Is there a casual relation between air pollution and dementia?

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Received: 6 June 2022 / Accepted: 20 September 2022 / Published online: 2 November 2022
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Abstract
Dementia has been cited as a critical public health risk in the contemporary world, while few empirical researchers try to reveal the casual relationship between air pollutant concentrations (APCs) and dementia, especially given the increasing prevalence of air pollution on a global scale. Accordingly, this paper tries to infer the causal relationship between APCs and dementia. The 59,605 valid data was compiled through a combination of the statistic from the China Family Panel Study, China Environmental Statistics Yearbook, World Meteorological Association and China National Bureau of Statistics. The RD design of this study utilizes the discontinuous variation in APCs and dementia as one crosses the Huai River boundary, which is an arbitrary heating policy that causes the significant difference in APCs between the north and south of China. We used stata17.0 to analyze the data. The results of the RD regression indicated that a 100 μg/m³ rise in APCs led to an increase of 42.4% in the hazard ratio of suffering dementia (Coeff=-0.58, SD=0.23, P < 0.05). Meanwhile, heterogeneous models revealed that the hazard ratio of suffering dementia by APCs was more significant in the older compared to younger (coeff=1.35 vs coeff=1.55, P < 0.05), male compared to female (coeff=1.62 vs coeff=0.71, P < 0.05), smoking compared to non-smoke (coeff=2.12 vs coeff=0.93, P < 0.05), and thin groups compared to medium and obesity (coeff=2.05 vs coeff=1.22, coeff=1.28, P < 0.05). In addition, the O3 and SO2 were the air pollutants with the highest (coeff=1.54, P < 0.05) and lowest effects (coeff=0.81, P < 0.05) on the hazard ratio of suffering dementia among the five APCs, respectively. And the robustness of the results was ensured by changing the RD bandwidth, polynomial order. The results indicated that APCs significantly induced the hazard ratio of suffering dementia of Chinese residents, which provides empirical evidence in supporting the Chinese government to invest more in combating air pollution and ensure the public health of Chinese residents.

Keywords Air pollutants · Dementia · Geographical analysis · Health Inequalities · RD design

Introduction
Dementia has been cited as a critical public health risk in the contemporary world (Bianchetti et al. 2022). Relevant researches indicate that the number of people with dementia was 43.8 million in 2016, and will exceed 130 million by 2050 (Ma et al. 2022). Meanwhile, The estimated global cost of dementia was 818 billion dollar in 2015, with an annual increase of 35% since 2010, and the cost will be approximately 2 trillion dollar in 2030 (Livingston et al. 2020). Dementia is particularly serious in China, where the total number of patients was approximately 20 million in 2021, equivalent to 60% of the total US population (Jiang et al. 2021). Taken together, the cost caused by dementia imposes a tremendous economic burden worldwide, especially in China, where medical care is underdeveloped. Accordingly, it is necessary to reveal the potential factors lead to dementia.

Of interest, although abundant empirical studies have analyzed the association between dementia and conventional factors such as gender, wage, medical management, smoking, and screen time (Auer et al. 2018; Choi et al. 2018; Frederiksen et al. 2020; Naue and Kroll 2009; Neophytou et al. 2021), few studies tried to reveal the casual relation between air pollutants and dementia.
If the causal relationship between air pollutants and dementia cannot be isolated, but merely follows a correlation analysis, a biased conclusion may be reached, increasing economic expenditures and tremendously endangering the public health of the residents. From a clinical perspective, air pollutants, particularly PM10, significantly influence the probability of suffering dementia. More specifically, PM10 could induce dementia directly through induction of systemic or brain-based oxidative stress and inflammation (Power et al. 2015). Several literatures discover that air pollutants, especially PM10, cause systemic or brain-based oxidative stress and inflammation (Calderon-Garciduenas et al. 2003), which significantly damage cytokine signaling. And then, cytokines, a broad and loose category of small proteins, play an important role in regulating brain functions including neural circuitry of memory. Finally, dysregulation in cytokine results in several cognitive dysfunctions such as forgetfulness, dementia, and even Alzheimer (Dehghani et al. 2022).

However, the above findings are based merely on several representative non-human animals controlled laboratory experiments. Because of rigid ethical constraints, it’s extremely difficult to experimentally verify the causal effect of air pollutants on human dementia. Accordingly, researchers try to use the large population-based cohort data, and rely on methodological innovations, to simulate the quasi-experiments.

Despite some meaningful attempts, there are still several methodological limitations such as (a) Omitted variable bias. More specifically, several confounders are omitted, and if these confounders positively or negatively influence the dementia, the coefficients would be overestimated or underestimated, respectively. Although some researchers use Propensity Scoring Matching (PSM) to balance the bias, they can only balance the observable bias, not the unobservable bias and (b) Reverse causality bias. More specifically, the dementia may lead to lower labor supply and affect the pollutant emissions, and confounder the estimation. While it is possible to use the difference-in-difference model to eliminate the reverse causality of covariates that do not vary over time, the covariates that do vary over time are difficult to consider.

