# ENVIRONMENTAL EXPOSURE

# Association between air pollution and general practitioner visits for respiratory diseases in Hong Kong

T W Wong, W Tam, I Tak Sun Yu, Y T Wun, A H S Wong, C M Wong

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**Background:** Few studies have explored the relation between air pollution and general practitioner (GP) consultations in Asia. Clinic attendance data from a network of GPs were studied, and the relationship between daily GP consultations for upper respiratory tract infections (URTI) and non-URTI respiratory diseases and daily air pollutant concentrations measured in their respective districts was examined. **Methods:** A time series study was performed in 2000–2002 using data on daily patient consultations in 13

GP clinics distributed over eight districts. A Poisson regression model was constructed using the generalised additive model 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 the GP for URTI per unit increase in concentration for each

See end of article for authors' affiliations

Correspondence to: Professor T W Wong, School of Public Health, Prince of Wales Hospital, Shatin, Hong Kong, China; twwong@cuhk.edu.hk

Received 15 August 2005 Accepted 26 February 2005 **Published Online First** 14 March 2006 air pollutant was derived using a random effect model. First visits for non-URTI respiratory diseases were analysed 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 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:** These results provide further evidence that air pollution contributes to GP visits for URTI and non-URTI respiratory diseases in the community.

any 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 outpatient consultations in the private and public sector, respectively, were for respiratory illnesses.<sup>13</sup><sup>14</sup> The total number of GP consultations for respiratory illnesses has been estimated to be about 23 million in Hong Kong in 2001.15 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 healthcare 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 GP clinics over a 3 year period from 2000 to 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 1 year data (2000) from seven GP clinics, have been reported earlier.<sup>23</sup>

### 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 to 36 months, depending on the time of their recruitment and withdrawal. The following diseases/symptoms were recorded:

- Respiratory diseases/symptoms: upper and lower respiratory tract infections, influenza, asthma, chronic obstructive pulmonary diseases, allergic rhinitis, cough and other respiratory diseases.
- Cardiovascular diseases/symptoms: cardiac arrhythmias, angina, hypertension and other circulatory diseases.
- 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 3 digit system which identifies the "episode" of doctor consultation by system and diagnosis or reason for encounter. The system is partly compatible with the 10th revision of the International Classification of Diseases (ICD-10). The following information was recorded: 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

**Abbreviations:** NO<sub>2</sub>, nitrogen dioxide; O<sub>3</sub>, ozone; PM<sub>10</sub>, PM<sub>2.5</sub>, particulates with an aerodynamic diameter less than 10  $\mu$ m or 2.5  $\mu$ m; RR, relative risk; SO<sub>2</sub>, sulphur dioxide; TSP, total suspended particles; URTI, upper respiratory tract infections



(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  $(NO_2)$ , sulphur dioxide  $(SO_2)$ , ozone  $(O_3)$ , and particulates with an aerodynamic diameter less than 10 µm (PM<sub>10</sub>)—were measured in air monitoring stations located in eight districts throughout Hong Kong by the Environmental Protection Department (EPD). In addition, particulates with an aerodynamic diameter less than 2.5 µm  $(PM_{2.5})$  were monitored in one station. SO<sub>2</sub> was measured by UV fluorescence (Model 43A SO2 Analyzer, Thermo Environmental Instruments Inc, USA); NO2 was measured by chemiluminescence (Model 42 Chemiluminescence NO-NO<sub>2</sub>-NO<sub>X</sub> Analyzer, Thermo Environmental Instruments Inc, USA); O3 was measured by UV absorption (ML8840 NOX Analyzer, Monitoring Lab Inc, USA); PM<sub>10</sub> was measured by the Tapered Element Oscillating Microbalance (TEOM) (Rupprecht & Patashnick Co Inc, TEOM Series 1400a-AB PM10 Monitor, USA), and PM2.5 was measured by TEOM (R & P Partisol Plus, Model 2025, USA). 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

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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 corresponding data from the nearest station. 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.

