

# BMJ Open Association of ambient air pollution and Air Quality Index with risk of sudden sensorineural hearing loss: a cross-sectional study

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## ABSTRACT

**Objectives** To explore the associations of air pollutants and Air Quality Index (AQI) with risk of sudden sensorineural hearing loss (SSNHL)

**Design** Cross-sectional study

**Setting** Medical record data and local population data collected between 2014 and 2022 in Changshu, China were retrospectively reviewed.

**Participants** Adults aged 18 years and above who were diagnosed with SSNHL in Changshu No. 1 People's Hospital or Changshu No. 2 People's Hospital from the spring of 2014 to the fall of 2022 were included in the study.

**Outcome measure** SSNHL was diagnosed by clinicians using the Chinese diagnostic criteria for SSNHL.

**Results** Compared with those exposed to the lowest tertile of carbon monoxide (CO), the prevalence ratio for those exposed to middle and high tertiles of CO were 1.113 (95% CI 1.022 to 1.213) and 1.230 (95% CI 1.105 to 1.369), respectively. The risk of SSNHL was increased by 30.6% (95% CI 9.9% to 55.4%) per doubling increment of CO. No categorical association was found between ozone (O<sub>3</sub>) exposure and risk of SSNHL, however, an increased risk of 22.2% (0.8%–48.2%) was identified for each doubling of O<sub>3</sub>. No association was identified between other pollutants and AQI and risk of SSNHL.

**Conclusions** In this study, CO and O<sub>3</sub> were associated with an increased risk of SSNHL in Changshu, China. Further studies are warranted to confirm our findings.

## INTRODUCTION

Sudden sensorineural hearing loss (SSNHL), referred to as 'sudden deafness', is an acute, idiopathic sensorineural hearing loss. It is defined as abrupt onset, unexplained sensorineural hearing loss of at least 20 decibels across two adjacent frequencies, occurring within a 72-hour window according to the Chinese diagnostic and therapeutic criteria.<sup>1</sup>

The incidence of SSNHL has been notably increasing globally in the past decades. For instance, in Germany, the incidence escalated from 20/100 000 in 2004<sup>2</sup> to 160–400/100 000 in 2011.<sup>3</sup> A similar trend was observed in Japan, where the incidence climbed from

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study investigated the associations between air pollutants and risk of sudden sensorineural hearing loss (SSNHL) in a moderately polluted to highly polluted environment.
- ⇒ This study included a broad period and more than 4000 patients with SSNHL in Changshu, China.
- ⇒ Since this study was conducted at the group level instead of the individual level, the data should be interpreted with caution.

3.9/100 000 in 1972 to 27.5/100 000 in 2001.<sup>1</sup> In the USA, the incidence of SSNHL rose from 5 to 20 per 100 000 persons in 1977,<sup>4 5</sup> to 27/100 000 in 2006–2007.<sup>6</sup> In Taiwan, the reported incidence varied from 6.5 per 100 000 in 1998 to 10.2 per 100 000 in 2002.<sup>7</sup>

Various factors, including autoimmune diseases, viral infections, functional metabolic abnormalities and traumatic factors have been identified as potential contributors to the onset of SSNHL.<sup>8</sup> Pathologically, the condition is often characterised by an increase in inflammatory factors and related stress proteins, disruption of cochlear ionic homeostasis, and ultimately damage to the inner ear's hair cells.<sup>9–12</sup>

Concerning the rising incidence of SSNHL, there is a growing interest in the potential role of environmental factors, particularly in industrialisation. Hospital visits for Meniere's disease were associated with measured concentrations of ambient air pollutants sulfur dioxide (SO<sub>2</sub>), nitrogen dioxide (NO<sub>2</sub>), carbon monoxide (CO) and mean particulate matter with a diameter of 10 µm or less (PM<sub>10</sub>) in Korea.<sup>13</sup> Higher mean particulate matter with a diameter of 2.5 µm or less (PM<sub>2.5</sub>) concentrations were also associated with a higher risk of acute otitis media incidents in children.<sup>14</sup> Airborne pollutants, for example, have been linked to aggravated respiratory symptoms and reduced

lung function.<sup>15</sup> Exposure to nitrogen oxides (NO<sub>x</sub>) and particulate matter (PM) has been associated with a higher incidence of eczema in older women,<sup>16</sup> and higher levels of PM<sub>2.5</sub> have been correlated with reduced white matter volume.<sup>17</sup> Moreover, NO<sub>2</sub> has been shown to enhance thrombin production in vitro,<sup>18</sup> potentially increasing risks of stroke, myocardial ischaemia and coronary heart disease,<sup>19</sup> and NO<sub>2</sub> has been strongly associated with the development of diabetes.<sup>20</sup>

