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# The impact of prolonged exposure to air pollution on the incidence of chronic non-communicable disease based on a cohort in Tianjin

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# ABSTRACT

Evidence on the associations of prolonged ambient pollutants exposure with chronic non-communicable diseases among middle-aged and elderly residents is still limited. This prospective cohort study intends to investigate the long-term effects of ambient pollution on hypertension and diabetes incidence among relatively older residents in China. Individual particulate matter exposure levels were estimated by satellite-based model. Individual gaseous pollutants exposure levels were estimated by Inverse Distance Weighted model. A Cox regression model was employed to assess the risks of hypertension and diabetes morbidity linked to air pollutants exposures. The crossproduct term of ambient pollutants exposure and covariates was further added into the regression model to test whether covariates would modify these air pollution-morbidity associations. During the period from 2014 to 2018, a total of 97,982 subjects completed follow-up. 12,371 incidents of hypertension and 2034 of diabetes occurred. In the multi-covariates model, the hazard ratios (HR) and 95% confidence interval (CI) were 1.49 (1.45-1.52), 1.28 (1.26-1.30), 1.17 (1.15-1.18), 1.21 (1.17-1.25) and 1.33 (1.31-1.35) for hypertension morbidity per  $10 \ \mu g/m^3$  increment in PM<sub>1</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub> and SO<sub>2</sub>, respectively. For diabetes onsets, the HR (95% CI) were 1.17 (1.11-1.23), 1.09 (1.04-1.13), 1.06 (1.02-1.09), 1.02 (0.95-1.10), and 1.24 (1.19-1.29), respectively. In addition, for hypertension analyses, the effect estimates were more pronounced in the participants with age <60 years old, BMI  $\ge 24$  kg/m<sup>2</sup>, and frequent alcohol drinking. These findings provided the evidence on elevated risks of morbidity of hypertension and diabetes associated with prolonged ambient pollutants exposure at relatively high levels.

## 1. Introduction

Hypertension and diabetes are two well-known major risk factors of cardiometabolic diseases in developing countries such as China, causing a large number of prevalent patients worldwide. It is predicted to reach around 300 million of patients with hypertension by 2025 and 578 million cases with diabetes by 2030 (Huang et al., 2019; Wang et al., 2020), respectively. The percentage of hypertensive patients and diabetics has been enhancing continuously in China. The reported prevalence of hypertension ranged from 25.2% to 27.9% during 2015–2017, and the prevalence of diabetes increased from 10.4% to 11.2% during 2013–2015 (Diabetes Branch of Chinese Medical Association, 2021;

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Hypertension Branch of Chinese Geriatric Medical Association, 2019). For decades, the population aging problem in China remains serious (Wu et al., 2017). To our best knowledge, the prevalence and incidence of hypertension and diabetes increased across age (Dorobantu et al., 2018; Li et al., 2015; Menke et al., 2015; Sinnott et al., 2017; Wang et al., 2017a). As reported, hypertension and diabetes have influenced around 16.9%–50% of Chinese middle-aged and elderly population (Li et al., 2015; Wang et al., 2017a). Hence, attention attached to the risks of hypertension and diabetes among the adults of aged  $\geq$ 45 years is of great significance in China.

Apart from several traditional risk factors, several literatures indicated that environmental pollution may substantially contribute to the development of hypertension and diabetes (Baudin et al., 2001; Huang et al., 2019; Maddatu et al., 2017; Shan et al., 2020; Zhang et al., 2020a). Especially, the increased incidence of hypertension and diabetes linked to ambient pollutants exposure have attracted focus of researchers.

An accumulating investigations have explored the long-term impacts of air pollutants exposure on both hypertension and diabetes in China. However, the design of most studies is cross-sectional study, which is unable to explore the effects of time-varying air pollutants exposure levels on these two diseases (Du et al., 2021; Li et al., 2019a; Liu et al., 2016; Xie et al., 2018; Yang et al., 2018, 2019a). Till now, only two longitudinal cohorts have been established to investigate the associations of long-term exposure to air pollutants with morbidity of hypertension and diabetes among adults in mainland China. One cohort was based on general participants came from four cities in northern China (Li et al., 2021; Shan et al., 2020; Yan et al., 2020), however, it was a retrospective cohort. Another one used data from the China-PAR project with four prospective cohorts covering the entire range of China (Huang et al., 2019; Liang et al., 2019). But it only revealed a significant relationship between PM2.5 with incidence of hypertension or diabetes, it did not explore the effects of other ambient pollutants such as PM<sub>1</sub>, PM<sub>10</sub>, NO<sub>2</sub> and SO<sub>2</sub>. What's more, the subjects in these two cohorts were general adults (≥18 years old). Yet, compared with younger adults, middle-aged and elderly individuals may be more susceptible to air pollutants (Liu et al., 2019). In addition to these mainland data, the adverse effect estimates of PM2.5-induced onset of diabetes were also found among the cohorts in Hongkong and Taiwan (Lao et al., 2019; Qiu et al., 2018). However, the levels of PM<sub>2.5</sub> in these settings were relatively lower than that in northern China such as Tianjin. Considering these heterogeneities, the findings obtained from studies in relatively low concentrations of air pollutants might not directly extend to those in high pollution regions.

Based on health examination data, this prospective cohort study aimed to examine the incidence of hypertension and diabetes in association with ambient pollutants exposure among middle-aged and elderly residents in Tianjin (an area with high pollutants levels in China), and to provide the concentration-response (C-R) curves of these relationships.

### 2. Materials and methods

## 2.1. Study area and population selection

We performed this cohort study in the Binhai New Area. The detailed information of geographical location was described in a published literature (Lin et al., 2020b). Briefly, as the center of the Bohai Economic Circle, the Binhai New Area lies eastern coastal of Tianjin in northern China. It comprises three administrative districts (Tanggu, Hangu and Dagang district) with a total area of 2270 square kilometers and a total number of 2.97 million population.

According to the design, the cohort in this study included subjects from 37 health examination system of community hospitals who took the regular free physical examinations during the period from 2014 to 2018 in Tianjin Binhai New Area. This cohort was established in 2014. Originally, approximately 223,000 residents participated in the regular free physical examinations in 2014. After excluding the subjects with missing/incomplete addresses, missing basic information, and repeated physical examinations within one year, there were 112,394 participants at baseline (from January 1st, 2014 to December 31st, 2014) in the study cohort. The follow-up survey was conducted every year from January 1st, 2015 to December 31st, 2018. At last, a total of 97,982 (87.18%) participants completed the follow up successfully, and all of them were alive during the study period.