Taken together, it’s still hard to isolate a net, causal effect between air pollutants and dementia. Fortunately, an arbitrary heating policy in China provides a natural quasi-experimental design for estimating the causal relation between air pollutants and dementia. More specifically, in the 1960s, the Mao’s government introduced the Huai River Policy (HRP), which arbitrarily divided China into two parts, North and South, according to the relative position of the provinces to the Huai River (HR). The HRP mandatorily built thermal power stations north of the border, which provided free hot water to northern residents through the burning of fossil fuels. The burning of fossil fuels produced a large amount of air pollutants, including PM10, SO2, CO, NO2, and O3, which pose a potential threat to people’s mental health. This policy is still in use today.

While from a methodological perspectives, the HPR is extremely useful in studying the causal relationship between air pollutants and dementia. Because the Huai River is not a boundary used for administrative purposes and even cuts through several provinces (the economic and demographic characteristics of the cities in a given province remain generally consistent in China). This unique feature makes the cities near the boundary to vary smoothly in economic and demographic characteristics, but with significant differences in air pollutants. Furthermore, these facts coincide with the principle of the Regression Discontinuity (RD) design, i.e., if we take the Huai River as the boundary of the RD design, we will get the following pair of samples: (a) treatment group, located north of the boundary, with more air pollutants, and (b) control group, located south of the boundary, with less air pollutants. Meanwhile, the two samples remain close consistent in terms of the economic and demographic characteristics. Furthermore, the RD design is very helpful in addressing the two methodological dilemmas presented above, namely the RD design can isolate the net association between air pollutants and dementia, controlling for other demographic characteristics conditional, and effectively addressed the omitted variable bias and reverse causality bias.

Therefore, the aim of this paper is to explore the causal relationship between air pollutants and dementia with the RD design by the HR. This paper is organized as follows. The “Materials and methods” section presents the methodological framework and introduces data and variables. The outcomes including data describing, graphical analysis, main results, robustness tests, heterogeneity analysis are systematically explained in the “Results” section. The “Discussion” and “Conclusion” sections present the discussion and conclusion, respectively.

Materials and methods

Population and study design

The subjects in this study were drawn from the China Family Panel Studies (CFPS) executed by the Chinese Social Science Survey Center (CSSSC) of Peking University. CFPS had conducted seven rounds since 2010, with over 300,000 individuals included, which was a interdisciplinary, multi-ethnic, cohort survey. For the comparability, the CFPS 2016, 2018, and 2020 were selected for this study and combined into the panel data. After removing invalid samples, the final valid sample covered 59,605 individuals from
14 nationalities in 125 cities. Each individual was marked with the distance from the Huai River by the Arcgis 12.0. The sample consisted of 30,802 individuals located north of the Huai River and 28,803 individuals located south of the Huai River.

**Determination of variables**

**Huai River policy**

China is the third largest country in the world, spanning 50 latitudes, with the southernmost Zengmuhe in the Spratly Islands (3° 52′ N) and the northernmost Mohe in Heilongjiang Province (53° 33′ N). This characteristic shapes the unique climate difference among the north and south cities in China, with the average winter temperatures below 0°C; in north cities (Monsoon Climate of Medium Latitudes), and the average winter temperatures above 0°C; in south cities (Subtropical Monsoon Climate). Notably, the boundary between the southern and northern cities of China is the HR. The geographical characteristics of China were graphically shown in Fig. 1.

Accordingly, Chinese residents north of the Huai River live in low temperature which hinders daily productive activities and affects their health for thousands years. Accordingly, in 1960, the Mao’s government introduced the HRP, which compulsory supplied the free heating for the cities north of the Huai River boundary, by building a large number of thermal power plants and burning fossil fuels. This policy enabled the residents of the north to engage in productive outdoor activities in the winter, and improved the Chinese economy significantly. However, an inevitable problem was that free heating in China resulted in the emission of large amounts of air pollutants, which posed a significantly hazardous to the public health. Taken together, the arbitrary HRP resulted in northern Chinese residents living with worse air pollutants, compared with their southern counterparts.

Additionally, a typical characteristic of the Huai River boundary enables researchers to reveal the casual relation between air pollutants and dementia, namely the delineation of the Huai River boundary is based exclusively on geographical features rather than administrative purposes. It is generally known that China is a typical socialist country, where administrative divisions uniquely determine the demographic and economic characteristics of a given region. In other words, the non-political purpose of the boundary shape that the demographic and
economic characteristics of the cities around the Huai River remain largely consistent. Accordingly, if the suitable sample was selected, we can isolate the net effects of air pollutants on dementia.

