rate		Male morbidity rate		Female morbidity rate	
	2010 ~ 2011	2012 ~ 2013	2010 ~ 2011	2012 ~ 2013	2010 ~ 2011	2012 ~ 2013	2010 ~ 2011	2012 ~ 2013
Liwan	96.79	98.94	46.81	49.34	100.71	103.27	52.64	53.00
Yuexiu	80.42	73.47	35.93	35.62	72.07	80.40	39.44	39.11
Haizhu	84.64	86.93	38.26	39.51	108.74	101.77	49.85	54.49
Tianhe	38.30	38.09	15.38	17.31	57.51	57.86	29.28	35.51
Baiyun	46.53	49.83	20.52	22.38	64.52	60.73	29.86	27.60
Huangpu	57.83	49.81	31.24	26.68	71.36	62.15	39.85	33.49
Panyu	57.32	61.97	26.20	28.54	59.92	67.67	29.89	35.89
Huadu	33.19	34.56	14.52	13.56	46.34	50.82	20.17	23.85
Nansha	38.94	52.81	9.86	20.66	61.28	52.27	19.72	23.92
Luogang	29.22	38.64	10.81	12.03	32.80	35.78	17.84	22.55
Zengcheng	37.08	42.35	15.72	18.22	38.49	43.28	15.84	17.98
Conghua	30.72	35.15	11.33	13.66	36.39	49.08	15.93	16.74
Total	57.37	58.53	25.63	26.81	65.94	67.98	32.14	34.06

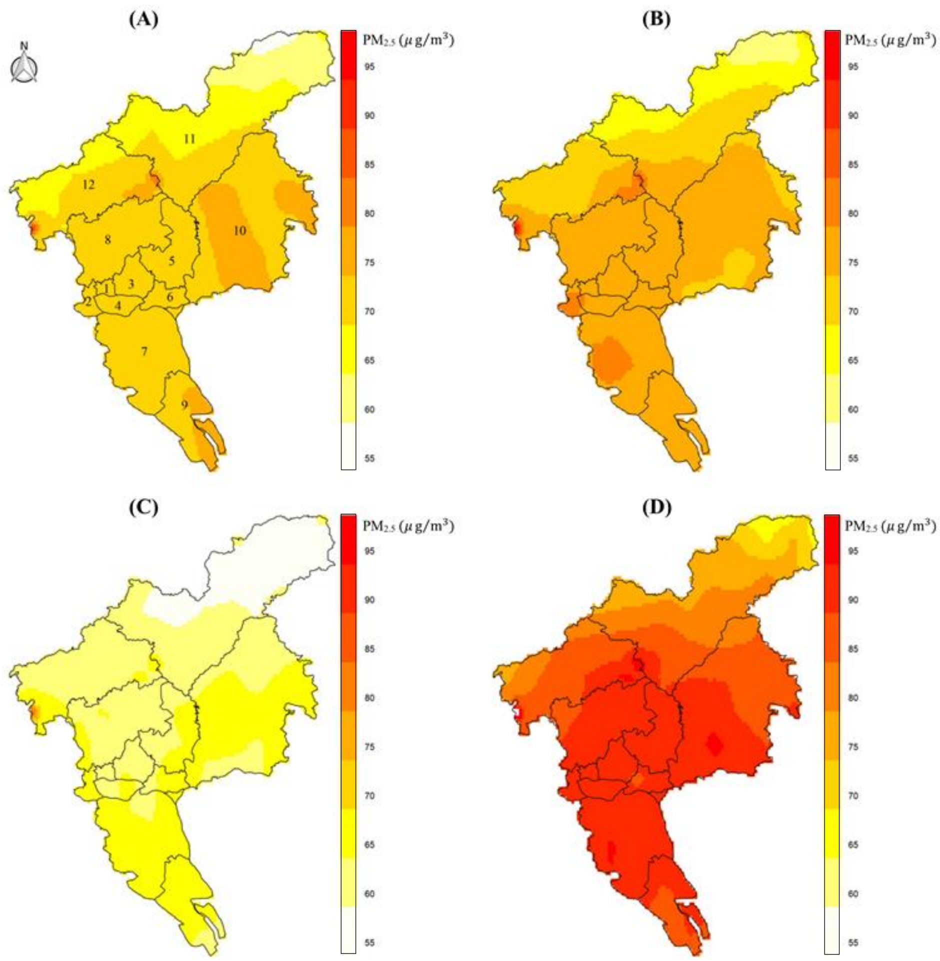

Figure 1. Spatial-temporal distribution of ambient $PM_{2.5}$ concentrations (μg/m^3) in Guangzhou, China, 2010 ~ 2013.