This emerging evidence prompts a critical question: Is there an association between the air quality and air pollutants in the patient's environment and risk of SSNHL? There were eight studies on this, including three cross-sectional studies and five cohort studies, distributed among four countries: Korea, Taiwan, Turkey and the UK.<sup>21</sup> Some studies, such as the one conducted in Korea, suggested a possible link between PM<sub>2.5</sub> and sudden deafness.<sup>22</sup> Another Turkish research has found that certain meteorological factors may affect the prognosis of sudden deafness, although a clear link with air pollutants has not been established.<sup>23</sup> Studies in the UK and Taiwan have shown a link between air pollutants and sudden deafness.<sup>24 25</sup> Despite these findings, research specifically investigating the association between air quality and the onset of SSNHL in Mainland China remains lacking. This gap in research underscores the need for more comprehensive studies to understand the environmental dimensions of this increasingly prevalent condition, especially in Mainland China. Therefore, we examined the cross-sectional association of air pollutants and risk of SSNHL by retrospectively reviewing medical record data coupled with local population data.

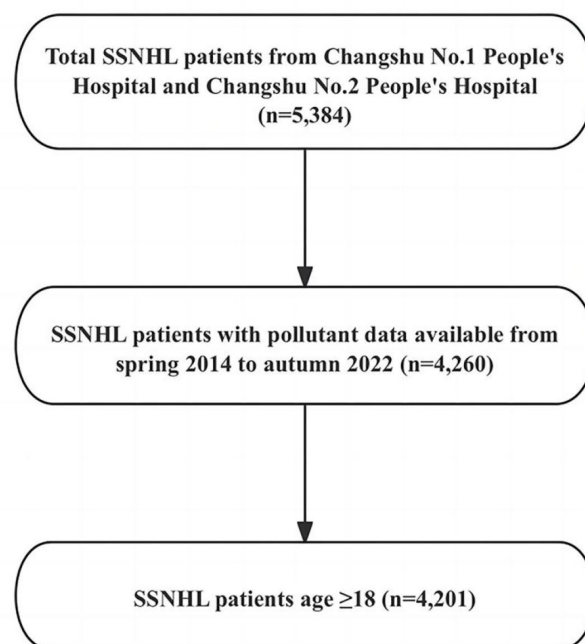
## METHODS

### Study design and population

This cross-sectional analysis primarily encompassed patients who were initially diagnosed with SSNHL and admitted to Changshu No. 1 People's Hospital or Changshu No. 2 People's Hospital, Jiangsu Province, China, from March 2014 to November 2022. A total of 5384 patients met the Chinese diagnostic criteria for SSNHL. Of these, 4260 patients had corresponding air pollutant data available. Furthermore, 59 patients who developed the disease before the age of 18 years were excluded, considering the rarity of SSNHL in teenagers and children. Consequently, 4201 patients were included in the final analysis (figure 1).

### Outcome

The outcome was SSNHL, diagnosed by clinicians using the Chinese diagnostic criteria for SSNHL. It was defined as abrupt onset, unexplained sensorineural hearing loss of at least 20 decibels across two adjacent frequencies, occurring within a 72-hour window. The date of onset was defined as the day the patient self-reported experiencing sudden hearing loss.



**Figure 1** Case screening process. SSNHL, sudden sensorineural hearing loss.

### Exposure

The daily average concentrations of air pollutants during the same period were sourced from the official portal of Changshu city.<sup>26</sup> The pollutants included PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, CO, ozone (O<sub>3</sub>) and Air Quality Index (AQI). In this study, PM<sub>2.5</sub> and PM<sub>10</sub> were measured by the gravimetric method [Huanjing (HJ, means "Environment") 618–2011], SO<sub>2</sub> was measured by the tetrachloromercurate-pararosaniline method (HJ 483–2009), NO<sub>2</sub> was measured by the ethylene diamine dihydrochloride spectrophotometric method (HJ 479–2009), CO was measured by non-dispersive infrared spectrometry [Guobiao (GB, means "National standard") 9801], and O<sub>3</sub> was measured by indigo disulphonate spectrophotometry (HJ 504–2009). All pollutants and AQI measurements were made in accordance with technical guidelines on environmental monitoring quality management (HJ 630–2011) and ambient air quality monitoring norms.<sup>27</sup> Data came from automatic monitoring stations.

### Covariates

Covariates included each patient's gender, age, year and season of onset, and meteorological data.

