

Title: The Association between Air Pollution and General Practitioner Visits for Respiratory Diseases in Hong Kong

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## Abstract

**Background:** Few studies explore the relation between air pollution and general practitioner (GP) consultations in Asia. We studied clinic attendance data from a network of GPs and examined the relations of daily GP consultations for upper respiratory tract infections (URTI) and non-URTI respiratory diseases with daily air pollutant concentrations measured in their respective districts.

**Methods:** A time series study was performed, using data on daily patient consultations in 13 GP clinics distributed over eight districts, from 2000 – 2002. A Poisson regression model was constructed using the generalised additive model (GAM) approach for each GP clinic, and associations with daily numbers of first visits for URTI were sought for daily concentrations of the following air pollutants: SO<sub>2</sub>, NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>. A summary relative risk of first visits to GP for URTI per unit increase in concentration for each air pollutant was derived using a random effect model. First visits for non-URTI respiratory diseases were analyzed in three GP clinics.

**Results:** Significant associations were observed between first visits for URTI and an increase in the concentrations of NO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub> and PM<sub>2.5</sub>. The excess risk (ER) was highest for NO<sub>2</sub> (3.0%), followed by O<sub>3</sub> (2.5%), PM<sub>2.5</sub> (2.1%) and PM<sub>10</sub> (2.0%). Similar associations with these air pollutants were found for non-URTI respiratory diseases.

**Conclusions:** Our findings give further evidence that air pollution contributes to GP visits for URTI and non-URTI respiratory diseases in the community.

(234 words)

## Introduction

Many epidemiological studies on air pollution focus on hospital admissions and mortalities as health outcomes.<sup>1-12</sup> These outcomes represent, respectively, serious morbidities and the ultimate health consequences of air pollution. Illnesses seen in primary health care settings, by contrast, form the much wider base of the pyramid of air pollution-related illnesses. Although most of these illnesses are minor in nature with minimal long-term effects on health, they represent a substantial proportion of the overall morbidity in the community. In a local cross-sectional morbidity study, 41% and 48% of out-patient consultations, in the private and public sector respectively, were for respiratory illnesses.<sup>13,14</sup> The total number of GP consultations for respiratory illnesses has been estimated to be about 23 million in Hong Kong in 2001.<sup>15</sup> The direct medical cost exceeds HK\$3.4 billion (US\$442 million). With the associated productivity loss, these illnesses constitute a substantial economic burden on the community. Despite the significant health and economic impact of air pollution, few epidemiological studies on air pollution and health have been conducted in the primary health care sector.<sup>16-22</sup> An important reason for the paucity of such studies is the absence of routinely collected data on primary health care in both private and public sectors in most countries. To study the effect of air pollution on morbidities in the primary care setting, we prospectively collected data on daily visits for upper respiratory tract infections (URTI) and other diseases from 13 GPs' clinics, over a three-year period from 2000 – 2002 inclusive, and looked for associations with daily variations in the concentrations of the following air pollutants: NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>, PM<sub>10</sub> and PM<sub>2.5</sub>, using a time series approach. Our preliminary findings, based on one-year data (2000) from seven GP clinics, have been reported earlier.<sup>23</sup>

## Subjects and Methods

### *Data from GP clinics*

From January 2000 to December 2002, we recruited 13 GPs in eight districts of Hong Kong to collect data on the daily number of first visits for respiratory and other diseases at their clinics. The length of their participation in the study varied from 12 – 36 months, depending on the time of their recruitment and withdrawal. The following diseases / symptoms were recorded: (i) Respiratory diseases / symptoms: upper and lower respiratory tract infections, influenza, asthma, chronic obstructive pulmonary diseases, allergic rhinitis, cough and other respiratory diseases; (ii) Cardiovascular diseases / symptoms: cardiac arrhythmias, angina, hypertension and other circulatory diseases; (iii) Diseases of the other systems. Diseases or symptoms were coded according to the International Classification of Primary Care 2nd edition (ICPC-2).<sup>24</sup> This is an alphanumeric, three-digit system, which identifies the ‘episode’ of doctor consultation by system and diagnosis or reason for encounter. The system is partly compatible with the Tenth Revision of the International Classification of Diseases (ICD-10). The following information was recorded: the age and sex of the patients; their place of residence and work by district; whether it was a first visit, or a follow-up visit for the same disease episode; the diagnoses (categorised according to the ICPC-2); their employment status; and the duration of sick leave granted by the doctor.

### *Data on air pollutants*

Daily mean concentrations of four ‘criteria pollutants’: nitrogen dioxide (NO<sub>2</sub>), sulphur dioxide (SO<sub>2</sub>), ozone (O<sub>3</sub>) and particulates with an aerodynamic diameter less than 10 µm (PM<sub>10</sub>) were measured in air monitoring stations located in 8 districts throughout Hong Kong by the Environmental Protection Department (EPD).<sup>\*</sup> In addition, particulates with an aerodynamic diameter less than 2.5 µm (PM<sub>2.5</sub>) were monitored in one station. Each of the 13 GP clinics was matched with a corresponding set of air pollutant data in his/her district.