Note: $PM_{2.5}$, particulate matter with aerodynamic diameter < 2.5 μm. Gridded $PM_{2.5}$ concentrations were estimated by the relationship between ground-level $PM_{2.5}$ and aerosol optical depth (AOD), data of which were extracted from publicly available remote satellite images on the CIESIN website (BMI and CIESIN, 2018). Districts are labeled by consecutive numbers ranging from 1 to 12: 1 = Yuexiu; 2 = Liwan; 3 = Tianhe; 4 = Haizhu; 5 = Luogang; 6 = Huangpu; 7 = Panyu; 8 = Baiyun; 9 = Nansha; 10 = Zengcheng; 11 = Conghua; 12 = Huadu. Years are labeled by capital letters: A = 2010; B = 2011; C = 2012; D = 2013.

sampling values for each exposure concentration was used as the central estimate, with 95% UI deriving from the 2.5% and 97.5% of the iterated posterior distribution.

To display on maps the spatial distribution of attributable DALY, we implemented universal kriging interpolation with Gaussian kernel estimation, a spatial analysis method that is commonly used for public health assessment and pollution control (Oliver and Webster, 1990; He et al., 2018). We used adaptive Gaussian bandwidths, which is more flexible and robust for estimating the spatially-distributed RR (Davies and Hazelton, 2010). Other kernels such as naive Nugget kernel and Wave kernel (Oliver and Webster, 1990) were also considered in the preliminary spatial analysis (see Table S3). We then compared the goodness-of-fit of different models using sum of squares of residuals, root mean squared error, and proportion of variance explained (Hijmans and van Etten, 2014). Next, we further checked model predictive performance with 10-fold cross-validation test, where mean squared error and mean square normalized error were calculated. Given consideration of model goodness-of-fit and predictive power, Gaussian kernel model fitted with $PM_{2.5}$ outperformed the other models and was used in the kriging interpolation for the spatially-estimated attributable DALY in the study. All analyses were performed in R software (version 3.4.3), with raster, sp, gstat, and RStan packages.

3. Results

3.1. Summary of Target Population

Table 1 summarizes the mortality and morbidity rates for the 12 administrative districts of Guangzhou, and also the city-level rates for each indicator. The city-level mortality rates for males in the two periods were 57.37 per 100000 (for 2010 ~ 2011) and 58.53 per 100000 (for 2012 ~ 2013), respectively. The city-level mortality rates for females were only half as those for males in the respective periods. The city-level morbidity rates for males were also higher than those for females. Age-district-specific population counts in 2010 ~ 2013 are presented in Table S1. It shows that Liwan, Yuexiu and Haizhu were populated with people aged above 60 years, but Luogang and Conghua had smaller percentages of aged population.

3.2. Population Exposure Levels

The population-weighted $PM_{2.5}$ in Guangzhou increased by 25.9%, from 2010 (Mean ± Standard deviation (SD): 71.1 ± 3.8 μg/m^3) to 2013 (Mean ± SD: 89.5 ± 6.3 μg/m^3) (see Figure S1). In Guangzhou, $PM_{2.5}$ dropped to the lowest (Mean ± SD: 63.1 ± 3.0) in 2012, but increased sharply since then. Among the 12 administrative districts, $PM_{2.5}$ exposure in Panyu and Nansha had remained at a high level (> 64.6 μg/m^3) since 2012. Figure 1 shows that even though the district-specific popular-tion-weighted $PM_{2.5}$ concentrations varied annually, the spatial distribution of $PM_{2.5}$ exposure is shifting from the north to the south (from Conghua and Huadu, down to Panyu and Nansha). Furthermore, ambient $PM_{2.5}$ pollution in 2013 was the most severe, compared to those in previous years. Figure 2 demonstrates the spatial-temporal distribution of RR ascribed to $PM_{2.5}$ exposure, and the patterns of RR are almost consistent with Figure 1. Residents in districts exposed to higher $PM_{2.5}$ concentrations had a higher risk for developing lung cancer, and the RRs of the 12 districts were estimated to range between 1.37 (95% UI: 1.04 ~ 1.86) and 1.99 (95% UI: 1.12 ~ 3.19).