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 overdispersion.27 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 3 days) to the model. After the confounding effects of seasonality, days of the week, and climatic variables had 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

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
GP 1 26 months (Jan 2000–Feb 2002)	8465	8030 (94.9%)	6215 (73.4%)	6021 (71.1%)	4056 (47.9%)
GP 2 12 months	10286	6810 (66.2%)	3065 (29.8%)	1526 (14.8%)	1049 (10.2%)
(Jan-Dec 2000) GP 3 36 months	40186	38350 (95.4%)	32031 (79.7%)	20436 (50.9%)	19558 (48.6%)
(Jan 2000–Dec 2002) GP 4 36 months	29731	29146 (98.0%)	20812 (70.0%)	12438 (41.8%)	10177 (34.2%)
(Jan 2000–Dec 2002) GP 5 12 months	8520	8306 (97.4%)	6357 (74.6%)	2068 (24.2%)	1760 (20.7%)
(Jan-Dec 2000) GP 6 36 months	35967	35392 (98.4%)	32403 (90.1%)	24366 (67.7%)	23686 (65.9%)
(Jan 2000–Dec 2002) GP 7 36 months	27212	26492 (97.4%)	22130 (81.3%)	14272 (52.4%)	12319 (45.3%)
(Jan 2000–Dec 2002) GP 8 33 months	21321	20131 (94.4%)	15256 (71.6%)	9456 (44.4%)	8837 (41.4%)
(Apr 2000-Dec 2002) GP 9 33 months	45844	43534 (95.0%)	34726 (75.7%)	18866 (41.1%)	14729 (32.1%)
(Apr 2000–Dec 2002) GP 10 33 months	34553	31920 (92.4%)	8757 (25.3%)	6141 (17.8%)	4540 (13.1%)
(Apr 2000–Dec 2002) GP 11 33 months	20851	19039 (91.3%)	15422 (74.0%)	10949 (52.5%)	10247 (49.1%)
(Apr 2000-Dec 2002) GP 12 24 months	9389	9114 (97.1%)	7086 (75.5%)	6973 (74.2%)	3233 (34.4%)
(Jan 2001–Dec 2002) GP 13 24 months	22189	20108 (90.6%)	15129 (68.2%)	14012 (63.1%)	7864 (35.4%)
(Jan 2001–Dec 2002) Total	314514	296372 (94.2%)	219389 (69.8%)	147524 (46.9%)	122055 (38.8%)

station located in each district) were added to each core model to determine the relative risk (RR) of GP visits for a  $10 \ \mu g/m^3$  increase in each of these air pollutants. Data on daily concentrations of PM2.5 were used in three models which took data from GP 9 (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 3 lag days (lag 3) and cumulative lags by 2 (lag 0 and 1), 3 (lag 0, 1 and 2), and 4 days (lag 0 to 3), were tested in each model. The lag day with the air pollutant concentration that yielded the smallest p value (that is, the largest  $\gamma^2$ ) 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).28 29 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 only counts of daily patient consultations were obtained from the GPs, stratified by various parameters without the individual patient's identity. Data on air pollution were provided by the Environmental Protection Department.

### RESULTS GP consultations

# Table 1 shows the summary statistics of consultations by 13 GPs in eight districts. The duration of their participation ranged 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 cardiovascular diseases were few in number.

Table 2 shows the means, ranges, and percentiles of daily air pollutant concentrations in eight air monitoring stations during the study period.  $NO_2$  and  $PM_{10}$  are the dominant air pollutants in five districts (Eastern, Kwun Tong, Tsuen Wan, Kwai Chung and Yuen Long). The corresponding concentrations of  $O_3$  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 and Western), with relatively low  $NO_2$  and  $PM_{10}$  levels but high levels of  $O_3$ .  $PM_{2.5}$  was highly correlated with  $PM_{10}$  (correlation

Table 2	Summary statistics of daily air pollutant concentrations in eight air monitoring stations (January 2000–December
2002)	

Stations (corresponding to GPs)	Pollutant	N (days)	Mean concentration (µg/m <sup>3</sup> )	SD	Min	25%	50%	75%	Max
Central and Western	NO <sub>2</sub>	950	50.9	21.4	10	36	49	62	170
(GP 8)	PM <sub>10</sub>	960	48.8	27.9	9	27	43	64	200
,	O3	953	33.8	19.8	3	19	29	48	115
	SO <sub>2</sub>	950	19.6	15.8	0	9	15	24	105
Eastern (GP 3)	NO <sub>2</sub>	960	55.0	19.0	11	42	56	66	169
	PM10	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
Kwai Chung	NO <sub>2</sub>	1084	68.2	22.6	12	54	64	77	211
(GPs 1 and 4)	PM10	1091	56.9	43.6	14	35	46	34	290
, ,	O <sub>3</sub>	1091	24.1	17.4	0	9	21	65	99
	SO <sub>2</sub>	1090	23.4	20.1	0	9	15	37	130
Kwun Tong	NO <sub>2</sub>	814	71.5	23.4	7	56	72	85	179
(GPs 2, 6 and 10)	PM <sub>10</sub>	877	55.0	24.9	14	37	51	68	186
	O3	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
Shatin (GP 11)	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
Tai Po	NO <sub>2</sub>	955	47.8	19.4	10	35	45	57	156
(GPs 5 and 12)	PM10	1030	47.7	24.6	11	29	42	61	165
	O3	951	44.6	21.5	1	28	41	60	119
	SO <sub>2</sub>	953	12.0	10.1	0	5	10	16	99
Tsuen Wan	NO <sub>2</sub>	1086	62.5	20.2	17	48	60	73	152
(GP 9)	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
Yuen Long	NO <sub>2</sub>	958	57.7	20.2	16	43	55	70	148
(GPs 7 and 13)	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