**Air pollutant concentration**

_Air pollutant concentration (APCs)_ was the dependent variable in this study, which was conceptualized as the mass of air pollutants in a cubic meter of a given city. It is worth noting that we use the PM10 concentration per cubic meter in our work to represent APCs, and in the “Robustness” section, we use PM10, PM2.5, SO2, NO2, CO and O3, respectively, to represent the APCs (Auer et al. 2018; Frederiksen et al. 2020; Naue and Kroll 2009), to verify the consistency of the results among different types of air pollutants. Accordingly, APCs was a continuous variable taking values in the range of 11–164 μg/m³, indicated the PM10 concentration per cubic meter in the city where the respondent lives. The APCs obtained by the following steps:

First, we downloaded the China Environment Yearbook 2016–2020 from the official website of the Chinese Ministry of Ecology and Environment, which contained the concentrations of five kinds of air pollutants (PM10, NO2, SO2, CO, O3) for 31 cities.

Secondly, we checked the information on 31 cities against the CFPS city catalogue, and got a catalogue of 94 cities which the APCs concentration was missing.

Thirdly, we visited the official websites of these 94 cities respectively, and downloaded their annual government work reports for 2016–2020. The information on APCs of 94 cities was included in each work report.

Finally, we combined the valid information from steps 1 to 3, and obtained the comprehensive APCs information for 125 valid cities, namely city-level APCs panel data.

To further describe the distribution of APCs near the HR boundary, we used the Arcgis 12.0 to graphically depict the APCs, as shown in Fig. 2. The solid blue line indicated the HR, which was the proposed breakpoint in our RD design. A higher APCs could be clearly identified for cities south of the boundary, compared with their south counterparts.

**Dementia**

_Dementia_ was the independent variable. The CFPS used a standardized brief screening scale for dementia to determine whether a respondent suffered dementia, covered 30 questions and included six items: picture memory, verbal memory, point-in-time memory, place memory, short-term memory, and object naming memory. One point was awarded for each correct answer, but no points were awarded for incorrect answers.
awarded for incorrect answers. Respondents’ total scores were normalized to obtain a continuous variable. To be consistent with the subsequent analysis, we reversed the results, and got a continuous variable with values ranging from 1 to 5, where the score bigger than 4 was defined as dementia. According to relevant studies (Choi et al. 2018; Neophytou et al. 2021). More specifically, the dementia was obtained by the following three steps:

First, we downloaded the latest three rounds of CFPS panel data (2016, 2018, 2020) with 65,326 individuals.

Second, we removed 5721 respondents with missing dementia information.

Third, we used the merge command in Stata, with “cityid” as the match variables, to obtain a comprehensive database containing city-level APC panel information and individual-level dementia panel information, simultaneously.

Similarly, to reveal the spatial distribution of dementia among Chinese residents, we used Arcgis 12.0 to graphically describe the relationship between an individual’s geographical location and dementia, as Fig. 3. The depth of color was positively correlated with the dementia. It can be found that dementia was more severe within the cities north of the HR, although the relationship was not monotonic.

The sample selection process was systematically shown in Fig. 4.

Covariates

In addition, we added several covariates in our analysis based on the previous studies as follows: (a) Individual-Level Covariates, including conventional individual demographic characteristics such as age, sex, residence, wage, education, employment, Body Mass Index (BMI), physical activity, smoke (as shown in panel 3 of Table 2) and (b) City-Level Covariates, including city-level variables that have rarely been considered in previous studies, such as Gross Domestic Product (GDP), Per capita GDP, Proportion of Secondary Industry (SI), temperature, wind (as shown in panel 2 of Table 2). The (a) covariates were from the CFPS individual self-reported questionnaire, and the (b) covariates were compiled through a combination of the statistic from the World Meteorological Association and China National Bureau of Statistics.

Statistical analysis

Three metrological measures were progressively adopted to verify the potential causal correlation between APCs and

Fig. 3 China’s Huai River boundary and dementia
dementia. The Ordinary Least Squares (OLS) estimation was first used, as in Eq. 1:

\[ D_i = a_0 + y_1 Apci, j + \sum_{i=1}^{n} y_i Cov_i + \epsilon_j \]  

(1)

where \( Apci, j \) represented the APCs of individual \( i \) in City \( j \), \( Cov_i \) was a vector denoted the covariates. \( D_i \) denoted the dementia of individual \( i \), meanwhile the coefficient \( Cov_i \) indicated the impacts of APCs on dementia. \( y_1 \) and \( y_i \) were vectors representing the magnitude and direction of the correlation coefficient, respectively. \( \epsilon_j \) denoted the unobservable errors.