Based on the population-weighted $PM_{2.5}$ concentrations, population-weighted average of PAFs for Guangzhou were displayed in Figure S2, which depicted the same trend as those observed in $PM_{2.5}$ (see Figure S1). The PAFs increased with fluctuation, from 36.6% (95% UI: 6.0 ~ 56.5) to 44.6% (95% UI: 8.4 ~ 64.2), in 2010 ~ 2013. On average, 37.7% of the total DALY for lung cancer could be attributable to long-term $PM_{2.5}$ exposure.

3.3. Spatial-Temporal Distribution of Attributable DALYs

The gender-specific DALY of lung cancer attributable to ambient $PM_{2.5}$ is summarized in Table 2. The DALY of lung cancer attributable to ambient $PM_{2.5}$ also increased with fluctuation. In general, the attributable DALY in Guangzhou increased by 26.8%, from 2010 (34198.6 DALYs [95% UI: 5594.1 ~ 52795.1]) to 2013 (43352.7 DALYs [95% UI: 8157.9 ~ 62371.7]). Table 2 also shows that long-term exposure to $PM_{2.5}$ contributed to a total loss of 29677.5 (95% UI: 5584.6 ~ 42697.1) DALYs for males, and to a loss of 13675.2 (95% UI: 2573.3 ~ 19674.6) DALYs for females in 2013. The attributable DALYs due to $PM_{2.5}$ exposure were higher in males than in females, for each district and respective year. Figure 3 further displays the spatial-temporal distribution of attributable DALY due to $PM_{2.5}$ exposure for both genders combined. Yuexiu and Haizhu, had the first and second largest numbers of attributable DALYs, taking up 17.9 and 17.2% of the city totals. Luogang and Huangpu, on the other hand, had the smallest numbers of attributable DALYs, taking up only 1.4 and 2.7% of city totals. Consistent with Figure 1 and Figure 2, spatial distribution of $PM_{2.5}$ attributable DALY in the 12 districts largely reflects the $PM_{2.5}$ exposure patterns and the RRs for lung cancer. With higher exposure to $PM_{2.5}$ in 2013 (Figure 1), residents in Yuexiu, Haizhu, Liwan and Panyu had higher risks for developing lung cancer (Figure 2), and also had larger numbers of lung cancer DALYs attributable to $PM_{2.5}$ (Figure 3).

4. Discussion

To the best of our knowledge, this is the first local burden of disease study highlighting DALY of lung cancer attributable to ambient $PM_{2.5}$ exposure in different spatial districts of Guangzhou. Implementing both comparative risk assessment and geospatial statistical modelling, our study provides quantitative evidence regarding spatial-temporal distribution of RRs for developing lung cancer due to ambient $PM_{2.5}$ exposure in Guangzhou. Residents living in different administrative districts have different RRs for developing lung cancer, due to their different levels of $PM_{2.5}$ exposure. And particularly, those who live in Yuexiu, Haizhu, and Liwan, may be more likely to suffer from a higher loss of attributable DALYs of lung cancer (Figure 3), partly due to the higher ambient $PM_{2.5}$ exposure in these dis-