Age, gender, and year and season of onset were collected via medical records from Changshu No. 1 People's Hospital and Changshu No. 2 People's Hospital. The seasons were defined as follows: spring spanning March to May, summer from June to August, fall covering September to November, and winter from December to February. Meteorological data, which include daily

average temperature, humidity, wind speed, and precipitation, were acquired from the Xihe Energy Big Data platform.<sup>28</sup>

### Data preprocessing

Patient morbidity was categorised into 210 subgroups based on a combination of three factors: sex (male and female), age group (18–34 years, 35–59 years and ≥60 years) and season. The seasonal categorisation accounted for all four seasons across 8 years, except for 2022, which included only three seasons (spring, summer and fall). This categorisation was calculated as 2 (sexes) × 3 (age groups) × 35 (seasons across the years), resulting in 210 subgroups. For each subgroup, the number of morbidity episodes was tallied. Then, the number of residents of Changshu City, the average concentration of each air pollutant, and the average air quality were collapsed in each subgroup and merged together with the number of morbidity episodes. We matched local pollutant concentrations as well as meteorological data based on date of disease onset of patients. Additionally, meteorological factors on the day of each morbidity episode were considered, including average temperature, humidity, wind speed and precipitation, which were used for adjustment analysis and sensitivity analysis in model 4 and model 5.

### Statistical methods

Descriptive statistics were employed to summarise baseline characteristics including demographics, the season and the year of disease onset as well as air pollutants and the corresponding AQI. For continuous variables, mean (SD), median (IQR), minimum and maximum were calculated, and for categorical continuous variables, frequencies were counted, and the related frequencies were calculated. Values of *p* for the differences in these variables between men and women were obtained by using the *t* test for two independent samples,  $\chi^2$  test or rank-sum test, as appropriate.

Then, Spearman's rank correlation analysis was conducted to assess the relations among air pollutants and corresponding AQI and identify potential multicollinearity issues. Each pollutant and AQI was grouped into three levels based on their tertiles. Additionally, a logarithmic transformation (base 2) was applied, potentially aiding in the assessment of associations corresponding to every doubling of pollutant concentration or AQI.

Subsequently, the Poisson regression model was employed to investigate the associations between pollutants and AQI and risk of SSNHL. The corresponding prevalence ratio (PR) and its 95% CI were calculated. In the model, the number of cases served as the dependent variable (ie, *Y*), the concentration of the pollutant of current concern as the independent variable (*X*), and simultaneous adjustments were made for a variety of other parameters, while the population size was used as the offset term of the model. The independent variables were introduced into the model as two dummy variables (with the lowest level group acting as the control). For

linearity testing, these variables were entered in their logarithmic form (base 2) to examine the prevalence changes per onefold increase in pollutant concentration. We adopted a sequential modelling strategy, constructing the following models: model 1: without any adjustments; model 2: adjusted for the year and season of onset, along with patient gender and age at onset; model 3: addressed multicollinearity among pollutants. Building on model 2, Lasso regression was used to select relevant pollutant factors, with the primary pollutant under investigation locked in the model. For instance, in analysing the association of CO with risk of SSNHL, we further adjusted for PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub> and AQI using Lasso regression based on model 2, and only O<sub>3</sub> was finally selected and adjusted in model 3 with covariates in model 2. Model 4 expanded on model 3 by further adjusting for mean temperature, humidity, wind speed and precipitation on the day of disease onset.

Finally, in model 5, a sensitivity analysis was conducted to test the robustness of the model by adding mean barometric pressure, and the interaction term between mean temperature and mean barometric pressure to model 4.

All statistical analyses were conducted by using Stata V.18.0 (StataCorp, College Station, Texas, USA). A value of *p* ≤ 0.05 was considered statistically significant.

### Patient and public involvement

None.

## RESULTS

**Table 1** displays the demographic data of 4201 patients with SSNHL included in this study, detailing age, sex, year and season of disease onset. The mean age of the patients was 52.0 years (SD: 14.5), with a predominance of middle-aged individuals (approximately 50%) and the elderly (about a third). The distribution of the patients was roughly balanced between male and female, and no significant sex differences were observed in terms of age, year and season at disease onset (all values of *p* were greater than 0.05).

**Table 2** presents data on air quality and pollutant levels from Spring 2014 to Fall 2022, including their mean, median, and maximum and minimum values. Pollutant concentrations except for CO and AQI were similar between male and female patients with SSNHL (all values of *p* were greater than 0.05). For CO between male and female patients, there is a statistically significant difference in mean levels (male vs female patients: 0.79 mg/m<sup>3</sup> vs 0.77 mg/m<sup>3</sup>, *p*=0.033), but not in the medians (male vs female patients: 0.74 mg/m<sup>3</sup> vs 0.73 mg/m<sup>3</sup>, *p*=0.150).