### *Statistical modelling*

We used a statistical model developed from the APHEA II protocol that has been used for time series analyses of mortality and hospital admissions in Europe.<sup>25</sup> Missing air pollutant data in one station were predicted by a regression of data from that station on

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\* SO<sub>2</sub> was measured by UV fluorescence (Model 43A SO<sub>2</sub> Analyzer, Thermo Environmental Instruments Inc, U.S.); NO<sub>2</sub> was measured by chemiluminescence (Model 42 Chemiluminescence NO-NO<sub>2</sub>-NO<sub>x</sub> Analyzer, Thermo Environmental Instruments Inc, U. S.); O<sub>3</sub> was measured by UV absorption (ML8840 NO<sub>x</sub> Analyzer, Monitoring Lab. Inc., U.S.); PM<sub>10</sub> was measured by the Tapered Element Oscillating Microbalance (TEOM) (Rupprecht & Patashnick Co., Inc., TEOM Series 1400a-AB PM10 Monitor, U.S.), and PM<sub>2.5</sub> by TEOM (R & P Partisol Plus, Model 2025, U.S.).

corresponding data from the nearest station.<sup>†</sup> A generalised additive model<sup>26</sup> using a Poisson distribution with log-link function was constructed as a core model. This regressed the daily numbers of GP visits for respiratory diseases in each clinic on the time variable (day), day of the week variable, daily mean temperature and humidity, and a holiday indicator. Only first visits of the disease episodes by patients who lived, worked, or attended school in the same district as the GP clinic were included in the model. Smoothing of the time variable was used to control for long-term seasonal patterns of GP visits and smoothing splines were used as smoothers. The quasi-likelihood method was used to correct for over-dispersion.<sup>27</sup> Each core model was chosen based on the degree of freedom that gave the minimum AIC value.<sup>27</sup> Autocorrelation was adjusted by adding autoregressive terms (GP consultations in the previous day, up to three days) to the model. After the confounding effects of seasonality, days of the week and climatic variables have been controlled, daily concentrations of PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub> and O<sub>3</sub> (obtained from the monitoring station located in each district) were then added to each core model, to determine the relative risk (RR) of GP visits for a 10 µg/m<sup>3</sup> increase in each of these air pollutants. Data on daily concentrations of PM<sub>2.5</sub> were used in three models, which took data from GP9 (in the same district as the PM<sub>2.5</sub> monitoring station), and GPs 1 and 4 (in a contiguous district). Concentrations of all the air pollutants for the same day (lag 0) up to three lag days (lag 3) and cumulative lags by two (lag 0 and 1), three (lag 0, 1 and 2), and four days (lag 0 to 3), were tested in each model. The lag day with the air pollutant concentration that yielded the smallest p value, i.e., the largest  $\chi^2$  was chosen. The standard errors of the estimates were computed using the supplementary program used in the re-analysis of the National Morbidity, Mortality, and Air Pollution Study (NMMAPS).<sup>28, 29</sup> The RRs obtained from individual GPs were combined using a random effect model.<sup>30</sup> All calculations were performed with the software S-plus 4.0 using a more stringent convergence criteria in the gam(.) function.<sup>31</sup>

Ethical approval was not required as we obtained from the GPs only counts of daily patient consultations stratified by various parameters, without the individual patient's identity. Data on air pollution were provided by the Environmental Protection Department.

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<sup>†</sup> A regression was fitted for the daily concentrations of the pollutant with missing values (Y) on the corresponding values of the pollutant on the same day from the nearest station (X). The predicted values (Y1) obtained from the regression equation were then used to replace Y.

## Results

### *GP consultations*

Table 1 shows the summary statistics of consultations by 13 GPs in eight districts. The duration of their participation varied, ranging from 12 months (2 GPs) to 36 months (4 GPs), with a mean of 28.8 months and a median of 33 months. A total of 314,514 consultations were recorded from the 13 GPs. 296,372 (94.2%) consultations were by patients living, working, or attending schools in the same district. About three-quarters of these were first visits of disease episodes, two-thirds of which were for respiratory diseases (all types). Upper respiratory tract infection (URTI) accounted for 82.7% of all respiratory diseases. Other respiratory diseases and the cardiovascular diseases were few in number.