However, traditional OLS estimation didn’t allow researchers to take independent city-level variables into consider. Accordingly, we used the Hierarchical Linear Models (HLM) to further estimate the relationship between APCs and dementia as in Eq. 2.

\[ D_{i,j,t} = a_0 + a_1 R + a_2 f(L_{i,j,t}) + Cov_{i,j,t} + \theta_j \]  

(3)

\[ Apci_{i,j,t} = a_0 + a_1 R_{i,j,t} + a_2 f(L_{i,j,t}) + Cov_{i,j,t} + \theta_j \]  

(4)

where \( R \) represented the driving variable and took the values 0, 1 to indicate that city \( j \) was located north or south of the boundary, respectively. \( f(L_{i,j,t}) \) was a polynomial used to assess the degree north of the boundary for city \( j \).

Meanwhile, the RD design provided us with a method to explore the potential causal correlation between APCs and dementia. More specifically, we chose an appropriate bandwidth (namely the bins in RD design) to meet the following condition: that dementia was solely affected by APCs. Then, it was valid to treat Eq. 3 as the first stage in a two-stage least squares (2SLS) system of equations. In this way, 2SLS estimation was able to assess the causal relationship between APC and dementia as in Eq. 5.

\[ D_{i,j,t} = \rho_0 + \rho_1 Apci_{i,j,t} + \rho_2 f(L_{i,j,t}) + Cov_{i,j,t} + \epsilon_j \]  

(5)

Taken together, we combined Eqs. 3, 4 and 5 to obtain the causal effect of APCs on dementia.
Results

Data description

Table 1 systematically presented the descriptive statistics for the relevant variables, and preliminarily provided supports to verify the validity of the RD design. The means for individual variables for the full sample, the northern sample and the southern sample were shown in Columns (1), (2), (3), respectively. The mean difference between the northern and southern samples was shown in Column (4). Additionally, Column (5) presented the similar results as Column (4), except introduced a cubic polynomial in degrees north of the HR, to verify the potential discontinuous change of relevant variables at the HR. A fundamental precondition of the RD design was that the covariates varied smoothly around the boundary, while the independent and dependent variables varied discontinuously. The results in column (5) indicated that there was no significant difference between the southern and northern samples with respect to the covariates, after adjusting for a cubic polynomial in degrees north of the boundary. Of interest, it was clear that APCs and dementia changed discontinuously near the boundary. More specifically, the distribution of individuals around the boundary was similar to a natural quasi-experimental design, where the probability of an individual being treated (namely the odds of located in a highly polluted city) was randomized. Methodologically, the unique factor that related dementia

Table 1 Characteristics of the study population (n = 59,605)

| Variables | Overall (N = 59,605) | North (N = 26,180) | South (N = 33,425) | Mean Difference (4) | Adjusted difference (5) | P-value |
|-----------|----------------------|--------------------|--------------------|---------------------|-------------------------|--------|
| Panel 1: Air pollution exposure and mental health difference between the China’s Huai River | | | | | | |
| Dementia | 2.87 (1, 5) | 2.91 (1, 5) | 2.83 (1, 5) | 0.75** | 1.31*** | <0.001/ <0.001 |
| PM10 | 57.21 (11.164) | 66.56 (18.164) | 45.32 (11,105) | 21.247*** | 16.08*** | <0.001/ <0.001 |
| NO2 | 41.85 (7.160) | 47.20 (14.160) | 34.95 (7.114) | 12.254*** | 12.62*** | <0.001/ <0.001 |
| SO2 | 35.51 (2.272) | 49.35 (18,164) | 17.66 (11,105) | 31.69*** | 34.30*** | <0.001/ <0.001 |
| CO | 35.51 (0.3, 9.5) | 2.32 (0.5, 9.5) | 1.31 (0.3, 3) | 1.00*** | 1.08*** | <0.001/ <0.001 |
| O3 | 109.94 (7.224) | 104.07 (7.224) | 117.51 (8.186) | −13.436*** | −15.37*** | <0.001/ <0.001 |
| Panel 2: Economic and climate difference between the China’s Huai River | | | | | | |
| Ln(GDP) | 17.14 (15.01, 19.76) | 16.83 (15.01, 19.68) | 17.54 (15.23, 19.76) | 17.54*** | 17.92*** | <0.001/ <0.001 |
| Ln(PGDP) | 10.83 (9.45, 12.10) | 10.66 (9.45, 12.01) | 10.05 (10.10, 12.10) | 11.05*** | 11.23*** | <0.001/ <0.001 |
| Proportion | 39.43 | 38.71 | 40.31 | 40.30*** | 40.75*** | <0.001/ |
| SI | (12.08, 65.05) | (12.08, 65.05) | (21.7, 56.54) | <0.001 |
| Temperature | 2.42 (-23.5, 21) | −2.73 (-23.5, 11.5) | 8.91 (-2.5, 21) | 8.91*** | 6.18*** | <0.001/ <0.001 |
| Wind | 2.72 (1.5) | 2.66 (1.5) | 2.79 (1.5) | 2.79*** | 2.44*** | <0.001/ <0.001 |
| Panel 3: Demographic features difference between the China’s Huai River | | | | | | |
| Age | 46.35 (9,104) | 46.32 (9,104) | 46.40 (9,104) | −0.08 | −0.08 | 0.601/ 0.600 |
| Sex | 32,008 | 14,347 | 17,661 | 0.01* | < 0.01 | 0.063/ |
| (Female) | (49.00%) | (49.41%) | (48.67%) | | | 0.582 |
| Hukou | 40,178 | 23,071 | 17,107 | −0.06*** | 0.02 | < 0.001/ |
| (city) | (71.67%) | (73.37%) | (69.51%) | | | 0.124 |
| Ln(wage) | 10.14 (4.03, 13.82) | 10.05 (4.03, 13.82) | 10.24 (4.79, 13.12) | −0.19*** | −0.023 | < 0.001/ 0.692 |
| Eduyear | 7.69 (0.22) | 7.81 (0.22) | 7.53 (0.22) | 0.28*** | 0.18 | < 0.001/ 0.279 |
| Employment | 40,433 | 22,653 | 17,780 | −0.01 | −0.12 | < 0.001/ |
| (employed) | (74.58%) | (74.62%) | (74.53%) | | | 0.818 |
| BMI | 22.66 (8.16, 130) | 23.01 (8.86, 130) | 22.19 (8.16, 90.91) | 0.82*** | −0.16 | < 0.001/ 0.307 |
| Physical | 95.33 | 97.96 | 92.07 | 5.89*** | −2.614 | < 0.001/ |
| Activity | (0, 2500) | (0, 2500) | (0, 2000) | | | < 0.001/ |
| Smoke | 15,791 | 9,046 | 6,745 | 0.01*** | < 0.01 | 0.01/ 0.180 |
| (smoked) | (26.45%) | (27.03%) | (25.71%) | | | 0.180 |