Spearman's rank correlation analysis results, as depicted in **figure 2**, show the following relations between the AQI and various pollutants: AQI has the strongest correlation with PM<sub>2.5</sub> and PM<sub>10</sub>, exceeding 0.90. SO<sub>2</sub>, NO<sub>2</sub> and CO show modest correlations (0.46 to 0.66) with AQI, PM<sub>2.5</sub> and PM<sub>10</sub>. The correlations between SO<sub>2</sub>, NO<sub>2</sub> and CO ranged from 0.25 to 0.41. O<sub>3</sub> exhibits almost no relation

**Table 1** Demographics, season and year at disease onset for patients with SSHNL, Changshu, China, 2014–2022 (n=4201)\*

Characteristics	Overall	Male	Female	P value
Patients, n (%)	4201 (100.0)	1995 (47.5)	2206 (52.5)	
Age at symptom onset, years				
Mean (SD)	52.0 (14.5)	52.1 (14.7)	52.0 (14.3)	0.797
Median (Q <sub>1</sub> , Q <sub>3</sub> )	53 (42, 63)	53 (42, 63)	52.5 (43, 63)	0.676
Min, Max	18, 93	18, 87	18, 93	–
Age group at diagnosis, n (%)				0.300
18–34 years	599 (14.3)	291 (14.6)	308 (14.0)	
35–59 years	2188 (52.1)	1014 (50.8)	1174 (53.2)	
≥60 years	1414 (33.7)	690 (34.6)	724 (32.8)	
Season at diagnosis, n (%)				0.081
Spring	1089 (25.9)	510 (25.6)	579 (26.2)	
Summer	1080 (25.7)	547 (27.4)	533 (24.2)	
Autumn	1107 (26.4)	521 (26.1)	586 (26.6)	
Winter	925 (22.0)	417 (20.9)	508 (23.0)	
Year at diagnosis, n (%)				0.196
2014	406 (9.7)	189 (9.5)	217 (9.8)	
2015	545 (13.0)	241 (12.1)	304 (13.8)	
2016	577 (13.7)	290 (14.5)	287 (13.0)	
2017	513 (12.2)	263 (13.2)	250 (11.3)	
2018	631 (15.0)	283 (14.2)	348 (15.8)	
2019	565 (13.4)	279 (14.0)	286 (13.0)	
2020	500 (11.9)	228 (11.4)	272 (12.3)	
2021	282 (6.7)	139 (7.0)	143 (6.5)	
2022	182 (4.3)	83 (4.2)	99 (4.5)	

\*Values of p for the differences between men and women were obtained by using the t-test for two independent samples,  $\chi^2$  test or rank-sum test, as appropriate.

Max, maximum; Min, minimum; Q, quartile; SSHNL, sudden sensorineural hearing loss.

with AQI, and negative correlations with several other pollutants, notably a  $-0.35$  correlation with  $\text{NO}_2$ .

We further examined the exposure-response relationship between each pollutant, AQI and the onset of SSHNL in turn.

### CO concentration and SSHNL onset

Compared with those exposed to low levels of CO, patients exposed to moderate and high levels of CO showed an increased risk of SSHNL across all four sequential models. Model 4 (the final model) showed an 11.3% (95% CI 2.2% to 21.3%) and 23.0% (95% CI 10.5% to 36.9%) increase in SSHNL prevalence for moderate and high levels of CO exposure, respectively, compared with low levels. Additionally, each unit of increase in  $\log_2(\text{CO})$  (ie, for each doubling of the concentration of CO) was associated with 30.6% (95% CI 9.9% to 55.4%) increase in SSHNL prevalence ( $p=0.002$ ). Sensitivity analyses in model 5 confirmed these findings (table 3).

### SO<sub>2</sub> concentration and SSHNL onset

Models 2 and 3 showed an increased SSHNL prevalence with moderate SO<sub>2</sub> exposure (PR=1.212, 95% CI 1.024 to 1.435; PR=1.198, 95% CI 1.005 to 1.427). However, after adjusting meteorological factors in model 4, the association between SO<sub>2</sub> and SSHNL onset was not significant. This conclusion was materially unchanged in the sensitivity analysis of model 5 ( $p>0.05$  for linear trend) (see table 4).

### O<sub>3</sub> concentration and SSHNL onset

There was a linear relationship between O<sub>3</sub> exposure and SSHNL onset. In model 4, each unit of increase in  $\log_2(\text{O}_3)$  (equivalent to each doubling of O<sub>3</sub>) was associated with a 22.2% (95% CI 0.8% to 48.2%) increase in SSHNL prevalence ( $p=0.041$ ). Sensitivity analyses in model 5 revealed consistent results (see table 5).