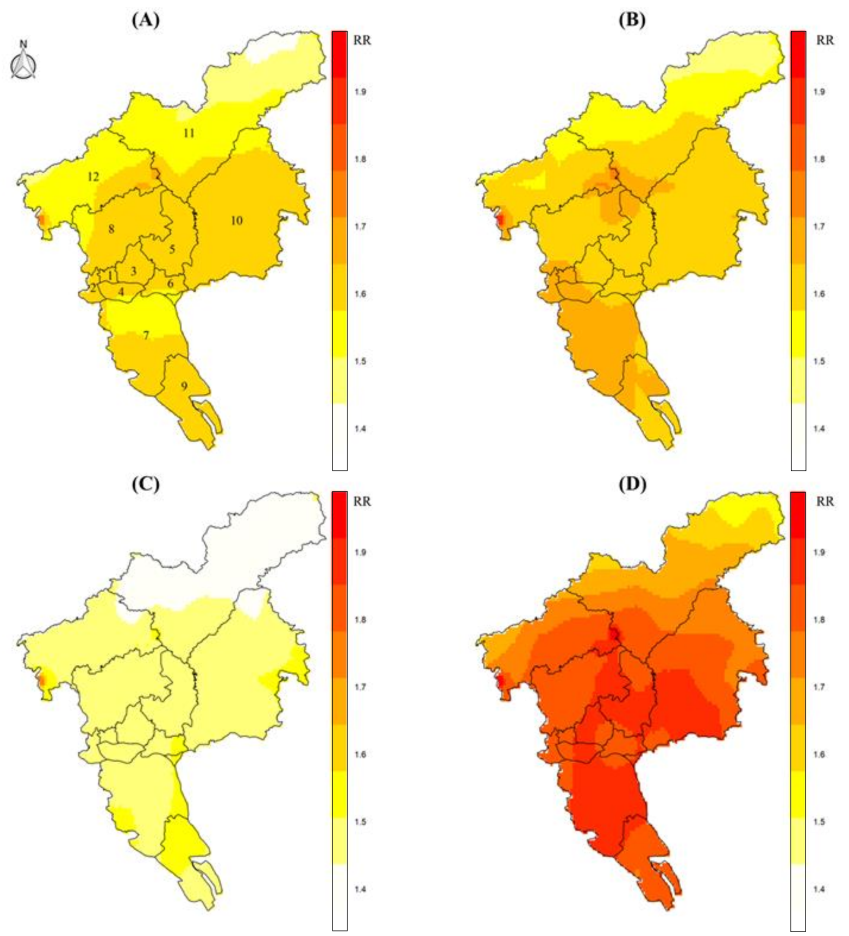

Figure 2. Spatial-temporal distribution of relative risks ascribed to ambient $PM_{2.5}$ for lung cancer in Guangzhou, China, 2010 ~ 2013.

Note: $PM_{2.5}$, particulate matter with aerodynamic diameter < 2.5 μm; RR, relative risk. Redder/Darker color indicates a higher RR due to exposure to ambient $PM_{2.5}$ pollution. Districts are labeled by consecutive numbers ranging from 1 to 12: 1 = Yuexiu; 2 = Liwan; 3 = Tianhe; 4 = Haizhu; 5 = Luogang; 6 = Huangpu; 7 = Panyu; 8 = Baiyun; 9 = Nansha; 10 = Zengcheng; 11 = Conghua; 12 = Huadu. Years are labeled by capital letters: A = 2010; B = 2011; C = 2012; D = 2013.

tricts (Figure 2) and to the higher proportion of aged population (Table S1). These findings are consistent with previous local burden of disease studies conducted in Guangzhou (Yu et al., 2017; Luo et al., 2019), where residents in the aged areas such as Yuexiu, Haizhu, and Liwan districts were reported to carry a higher DALY burden for malignant neoplasm.

Our estimated RRs for developing lung cancer are basically consistent with previous GBD studies (Burnett et al., 2014; Cohen et al., 2017), which found similar RRs ranging between 1.0 and 2.0. Besides, the estimated RRs for the aged districts or areas of Guangzhou coincide with the spatial distribution of exposure levels of $PM_{2.5}$, indicating that residents living in much polluted and aged areas may be more likely to suffer from a higher relative risk of lung cancer (Brauer et al., 2016; Cohen et al., 2017; Yu et al., 2017). However, the average population-weighted PAFs and city-level attributable DALYs are higher than those reported in previous studies (Gakidou et al., 2017; Yu et al., 2017). For PAF, it is estimated in the GBD 2016 (Gakidou et al., 2017), that the weighted PAF in China has reached 23.8% (95% UI: 15.6 ~ 32.7%). For DALY, it is estimated that the city-level attributable lung cancer burden due to $PM_{2.5}$ exposure was 16489.3 DALYs (95% UI: 10902.8 ~ 21228.8) in Guangzhou (Yu et al., 2017). The reasons for higher estimates in the current study may be threefold. Firstly, the current study incorporates higher resolution gridded population data in the estimation, which makes it possible to identify more spatial features for calculation of PAF. The gridded data with higher resolution may result in PAF with a wider range of values, because higher resolution data for a given area are comprised of more grid cells and it tends to offer more spatial information (Atkinson and Tate, 1999). Thus, it provides more spatial features for grid-cell level population-weights in estimating PAF (Figure S2). Secondly, lower resolution $PM_{2.5}$ data may not fully capture the spatial variation of ambient $PM_{2.5}$ on a district level, and thus might contribute less information to the calculation of city-level PAF. For instance, Yu et al. (2017) estimated the average PAF for Guangzhou based on low resolution $PM_{2.5}$ data (0.1° by 0.1°), which were extracted from the GBD 2013 study. These datasets were suitable to derive large-scaled estimates on the global and national levels (Brauer et al.,