	NO <sub>2</sub>	O <sub>3</sub>	SO <sub>2</sub>	PM10	*PM <sub>2.5</sub>
GP 1	1.026 {0-1}	1.018 {2}	1.032 {0}	1.021 {1}	1.028 {1}
	(1.002 to 1.051)	(0.992 to 1.045)	(1.010 to 1.055)	(1.005 to 1.037)	(1.002 to 1.056)
GP 2	1.037 {3}	1.117 {3}	1.173 {2}	1.075 {3}	
	(0.982 to 1.095)	(1.008 to 1.238)	(1.022 to 1.346)	(1.018 to 1.135)	
GP 3	1.045 {0-1}	1.035 {1}	0.987 {2}	1.026 {1}	-
	(1.028 to 1.062)	(1.018 to 1.053)	(0.973 to 1.003)	(1.017 to 1.036)	
GP 4	1.006 {0-1}	1.028 {0-3}	0.988 {0-1}	1.012 {0}	1.017 {0}
	(0.998 to 1.014)	(1.001 to 1.056)	(0.975 to 1.001)	(0.998 to 1.026)	(1.001 to 1.034)
GP 5	1.077 {1}	0.949 {0-3}	0.909 {0}	1.047 {0-3}	
	(1.021 to 1.135)	(0.883 to 1.019)	(0.756 to 1.093)	(0.960 to 1.142)	
GP 6	1.027 {0}	1.028 {2}	0.977 {2}	1.015 {1}	-
	(1.013 to 1.041)	(1.013 to 1.044)	(0.962 to 0.992)	(1.005 to 1.024)	
GP 7	1.037 {0-1}	1.017 {1}	0.980 {0-1}	1.022 {0-1}	-
	(1.020 to 1.055)	(0.998 to 1.036)	(0.959 to 1.002)	(1.009 to 1.035)	
GP 8	1.036 {0}	1.062 {2}	0.976 {2}	1.045 {0-3}	-
	(1.013 to 1.059)	(1.036 to 1.089)	(0.949 to 1.003)	(1.015 to 1.076)	
GP 9	1.025 {0}	1.027 {1}	1.018 {0}	1.020 {0-3}	1.022 {0}
	(1.009 to 1.041)	(1.010 to 1.045)	(1.003 to 1.033)	(1.000 to 1.041)	(1.005 to 1.040)
GP 10	1.073 {0-3}	1.041 {2}	0.958 {0-2}	1.019 {2}	
	(1.028 to 1.119)	(1.017 to 1.065)	(0.926 to 0.991)	(1.001 to 1.037)	
GP 11	1.019 {3}	1.014 {2}	1.021 {3}	1.016 {1}	-
	(1.005 to 1.033)	(1.002 to 1.026)	(1.000 to 1.043)	(1.001 to 1.031)	
GP 12	1.017 {0}	1.027 {2}	1.046 {3}	1.019 {2}	-
	(0.987 to 1.049)	(0.986 to 1.069)	(1.011 to 1.083)	(0.997 to 1.041)	
GP 13	1.041 {0-3}	0.998 {0-3}	1.010 {0-1}	1.027 {0-3}	-
	(0.997 to 1.088)	(0.994 to 1.003)	(0.998 to 1.022)	(1.004 to 1.050)	
Combined RR	1.030	1.025	1.000	1.020	1.021
	(1.020 to 1.040)	(1.012 to 1.038)	(0.987 to 1.013)	(1.016 to 1.025)	(1.010 to 1.032)
Combined RR after	1.030	1.024	0.999	1.020	1.021
excluding GP 2†	(1.019 to 1.041)	(1.011 to 1.036)	(0.986 to 1.011)	(1.017 to 1.023)	(1.010 to 1.032)

Statistically most significant lag days (either single or cumulative) are shown in curly brackets. \*PM<sub>2.5</sub> data were available only in the district of GP 9 (Tsuen Wan). GPs 1 and 4 were located in an adjoining district (Kwai Chung).