Based on the aim of the present study, exclusion of participants was as follows. (1) Residents with age below 45 years old; (2) Subjects resided in the baseline address for less than 5 years since baseline. We further eliminated the participants who had duplicated physical examinations within the same year, incomplete residential information, lack of data on disease during the follow-up, and individuals who suffered related diseases at baseline. For instance, baseline hypertensive patients were excluded in analyses of hypertension-related cohort. The participants with diabetes, a 2-h oral glucose tolerance level of  $\geq 11.1 \text{ mmol/L}$ , or fasting plasma glucose (FPG) level of  $\geq 7.0 \text{ mmol/L}$  were removed in analyses of diabetes-related cohort. The details of population screening were shown in Fig. 1. Finally, there were 48,357 people available for hypertension analysis and 72,869 for diabetes analysis.

The study was approved by the ethical committee of the coordinating center of Chu Hsien-I Memorial Hospital.

# 2.2. Health data collection and disease diagnosis

The incident dates of hypertension and diabetes among residents from 2014 to 2018 in Tianjin Binhai New District were obtained via the Tianjin Community Health Service Information System. The detailed information of health examination data was described in a published literature (Lin et al., 2020b), and it was shown in **Supplementary Materials**.

The defined chronic non-communicable diseases were coded based on the International Classification of Diseases, Revision 10 (ICD-10, I10-15 for hypertension; E10-14 for diabetes). New-onset diseases were diagnosed in community hospitals initially, subsequently, whether the patients were really new cases was diagnosed by higher-level hospitals. The diagnosed date of new-onset diabetes was defined as followings, (1) Medical personnel-diagnosed date or self-reported physician diagnosed date; (2) If a person took antidiabetic drugs or therapy of insulin within the 12 months before the medical examination, the treatment day was the diagnosed date of diabetes; (3) The date of medical recommendations for diabetes diet and physical activity programs. Considering that type 2 diabetes mellitus (T2DM) accounts for around 90% of diabetes among adults, and this research aimed at individuals aged >45 years, thus, it can be assumed that most cases of diabetes were T2DM in this study (Alberti and Zimmet, 1998; Diabetes Branch of Chinese Medical Association, 2021). The incident time of new cases of hypertension was based on (1) the date of medical personnel- or self-reported physician diagnosis in hospitals; (2) the date when a person took antihypertensive agents initially. As we know, participants' self-reported diagnosed time of chronic disease onset may induce recall bias. However, in this study, each study subject was followed up once a year, and they recalled diagnosed time of chronic disease within 1 year. Because the recalling time interval (1 year) was relatively short, and hence, we assumed that the bias on main results caused by this phenomenon was relatively small. In addition, the histories of individual medication or treatment of disease were collected during the follow-up, which further improves the accuracy of recalled diagnosed time.

# 2.3. Air pollution and exposure assessment

In this study, evaluation of personal air pollution exposure level was derived from the following two methods. (1) Annual mean particulate matter (PM) concentrations were estimated by satellite-based model; (2) Annual average gaseous pollutants levels were evaluated through the



Fig. 1. The flow chart of the participants selection.

Inverse Distance Weighted (IDW) modeling method.

The annual mean ambient  $PM_1$ ,  $PM_{2.5}$  and  $PM_{10}$  levels at 1-km spatial resolution in China were collected from the CHAP dataset (available at https://weijing-rs.github.io/product.html), which was calculated using satellite remote sensing and machine learning that considers the spatiotemporal heterogeneity of air pollution (Wei et al., 2019a, 2019b, 2020, 2021a, 2021b). A detailed methodology of the proposed spatiotemporal model was descried in **Supplementary Materials**. To estimate prolonged PM exposure levels among the individuals in the cohort study, the annual average concentration of PM during the study period from 2014 to 2018 was assigned as a time-varying exposure. Subsequently, these data were allocated to each participant's latitude and longitude geocoded by individual residential address.

The personal annual average exposure levels of ambient  $NO_2$  and  $SO_2$  were estimated through IDW modeling method using the real-time data on air pollution acquired from Air Quality Monitoring (AQM) stations. First, 24-h average concentrations of  $NO_2$  and  $SO_2$  between January 1, 2014 to December 31, 2018 were obtained from all fixed AQM stations in Tianjin Environmental Protection Bureau (a government agency that collects available data of air pollution in China). According to daily monitoring levels, monthly and annual average air pollutants levels of each monitoring site were calculated. Subsequently,

Baidu Map Application Programming Interface (http://lbsyun.baidu. com/) was used to acquire (1) geocoded latitude and longitude in WGS84 coordinates of individual residential address; (2) the absolute distances between residential addresses and nearby monitoring stations. Second, we used IDW model to calculate annual mean NO<sub>2</sub> and SO<sub>2</sub> concentrations exposed to each participant via combining with the latitude and longitude coded residential address and air pollutants' data derived from AQM stations. Accounting for the temporal variations of pollutants during 2014-2018, the annual mean levels of each ambient pollutant were calculated as a time-varying exposure, which is timevarying ambient pollutants exposure on 1-calendar year scale, and they were assigned to each participant who was alive or not suffering the study diseases (hypertension for hypertension-related analysis, diabetes for diabetes-related analysis) in that year during the follow-up period based on the individual coded address (Yang et al., 2019c; Zhang et al., 2020b). IDW modeling method selected data through the following principles. Commonly, the data of three closest monitoring sites were selected. If the pollution data were unavailable in the second or third nearest AQM station, the levels of the fourth nearest site would be selected (Milillo and Gardella, 2008). In environmental science, IDW is commonly used to conduct the estimation of individual exposure levels based on the data from fixed monitoring sites.

# 2.4. Meteorological data

Daily mean temperature and relative humidity data of three administrative districts in the Binhai New District were available from China Meteorological Data Sharing Service System (http://data.cma. cn/). And then, we calculated annual average temperature levels in three districts, and they were assigned to participants during the study period from 2014 to 2018.

## 2.5. Statistical analyses

Characteristics of study subjects at baseline were displayed as numbers (percentages) for categorical variables and mean  $\pm$  standard derivations for continuous variables. For hypertension-related cohort, the person-years of follow-up were calculated since January 1, 2014 until incident hypertension, or subjects who completed the follow-up period were censored on December 31st, 2018, whichever occurred first. For diabetes-related cohort, the person-years of follow-up were calculated since January 1, 2014 until the time of incident diabetes, or persons who completed the follow-up period were censored on December 31st, 2018, whichever censored on December 31st, 2018, whichever censored on December 31st, 2018, whichever came first.

Given that the annual mean PM<sub>2.5</sub> levels changed by years over the follow-up period, the annual mean PM<sub>2.5</sub> levels were calculated as timevarying exposure, and they were used to analyze the relationships of air pollutants and disease events through Cox proportional hazards model. Air pollutants' levels were introduced in analyses as continuous variable. The selected multi-covariates adjusted in the present study were time-varying age and body mass index (BMI), sex, smoking status, drinking frequency, and leisure exercise frequency, humidity and temperature. All analyses were performed by introducing certain risk factors gradually in adjustment models. In the crude model, no covariates were introduced. Subsequently, we performed the analyses with inserting the time-varying age and BMI, and sex in Model 1. Model 2 additionally expanded smoking status, drinking frequency, and status of leisure exercise as adjusted confounders. Apart from single-pollutant models, twopollutant models were further performed to evaluate the influences of multiple air pollution exposures on chronic diseases morbidity. The combinations of the double-pollutant model were PM1-NO2, PM2.5-NO2, PM<sub>10</sub>-NO<sub>2</sub>, and NO<sub>2</sub>-SO<sub>2</sub> models. Because in other bi-pollutant models, the results acquired from Pearson correlation analysis revealed that air pollutants were highly correlated with each other, these bi-pollutant models were not statistically analyzed (Table S1).