Table 2. Disability-Adjusted Life-Years (DALYs) of Lung Cancer Attributable to Ambient $PM_{2.5}$ in Guangzhou during 2010 ~ 2013, by Gender and Administrative District

Administrative district	Male (95% UI)				Female (95% UI)			
	2010	2011	2012	2013	2010	2011	2012	2013
Liwan	3241.8 (531.2, 4997.9)	3563.7 (615.4, 5300.6)	3023.4 (478.6, 4870.1)	4228.3 (810.5, 6034.5)	1656.4 (271.4, 2553.7)	1820.9 (314.4, 2708.4)	1432.7 (226.8, 2307.8)	2003.6 (384.0, 2859.6)
Yuexiu	4202.7 (687.8, 6483.1)	4554.2 (777.0, 6814.0)	3464.9 (543.6, 5605.6)	4933.9 (948.5, 7031.4)	2032.4 (332.6, 3135.2)	2202.3 (375.8, 3295.2)	1800.2 (282.4, 2912.3)	2563.3 (492.8, 3653.1)
Haizhu	3912.9 (640.1, 6036.4)	4227.0 (719.5, 6332.1)	3603.4 (567.8, 5817.5)	5124.3 (989.7, 7286.5)	1866.0 (305.3, 2878.7)	2015.8 (343.1, 3019.8)	1623.5 (255.8, 2621.2)	2308.8 (445.9, 3283.0)
Tianhe	1495.6 (245.8, 2302.6)	1568.3 (262.6, 2368.4)	1364.7 (213.3, 2212.1)	1961.7 (378.3, 2791.2)	685.5 (112.7, 1055.4)	718.8 (120.3, 1085.5)	661.9 (103.5, 1073.0)	951.5 (183.5, 1353.9)
Baiyun	2066.1 (339.2, 3183.0)	2182.7 (366.8, 3290.1)	1914.4 (298.4, 3108.3)	2749.3 (527.8, 3920.3)	981.1 (161.0, 1511.4)	1036.4 (174.2, 1562.2)	858.9 (133.9, 1394.6)	1233.5 (236.8, 1759.0)
Huangpu	635.8 (103.9, 981.4)	665.6 (110.6, 1008.4)	526.4 (83.8, 845.2)	726.3 (138.7, 1038.2)	315.4 (51.5, 486.8)	330.2 (54.9, 500.3)	265.5 (42.3, 426.3)	366.3 (69.9, 523.6)
Panyu	3174.4 (517.3, 4906.2)	3475.3 (594.6, 5192.6)	2406.1 (383.4, 3862.7)	3392.8 (660.5, 4808.4)	1520.0 (247.7, 2349.3)	1664.1 (284.7, 2486.4)	1168.9 (186.3, 1876.5)	1648.2 (320.9, 2336.0)
Huadu	1155.5 (186.6, 1794.2)	1213.4 (199.8, 1848.1)	1135.9 (176.7, 1847.0)	1573.5 (292.2, 2277.4)	522.4 (84.4, 811.2)	548.6 (90.3, 835.5)	449.5 (69.9, 731.0)	622.7 (115.6, 901.3)
Nansha	422.0 (70.7, 644.2)	436.6 (73.7, 656.9)	952.7 (153.5, 1520.2)	1285.0 (244.4, 1840.1)	94.5 (15.8, 144.3)	97.8 (16.5, 147.1)	367.9 (59.3, 587.0)	496.1 (94.4, 710.5)
Luogang	291.3 (47.8, 448.8)	305.3 (51.0, 461.4)	383.4 (60.3, 619.4)	547.2 (105.8, 777.7)	120.7 (19.8, 185.9)	126.5 (21.1, 191.1)	119.1 (18.7, 192.4)	169.9 (32.9, 241.5)
Zengcheng	1722.4 (289.3, 2626.1)	1729.6 (286.3, 2626.5)	1707.0 (269.6, 2752.9)	2404.9 (462.3, 3427.1)	803.1 (134.9, 1224.5)	806.5 (133.5, 1224.6)	756.3 (119.5, 1219.6)	1065.5 (204.8, 1518.3)
Conghua	959.7 (149.7, 1516.8)	1002.4 (158.7, 1556.8)	973.4 (145.9, 1616.8)	1338.6 (234.8, 1988.6)	388.6 (60.6, 614.1)	405.9 (64.3, 630.4)	387.2 (58.0, 643.2)	532.5 (93.4, 791.1)
Total	23235.5 (3800.8, 35870.5)	24055.6 (3967.8, 36598.2)	21169.4 (3302.9, 34374.0)	29677.5 (5584.6, 42697.1)	10963.1 (1793.3, 16924.6)	11350.0 (1872.1, 17268.0)	9754.8 (1522.0, 15839.4)	13675.2 (2573.3, 19674.6)