**Table 2** Pollutant index and several contaminants at SSNHL diagnosis, Changshu, China, 2014–2022 (n=4201)\*

	Overall	Male patients	Female patients	P value
Patients, n (%)	4201 (100.0)	1995 (47.5)	2206 (52.5)	
AQI				
Mean (SD)	69.38 (34.00)	68.93 (33.07)	69.78 (34.82)	0.397
Median (Q <sub>1</sub> , Q <sub>3</sub> )	61 (45, 85)	61 (45, 84.5)	61 (45.25, 85)	0.767
Min, Max	6, 272	15, 248	6, 272	–
PM <sub>2.5</sub> (µg/m <sup>3</sup> )				
Mean (SD)	43.42 (28.53)	43.07 (27.76)	43.73 (29.20)	0.452
Median (Q <sub>1</sub> , Q <sub>3</sub> )	36 (23, 55)	35 (23, 55)	36 (23, 55)	0.805
Min, Max	3, 221	5, 199	3, 221	
PM <sub>10</sub> (µg/m <sup>3</sup> )				
Mean (SD)	68.09 (38.32)	67.42 (37.43)	68.69 (39.10)	0.276
Median (Q <sub>1</sub> , Q <sub>3</sub> )	58 (40, 86)	58 (40, 86)	58 (40, 86)	0.483
Min, Max	5, 265	9, 265	5, 265	–
SO <sub>2</sub> (µg/m <sup>3</sup> )				
Mean (SD)	15.31 (7.68)	15.31 (7.78)	15.31 (7.59)	0.986
Median (Q <sub>1</sub> , Q <sub>3</sub> )	14 (10, 18)	14 (10, 18)	14 (10, 18)	0.835
Min, Max	0, 69	3, 69	0, 69	–
NO <sub>2</sub> (µg/m <sup>3</sup> )				
Mean (SD)	36.88 (16.10)	36.83 (15.91)	36.93 (16.27)	0.860
Median (Q <sub>1</sub> , Q <sub>3</sub> )	33 (26, 45)	33 (26, 44)	33 (26, 45)	0.864
Min, Max	6, 124	6, 124	6, 114	–
CO (mg/m <sup>3</sup> )				
Mean (SD)	0.78 (0.28)	0.79 (0.29)	0.77 (0.28)	0.033
Median (Q <sub>1</sub> , Q <sub>3</sub> )	0.74 (0.59, 0.93)	0.74 (0.595, 0.95)	0.73 (0.59, 0.92)	0.150
Min, Max	0, 2.17	0, 2.17	0, 1.93	–
O <sub>3</sub> (µg/m <sup>3</sup> )				
Mean (SD)	65.37 (28.60)	65.84 (28.42)	64.96 (28.75)	0.363
Median (Q <sub>1</sub> , Q <sub>3</sub> )	63 (44, 83)	64 (45, 83)	63 (43, 82.75)	0.343
Min, Max	0, 183	0, 183	0, 183	–

\*Values of p for differences between male and female patients were obtained by using the t-test for two independent samples,  $\chi^2$  test or rank-sum test, as appropriate.

.AQI, Air Quality Index; CO, carbon monoxide; Max, maximum; Min, minimum; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; PM<sub>10</sub>, mean particulate matter with a diameter of 10 µm or less; PM<sub>2.5</sub>, mean particulate matter with a diameter of 2.5 µm or less; Q, quartile; SO<sub>2</sub>, sulfur dioxide; SSNHL, sudden sensorineural hearing loss.

### Concentration of other pollutants, AQI and SSNHL onset

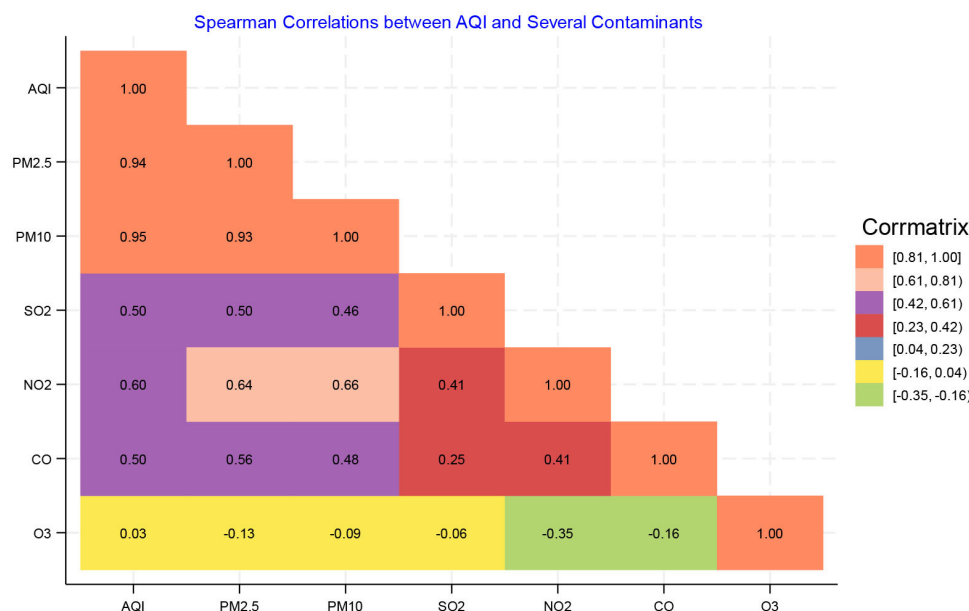
No significant associations were found between PM<sub>2.5</sub>, PM<sub>10</sub>, NO<sub>2</sub>, AQI and the onset of SSNHL ( $p \geq 0.05$ ) (online supplemental tables 1–4).