Modification effects by the confounders were tested using stratified analyses based on Model 2. The statistical interactions between ambient pollutants exposure and each subgroup characteristic were further assessed through a cross-product term in the Cox regression model.

To explore the C-R relationships of chronic cardiometabolic disease morbidity linked to long-term exposure to ambient PM pollutants, C-R curves were performed with restricted cubic spline (RCS) functions by adjusting for potential covariates in Model 2, using the medians of each PM exposure level as the reference. RCS was commonly used in cohort studies to evaluate the associations of prolonged exposure to ambient pollutants with human health combined with the Cox regression model (Chen et al., 2020; Grande et al., 2021; Hu et al., 2021a, 2021b; Lin et al., 2020a). To balance best fit and overfitting in the main splines for morbidity of hypertension, and diabetes linked to air pollution, the number of knots was selected between 3 and 7. According to Regression Modeling Strategies indicated, when the knots is 4, the fitting of the model is better. Because it not only considered the smoothness of the curve, but also avoided the reduction of accuracy caused by over-fitting (Harrell, 2015). As such, we chose RCS with 4 knots as main result. The results with other knots number were displayed in Supplementary Materials.

To test robustness, we carried out some sensitivity analyses. First, part of self-reported diagnosed time of diseases may bring a little deviations from the real time of diseases onset. We performed a logistic regression analysis to examine the impacts of average annual levels of ambient pollutants on both diseases during the follow-up time. Second, to minimize the potential effects of other cardiovascular diseases (CVD), we excluded cerebrovascular diseases, mental disease, and abnormal blood indicators at baseline, and conducted the analysis by the Cox regression model. Third, sugar or salt intake, and dust exposure may increase the risks of chronic non-communicable diseases incidence (Fecht et al., 2016; Genovesi et al., 2021; Khan and Sievenpiper, 2016; Vos et al., 2017), and hence the hazard ratios (HR) were re-calculated after excluding baseline salt addicts in hypertension analysis, sugar addicts in diabetes analysis, or participants who were exposure to occupational PM/dust in both diseases analyses, respectively. Last, because some studies indicated possible inverse associations between ambient temperature and blood pressure and/or diabetes (Su et al., 2014; Wang et al., 2017b), annual average temperature was further controlled on the basis of covariates in Model 3.

All statistical analyses were performed using the R (version 4.1.1) and SAS (version 9.4) Statistics Software. A two-sided test and *P*-value below 0.05 were used to detect significance.

# 3. Results

## 3.1. Description of the study subjects

Table 1 illustrated the baseline characteristics in the cohort of hypertension and diabetes.

A total of 48,357 participants with 198,261.61 person-years during the follow-up, among which 12,371 were onsets of hypertension. The mean age of the subjects was  $65.22 \pm 6.64$  years at the baseline, and BMI was  $24.35 \pm 2.92$  kg/m<sup>2</sup>. For diabetes cohort, 72,869 subjects were included in the final analysis, with 356,436.09 person-years and 2034 new incidents. The average age of the cohort was  $65.76 \pm 7.18$  years at baseline, and mean BMI was  $24.65 \pm 3.02$  kg/m<sup>2</sup>. Besides, in the cohort of each chronic non-communicable disease, the proportion of female accounted for approximately 55.0% (54.6% for hypertension vs 55.2% for diabetes). More than one fifth persons smoked cigarettes (former and current smokers), and almost 15% consumed alcohol (occasional and frequent drinking status).

# Table 1

Baseline characteristics of study population in hypertension and diabetes cohorts.

Characteristics	Hypertension cohort	Diabetes cohort
Age (years)	$65.22\pm6.64$	$65.76 \pm 7.18$
Sex (%)		
Male	21,967 (45.4)	32,651 (44.8)
Female	26,390 (54.6)	40,218 (55.2)
BMI (kg/m <sup>2</sup> )	$24.35\pm2.92$	$24.65\pm3.02$
Exercise frequency (%)		
Never	12,733 (26.3)	17,287 (23.7)
Occasionally	2749 (5.7)	3873 (5.3)
Frequently	32,595 (67.4)	51,397 (70.5)
Smoking status (%)		
Never	37,674 (77.9)	55,874 (76.7)
Former	1493 (3.1)	2650 (3.6)
Current	8904 (18.4)	14,027 (19.2)
Alcohol frequency (%)		
Never	41,356 (85.5)	61,653 (84.6)
Occasionally	3138 (6.6)	4923 (6.8)
Frequently	3485 (7.2)	5842 (8.0)
FBG (mmol/L)	$5.65 \pm 1.39$	$5.28 \pm 0.65$
SBP (mmHg)	$122.71 \pm 11.50$	$126.65 \pm 12.79$
DBP (mmHg)	$76.33 \pm 6.50$	$\textbf{77.95} \pm \textbf{7.04}$
New onsets (%)	12,371 (25.5)	2034 (2.8)
Total number	48,357 (100.0)	72,869 (100.0)

Abbreviation: BMI, Body mass index; FBG, Fasting blood glucose; SBP, Systolic blood pressure; DBP, Diastolic blood pressure.

# 3.2. Ambient pollution exposure and meteorological data

Fig. 2 showed the temporal trends of annual average levels of air pollution exposure during the study period for the initial cohort with 97,982 participants. Besides, the predicted concentrations of ambient pollutants in 2014 in Binhai New district were displayed in Fig. S1.

The mean concentrations of annual ambient pollutants exposure were 35.81  $\mu$ g/m<sup>3</sup> (Range: 29.53  $\mu$ g/m<sup>3</sup> to 49.78  $\mu$ g/m<sup>3</sup>) for PM<sub>1</sub>, 54.61  $\mu$ g/m<sup>3</sup> (Range: 44.47  $\mu$ g/m<sup>3</sup> to 69.22  $\mu$ g/m<sup>3</sup>) for PM<sub>2.5</sub>, 101.83  $\mu$ g/m<sup>3</sup> (Range: 87.58  $\mu$ g/m<sup>3</sup> to 120.60  $\mu$ g/m<sup>3</sup>) for PM<sub>10</sub>, 47.29  $\mu$ g/m<sup>3</sup> (Range: 39.86  $\mu$ g/m<sup>3</sup> to 52.84  $\mu$ g/m<sup>3</sup>) for NO<sub>2</sub>, 22.98  $\mu$ g/m<sup>3</sup> (Range: 12.12  $\mu$ g/m<sup>3</sup> to 41.17  $\mu$ g/m<sup>3</sup>) for SO<sub>2</sub>, respectively. The annual and overall average levels of all pollutants in hypertension and diabetes cohorts during the study period were illustrated in Table S2 (A), and the data in each cohort were approximately as same as those calculated from total 97,982 participants. What's more, the temperature and relative humidity by district in the Binhai New Area and calendar year were shown in Table S2 (B).