* DALY, disability-adjusted life-years; $PM_{2.5}$, particulate matter with aerodynamic diameter < 2.5 μm; UI, uncertainty interval.

2016), but we argue that it may be more reasonable to use higher resolution data for estimating PAF and attributable DALY in lower-scaled areas. Finally, using average data to evaluate city's overall status may lead to under-estimation of the total values. In previous studies (Pan et al., 2011; Yu et al., 2017), health outcome data were extracted from the annual report of Guangzhou cancer registry and reflected the city's average rates for cancer. As average values only reflect central tendency of parameters, we argue that using aver-age data may not be appropriate for estimating total DALYs for the whole city. In the present study, we calculated the city-level attributable DALYs by aggregating district-specific values instead. Such a method may incorporate information from a range of district-specific DALYs, and thus lead to more accurate city-level estimates. With those being said, the prior study con-ducted by Yu et al. (2017) was essentially a preliminary analysis of attributable burden in Guangzhou, and we have further updated the city-level estimates based on more refined data and aggregation method. Nonetheless, we consider the current estimates to be more accurate, when compared with those in the previous study.

Our findings in the spatial-temporal distribution of ambient $PM_{2.5}$ may also reflect the pollution status and environmental efforts in Guangzhou over time. It is suggested by previous study that nearly 40% of $PM_{2.5}$ can be comprised of carbonaceous aerosol (Seinfeld and Pandis, 2016), a component of which is emitted dominantly by vehicle exhausts in Guangzhou (Tao et al., 2015). During 2010 ~ 2012, a series of air quality control efforts were made in Guangzhou (GZEPB, 2013), such as improving gasoline quality, restricting heavy-polluting vehicles in major areas of the city, promoting the use