### DISCUSSION

The interplay between environmental factors and human health is crucial for survival and well-being. The human body constantly interacts with its environment, exchanging substances and energy. This interaction becomes particularly important when considering the role of environmental pollutants in disease pathogenesis. Airborne pollutants, especially respirable particles,

are closely linked to functional impairments of the respiratory system.<sup>15</sup> Short-term exposure to air pollutants may induce a range of physiological alterations such as systemic inflammation, oxidative stress, endothelial dysfunction, coagulation and lipid metabolism disorders.

One study found that acute PM exposure was associated with increased hospital visits for Meniere's disease based on the hospital visit data of 210 000 men and women who resided in Seoul, Korea from 2007 to 2010.<sup>29</sup> One systematic review found that higher air pollution exposure, especially NO<sub>2</sub>, is associated with a greater prevalence of otitis media in infants and children.<sup>30</sup> Notably, fluctuations in airborne



**Figure 2** Rank correlation matrix between the AQI and pollutants. AQI, Air Quality Index; CO, carbon monoxide; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; PM<sub>10</sub>, mean particulate matter with a diameter of 10 µm or less; PM<sub>2.5</sub>, mean particulate matter with a diameter of 2.5 µm or less; SO<sub>2</sub>, sulfur dioxide.

NO<sub>2</sub> concentrations have been associated with an increased risk of ST segment elevation myocardial infarction.<sup>19</sup> Long-term exposure to environmental pollution, metals, PM and organic pollutants extends these effects, potentially leading to metabolic dysfunction such as fatty liver disease.<sup>31</sup> Moreover, factors

like PM<sub>2.5</sub>, water pollutants, extreme weather and natural disasters are increasingly recognised as significant contributors to kidney disease morbidity and mortality.<sup>32</sup>

Along with the development of modern industrial society, air quality has emerged as a critical environmental

**Table 3** Associations [PR (95% CI)] between CO concentration and risk of SSNHL\*

	Tertiles of CO			<i>log</i> <sub>2</sub> <sup>(CO)</sup>	
	T1 (lowest)	T2	T3 (highest)	↑ 1 unit	P value
CO, (mg/m <sup>3</sup> )					
Median	0.643	0.768	0.921	—	—
Min, Max	0.425, 0.726	0.727, 0.808	0.809, 1.175	—	—
No. of event	1271	1394	1536	—	—
Model 1†	1 (Ref.)	1.133 (1.050, 1.223)	1.241 (1.152, 1.337)	1.178 (1.039, 1.336)	0.011
Model 2‡	1 (Ref.)	1.099 (1.013, 1.193)	1.210 (1.096, 1.334)	1.273 (1.084, 1.494)	0.003
Model 3§	1 (Ref.)	1.098 (1.011, 1.192)	1.209 (1.096, 1.334)	1.285 (1.095, 1.509)	0.002
Model 4¶	1 (Ref.)	1.113 (1.022, 1.213)	1.230 (1.105, 1.369)	1.306 (1.099, 1.554)	0.002
Model 5**	1 (Ref.)	1.122 (1.029, 1.224)	1.216 (1.092, 1.3550)	1.276 (1.071, 1.522)	0.007

\*All the models were constructed using Poisson regression with SSNHL patient count as the dependent variable and related population size as the offset.

†Model 1: no adjustment for any covariates.

‡Model 2: adjusted for year at diagnosis, season at diagnosis, age group (18–24 years, 35–59 years and ≥60 years) and sex.

§Model 3: adjusted for all the covariates in model 2 plus O<sub>3</sub> in log scale with 2 as the base, which was selected using adaptive lasso among the candidates from the list including PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub> and AQI. All the candidates are transformed variables in log scale with 2 as the base.

¶Model 4: adjusted for all the covariates in model 3 plus MT (continuous), MRH (continuous), wind speed (continuous) and precipitation (continuous).

\*\*Model 5: adjusted for all the covariates in model 4 plus MAP (continuous), and the interaction term between MT and MAP.

AQI, Air Quality Index; CO, carbon monoxide; MAP, mean atmosphere pressure; Max, maximum; Min, minimum; MRH, mean relative humidity; MT, mean temperature; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; PM<sub>10</sub>, mean particulate matter with a diameter of 10 µm or less; PM<sub>2.5</sub>, mean particulate matter with a diameter of 2.5 µm or less; PR, prevalence ratio; SO<sub>2</sub>, sulphur dioxide; SSNHL, sudden sensorineural hearing loss; T, tertile.