The values in brackets indicate the range (for continuous variables) or the percentage (for categorical variables) of each variable. *Significant at 10 percentage, **significant at 5 percentage, ***significant at 1 percentage

Data source: a combination of China Environmental Statistics Yearbook (2016–2020), World Meteorological Association (2016–2020), China National Bureau of Statistics (2016–2020) and Chinese Family Panel Studies (2016–2020)
was the APCs. Taken together, the results in Table 1 allowed us to explore the causal link between APCs and dementia.

**Graphical analysis**

The difference in APCs and dementia between northern and southern residents on HR boundary was graphically represented in Figs. 5 and 6. A valuable information was that the HR resulted in a 0.04–0.14-unit increase in the hazard ratio of suffering dementia (because dementia is a continuous variable with values from 1 to 5, it corresponds to a 0.8% to 2.8% increase in the hazard ratio of suffering dementia) and 11.4–19.4 μg/m³ increase in APCs of the northern residents, compared with their southern counterparts. Taken together, the graphical results demonstrated the discontinuous variations in APCs and dementia near the HR.

And then, Fig. 7 graphically examined the validity of the RD design, plotting by predicting expected dementia differences (calculated as the fitted value from a hierarchical linear models (HLM) regression of dementia on all covariates except APCs) at the HR. Particularly, the potential deviation in dementia was explained by the covariate cluster by 7.42 percentage (R² = 0.0742). Interestingly, the difference in suffering dementia between the residents of the north and south of HR was not significant, after isolating the influence of APCs. Combining the findings in Figs. 5, 6 and 7, the covariates didn’t effectively predict the differences in dementia between residents north and south of the boundary. That is to say, uncontrolled factor (APCs) might have potential influence on dementia.

**Regression results of APCs and dementia**

The results of OLS and HLM

The results in Table 2 presented the linear correlation between APCs and dementia by OLS (columns 1, 2) and HLM (column 3), respectively. The OLS results (Columns (1) and (2)) indicated that, after controlling for individual-level covariates, a 100 μg/m³ increase in APCs was associated with a 0.1-unit increase in the hazard ratio of suffering dementia (equivalent to a 2% increase in the hazard ratio of

![Graphical representation of APCs and dementia](image-url)
suffering dementia), statistically significant. Similarly, the HLM results showed that after controlling for both individual and city-level covariates, a 100 $\mu g/m^3$ increase in APCs was associated with a 0.3-unit increase in the hazard ratio of suffering dementia (equivalent to a 6% increase in the hazard ratio of suffering dementia), statistically significant.

However, neither of these two methods controlled for the endogeneity problems arose from omitted variables and reverse causality. In other words, OLS and HLM only partially estimated the correlation between APCs and dementia, which were far from causal relation. Therefore, we would continue exploring the causal relation between the APCs and dementia through the RD design in the next section.

The results of RD design

The RD design was to explore the causal relation between APCs and dementia, and the results were systematically presented in Table 3. Columns (1) and (2) both restricted the sample to the 2° latitude from the boundary, but used linear, quadratic polynomial to estimates of the coefficients, respectively. Columns (3)–(7) presented the first-order, second-order polynomial estimation which restricted the sample to 5° and 8°, respectively.