## 3.3. Association between ambient pollution and incidence

As revealed in Table 2, long-term exposure to single ambient pollutant increased the morbidity of hypertension in both crude and multi-adjusted models. The HR and 95% confidence intervals (CI) in final model were 1.49 (95% CI: 1.45, 1.52), 1.28 (95% CI: 1.26, 1.30), 1.17 (95% CI: 1.15, 1.18), 1.21 (95% CI: 1.17, 1.25), 1.33 (95% CI: 1.31, 1.35) for per 10  $\mu$ g/m<sup>3</sup> increment of PM<sub>1</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, and SO<sub>2</sub>, separately. The similar significant positive relationships were also obtained for the relationship of diabetes incidence linked to PM<sub>1</sub>, PM<sub>2.5</sub>, PM<sub>10</sub>, and SO<sub>2</sub>, with the HR of 1.17 (95% CI: 1.11, 1.23), 1.09 (95% CI: 1.04, 1.13), 1.06 (95% CI: 1.02, 1.09), and 1.24 (95% CI: 1.19, 1.29) in multivariate model, respectively. For prolonged NO<sub>2</sub> exposure, although the effect estimate was not significant, it still revealed an adverse impact on diabetes onset with the HR of 1.02 (95% CI: 0.95, 1.10).

In double-pollutant models (Table 3), the effect estimates of  $PM_1$  levels on hypertension were enhanced after adjustment for  $NO_2$  exposure levels. Similar increasing relationships were also observed of  $PM_1$ ,  $PM_{2.5}$ ,  $PM_{10}$  or  $SO_2$  levels and diabetes after  $NO_2$  levels were controlled. Overall, the results of these two-pollutant analyses were consistent with that in the single-pollutant models.

Fig. 3 illustrated the shapes of C-R curve between PM and the occurrence of hypertension or diabetes after adjustment for multicovariates in the single-pollutant model. In the shape of hypertension risk estimates, as the increase of  $PM_1$  and  $PM_{2.5}$  concentrations, the shape of curve showed a steeply increasing linear pattern. For  $PM_{10}$ , it rose somewhat faster before the concentration of around 115  $\mu$ g/m<sup>3</sup>, and then slightly stabilized at higher levels. Also, the risk of  $PM_1$  over the entire concentration range with diabetes morbidity revealed the consistent trend as that in hypertension. However, for other PM-linked-



Fig. 2. The temporal trends of annual average levels of ambient pollution exposure in the initial study population (N = 97,982) during the study period from 2014 to 2018.

to diabetes onsets, the curves were close horizontal at the lower concentration ranges ( $PM_{2.5} < nearly 48 \ \mu g/m^3$ ;  $PM_{10} < nearly 95 \ \mu g/m^3$ ). Then, it increased almost linearly, and became apparently steeper at higher levels.

## 3.4. Stratified analyses and sensitivity analyses

The results of stratified Cox models for diseases linked to prolonged air pollution exposure were summarized in Tables 4–5. The impacts of air pollutants exposure on hypertension incidence were stronger in younger adults, people with high BMI, and frequent alcohol intake (*P*value for interaction <0.05). For diabetes, the more pronounced effects in modifications by age were consistent with those reported from hypertension. In the subgroups of BMI, apart from NO<sub>2</sub>, the higher associations between ambient pollutants exposure and the incidence of diabetes exited in participants with high BMI, which were similar to the results derived from hypertension analyses. Besides, the results of twopollutant stratified models were summarized in Tables S3–S6, and the results of both diseases with ambient pollution were similar to those from each single-pollutant model.

The data on sensitivity analyses were reported in Table S7. For incidence of hypertension, the effect estimates from the logistic regression analysis were consistent with the results obtained from Cox regression models. Moreover, among individuals with no occupational dust exposure, no excessive salt intake, and no potential affected diseases (not suffered other CVD, cerebrovascular diseases, mental disease, and abnormal blood indicators) at baseline, the directions of ambient pollution-morbidity associations did not change. After adding ambient temperature as a covariate, we found the HR decreased for hypertension morbidity linked to prolonged PM and SO<sub>2</sub> exposure, and a slightly elevated HR revealed for NO2 exposure. But these little changes of HR did not alter the directions of main associations. As to the associations of diabetes morbidity with PM10, PM2.5, and SO2, the HR directions displayed from multi-covariates model were consistent with the main effects in each selected population. No significant associations were obtained for NO<sub>2</sub>- morbidity in most sensitivity analyses (P-value  $\geq$ 0.05). However, across these sensitivity analyses, apart from the results of adding meteorological factors as covariates, the weakest effect revealed after sugar addicts were removed at baseline, and the HR was 1.02 (95% CI: 0.95, 1.09), which still suggested a positively adverse influence. Generally, whether for hypertension or diabetes, the results in sensitivity analysis were equivalent to the main analyses.

## 4. Discussion

This prospective cohort study showed the risk of hypertension and diabetes incidence increased by long-term exposure to  $PM_1$ ,  $PM_{2.5}$ ,  $PM_{10}$ ,  $NO_2$ , and  $SO_2$  at high levels among middle-aged and elderly residents living in Tianjin. In single models, the strongest HR revealed in  $PM_1$ , followed by  $SO_2$ ,  $PM_{2.5}$ ,  $NO_2$ , and  $PM_{10}$  in hypertension analysis. For diabetes analysis, the strongest HR revealed in  $SO_2$ , followed by  $PM_1$ ,  $PM_{2.5}$ ,  $PM_{10}$ , and  $NO_2$ . The significant effect estimates in the two-pollutant models were found except for  $NO_2$ -diabetes. The findings also suggested that participants less than 60 years old, with  $BMI \ge 24$  kg/m<sup>2</sup>, and frequent alcohol intake were more sensitive to ambient pollutants exposure in hypertension.