The RRs for GP 2 were much higher than those of other GPs. The combined RR was recalculated without GP 2 as a sensitivity analysis.

coefficient r = 0.94). NO<sub>2</sub> was moderately correlated with  $PM_{10}$  (median r = 0.68; range 0.38–0.75) and  $SO_2$  (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  $PM_{10}$  (median r = 0.40; range 0.14–0.48) but poorly correlated with SO<sub>2</sub> (median r = -0.13; range -0.04to -0.42). SO<sub>2</sub> was poorly correlated with PM<sub>10</sub> (median r = 0.28; range 0.19-0.51).

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  $10 \ \mu g/m^3$  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 found for  $O_{3}$ ,  $NO_{2}$ ,  $PM_{10}$  and  $PM_{2.5}$ , but not for  $SO_{2}$ . The magnitudes of the excess risk of GP visits for URTI, given by  $100 \times (RR - 1)\%$ , were 3.0% for NO<sub>2</sub>, 2.5% for O<sub>3</sub>, 2.0% for

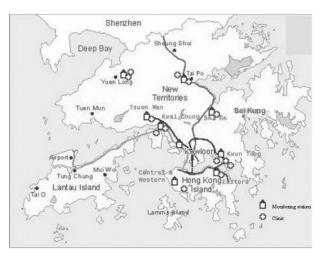


Figure 1 Location map of the GP clinics and the air monitoring stations.

	concentrations of air pollutants (2000–2002)						
	NO <sub>2</sub>	O <sub>3</sub>	SO <sub>2</sub>	PM10			
GP 9	1.015 {0-3}	1.036 {0-3}	1.014 {2}	1.021 {3}			
	(0.997 to 1.033)	(1.008 to 1.064)	(0.998 to 1.030)	(1.006 to 1.036)			
GP 12	1.050 {0–1}	1.020 {1}	0.956 {0–1}	1.020 {0}			
	(1.028 to 1.073)	(0.996 to 1.045)	(0.913 to 1.000)	(1.005 to 1.036)			
GP 13	1.047 {0-3}	1.025 {0-2}	1.023 {0-3}	1.029 {0-3}			
	(1.030 to 1.062)	(1.006 to 1.043)	(0.998 to 1.049)	(1.019 to 1.039)			
Combined RR	1.038	1.026	1.012	1.025			
	(1.028 to 1.048)	(1.013 to 1.039)	(0.999 to 1.025)	(1.018 to 1.032)			

 $PM_{10}$ , and 2.1% for  $PM_{2.5}$ . The individual and combined RR of first visits for non-URTI 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 GP 2 (who contributed 1 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 GP 2 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 fig 1.

### 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 the GP for URTI are statistically significant and above unity for a  $10 \ \mu g/m^3$ increase in four out of five air pollutants-namely, NO2, O3, PM<sub>10</sub>, and PM<sub>2.5</sub>. The association between air pollution and GP visits due to non-URTI respiratory diseases was analysed in three GP datasets and the results were similar to those for URTI. The RRs for PM<sub>2.5</sub> closely mirror those for PM<sub>10</sub>, which reflects the strong correlation between the two pollutants. The magnitude of the RR for PM2.5 was uniformly higher than that for PM<sub>10</sub>. 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 which found that  $\mathrm{PM}_{2.5}$  was more strongly associated than  $\mathrm{PM}_{10}$  with acute health outcomes.33-35 It should be cautioned, however, that only one of three GP datasets (GP 9 in Tsuen Wan) used for calculating the RR for PM2.5 was from the district where PM2.5 concentrations were monitored. The other two GP clinics (GPs 1 and 4) were situated in the neighbouring district of Kwai Chung. Our decision to use PM2.5 data from Tsuen Wan for these two GPs was based on a higher propensity for PM<sub>2.5</sub> to be more evenly dispersed than PM<sub>10</sub>.

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 used 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  $PM_{2.5}$ ). 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 mean values from different numbers of stations for different pollutants in various locations. There have been concerns that exposure estimates based on central monitor values do not accurately reflect individual personal exposure.36 However, Schwartz et  $al^{34}$  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. 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.28 29 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.13 14 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.16-22 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.1-5 8-12 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 to link air pollutants with specific respiratory morbidity seeking primary medical care in the community. That study differed from ours in that it used retrospective datasets from a larger number of GPs (45–47) for a 3 year period. Asthma and lower respiratory tract infections were found 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  $SO_2$  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 TSP, which is predominantly made up of larger particles that may cause irritation and inflammation of the upper respiratory tract. Hence, the associations of  $PM_{2.5}$  and  $PM_{10}$  with URTI are biologically plausible. We could not explain the lack of significant association between URTI and non-URTI respiratory diseases and  $SO_2$ , other than the small effect size of the latter. The concentration of  $SO_2$  in Hong Kong has decreased substantially since 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  $SO_2$  concentrations in their corresponding districts.