The results of panel 1 in Table 3 confirmed the validity of the RD design as follows: after adjusting for covariates, there was a statistically significant difference in APCs and dementia between residents of the north and south of the HR, simultaneously. The discontinuous deviations among the northern and southern resident of the boundary were 11.60–24.49 $\mu g/m^3$ in APCs and 0.05–0.19 units in the hazard ratio of suffering dementia (equivalent to a 1%–3.8% increase in the hazard ratio of suffering dementia), respectively.

Next, we used the “rdrobust” command to explore the causal relation between APCs and dementia, the results were presented in Table 3 panel 2. According to the AIC, BIC optimality principle, we chose to report the results of Column (2). A 100 $\mu g/m^3$ increase in APCs was associated with a 2.13-unit (27.28 in APCs was equivalent to hazard ratio in 0.58, so 100 APCs was equivalent to hazard ratio in 2.13) increase in the hazard ratio of suffering dementia.
Heterogeneity analysis

Table 4 systematically revealed the casual influence of APCs on dementia among different samples. All
heterogeneities in coefficients between elected groups were systematically shown in Fig. 8 and statistically significant. We first focused on the difference in coefficients between the youth and aged groups. APCs positively predicted the hazard ratio of suffering dementia in youth and aged, but the influence was more pronounced for the older group (coeff=1.35 vs coeff=1.55, \( p < 0.05 \)). Second, male were more likely to get dementia due to the rising of the APCs, compared with their female counterparts (coeff=1.62 vs coeff=0.71, \( p < 0.05 \)). Third, smokers were more than twice as likely to suffer from dementia due to the increasing in the APCs, compared to the non-smokers (coeff=2.12 vs coeff=0.93, \( p < 0.05 \)). Fourth, the rising of APCs was more likely to cause dementia in those who were thin, compared to the medium and obesity (coeff=2.05 vs coeff=1.22, coeff=1.28, \( p < 0.05 \)).

**Robustness**

Finally, we analyzed the influence of different kinds of APCs (including PM10, NO2, SO2, CO, O3) on

### Table 3  Association between APCs and dementia through RD

| Variables | (1) | (2) | (3) | (4) | (6) | (7) |
|-----------|-----|-----|-----|-----|-----|-----|
| APCs      | 24.49*** | 27.28*** | 12.48*** | 13.55*** | 12.53*** | 11.60*** |
| Dementia  | -0.13*** | -0.19*** | -0.06*** | -0.05 | -0.09*** | -0.07*** |
| Panel 1: Impact of “North” on the listed variable, RD robust with OLS |
| APCs      | (0.67) | (0.70) | (0.47) | (0.55) | (0.41) | (0.47) |
| Dementia  | (0.06) | (0.08) | (0.03) | (0.04) | (0.03) | (0.03) |
| Panel 2: Impact of dementia on the listed variable, RD robust with two-stage least squares |
| APCs      | -0.30*** | -0.58*** | -0.08*** | -0.07 | -0.10*** | -0.08*** |
| Dementia  | (0.15) | (0.23) | (0.04) | (0.05) | (0.03) | (0.04) |
| RD type   | Polynomial | Polynomial | Polynomial | Polynomial | Polynomial | Polynomial |
| Polynomial | Linear | Second | Linear | Second | Linear | Second |
| Sample    | 2% | 2% | 5% | 5% | 8% | 8% |

*Significant at 10 percentage, **significant at 5 percentage, ***significant at 1 percentage

### Table 4  Heterogeneity in the effect of PM10 concentrations on samples with different demographic characteristics

| Variables | Age group | Gender group | Smoke group | BMI group |
|-----------|-----------|--------------|-------------|-----------|
| PM10      | Young     | 1.35         | 0.71        | 2.12      | 2.05      | 1.22      | 1.28      |
|           | Aged      | 1.55         | 1.62        | 0.93      | 2.05      | 1.22      | 1.28      |
|           | Male      |***           |***          |***        |***        |***        |***        |
|           | Female    |***           |***          |***        |***        |***        |***        |
| Polynomial| liner     |***           |***          |***        |***        |***        |***        |
| Sample    | 2”        | 2”           | 2”          | 2”        | 2”        | 2”        | 2”        |

*Significant at 10 percentage, **significant at 5 percentage, ***significant at 1 percentage