**Table 4** Associations [PR (95% CI)] between SO<sub>2</sub> concentration and risk of SSNHL\*

	Tertiles of SO <sub>2</sub>			log <sub>2</sub> <sup>(SO<sub>2</sub>)</sup>	P value
	T1 (lowest)	T2	T3 (highest)	↑ 1 unit	
SO <sub>2</sub> , (µg/m <sup>3</sup> )				—	—
Median	8.484	13.674	20.974	—	—
Min, Max	6.710, 10.950	11.040, 16.040	16.330, 34.830	—	—
No. of event	966	1651	1584	—	—
Model 1†	1	1.697 (1.551, 1.818)	1.532 (1.414, 1.660)	1.351 (1.280, 1.425)	<0.001
Model 2‡	1	1.212 (1.024, 1.435)	1.170 (0.961, 1.425)	1.064 (0.938, 1.208)	0.334
Model 3§	1	1.198 (1.005, 1.427)	1.050 (0.853, 1.293)	0.951 (0.827, 1.094)	0.483
Model 4¶	1	1.137 (0.939, 1.376)	0.969 (0.769, 1.222)	0.880 (0.750, 1.034)	0.120
Model 5**	1	1.119 (0.919, 1.361)	0.950 (0.750, 1.202)	0.860 (0.731, 1.012)	0.070

\*All the models were constructed using Poisson regression with SSNHL patient count as the dependent variable and related population size as the offset.

†Model 1: no adjustment for any covariates.

‡Model 2: adjusted for year at diagnosis, season at diagnosis, age group (18–24 years, 35–59 years and ≥60 years), and sex.

§Model 3: adjusted for all the covariates in model 3 plus O<sub>3</sub> in log scale with 2 as the base, which was selected using adaptive lasso among the candidates from the list including PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub> and AQI. All the candidates are transformed variables in log scale with 2 as the base.

¶Model 4: adjusted for all the covariates in model 3 plus MT (continuous), MRH (continuous), wind speed (continuous) and precipitation (continuous).

\*\*Model 5: adjusted for all the covariates in model 4 plus MAP (continuous), and the interaction term between MT and MAP.

AQI, Air Quality Index; MAP, mean atmosphere pressure; MRH, mean relative humidity; MT, mean temperature; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; PM<sub>10</sub>, mean particulate matter with a diameter of 10 µm or less; PM<sub>2.5</sub>, mean particulate matter with a diameter of 2.5 µm or less; PR, prevalence ratio; SO<sub>2</sub>, sulfur dioxide; SSNHL, sudden sensorineural hearing loss; T, tertile.

variable attracting widespread academic attention. For instance, a study by Choi *et al* in Korea linked high concentrations of NO<sub>2</sub> to the onset of idiopathic deafness.<sup>33</sup>

However, studies in Taipei examining the correlation between air quality and SSNHL have yielded different results, likely due to variations in data sources, statistical

**Table 5** Associations [PR (95% CI)] between O<sub>3</sub> concentration and risk of SSNHL\*

	Tertiles of O <sub>3</sub>			log <sub>2</sub> <sup>(O<sub>3</sub>)</sup>	P value
	T1 (lowest)	T2	T3 (highest)	↑ 1 unit	
O <sub>3</sub> , (µg/m <sup>3</sup> )				—	—
Median	44.555	66.681	84.359	—	—
Min, Max	22.000, 54.780	55.140, 74.060	74.570, 102.080	—	—
No. of event	1334	151	1357	—	—
Model 1†	1	1.132 (1.052, 1.219)	1.007 (0.934, 1.086)	1.087 (1.011, 1.168)	0.024
Model 2‡	1	1.110 (0.992, 1.241)	1.098 (0.952, 1.267)	1.195 (1.004, 1.424)	0.045
Model 3§	1	1.118 (0.998, 1.251)	1.117 (0.967, 1.290)	1.215 (1.020, 1.447)	0.029
Model 4¶	1	1.115 (0.990, 1.257)	1.114 (0.948, 1.311)	1.222 (1.008, 1.482)	0.041
Model 5**	1	1.115 (0.989, 1.258)	1.107 (0.941, 1.303)	1.218 (1.002, 1.481)	0.047

\*All the models were constructed using Poisson regression with SSNHL patient count as the dependent variable and related population size as the offset.

†Model 1: no adjustment for any covariates.

‡Model 2: adjusted for year at diagnosis, season at diagnosis, age group (18–24 years, 35–59 years and ≥60 years) and sex.

§Model 3: adjusted for all the covariates in model 3 plus O<sub>3</sub> in log scale with 2 as the base, which was selected using adaptive lasso among the candidates from the list including PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub> and AQI. All the candidates are transformed variables in log scale with 2 as the base.

¶All the candidates are transformed variables in log scale with 2 as the base.

\*\*Model 5: adjusted for all the covariates in model 4 plus MAP (continuous), and the interaction term between MT and MAP.