## 4.1. Hypertension

Air pollution has been considered as a risk factor for hypertension. Several studies have reported that the long-term exposure to ambient pollution was significantly related to the increased risk of hypertension incidence in all-aged populations, but the data obtained from cohort studies was limited, especially among middle-aged and elderly persons. Four epidemiological studies (Dong et al., 2013; Liu et al., 2017; Wu et al., 2021; Xie et al., 2018; Yang et al., 2019a) carried out in northern Table 2

Items	HR (95% CI) for single-pollutant model								
	PM <sub>1</sub> PM <sub>2.5</sub>		PM10	NO <sub>2</sub>	SO <sub>2</sub>				
Hypertension									
Crude model	1.53 (1.50-1.56)	1.31 (1.29–1.33)	1.19 (1.18–1.21)	1.27 (1.23–1.32)	1.36 (1.34–1.38)				
Model 1	1.49 (1.45–1.52)	1.28 (1.26–1.30)	1.17 (1.15–1.18)	1.23 (1.19–1.28)	1.33 (1.31–1.35)				
Model 2	1.49 (1.45–1.52)	1.28 (1.26–1.30)	1.17 (1.15–1.18)	1.21 (1.17–1.25)	1.33 (1.31–1.35)				
Diabetes									
Crude model	1.24 (1.18–1.31)	1.14 (1.09–1.18)	1.09 (1.06–1.13)	1.07 (0.99–1.15)	1.30 (1.25–1.35)				
Model 1	1.17 (1.11–1.24)	1.09 (1.05–1.14)	1.06 (1.03-1.09)	1.04 (0.96–1.11)	1.24 (1.20-1.29)				
Model 2	1.17 (1.11–1.23)	1.09 (1.04–1.13)	1.06 (1.02–1.09)	1.02 (0.95–1.10)	1.24 (1.19–1.29)				

Adjusted HR (95%CI) of hypertension and diabetes morbidity linked to each  $10 \ \mu g/m^3$  increase in air pollutants. (Single-pollutant model).

Abbreviation: HR: Hazard ratios; PM<sub>1</sub>: Ultrafine particulate matter; PM<sub>2.5</sub>: Fine particulate matter; PM<sub>10</sub>: Inhalable particulate matter; NO<sub>2</sub>: Nitrogen dioxide; SO<sub>2</sub>: Sulphur dioxide.

Crude model, adjusted no covariates; Model 1, adjusted for sex (male and female), age (continuous variable), and BMI (continuous variable); Model 2, Model 1+adjusted for smoking status (never, former, or current), frequency of alcohol intake (never, occasionally, or frequently), and frequency of exercise (never, occasionally, frequently).

#### Table 3

Adjusted HR (95%CI) of hypertension and diabetes morbidity linked to each 10 µg/m<sup>3</sup> increase in air pollutants. (Double-pollutant model).

Items	HR for double-pollutant model A HR for double-p		HR for double-poll	lutant model B HR for doub		utant model C	HR for double-pollutant model D	
	PM <sub>1</sub>	NO <sub>2</sub>	PM <sub>2.5</sub>	NO <sub>2</sub>	PM <sub>10</sub> NO <sub>2</sub>		SO <sub>2</sub>	NO <sub>2</sub>
Hypertension								
Crude model	1.54 (1.51–1.58)	0.98 (0.94–1.01)	1.32 (1.29–1.34)	0.98 (0.94–1.02)	1.17 (1.16–1.19)	1.14 (1.10–1.18)	1.37 (1.34–1.39)	0.98 (0.95–1.02)
Model 1	1.50 (1.46–1.54)	0.97 (0.94–1.01)	1.29 (1.26–1.31)	0.98 (0.94–1.02)	1.15 (1.14–1.17)	1.14 (1.10–1.18)	1.34 (1.31–1.36)	0.98 (0.95–1.02)
Model 2	1.51 (1.47–1.55)	0.94 (0.91–0.98)	1.29 (1.27–1.31)	0.95 (0.91–0.99)	1.15 (1.14–1.17)	1.10 (1.06–1.14)	1.34 (1.32–1.37)	0.95 (0.92-0.99)
Diabetes								
Crude model	1.33 (1.25–1.41)	0.77 (0.71-0.85)	1.21 (1.16–1.27)	0.76 (0.69–0.84)	1.11 (1.08–1.15)	0.84 (0.77–0.92)	1.38 (1.32–1.44)	0.73 (0.67–0.80)
Model 1	1.25 (1.18–1.33)	0.78 (0.71-0.85)	1.16 (1.10–1.21)	0.78 (0.70–0.84)	1.08 (1.04–1.12)	0.84 (0.77–0.91)	1.32 (1.26–1.38)	0.73 (0.67–0.80)
Model 2	1.25 (1.18–1.33)	0.76 (0.70–0.83)	1.15 (1.10–1.21)	0.76 (0.69–0.83)	1.08 (1.04–1.11)	0.82 (0.76–0.90)	1.32 (1.26–1.38)	0.72 (0.66–0.79)

Abbreviation: HR: Hazard ratios; PM<sub>1</sub>: Ultrafine particulate matter; PM<sub>2.5</sub>: Fine particulate matter; PM<sub>10</sub>: Inhalable particulate matter; NO<sub>2</sub>: Nitrogen dioxide; SO<sub>2</sub>: Sulphur dioxide.

Crude model, adjusted no covariates; Model 1, adjusted for sex (male and female), age (continuous variable), and BMI (continuous variable); Model 2, Model 1+adjusted for smoking status (never, former, or current), frequency of alcohol intake (never, occasionally, or frequently), and frequency of exercise (never, occasionally, frequently).

China have documented significantly positive associations between prolonged PM (PM2.5, and PM10) exposure and prevalence of hypertension, with the odds ratio (OR) and 95% CI ranges from 1.03 (95% CI: 1.00, 1.07) to 1.12 (95% CI: 1.08, 1.16). Besides, the significant associations of hypertension prevalence linked to long-term PM exposure were also reported among children and adolescents, and these subjects came from both northern and southern settings in China (Dong et al., 2014; Wu et al., 2020; Zhang et al., 2019, 2020b). However, the participants above were relatively younger than recruiters in our study, and the age heterogeneity may cause differences in risk effects. Two community-based studies (Li et al., 2019a; Yang et al., 2018) have evaluated the adverse risk effects of prolonged PM1 pollution on hypertension and blood pressure levels, but the average accumulated concentrations of PM<sub>1</sub> reached to 55.99 and 66.00  $\mu$ g/m<sup>3</sup> in these two work, which were higher than that in our study (35.81  $\mu$ g/m<sup>3</sup>). All above literatures were based on cross-sectional design, which induced the limitation in addressing the temporal relationships between air pollutants levels and hypertension incidence over a long period, leading to the bias for risk estimates. To our best knowledge, two established cohorts from China-PAR project and China-NFC found that the HR were up to 1.11 (95% CI: 1.05–1.17) and 1.537 (95% CI: 1.515, 1.560) when people were exposed to PM2.5 and PM10 for a long time, respectively (Huang et al., 2019; Li et al., 2021). Yet, only China-NFC cohort (Li et al., 2019b; Yan et al., 2020) were performed to explore the incident risk of hypertension in association with gaseous pollutants such as NO2 and SO2, but it did not take the effects of time-varying changes of air pollutants level into account. Also, it was a retrospective study and the diagnosed date was only obtained through recalling. Compared with the professional doctors' diagnostic information, it may result to inaccurate results.