### Fig. 8  Heterogeneity in the effect of PM10 concentrations on samples with different demographic characteristics
dementia, to verify the robustness. Table 5 demonstrated the heterogeneity of the influences of the five APCs (PM10, NO2, SO2, CO, O3) on dementia, under the bins of 2°, 5°, 8° and the polynomial of liner, second, third, respectively. It can be clearly found that all five APCs were positively associated with the hazard ratio of suffering dementia, statistically significantly. A valuable information was that O3 and SO2 concentrations were the pollutants with the highest and lowest positive benefits for the hazard ratio of suffering dementia among the five APCs, respectively. An increase of 100 μg/m³ in the concentration of O3 and SO2 led to an increase of 30.8% (coeff = 1.54, p < 0.05) and 16.2% (coeff = 0.81, p < 0.05) in the hazard ratio of suffering dementia, respectively. In addition, an increase of 100 μg/m³ in PM10, NO2 and CO was associated with a 21.2% (coeff = 1.06, p < 0.05), 23.8% (coeff = 1.19, p < 0.05) and 20.6% (coeff = 1.03, p < 0.05) increase in the hazard ratio of suffering dementia, respectively. The heterogeneous influences of the five APCs on dementia under different conditions were graphically illustrated in Fig. 9.

### Table 5 Heterogeneity in the effects of different air pollutants on dementia

|       | Liner polynomials | Second polynomials | Third polynomials |
|-------|-------------------|--------------------|-------------------|
|       | 2°    | 5°    | 8°    | 2°    | 5°    | 8°    | 2°    | 5°    | 8°    |
| PM10  | 1.25***| 0.38***| 0.31***| 1.06***| 0.78***| 0.44***| 0.65***| 0.85***| 0.73***|
| NO2   | 1.4*** | 0.55***| 0.46***| 1.19***| 1.06***| 0.57***| 0.59***| 1.01***| 0.93***|
| SO2   | 0.85***| 0.46***| 0.35***| 0.81***| 0.86***| 0.52***| 0.46***| 0.84***| 0.82***|
| CO    | 1.28***| 0.54***| 0.38***| 1.03***| 1.01***| 0.56***| 0.64***| 0.98***| 0.87***|
| O3    | 2.15***| 0.50***| 0.34***| 1.54***| 1.12***| 0.53***| 0.69***| 1.31***| 0.97***|

*Significant at 10 percentage, **significant at 5 percentage, ***significant at 1 percentage

### Discussion

This paper sought to fill the gap of the casual relationship between APCs and dementia, especially given the increasing prevalence of air pollution on a global scale. The results of the RD regression indicated that a 100 μg/m³ rise in APCs led to an increase of 42.4% in the hazard ratio of suffering dementia, statistically significant, after restricting the sample to the 2° latitude from the HR boundary. Of interest, this estimate was 5.3 and 2.65 times larger than using the conventional OLS and HLM. The bias was mainly due to the following two reason as (a) confounders in conventional regressions are negatively correlated with the random error term and bias the estimates downwards and (b) self-selection confounds the estimation, namely where people suffer severe dementia may prefer cleaner air and choose to move to areas with less APCs, and this self-selection behavior confounds the estimation. Meanwhile, heterogeneous models revealed that the hazard ratio of dementia by APCs was more significant in the older (compared to younger), male (compared to female), smoker (compared to non-smoker), and thin groups.
Heterogeneity among these populations deserves special attention, as previous studies have mostly controlled for the demographic characteristics. Related studies have found that the HR for dementia was higher in older (OR = 3.2, 95% CI 1.0–12.2 for older, and OR = 1.7, 95% CI 0.7–4.1 for younger) (Johansson et al., 2019), male (OR = 1.06, 95% CI 1.04–1.09 for male, and OR = 0.99, 95% CI 0.95–1.02 for female) (Dal Forno et al., 2005), smoker (OR = 1.95, 95% CI 1.34–2.83 for smoker, and OR = 0.99, 95% CI 0.76–1.28 for non-smoker) (Chen et al., 2013), thin groups (compared with people of a healthy weight, thin people (BMI < 20 kg/m²) had a 34% higher (95% CI 29–38) risk of dementia) (Qizilbash et al., 2015). Accordingly, for a given group of residents, the rise in APCs can magnify health inequalities associated with heterogeneity in demographic characteristics, in terms of the risk of developing dementia. In addition, robustness test presented that O3 and SO2 were the air pollutants with the highest and lowest effects on dementia among the five APCs, respectively.

Furthermore, the coefficients in our estimation were much smaller compared with a recent representative study (Renna et al., 2018), and Table 6 presents a systematic comparison of our study with it. In addition to using more abundant databases, we used a causal inference tool, namely the RD design, rather than traditional regression, and reduced the bias of confounders on the results.

Meanwhile, several meaningful cross-country conclusions can be drawn from the comparison of this paper and five relevant empirical researches. We compared five cohort studies focusing on the relationship between PM10 and dementia, all of which are from low-pollution countries such as the USA, Canada and Australia (Grande et al., 2020; Ilango et al., 2020; Paul et al., 2019; Vali et al., 2021). The results systematically indicated that in low-pollution countries, a 100 µg/m³ increase in APCs was associated with a 14–32% increase in the hazard ratio of suffering dementia. However, according to the results of this paper, a 100 µg/m³ rise in APCs was associated with 42.4% increase in the HR of suffering dementia in China, close to 1.5 times that of low-pollution countries. We graphically described the cross-country comparison in Fig. 10. China is known to be one of the most polluted countries in the world, and cross-national evidence supports that the induction of dementia by APCs is more pronounced in highly polluted countries (Table 7).