**Table 1: Summary statistics of visits to GPs by clinic**

GP code / duration / time period of study	Total no. of visits	Visits made by patients in the same district	No. of first visits in the same district	First visits for: any respiratory diseases, same district	First visits for: URTI, same district
GP1 / 26 months Jan 2000–Feb 2002	8465	8030 (94.9%)	6215 (73.4%)	6021 (71.1%)	4056 (47.9%)
GP2 / 12 months Jan–Dec 2000	10286	6810 (66.2%)	3065 (29.8%)	1526 (14.8%)	1049 (10.2%)
GP3 / 36 months Jan 2000–Dec 2002	40186	38350 (95.4%)	32031 (79.7%)	20436 (50.9%)	19558 (48.6%)
GP4 / 36 months Jan 2000–Dec 2002	29731	29146 (98.0%)	20812 (70.0%)	12438 (41.8%)	10177 (34.2%)
GP5 / 12 months Jan–Dec 2000	8520	8306 (97.4%)	6357 (74.6%)	2068 (24.2%)	1760 (20.7%)
GP6 / 36 months Jan 2000–Dec 2002	35967	35392 (98.4%)	32403 (90.1%)	24366 (67.7%)	23686 (65.9%)
GP7 / 36 months Jan 2000–Dec 2002	27212	26492 (97.4%)	22130 (81.3%)	14272 (52.4%)	12319 (45.3%)
GP8 / 33 months Apr 2000–Dec 2002	21321	20131 (94.4%)	15256 (71.6%)	9456 (44.4%)	8837 (41.4%)
GP9 / 33 months Apr 2000–Dec 2002	45844	43534 (95.0%)	34726 (75.7%)	18866 (41.1%)	14729 (32.1%)
GP10 / 33 months Apr 2000–Dec 2002	34553	31920 (92.4%)	8757 (25.3%)	6141 (17.8%)	4540 (13.1%)
GP11 / 33 months Apr 2000–Dec2002	20851	19039 (91.3%)	15422 (74.0%)	10949 (52.5%)	10247 (49.1%)
GP12 / 24 months Jan 2001–Dec 2002	9389	9114 (97.1%)	7086 (75.5%)	6973 (74.2%)	3233 (34.4%)
GP13 / 24 months Jan 2001–Dec 2002	22189	20108 (90.6%)	15129 (68.2%)	14012 (63.1%)	7864 (35.4%)
Total	314514	296372 (94.2%)	219389 (69.8%)	147524 (46.9%)	122055 (38.8%)

Note: Values in parentheses are percentages of the total number of visits at each clinic

Table 2 shows the means, ranges, and percentiles of daily air pollutant concentrations in eight air-monitoring stations during the period. NO<sub>2</sub> and PM<sub>10</sub> are the dominant air pollutants in five districts (Eastern, Kwun Tong, Tsuen Wan, Kwai Chung and Yuen Long). The corresponding concentrations of O<sub>3</sub> in these districts (with the exception of Eastern and Yuen Long) are low. This pattern is reversed in three districts (Shatin, Tai Po and Central & Western), with relatively low NO<sub>2</sub> and PM<sub>10</sub> but high levels of O<sub>3</sub>. PM<sub>2.5</sub> was highly correlated with PM<sub>10</sub> (correlation coefficient,  $r = 0.94$ ). NO<sub>2</sub> was moderately correlated with PM<sub>10</sub> (median  $r = 0.68$ ; range: 0.38 – 0.75) and SO<sub>2</sub> (median  $r = 0.47$ ; range: 0.36 – 0.64), but poorly correlated with O<sub>3</sub> (median  $r = 0.12$ ; range: -0.15 – 0.31). O<sub>3</sub> was moderately correlated with PM<sub>10</sub> (median  $r = 0.40$ ; range: 0.14 – 0.48), but poorly correlated with SO<sub>2</sub> (median  $r = -0.13$ ; range: -0.04 – -0.42). SO<sub>2</sub> was poorly correlated with PM<sub>10</sub> (median  $r = 0.28$ ; range: 0.19 – 0.51).

**Table 2: Summary statistics of daily air pollutant concentrations in 8 air monitoring stations, January 2000 – December 2002**