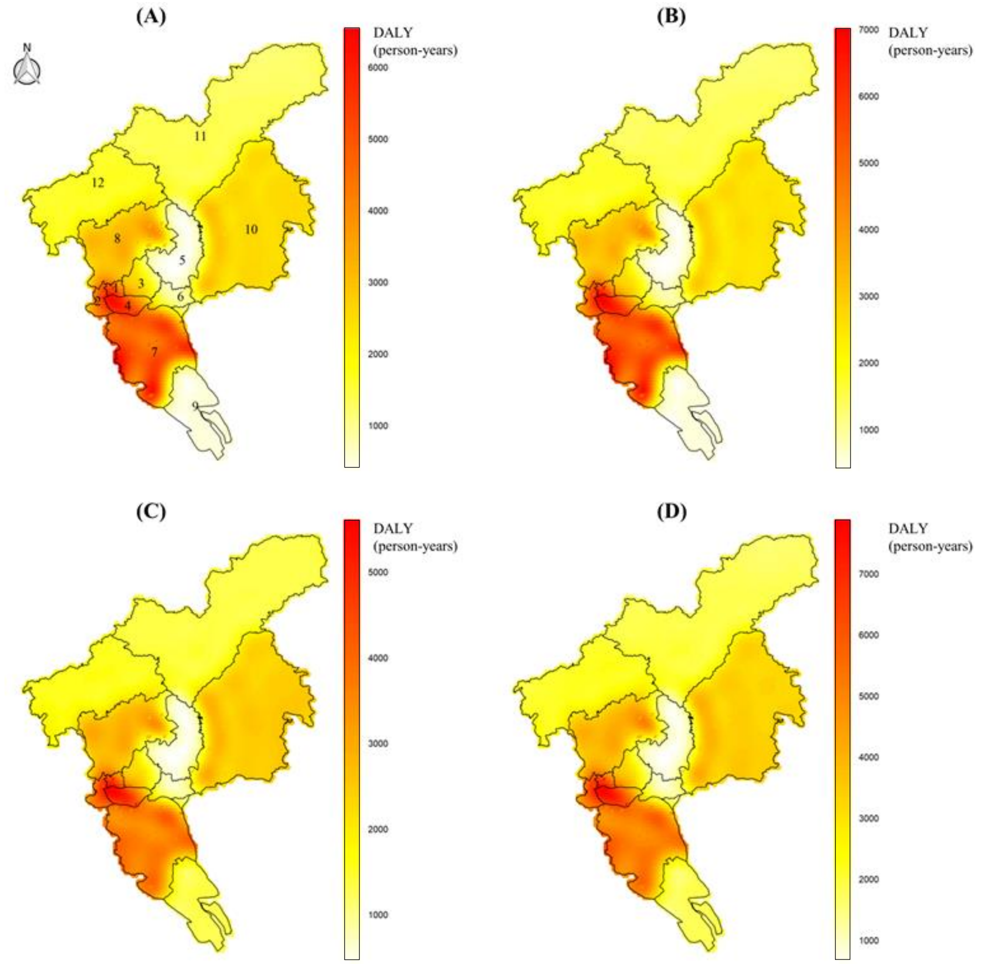

Figure 3. Spatial-temporal distribution of disability-adjusted life-years of lung cancer attributable to ambient $PM_{2.5}$ in Guangzhou, China, 2010 ~ 2013.

Note: DALY, disability-adjusted life-years; $PM_{2.5}$, particulate matter with aerodynamic diameter < 2.5 μm. Redder/Darker color indicates a higher attributable DALY due to exposure to ambient $PM_{2.5}$ pollution. Districts are labeled by consecutive numbers ranging from 1 to 12: 1 = Yuexiu; 2 = Liwan; 3 = Tianhe; 4 = Haizhu; 5 = Luogang; 6 = Huangpu; 7 = Panyu; 8 = Baiyun; 9 = Nansha; 10 = Zengcheng; 11 = Conghua; 12 = Huadu. Years are labeled by capital letters: A = 2010; B = 2011; C = 2012; D = 2013.

of new energy vehicles, shutting down heavily-polluting companies, etc. In particular, a more aggressive regulatory approach was exerted during the event of Asian Games in 2010, when a combination of eight steps of air pollution abatement strategy was implemented (Liu et al., 2013). A previous study has proven the effectiveness of emission control measures exerted in Guangzhou via quantitative simulation models (Liu et al., 2013). Altogether, these evidences may explain the temporal trends of $PM_{2.5}$ presented in Figure 1. The annual mean $PM_{2.5}$ concentrations during 2010 ~ 2012 in the current study were found to fall within the concentration range reported by previous studies (Liu et al., 2013; Tao et al., 2015), and the consistency adds credibility to the findings of the present study. However, as presented in Figure 1, we also find higher annual mean $PM_{2.5}$ concentration in 2013, particularly for Panyu and Nansha districts. The uprising trend for $PM_{2.5}$ in 2012 ~ 2013 was presented in the official environmental report (GZEPB, 2018). We suspect that the increase of $PM_{2.5}$ concentration might be due to the development plans exerted for those districts (GZG, 2012; Li et al., 2016). The causality relationship between the implemented plans and $PM_{2.5}$ pollution should warrant future research, but it is beyond the scope of the study.

In the present study, the spatial variation of RR reflects, to some extent, the variation of $PM_{2.5}$ exposure in the population. Using the comparative risk assessment framework and spatially-gridded data, we are able to pinpoint the spatial distribution of RR ascribed to $PM_{2.5}$ exposure in each grid cell (Figure 2). Under this framework, we implemented the IER model that has been validated in previous meta-analysis studies (Burnett et al., 2014; Cohen et al., 2017), and also by our preliminary analysis in Table S2. Specifically, the IER model describing the relationship between $PM_{2.5}$ exposure and relative risks of lung cancer was based on a collection of long-term cohort studies (Pope et al., 2002; Pope et al., 2011). The model is thus able to combine previous information on lung cancer mortality from four sources of $PM_{2.5}$ (Burnett et al., 2014), adjust intrinsically for potential confounding factors such as exposure duration (Pope et al., 2011), and finally predict the RR for observed $PM_{2.5}$ in each grid cell. Due to the high statistical power of meta-analysis, it is our belief that the current study could provide a high degree of evidence for estimating RR ascribed to $PM_{2.5}$ exposure.