Unfortunately, it is hard to take the COVID-19 epidemic into our consideration because the CFPS did not address the relevant individual characteristics. However, with China’s nationwide lockdown policy, we think that the impact of the epidemic on the causal relationship between APCs and dementia is negligible, especially with the RD design. More specifically, the impact of the epidemic on the dementia of all Chinese residents is almost homogeneous, namely, the impact of the epidemic on residents’ dementia will be the random error term in our regression.

| Methods   | Study design | Location       | N    | APCs     | Conclusion          |
|-----------|--------------|----------------|------|----------|---------------------|
| Ologit    | Cohort       | UK (London)    | 130978 | PM2.5    | PM2.5 increase HR 7.37 |
|           |              | China (nation wide) | 65326 | NO2      | NO2 increase HR 2.27 |
| RD design | Cohort       |                |      | PM10     | PM10 increase HR 1.06 |
|           |              |                |      | NO2      | NO2 increase HR 1.19 |
|           |              |                |      | SO2      | SO2 increase HR 0.81 |
|           |              |                |      | CO       | CO increase HR 1.03  |
|           |              |                |      | O3       | O3 increase HR 1.54  |

**Table 6** Comparison of this study with a recent representative study

**Fig. 10** Cross-country comparison in the effects of different APCs on dementia
Additionally, there are several limitations to be interpreted carefully as follows: (a) As for the RD design, the time-fixed effects are not taken into our consideration, this is the common limitation of contemporary empirical researchers dealing with RD design on the cohort data, and may result in some estimation bias and (b) Although containing 125 cities distributed on both sides of the HR boundary, our data still do not cover the entire potential sample and (c) We only obtain information on APCs at the city level and cannot detect individual exposure levels and (c) Although less frequent, there are still cases of heating via electricity, especially in the southeastern of China (provinces far from HR), thus potentially resulting in RD designs based on differences in heating systems that might do not perfectly independent of the net effect on dementia. Despite above limitations, this research was still theoretically and empirically meaningful with a relatively perfect and robust estimate of the casual relation between APCs and dementia.

In a policy context, our findings strongly supported the efforts of the Chinese government and Non-governmental organizations in reducing the air pollutants. Although President Xi Jinping has been adopting a tougher policy towards the other countries, environmental protection is still the most important parts of cooperation between China and the rest of the world, especially between China and the USA. If China could continue to cooperate with other countries, such as the USA, in combating air pollutants, it would reduce significant medical expenditures and protect Chinese residents from diseases such as dementia.

This paper is pioneering in attempting to apply the RD design to infer the causal relationship between APCs and dementia, and accordingly, provides several meaningful insights for future research as follows (a) more cross-national studies based on the RD designs are extremely meaningful, especially in comparing the heterogeneous effects of APCs on the dementia between developing and developed countries and (b) future research needs to pay more attention to reveal the potential correlation between APCs and dementia. In particular, whether impairments in cardiorespiratory function or changes in brain structure are indirectly involved as mediating variables in the association between the APCs and dementia (Dehghani et al. 2022), needs to be discussed farther and (c) it would be worthwhile to investigate how to methodologically implement a cross-level RD design, as air pollutant concentrations tend to be a city-level variable and dementia tends to be an individual-level variable, if the HLM can be combined with the RD design, it will help to isolate the net effects between APCs and dementia.

**Conclusion**

In this large population-based cohort word, we used the RD design relying on an arbitrary heating policy of China, to reveal the casual relation between air pollutants and dementia. We found that exposure to air pollutants led to a significant increase in the hazard ratio of suffering dementia, the induction of dementia by air pollutants was more significant in the older (compared to younger), male (compared to female), smoker (compared to non-smoker), and thin groups (compared to medium and obesity). In addition, O3 and SO2 were the air pollutants with the highest and lowest effects on the hazard ratio of suffering dementia among the five APCs, respectively.

**Author contribution** J.X.: formal analysis, methodology, writing original draft. C.L.: supervision, methodology. J.X.: supervision, conceptualization, writing review and editing. J.X.: conceptualization.

**Funding** Not applicable.

**Availability of data and materials** The datasets used in this study are available from the corresponding author on reasonable request.

**Declarations**

**Ethics approval** The studies involving human participants were reviewed and approved by the Ethics Committee of the School of Xi’an Jiaotong University and the legal guardians of all participants. All methods were performed in accordance with relevant guidelines and regulations. Written informed consent to participate in this study was provided by themselves.

**Conflict of interest** The authors declare no competing interests.

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