Stations (corresponding to GPs)	Pollutant	N (days)	Mean concentration ( $\mu\text{g}/\text{m}^3$ )	S.D.	Min	25%	50%	75%	Max
1. Central & Western (GP8)	NO <sub>2</sub>	950	50.9	21.4	10	36	49	62	170
	PM <sub>10</sub>	960	48.8	27.9	9	27	43	64	200
	O <sub>3</sub>	953	33.8	19.8	3	19	29	48	115
	SO <sub>2</sub>	950	19.6	15.8	0	9	15	24	105
2. Eastern (GP3)	NO <sub>2</sub>	960	55.0	19.0	11	42	56	66	169
	PM <sub>10</sub>	1082	43.4	23.1	12	25	39	56	150
	O <sub>3</sub>	966	32.4	14.5	2	22	32	40	99
	SO <sub>2</sub>	959	12.2	9.5	1	7	10	10	52
3. Kwai Chung (GP1, GP4)	NO <sub>2</sub>	1084	68.2	22.6	12	54	64	77	211
	PM <sub>10</sub>	1091	56.9	43.6	14	35	46	65	290
	O <sub>3</sub>	1091	24.1	17.4	0	9	21	37	99
	SO <sub>2</sub>	1090	23.4	20.1	0	9	15	34	130
4. Kwun Tong (GP2, GP6, GP10)	NO <sub>2</sub>	814	71.5	23.4	7	56	72	85	179
	PM <sub>10</sub>	877	55.0	24.9	14	37	51	68	186
	O <sub>3</sub>	806	24.7	12.4	4	14	23.5	33	63
	SO <sub>2</sub>	812	16.6	12.9	0	9	13	19	109
5. Shatin (GP11)	NO <sub>2</sub>	1076	47.4	20.2	10	34	44	57	146
	PM <sub>10</sub>	1070	46.7	23.9	7	29	40	60	164
	O <sub>3</sub>	1077	36.4	22.7	4	18	31	51	123
	SO <sub>2</sub>	1078	15.8	11.3	0	8	12	19	80
6. Tai Po (GP5, GP12)	NO <sub>2</sub>	955	47.8	19.4	10	35	45	57	156
	PM <sub>10</sub>	1030	47.7	24.6	11	29	42	61	165
	O <sub>3</sub>	951	44.6	21.5	1	28	41	60	119
	SO <sub>2</sub>	953	12.0	10.1	0	5	10	16	99
7. Tsuen Wan (GP9)	NO <sub>2</sub>	1086	62.5	20.2	17	48	60	73	152
	PM <sub>10</sub>	1092	51.1	23.7	13	34	45	65	167
	O <sub>3</sub>	1086	23.1	15.7	2	10	20	32	88
	SO <sub>2</sub>	1088	35.0	25.8	2	14	25	53	141
	PM <sub>2.5</sub>	725	35.7	16.7	9	23	32	44	120
8. Yuen Long (GP7, GP13)	NO <sub>2</sub>	958	57.7	20.2	16	43	55	70	148
	PM <sub>10</sub>	1063	55.0	28.1	13	33	49	72	176
	O <sub>3</sub>	955	30.4	16.1	0	19	27	40	92
	SO <sub>2</sub>	958	17.6	13.0	0	9	15	23	114

The degrees of freedom used to control the seasonality in our statistical models differed for individual GPs. The mean, standard deviation and median degrees of freedom for the 13 models are 80.8, 51.2 and 70 respectively.

The individual relative risks (RRs) of patients' first visits for URTI by clinic, and the summary RRs for all clinics (per  $10 \mu\text{g}/\text{m}^3$  increase in the concentrations of each air pollutant) are shown in Table 3. Statistically significant summary RRs (at 95% confidence level) of first visits to GP clinics for URTI were demonstrated for  $\text{O}_3$ ,  $\text{NO}_2$ ,  $\text{PM}_{10}$  and  $\text{PM}_{2.5}$ , except for  $\text{SO}_2$ . The magnitudes of the excess risk (ER) of GP visits for URTI, given by  $100 \times (\text{RR} - 1) \%$ , were 3.0% for  $\text{NO}_2$ , 2.5% for  $\text{O}_3$ , 2.0% for  $\text{PM}_{10}$ , and 2.1% for  $\text{PM}_{2.5}$ . The individual and combined RR of first visits for non-URT I respiratory diseases were calculated for three GPs (GPs 9, 12 and 13) with sufficiently large numbers of visits ( $> 2$  per day) for modelling (Table 4). The findings were similar to those for URTI. The daily numbers of first visits for individual respiratory diseases, and for cardiovascular diseases as a group, were too few for model construction.

As the RRs obtained from GP2 (who contributed one year's data, with a much lower proportion of patients coming from his own district) were considerably higher than the corresponding figures from other GP clinics for four pollutants, a sensitivity analysis was performed by excluding GP2 in calculating the summary RRs. The summary RRs and 95% confidence intervals were little changed, which did not affect the overall interpretation of our results.

A location map of the GP clinics and the air monitoring stations is shown in Figure 1.

**Table 3: Relative risks (95% confidence intervals) of first visits to 13 GPs for upper respiratory tract infections (URTI) per 10 µg/m<sup>3</sup> increase in the concentrations of air pollutants (2000-2002)**