The study has several strengths. First, we have proposed a complete analysis framework that combines the comparative risk assessment and spatial interpolation estimation, to evaluate attributable DALY burden for Guangzhou on the grid-cell level. The spatial interpolation estimation is implemented as a feature because it can predict unknown values for any spatial point data with known values (Oliver and Webster, 1990). Since DALY is calculated as a district-specific estimate, it only reflects the centroid value for each district (He et al., 2018) and it is, in its essence, a type of spatial point data. However, spatial point data is incapable of representing all spatial information within each grid cell and it may lead to potential difficulty of results interpretation (Dougenik et al., 1985). To tackle the issue, we fitted the attributable DALY against gridded $PM_{2.5}$ in the kriging interpolation model (see Table S3) and applied spatial information from both point data and gridded data to the estimates. Under the presented analysis framework, we are able to fully utilize the known spatial patterns from the gridded data and thus derive the attributable DALY on a grid-cell level. Besides, we believe that it is also possible to further generalize the analysis framework directly to other local burden of disease study, and to the study of other types of air pollutants.

Another strength of the study concerns with the estimation of high-resolution (1 km × 1 km) RR and attributable DALY burden in Guangzhou. By displaying on maps the RR and attributable DALY ascribed to $PM_{2.5}$ exposure, the high-resolution empirical findings may have important public health implications for air pollution control and lung cancer intervention. Specifically, it is our belief that the current findings can provide guidance to the authorities and policy-makers on prioritization of environmental health problems such as where exposure to $PM_{2.5}$ is severe and should be reduced, or where the limited health resources should be allocated to so that more burden attributable to $PM_{2.5}$ can be alleviated.

Several limitations should be acknowledged in this study. First, the temporal trend of the estimated attributable DALY during 2010 ~ 2013 was not changing as drastically as that of $PM_{2.5}$, possibly due to the comparatively short range of time. We suspect that, unlike air pollution agents that can change dramatically overtime, estimated DALY burden of lung cancer may not vary substantially because of intrinsic pathological characteristics of lung cancer (Schwartz et al., 2008), and the stability of age structure in a short range of time (Girosi and King, 2008). The current study did not extend the range of time for the attributable burden estimates due to unavailability of morbidity and mortality data. Also, due to the unavailability of daily health outcome data, the current study was not able to analyze the impact of daily exposure on the attributable disease burden, and did not account for the effects of daily internal movements of population between districts on pollution exposure. Future studies using data with a longer time period, daily health outcome, and district-internal travel patterns may reveal more information regarding the temporal trend of district-specific attributable DALY. Nonetheless, the proposed comprehensive methodology synthesizing both spatial information technologies and burden of disease evaluation may shed light on future study of the burden of disease attributable to $PM_{2.5}$ exposure at the local level. Second, confounding factors other than $PM_{2.5}$ may also affect the spatial variation within the kriging interpolation model. Traditional meteorological factors such as air pressure, wind speed and humidity (Lin et al., 2018a) may be one type of confounder. Another type of confounder, such as urban micro-climate factors (e.g. spatial geometry factors, heat effect, etc.) may also have an impact on the variation (Yang et al., 2014). Unfortunately, such detailed level of data was also not accessible. The confounding effects on the kriging model may warrant a future study.

5. Conclusions

We estimated grid-cell level RR ascribed to $PM_{2.5}$ exposure for lung cancer and reported attributable DALY of lung cancer due to $PM_{2.5}$ exposure in the 12 administrative districts of Guangzhou, China. Population residing in aged districts such as Yuexiu, Haizhu, and Liwan, may be more likely to suffer from a higher loss of DALYs of lung cancer, partly due to their higher chance of exposure to ambient $PM_{2.5}$. This evidence is crucial to tailor policies with regards to air pollution control and intervention strategies for lung cancer. Specifically, understanding the spatial and temporal distribution of lung cancer burden attributable to $PM_{2.5}$ exposure is essential for the authorities to prioritize pollution-related public health action, to allocate the limited health resources and to alleviate burden of disease over time.

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