#### 4.2. Diabetes

Numerous literatures have examined the prolonged PM exposure in relation to morbidity of diabetes. Two prospective cohorts derived from mainland China examined the HR of incident diabetes attributed to longterm PM<sub>2.5</sub> exposure, which were 1.16 (95% CI: 1.06-1.26) with a 10  $\mu g/m^3$  increment (Liang et al., 2019), and 1.16 (95% CI: 1.07–1.26) in the fourth quartile (Lao et al., 2019). Another research reported that the HR was 1.17 (95% CI: 1.08–1.26) per 10  $\mu$ g/m<sup>3</sup> increase of PM<sub>10</sub> (Wang et al., 2020). In addition, an elderly-based cohort conducted in Hong Kong (Oiu et al., 2018) revealed significant relationship between PM<sub>2.5</sub> and incidence of diabetes with HR up to 1.15 (95% CI: 1.05-1.25). In this literature, the mean annual  $PM_{2.5}$  level was 35.8  $\mu$ g/m<sup>3</sup>, which was lower than 54.61  $\mu$ g/m<sup>3</sup> in our study. However, all the mentioned literatures did not evaluate the influences of other ambient pollutants. Currently, the longitudinal effects of gaseous pollutants with diabetes were insufficient. Resemble to hypertension, only China-NFC cohort evaluated the risk of NO2 and SO2 for incident diabetes, but the assessment of individual air pollutant exposure was accumulated data other than temporal changes, and the self-reported diagnosed data of diabetes may induce bias of risk estimates.

By contrast, combined with time-varying pollution data, this largepopulation prospective cohort analyses provided the evidence on the elevated risks of incident hypertension and diabetes affected by air pollutants after long-term exposure among Chinese adults aged  $\geq$ 45 years. To diminish potential effects of other disease status and dietary consumption on study diseases, we additionally performed a series of sensitive analyses. Expectedly, the relationship results were robust. In addition, compared with the results in aforementioned studies conducted among China-NFC cohort and China-PAR (Huang et al., 2019; Li



**Fig. 3.** The concentration-response curve (knots = 4) for the relationships of prolonged  $PM_1$ ,  $PM_{2.5}$ , and  $PM_{10}$  exposure with cardiometabolic disease incidence. The X-axis is the mean levels of  $PM_1$ ,  $PM_{2.5}$  and  $PM_{10}$  in the cohort study. The Y-axis is the log relative risk. The blue solid lines represent the average effect estimate, and the light blue areas represent the 95% confidence intervals. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

et al., 2021; Liang et al., 2019; Yan et al., 2020), it might posit a slightly overestimated effect estimates in our study. The above difference might be explained by the relatively narrow range of air pollutants in our study. Although HR seemed stable in any sensitive analyses, to acquire more comprehensive effect estimations, further investigations should be conducted in regions with wide range levels of air pollution.

# 4.3. C-R curves

The shape of exposure-response curves between annual PM exposure

and hypertension onsets in our study was resemble to that for the association of long-term  $PM_{2.5}$  exposure with total coronary heart disease in China-PAR cohort (Li et al., 2020). Another recent published study also illustrated almost liner elevated trends for the relationship of short-term  $PM_{2.5}$  exposure and blood pressure (Hu et al., 2021a, 2021b). The plots of association between PM with diabetes onsets indicated that HR enhanced in a linear trend at high exposure levels of PM (over 54  $\mu g/m^3$  for  $PM_{2.5}$ , and over 100  $\mu g/m^3$  for  $PM_{10}$ ), whereas, no significant increase were observed at low levels (Fig. 3), These findings were slightly different from that displayed in  $PM_1$ . Till now, literatures on the

#### Table 4

Stratified analyses for HR (95% CI) of hypertension related to an increase of  $10 \,\mu\text{g/m}^3$  in ambient pollutants.

Stratified items	PM <sub>1</sub>		PM <sub>2.5</sub>		PM <sub>10</sub>		NO <sub>2</sub>		SO <sub>2</sub>	
	HR (95% CI) <sup>a</sup>	Pinteraction								
Age		< 0.001		< 0.001		< 0.001		< 0.001		< 0.001
<60 years	2.04		1.65				1.60		1.73	
	(1.93-2.16)		(1.59 - 1.72)				(1.45–1.76)		(1.66 - 1.80)	
$\geq$ 60 years	1.44		1.24		1.16		1.18		1.30	
	(1.41 - 1.48)		(1.22 - 1.27)		(1.14–1.17)		(1.14-1.23)		(1.28 - 1.32)	
Sex		0.280		0.136		0.115		0.251		0.207
Male	1.46		1.26		1.16		1.24		1.31	
	(1.42 - 1.51)		(1.23 - 1.29)		(1.13 - 1.18)		(1.18 - 1.31)		(1.28 - 1.35)	
Female	1.50		1.29		1.18		1.19		1.34	
	(1.46 - 1.55)		(1.26 - 1.32)		(1.16 - 1.20)		(1.14–1.25)		(1.32 - 1.37)	
BMI		< 0.001		< 0.001		< 0.001		< 0.001		< 0.001
$<24 \text{ kg/m}^2$	1.37		1.20		1.12		1.12		1.26	
	(1.33 - 1.42)		(1.18 - 1.24)		(1.10 - 1.14)		(1.06 - 1.18)		(1.23 - 1.29)	
$\geq$ 24 kg/m <sup>2</sup>	1.58		1.33		1.21		1.29		1.38	
	(1.54–1.63)		(1.31 - 1.36)		(1.19 - 1.23)		(1.24–1.35)		(1.35-1.41)	
Smoking status		0.299		0.218		0.027		0.002		0.122
Never	1.48		1.27		1.16		1.18		1.32	
	(1.44–1.52)		(1.25 - 1.29)		(1.14–1.18)		(1.14–1.23)		(1.30 - 1.35)	
Former	1.65		1.39		1.27		1.25		1.40	
	(1.50 - 1.82)		(1.29 - 1.49)		(1.20 - 1.35)		(1.06 - 1.47)		(1.30 - 1.50)	
Current	1.48		1.28		1.18		1.34		1.34	
	(1.41–1.55)		(1.23 - 1.32)		(1.15 - 1.22)		(1.24–1.45)		(1.30 - 1.39)	
Alcohol		< 0.001		< 0.001		< 0.001		< 0.001		< 0.001
frequency										
Never	1.47		1.27		1.16		1.19		1.32	
	(1.43 - 1.50)		(1.24 - 1.29)		(1.14–1.18)		(1.15 - 1.24)		(1.30 - 1.34)	
Occasionally	1.51		1.28		1.18		1.22		1.35	
	(1.40 - 1.62)		(1.22 - 1.35)		(1.13 - 1.23)		(1.08 - 1.37)		(1.28 - 1.42)	
Frequently	1.63		1.36		1.25		1.45		1.41	
	(1.51 - 1.75)		(1.29 - 1.43)		(1.20 - 1.31)		(1.29 - 1.63)		(1.34–1.49)	
Exercise		0.282		0.903		0.796		0.586		0.284
frequency										
Never	1.48		1.29		1.18		1.26		1.37	
	(1.42 - 1.54)		(1.25 - 1.33)		(1.15 - 1.21)		(1.17 - 1.35)		(1.33 - 1.41)	
Occasionally	1.30		1.14		1.08		1.03		1.20	
	(1.19–1.42)		(1.07 - 1.22)		(1.02 - 1.13)		(0.89–1.19)		(1.13 - 1.28)	
Frequently	1.51		1.28		1.17		1.21		1.33	
	(1.47–1.55)		(1.26–1.31)		(1.15–1.19)		(1.17–1.27)		(1.31–1.36)	