	<b>NO<sub>2</sub></b>	<b>O<sub>3</sub></b>	<b>SO<sub>2</sub></b>	<b>PM<sub>10</sub></b>	<b>*PM<sub>2.5</sub></b>
GP1	1.026 [0-1] (1.002, 1.051)	1.018 [2] (0.992, 1.045)	1.032 [0] (1.010, 1.055)	1.021 [1] (1.005, 1.037)	1.028 [1] (1.002, 1.056)
GP2	1.037 [3] (0.982, 1.095)	1.117 [3] (1.008, 1.238)	1.173 [2] (1.022, 1.346)	1.075 [3] (1.018, 1.135)	-
GP3	1.045 [0-1] (1.028, 1.062)	1.035 [1] (1.018, 1.053)	0.987 [2] (0.973, 1.003)	1.026 [1] (1.017, 1.036)	-
GP4	1.006 [0-1] (0.998, 1.014)	1.028 [0-3] (1.001, 1.056)	0.988 [0-1] (0.975, 1.001)	1.012 [0] (0.998, 1.026)	1.017 [0] (1.001, 1.034)
GP5	1.077 [1] (1.021, 1.135)	0.949 [0-3] (0.883, 1.019)	0.909 [0] (0.756, 1.093)	1.047 [0-3] (0.960, 1.142)	-
GP6	1.027 [0] (1.013, 1.041)	1.028 [2] (1.013, 1.044)	0.977 [2] (0.962, 0.992)	1.015 [1] (1.005, 1.024)	-
GP7	1.037 [0-1] (1.020, 1.055)	1.017 [1] (0.998, 1.036)	0.980 [0-1] (0.959, 1.002)	1.022 [0-1] (1.009, 1.035)	-
GP8	1.036 [0] (1.013, 1.059)	1.062 [2] (1.036, 1.089)	0.976 [2] (0.949, 1.003)	1.045 [0-3] (1.015, 1.076)	-
GP9	1.025 [0] (1.009, 1.041)	1.027 [1] (1.010, 1.045)	1.018 [0] (1.003, 1.033)	1.020 [0-3] (1.000, 1.041)	1.022 [0] (1.005, 1.040)
GP10	1.073 [0-3] (1.028, 1.119)	1.041 [2] (1.017, 1.065)	0.958 [0-2] (0.926, 0.991)	1.019 [2] (1.001, 1.037)	-
GP11	1.019 [3] (1.005, 1.033)	1.014 [2] (1.002, 1.026)	1.021 [3] (1.000, 1.043)	1.016 [1] (1.001, 1.031)	-
GP12	1.017 [0] (0.987, 1.049)	1.027 [2] (0.986, 1.069)	1.046 [3] (1.011, 1.083)	1.019 [2] (0.997, 1.041)	-
GP13	1.041 [03] (0.997, 1.088)	0.998 [0-3] (0.994, 1.003)	1.010 [0-1] (0.998, 1.022)	1.027 [0-3] (1.004, 1.050)	-
Combined RR	1.030 (1.020, 1.040)	1.025 (1.012, 1.038)	1.000 (0.987, 1.013)	1.020 (1.016, 1.025)	1.021 (1.010, 1.032)
Combined RR after excluding GP2**	1.030 (1.019, 1.041)	1.024 (1.011, 1.036)	0.999 (0.986, 1.011)	1.020 (1.017, 1.023)	1.021 (1.010, 1.032)

Statistically most significant lag days, either single or cumulative lag days are shown in square brackets

\* PM<sub>2.5</sub> data were available only in the district of GP9 (Tsuen Wan). GPs 1 and 4 were located in an adjoining district (Kwai Chung).

\*\* The RRs for GP2 were much higher than those of other GPs. The combined RR was re-calculated without GP2, as a sensitivity analysis.

Table 4: **Relative risks (95% confidence intervals) of first visits to 3 GPs for non- URTI respiratory diseases per 10 µg/m<sup>3</sup> increase in the concentrations of air pollutants (2000-2002)**

	<b>NO<sub>2</sub></b>	<b>O<sub>3</sub></b>	<b>SO<sub>2</sub></b>	<b>PM<sub>10</sub></b>
GP9	1.015 [0-3] (0.997, 1.033)	1.036 [0-3] (1.008, 1.064)	1.014 [2] (0.998, 1.030)	1.021 [3] (1.006, 1.036)
GP12	1.050 [0-1] (1.028, 1.073)	1.020 [1] (0.996, 1.045)	0.956 [0-1] (0.913, 1.000)	1.020 [0] (1.005, 1.036)
GP13	1.047 [0-3] (1.003, 1.062)	1.025 [0-2] (1.006, 1.043)	1.023 [0-3] (0.998, 1.049)	1.029 [0-3] (1.019, 1.039)
Combined RR	1.038 (1.028, 1.048)	1.026 (1.013, 1.039)	1.012 (0.999, 1.025)	1.025 (1.018, 1.032)

Statistically most significant lag days, either single or cumulative lag days are shown in square brackets

## **Discussion**

This is one of few time series studies on air pollution and community morbidity (as reflected in visits to GP) reported in the literature. For populations where routinely collected data are not available, GP consultation data have to be prospectively collected over a sufficiently long period for time series analysis, which accounts for the paucity of similar studies.