AQI, Air Quality Index; MAP, mean atmosphere pressure; MT, mean temperature; NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; PM<sub>10</sub>, mean particulate matter with a diameter of 10 µm or less; PM<sub>2.5</sub>, mean particulate matter with a diameter of 2.5 µm or less; PR, prevalence ratio; SO<sub>2</sub>, sulfur dioxide; SSNHL, sudden sensorineural hearing loss; T, tertile.

methods and the research approaches. For example, Chang *et al* found that NO<sub>2</sub> and CO are risk factors of SSNHL,<sup>24</sup> which was echoed by Tsai *et al* who also found that long-term exposure to PM<sub>2.5</sub>, NO, NO<sub>2</sub> and CO increased the risk of sudden deafness.<sup>34</sup> Similarly, Cheng *et al* highlighted the potential lag effect of PM<sub>2.5</sub>, O<sub>3</sub> and NO<sub>2</sub> on increased risk of SSNHL,<sup>35</sup> while Yuan *et al*'s study in the UK found a positive association of PM<sub>10</sub>, NOx and NO<sub>2</sub> with risk of SSNHL.<sup>25</sup> Notably, such studies are yet to be conducted in Mainland China.

Our study, set in Changshu, a county-level city in Jiangsu Province, fills this gap. Changshu's industrial backdrop, coupled with its geographical and climatic features, presents a unique setting for examining the impact of air pollution on health. Our findings indicate a significant adverse effect of airborne CO and O<sub>3</sub> on the development of SSNHL. We observed a clear exposure-response relationship with CO, where both moderate and high levels heightened SSNHL prevalence. Similarly, O<sub>3</sub> demonstrated a linear trend with SSNHL, showing a significant increase in risk with each concentration doubling, after adjusting for major potential confounders. Interestingly, no association was found between SSNHL and other pollutants like PM<sub>2.5</sub>, PM<sub>10</sub>, SO<sub>2</sub>, NO<sub>2</sub> or AQI. In addition, since potential confounding factors at individual level are not available, our conclusion on the association between air pollutants and risk of SSNHL should be explained with caution and further verified in future large-scale prospective cohort studies at the individual level.

The mechanisms underlying these associations are complex. CO, with its high affinity for haemoglobin, impairs oxygen exchange and can cause acute symptoms like headache and dizziness, and chronic neurological impairments such as aphasia, dementia, attention deficits and aberrant behaviours.<sup>36–40</sup> Long-term low-dose CO exposure, on the other hand, may also increase blood viscosity and thrombosis risk<sup>41</sup> and affect the microcirculations in the inner ear. Additionally, CO can stimulate the release of NO from endothelial cells,<sup>42</sup> and NO in the cochlea controls the stability of the cochlea's internal environment by participating in signalling and ionic regulatory pathways,<sup>43</sup> affecting neurotransmission and neuromodulation in the cochlea.<sup>44</sup> It has also been found that CO can inhibit cytochrome c oxidase, leading to oxidative stress and cellular damage,<sup>45–46</sup> potentially damaging inner ear hair cells.<sup>47</sup> O<sub>3</sub>, on the other hand, generates free radicals, affecting lung epithelial cells and causing DNA damage in epidermal keratinocyte,<sup>48–50</sup> with its impact on inner ear cells warranting further investigation.

This study is pioneering in Mainland China, covering a broad time span and large data set of 4201 cases of SSNHL in Changshu. The average concentrations of pollutants in the Changshu area from 2014 to 2022 are all higher than in Taiwan from 2011 to 2019.<sup>35</sup> Similarly, the pollutant concentrations in the Changshu area were also higher than those in the UK, Korea and Turkey during the study period<sup>22–23–25</sup> (online supplemental table 5). Pollutant concentrations in the Changshu area are at medium to high levels compared with South-East Asian areas.<sup>51–52</sup> Therefore, this study is also

the first to be conducted in a moderately polluted to highly polluted environment. In recent years, China's environmental protection measures have been strengthened and there have been some improvements in environmental pollution<sup>53–54</sup> (online supplemental figures 1–3). Moreover, Changshu is located in the economically developed region of the Yangtze River Delta in south-eastern China, with four distinct seasons. Its economic and climatic representativeness adds to the study's relevance.

However, this study also has some limitations. The study did not account for individual factors like socioeconomic status, smoking, alcohol consumption, nor did it consider other chronic diseases (eg, obesity, diabetes mellitus, etc). The potential impact of these factors on the associations under study has not been considered during the modelling process, which needs to be answered by future large-scale cohort studies. Additionally, the pollutants in the present study are at group level defined by age, sex and season, rather than individual level exposure.

## CONCLUSION

This study suggests a positive association between CO, O<sub>3</sub> and the risk of SSNHL, underscoring the need for emission reduction, enhanced air monitoring and increased public awareness of environmental protection. Further large-scale prospective cohort studies are warranted to confirm our findings and provide more insights into the topic.

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