Abbreviation: HR: Hazard ratios; PM<sub>1</sub>: Ultrafine particulate matter; PM<sub>2.5</sub>: Fine particulate matter; PM<sub>10</sub>: Inhalable particulate matter; NO<sub>2</sub>: Nitrogen dioxide; SO<sub>2</sub>: Sulphur dioxide.

<sup>a</sup> Multivariable covariates were controlled, including age, gender, BMI, smoke status, frequency of alcohol, and frequency of physical activity.

C-R relationship curves for diabetes linked to ambient pollution are rare, especially for long-term effects. The evidence provided in our study may have guiding significance for cardiometabolic management in susceptible populations. However, we were unable to determine the C-R curve in the lower ranges due to the heavy PM pollution in Tianjin. To our best knowledge, hypertension and diabetes are major cardiometabolic risk factors of CVD. Therefore, understanding the C-R curves between air PM pollution and these two diseases is crucial to reduce the morbidity and development of CVD. To determine the threshold that does not arouse harmful human health, more comprehensive and valid evidence are needed on the influence pattern of PM at a wider concentrations range on hypertension or diabetes morbidity. The graphical results with other differed number of knots were displayed as Figs. S2-S5. These findings showed that the trends of C-R plots with knots of 3 or 5 were basically similar to that with knots of 4. However, while knots is 6 or 7, the graphical results are overfitted.

## 4.4. Effect modifications

In the stratified analysis, age and BMI modified the effect of air pollutants on morbidity of both two diseases. In addition, alcohol frequency modified the effect of air pollutants on morbidity of hypertension. Compared with residents who aged less than 60 years old, older adults had lower HR. Another cohort exposed to high levels of ambient pollutants revealed the consistent trend (Shan et al., 2020; Yan et al., 2020; Li et al., 2021). In contrast to younger adults, the responsiveness of the elderly people to sympathetic and autonomic nervous system stimuli was relatively weak (Cohen et al., 2012; Zhang et al., 2019). Besides, younger individuals are more likely affected by risk factors of chronic diseases, such as environmental pressure, and unhealthy lifestyle (Mizia et al., 2021; Zhu et al., 2019). As to alcohol frequency, the highest HR was observed among participants with frequent alcohol consumption, followed by occasional and never ones in hypertension analyses. The similar trend was also observed in a prior study conducted in Chinese adults exploring the impacts of  $SO_2$  exposure with chronic disease, though null significant interactions were observed of ambient pollutants exposure and drinking status (Shan et al., 2020). Yet, the role of alcohol in this process remains unclear, which is a direction that requires further study and verification.

## 4.5. Possible mechanisms

The understanding of biological mechanism underlying air pollutionmediated hypertension and diabetes risks is still evolving. The general assumption is that air pollutant exposure may trigger oxidative stress, systematic inflammation response, autonomic nervous system imbalance, then induce insulin resistance and abnormal epigenetic changes. Subsequently, blood pressure and glucose levels elevated, inducing hypertension or diabetes (Rajagopalan et al., 2018). Additionally, PM<sub>1</sub> exerted the strongest associations in both chronic diseases, followed by

## Table 5

Stratified analyses for HR (95% CI) of diabetes related to an increase of  $10 \,\mu\text{g/m}^3$  in ambient pollutants.

Stratified items	$PM_1$		PM <sub>2.5</sub>		PM <sub>10</sub>		NO <sub>2</sub>		SO <sub>2</sub>	
	HR (95% CI) <sup>a</sup>	Pinteraction								
Age		< 0.001		< 0.001		< 0.001		0.023		< 0.001
<60 years	1.74		1.46		1.33		1.26		1.64	
-	(1.57 - 1.94)		(1.35 - 1.57)		(1.25 - 1.41)		(1.06 - 1.49)		(1.52 - 1.78)	
$\geq$ 60 years	1.11		1.04		1.03		1.00		1.20	
	(1.05 - 1.18)		(0.99–1.09)		(0.99 - 1.07)		(0.92 - 1.08)		(1.15-1.26)	
Sex		0.710		0.844		0.734		0.092		0.870
Male	1.26		1.09		1.09		1.10		1.30	
	(1.17 - 1.37)		(1.03 - 1.16)		(1.04–1.15)		(0.98 - 1.22)		(1.23 - 1.38)	
Female	1.23		1.08		1.10		0.97		1.29	
	(1.15 - 1.32)		(1.02 - 1.14)		(1.05 - 1.15)		(0.88 - 1.07)		(1.22–1.35)	
BMI		0.018		0.010		0.037		0.006		0.013
<24 kg/m <sup>2</sup>	1.08		1.02		1.01		1.10		1.16	
	(0.98 - 1.18)		(0.95–1.09)		(0.96 - 1.07)		(0.99 - 1.23)		(1.09 - 1.24)	
$\geq$ 24 kg/m <sup>2</sup>	1.22		1.13		1.08		0.97		1.28	
	(1.14–1.31)		(1.07 - 1.19)		(1.04 - 1.13)		(0.88 - 1.07)		(1.22–1.35)	
Smoking status		0.265		0.450		0.242		0.508		0.258
Never	1.15		1.08		1.04		1.00		1.22	
	(1.08 - 1.22)		(1.03 - 1.13)		(1.01 - 1.08)		(0.92 - 1.09)		(1.16–1.27)	
Former	1.47		1.24		1.19		1.41		1.52	
	(1.16 - 1.86)		(1.04 - 1.48)		(1.03 - 1.37)		(1.00 - 1.98)		(1.28 - 1.81)	
Current	1.19		1.09		1.07		1.03		1.25	
	(1.05 - 1.34)		(0.99 - 1.19)		(1.00 - 1.15)		(0.87 - 1.22)		(1.14–1.36)	
Alcohol		0.122		0.376		0.491		0.173		0.045
frequency										
Never	1.14		1.07		1.05		0.99		1.21	
	(1.08 - 1.21)		(1.02 - 1.12)		(1.01 - 1.08)		(0.91 - 1.07)		(1.16–1.27)	
Occasionally	1.45		1.28		1.17		1.55		1.40	
	(1.21 - 1.73)		(1.12–1.46)		(1.06 - 1.30)		(1.19 - 2.01)		(1.22 - 1.60)	
Frequently	1.18		1.03		1.02		1.00		1.32	
	(0.97 - 1.44)		(0.89 - 1.20)		(0.90 - 1.15)		(0.77 - 1.29)		(1.14–1.52)	
Exercise		0.777		0.694		0.583		0.185		0.504
frequency										
Never	1.20		1.11		1.08		1.12		1.28	
	(1.08 - 1.34)		(1.03 - 1.21)		(1.01 - 1.15)		(0.96 - 1.30)		(1.18 - 1.39)	
Occasionally	1.09		1.04		1.02		1.05		1.22	
	(0.88–1.37)		(0.88 - 1.22)		(0.90–1.16)		(0.78 - 1.42)		(1.04–1.44)	
Frequently	1.16		1.08		1.05		0.99		1.22	
	(1.09–1.24)		(1.03–1.14)		(1.01–1.09)		(0.91–1.08)		(1.17–1.28)	