The summary RR of first visits to GP for URTI are statistically significant and above unity for a  $10 \mu\text{g}/\text{m}^3$  increase in four out of five air pollutants, namely,  $\text{NO}_2$ ,  $\text{O}_3$ ,  $\text{PM}_{10}$ , and  $\text{PM}_{2.5}$ . The association between air pollution and GP visits due to non-URTI respiratory diseases was analyzed in three GP datasets and the results were similar to those for URTI. The RRs for  $\text{PM}_{2.5}$  closely mirror those for  $\text{PM}_{10}$ , which reflects the strong correlation between the two pollutants. The magnitude of the RR for  $\text{PM}_{2.5}$  was uniformly higher than that for  $\text{PM}_{10}$ . While the RRs for particulates of different sizes were found to be similar in some studies,<sup>32</sup> our results are consistent with a number of studies that demonstrated that  $\text{PM}_{2.5}$  was more strongly associated than  $\text{PM}_{10}$  with acute health outcomes.<sup>33-35</sup> It should be cautioned, however, that only one of three GP datasets (GP9 in Tsuen Wan) used for calculating the RR for  $\text{PM}_{2.5}$  was from the district where  $\text{PM}_{2.5}$  concentrations were monitored. The other two GP clinics (GP1, GP4) were situated in the neighbouring district of Kwai Chung. Our decision to use  $\text{PM}_{2.5}$  data from Tsuen Wan for these two GPs was based on a higher propensity for  $\text{PM}_{2.5}$  to be more evenly dispersed than  $\text{PM}_{10}$ .

Several GP clinics were spread over geographically diverse districts (corresponding to the locations of air monitoring stations) in Hong Kong. The clinic data were audited by systematic checks, and the data quality was satisfactory, with few errors or missing data. Data on air pollution were subject to quality control measures as stipulated by the Environmental Protection Department. Daily data obtained from individual GPs could not be combined to produce a large, single dataset for statistical modelling, as there were differences in the time period of their enrolment into the study. Instead, individual datasets were utilised to create models that yielded district-based RR. These were then combined into a single, summary RR for each air pollutant by methods used in meta-analysis. This approach circumvented the inherent instability of datasets from the individual clinics. Another advantage of the district-based approach was that only first GP visits for respiratory diseases by patients living, working or attending schools in the district were regressed with the air pollutant concentrations in the same district (with the exception of  $\text{PM}_{2.5}$ ). Hence, there was a better match between exposure and health outcome than if the pollutant concentrations were averaged over all stations in a territory-wide dataset. This district-based approach probably resulted in less exposure misclassifications than in the London study<sup>16-18</sup>, which used the averaged values from different numbers of stations for different pollutants in various locations. There has been concerns that exposure estimates based on central monitor values do not accurately reflect individual personal exposure.<sup>36</sup> However, Schwartz, et al, pointed out that in a time series approach, the number of health outcomes per day was calculated over the population. The relevant exposure should be the mean of personal exposures on that

day, which was probably more tightly correlated with monitoring station data than individual exposures.<sup>34</sup> The generalised additive model used is the most widely used statistical model in recent studies, and the more stringent criteria have been applied in the modelling to obtain a more accurate estimate of the RR and its standard error.<sup>28, 29</sup> From the clinical data, we could not detect any major influenza epidemics during the study period. Hence, the latter were not included in our models.

Our participant GPs were a selected, volunteer group, with the inherent problem of selection bias. To address this issue, we have checked the patient profile, the distribution of the diagnostic categories, the consultation hours, and the average workload of the doctors. In general, the above parameters for most of our GP clinics are fairly typical of those seen in a private GP practice in Hong Kong.<sup>13, 14</sup> There is no reason to believe that the observed associations between air pollutant concentrations and visits to GP for URTI and non-URTI respiratory diseases could only have occurred in our GPs but not in others. Moreover, the association could not be explained by some unidentified confounders. Hence, we conclude that the positive association between air pollution and respiratory diseases was likely to be true, as has been reported elsewhere.<sup>16-22</sup> These findings are supported by similar associations between hospital admissions for respiratory diseases and mortalities that have been reported in other local studies<sup>6, 7</sup> and numerous epidemiological studies elsewhere.<sup>1-5, 8-12</sup> Nevertheless, as in all ecological studies, we cannot conclude that a cause-effect relation exists between air pollution and GP visits.

The London study<sup>16-18</sup> on air pollution and GP consultation is one of few studies that link air pollutants with specific respiratory morbidity seeking primary medical care in the community. That study differs from ours in that it uses retrospective datasets from a larger number of GPs (45 - 47) for a three-year period. In this study, asthma and lower respiratory tract infections are shown to be significantly associated with an increase in air pollution (NO<sub>2</sub> and CO in children, and PM<sub>10</sub> in adults).<sup>16</sup> Allergic rhinitis was associated with SO<sub>2</sub> and O<sub>3</sub>, and other upper respiratory diseases were associated with PM<sub>10</sub>.<sup>17, 18</sup>

In another study in a hospital outpatient department in Beijing, positive associations were found between an increase in total suspended particulates (TSP) and SO<sub>2</sub>, and an increase in outpatient visits in certain specialties ("non-surgical", paediatrics and internal medicine). However, data on specific diseases or diagnostic codes were not available.<sup>19, 20</sup>

In our dataset, except for URTI (and non-URTI respiratory diseases for three GPs), daily consultations for individual respiratory diseases and cardiovascular diseases are too few for statistical modelling. URTI (the largest component of all respiratory diseases seen in general practice) are significantly associated with all air pollutants except SO<sub>2</sub>. Gaseous air pollutants are irritants to the respiratory tract and can cause inflammation and respiratory symptoms or diseases. PM<sub>2.5</sub> and PM<sub>10</sub> can penetrate deeply into the lower respiratory tract and would be expected to be associated with lower respiratory tract diseases rather than URTI. However, many respiratory symptoms such as cough, phlegm, chest tightness and others, could have resulted from irritation of both upper and lower airways. Some of these visits might have been labelled by our GPs as URTI. Moreover, both pollutants are statistically highly

correlated with total suspended particulates (TSP). TSP is predominantly made up of larger particles that may cause irritation and inflammation of the upper respiratory tract. Hence, the associations of PM<sub>2.5</sub> and PM<sub>10</sub> with URTI are biologically plausible. We could not explain the lack of significant association between URTI and non-URTI respiratory diseases and SO<sub>2</sub>, other than the small effect size of the latter. The concentration of SO<sub>2</sub> in Hong Kong has decreased substantially after to the mandatory use of low sulphur fuel in 1990.<sup>37</sup> However, the magnitude and significance of the RR derived from the individual GPs were not related to the mean SO<sub>2</sub> concentrations in their corresponding districts.

The excess risk (ER) in the London study cannot be directly compared with our findings because of the difference in the disease coding and the units of air pollutant concentration used – 10<sup>th</sup> to 90<sup>th</sup> centiles in the London study, and 10 µg/m<sup>3</sup> in this study. Owing to small numbers, our data could not be used for sub-group analysis by specific diseases or groups like asthma, lower respiratory diseases, and allergic rhinitis, except for non-URTI in three GP clinics. Likewise, we could not analyse our data separately for different age groups. In general, the ERs in the London study for SO<sub>2</sub> in allergic rhinitis are high (at 15.7% and 9.3% respectively for the age groups 0-14 and 15-64 years). SO<sub>2</sub> is also significantly associated with asthma, lower respiratory diseases (LRD), upper respiratory diseases (URD) and allergic rhinitis. By contrast, the RR for SO<sub>2</sub> was not significant in this study. The magnitudes of the ER of other pollutants (PM<sub>10</sub> and NO<sub>2</sub>) are broadly similar in both studies, despite the differences in the health outcomes. An anomalous finding in the London study is the significant negative association between O<sub>3</sub> and LRD and URD (for all three age groups), but significantly positively associated with allergic rhinitis. The authors gave no plausible explanation for this observation, but noted a negative association between O<sub>3</sub> and most other pollutants in winter. In our study, O<sub>3</sub> was positively associated with URTI and non-URTI respiratory diseases. The correlation between O<sub>3</sub> and most other air pollutants are weakly positive (except SO<sub>2</sub>, where *r* was negative). Pollutants such as Black Smoke and carbon monoxide have not been measured or analysed in our study. Although there are differences in the association between individual pollutants and the diseases / disease groups between the London study and ours, we share the overall conclusion that air pollutants are positively associated with GP consultations for respiratory diseases.

This study provides additional evidence of the effect of air pollutants encountered at current levels on the public's health. The results are broadly in agreement with other studies, with minor differences in specific relationships between individual air pollutants and diseases. In some time series studies on mortalities, there have been suggestions that air pollution might only exert a 'harvesting effect' on susceptible groups, such as the elderly and chronically sick, whose lifespan might have been short anyway. In hospital admission studies, the risk estimates were especially obvious for susceptible groups such as the elderly, the young, or the chronically sick. However, most time series studies have in fact shown a real increase in the disease burden, and a substantial shortening of life.<sup>38, 39</sup> Our study demonstrates that air pollution, besides affecting the 'at risk' populations, also affects the relatively healthy population – those who usually consult their GPs for URTI and other