Abbreviation: HR: Hazard ratios; PM<sub>1</sub>: Ultrafine particulate matter; PM<sub>2.5</sub>: Fine particulate matter; PM<sub>10</sub>: Inhalable particulate matter; NO<sub>2</sub>: Nitrogen dioxide; SO<sub>2</sub>: Sulphur dioxide.

<sup>a</sup> Multivariable covariates were controlled, including age, gender, BMI, smoke status, frequency of alcohol, and frequency of physical activity.

 $PM_{2.5}$ , then  $PM_{10}$ . A possible explanation is that, with the smaller size of particles, the ratio of surface area to mass was higher, which makes them easier to enter the lung alveolar tissue and the systemic circulation (Baudin et al., 2001; Chuang et al., 2005). Also, more harmful toxic constituents attached to smaller-sized particles, causing more serious deleterious effects (Wang et al., 2006). Unlike the pathway of PM, few studies revealed biological mechanisms leading to direct elevated glucose, insulin resistance or increased blood pressure after NO<sub>2</sub> or SO<sub>2</sub> exposure. However, some researchers have demonstrated that the levels of circumstantial biomarkers such as C-reactive protein or blood fibrinogen level may enhance mediated by PM<sub>2.5</sub>, PM<sub>10</sub>, or SO<sub>2</sub> (Lee et al., 2018; Wang et al., 2017a).

## 4.6. Strength and limitations

There are several strengths in this study. First, this is a prospective cohort study that provided the evidence on the associations between prolonged ambient pollutants exposure and onsets of hypertension and diabetes among middle-aged and elderly residents in China. Second, morbidity date of chronic-diseases were directly derived from physician diagnosis or participants' self-reported physician diagnosis, which would provide more accuracy of diagnostic results, thereby improving the persuasiveness of the effect estimates. What's more, PM exposure levels were estimated by STET model using satellite data with highresolution of 1 km, and the method ensured accuracy of data on PM exposure in the spatial distribution. For NO<sub>2</sub> and SO<sub>2</sub>, IDW model was used to evaluate individual exposure levels, and it is commonly employed in the valid assessments of gaseous pollutants derived from fix AQM stations. Finally, whether in single-pollutant model, doublepollutant model, stratified analyses, C-R curves, or sensitivity analyses such as the exclusion of salt or sugar addicts, the results for PM and SO<sub>2</sub> exposure were robust to some extent, whereas, the finding of NO<sub>2</sub> were unstable. Therefore, more reliable and comprehensive studies are required to evaluate chronic harmful health outcomes linked to NO<sub>2</sub>.

Despite the strengths mentioned, some limitations should not be ignored. First, because the variables such as personal education, and economic income were not available in the health examination system, the possible confounded effects of these factors could not be considered. Second, due to the lack of data, this study did not take indoor air pollution into account. Yet, for residents who warm and/or cook with biofuels, large amount of PM pollution exhausts may induce more apparent unfavorable effects than outdoor pollution (Dioni et al., 2011; Nandasena et al., 2012). Another limitation is that dietary habits such as vegetables, fruits, meat and poultry intake status were not obtained at the baseline and follow-up, although the results seemed steady after participants with excessive salt or sugar intake were excluded. It implies that studies are expected with more accuracy and comprehensive diet information in the future. In addition, an accumulated evidence indicated that noise was linked to adverse hypertension outcomes (Cai et al., 2018; Fecht et al., 2016; So et al., 2020). As a traffic-related pollutant,

NO<sub>2</sub> often appears couple with traffic noise, herein, traffic noise may intense the NO2-induced effect. Yet, noise was not available in our model for further analyses. Besides, after reviewing the previous literatures on the prolonged air pollution exposure with incidence of hypertension or diabetes, we found the follow-up time was commonly 5 years or more (Oba et al., 2020; Paoin et al., 2021; Renzi et al., 2018; Sørensen et al., 2011, 2012; Zhang et al., 2021). To ensure enough time to capture the outcomes, the population data was derived from 5-year follow-up period in this study. Yet, since hypertension and diabetes are chronic diseases, the results may be affected differently by the differed length of follow-up time (such as 5 years, 6-10 years, 10-15 years even more). Additional studies with a longer follow-up time are warranted to evaluate the above hypothesized associations (Park et al., 2015). At last, the problems of ambient pollution in northern China are more serious than that in southern China, hence, the findings at high ambient pollutants levels in this study among northern China may not expand to the effect estimates in the settings in south. More direct evidences derived from both northern and southern settings in China are necessary.

# 5. Conclusions

In sum, this cohort study revealed that chronic exposure to ambient pollutants with high concentrations were related to the morbidity of hypertension and diabetes among middle-aged and elderly residents in China. In general, HR slightly decreased after temperature and humidity were taken into potential confounders, and it suggested the modified influences of meteorological factors on the strengths of relationships between air pollutants and hypertension or diabetes incidence. Furthermore, the shapes of C-R curves showed significantly liner increasing trends of effect estimates with the increment of PM concentrations, and no thresholds existed. Part new findings broaden our knowledge on chronic non-communicable diseases morbidity related to prolonged exposure to ambient pollutants. Simultaneously, these results provided the local governments a clearer direction in implementing effective policies to promote human health by reducing air pollution in China.

# Credit author statement

Mengfan Yan: Conceptualization, Data curation, Formal analysis, Visualization of results, Validation of data, Roles/writing-original draft; Fang Hou: Data curation, Investigation, Validation of data; Jiahui Xu, Huanyu Liu: Data curation, Formal analysis; Hongyan Liu, Yourui Zhang, Hao Liu, Chunlan Lu: Data curation, Investigation; Pei Yu, Jing Wei, Nai-jun Tang: Project administration, Conceptualization, Supervision, Funding acquisition, Writing-review &editing.

# Declaration of competing interest

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

# Data availability

The authors are unable or have chosen not to specify which data has been used.

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# Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.114251.

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