respiratory diseases. Instead of attributing the association between air pollution and respiratory diseases to ‘harvesting’ of susceptible individuals, the hypothesis that air pollution could lead to otherwise healthy people falling ill and visiting GPs seems a more plausible explanation. Despite the minor nature of these ailments, the overall morbidity burden on the community and on the health care system is heavy. The epidemiological evidence of the impact on health of the air pollutants PM<sub>10</sub>, PM<sub>2.5</sub>, NO<sub>2</sub> and O<sub>3</sub> (and SO<sub>2</sub>, as shown in other studies) at current ambient levels, in the apparent absence of a ‘threshold effect’, in particular for particulates and O<sub>3</sub>,<sup>40</sup> provides a scientific basis for setting more stringent air quality standards than those currently used in Hong Kong. Our findings suggest that a reduction in the concentrations of air pollutants could be associated with a corresponding decline in the numbers of GP visits for URTI and non-URT I respiratory diseases. This hypothesis has important implications in the formulation of environmental health policies. Like most cities, the major local sources of air pollutants in Hong Kong are motor vehicles and power plants. More vigorous control of these sources is likely to confer substantial health benefits.

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**Competing interest statement**

No competing interests

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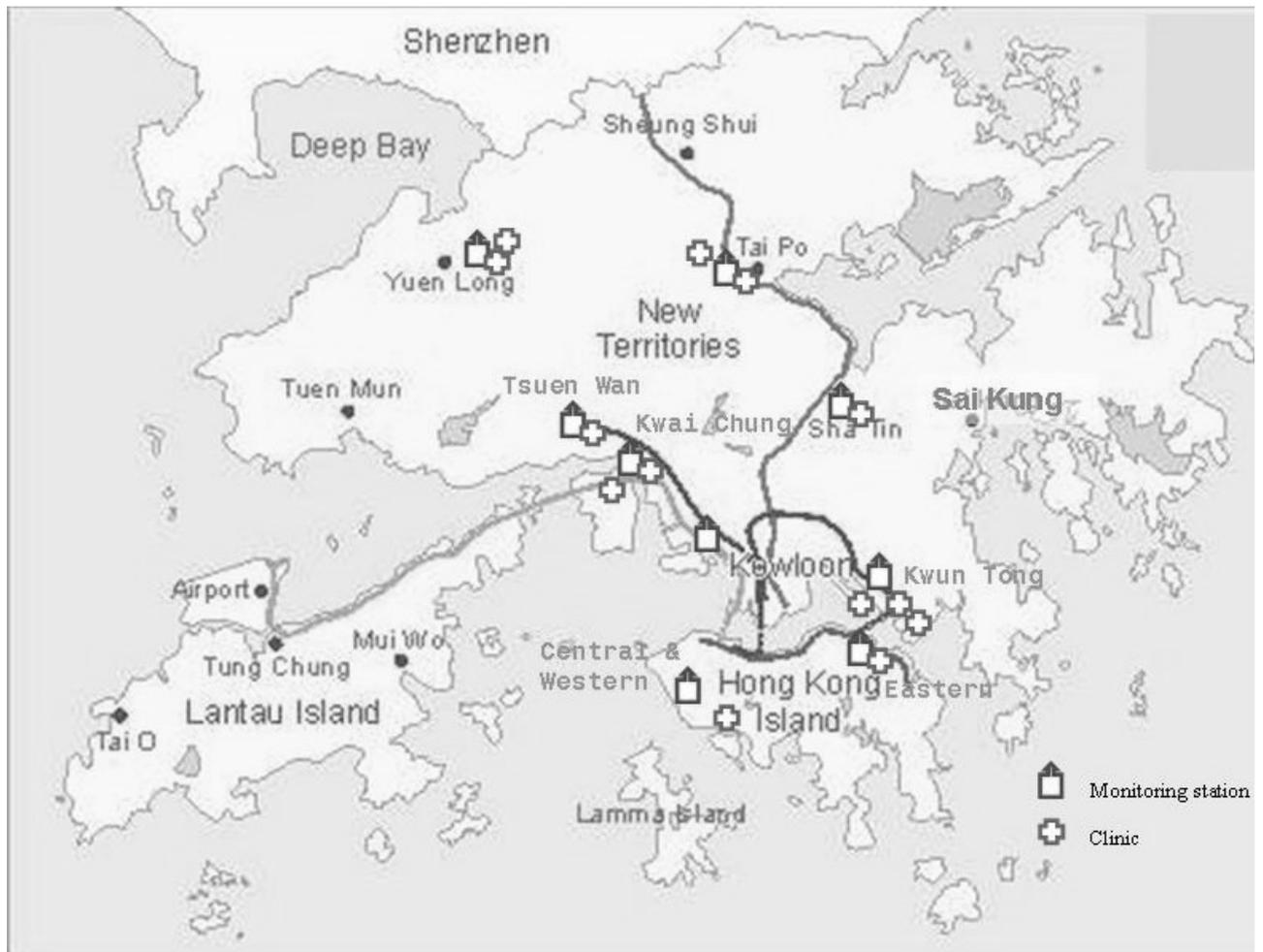


Figure 1: A location map of the GP clinics and the air monitoring stations