The excess risk 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 (10–90th centiles in the London study and 10  $\mu$ g/m<sup>3</sup> in this study). Owing to small numbers, our data could not be used for subgroup analysis by specific diseases or groups such as 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 excess risks in the London study for  $SO_2$  in allergic rhinitis were high (15.7% and 9.3%, respectively, for the age groups 0-14 and 15-64 years). SO<sub>2</sub> was also significantly associated with asthma, lower respiratory diseases, upper respiratory diseases, and allergic rhinitis. By contrast, the RR for SO<sub>2</sub> was not significant in this study. The magnitudes of the excess risk of other pollutants (PM<sub>10</sub> and NO<sub>2</sub>) were 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 O3 and lower respiratory diseases and upper respiratory diseases (for all three age groups) but the significantly positive association 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 O3 was positively associated with URTI and non-URTI respiratory diseases. The correlation between O<sub>3</sub> and most other air pollutants is 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 for the effect of air pollutants encountered at current levels on the health of the public. 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 mortality rates 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.38 39 Our study shows 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 healthcare 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 on the apparent absence of a "threshold effect", in particular for particulates and O3,40 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-URTI 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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## Authors' affiliations

T W Wong, W Tam, I Tak Sun Yu, Y T Wun, A H S Wong, Department of Community and Family Medicine, The Chinese University of Hong Kong,

Hong Kong, China C M Wong, Department of Community Medicine, The University of Hong Kong, Hong Kong, China

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### REFERENCES

- Katsouyanni K, Touloumi G, Spix C, et al. Short term effects of ambient sulphur dioxide and particulate matter on mortality in 12 European cities: results from time series data from the APHEA project. BMU 1997;314:1658–63.
- Samet JM, Dominici F, Curriero FC, et al. Fine particulate air pollution and mortality in 20 US cities, 1987–1994. N Engl J Med 2000;343:1742–9.
- 3 Kan H, Chen B. Air pollution and daily mortality in Shanghai: a time-series study. Arch Environ Health 2003;58:360–7.
- 4 Bremner SA, Anderson HR, Atkinson RW, *et al.* Short-term associations between outdoor air pollution and mortality in London 1992–4. *Occup Environ Med* 1999;56:237–44.
- 5 Neas LM, Schwartz J, Dockery D. A case-crossover analysis of air pollution and mortality in Philadelphia. Environ Health Perspect 1999;107:629–31.
- 6 Wong TW, Tam WS, Yu TS, et al. Associations between daily mortalities from respiratory and cardiovascular diseases and air pollution in Hong Kong, China. Occup Environ Med 2002;59:30–5.
- 7 Wong TW, Lau TS, Yu TS, et al. Air pollution and hospital admissions for respiratory and cardiovascular diseases in Hong Kong. Occup Environ Med 1999;56:679–83.
- Wordley J, Walters S, Ayres JG. Short term variations in hospital admissions and mortality and particulate air pollution. *Occup Environ Med* 1997;54:108–16.
   Atkinson RW, Anderson HR, Sunyer J, et al. Acute effects of particulate air
- 9 Atkinson RW, Anderson HR, Sunyer J, et al. Acute effects of particulate air pollution on respiratory admissions: results from APHEA 2 project. Air Pollution and Health: a European Approach, Am J Respir Crit Care Med 2001;164:1860–6.
- 10 Atkinson RW, Bremner SA, Anderson HR, et al. Short-term associations between emergency hospital admissions for respiratory and cardiovascular disease and outdoor air pollution in London. Arch Environ Health 1999;54:398–411.
- Schwartz J. Air pollution and hospital admissions for respiratory disease. Epidemiology 1996;7:20–8.
- 12 Schwartz J. Air pollution and hospital admissions for heart disease in eight U.S. counties. *Epidemiology* 1999;10:17–22.
- 13 Wun WT, Lee A, Chan KKC. Morbidity pattern in private and public sectors of family medicine/general practice in a dual health care system. *HK Pract* 1998;20:3–15.
- 14 Lee A, Chan KKC, Wun YT, et al. A morbidity survey in Hong Kong, 1994. HK Pract 1995;17:246–55.
- 15 Wong TW, Wun YT, Yu TS, et al. Short-term effects of air pollution on morbidity of the general population: a continuation study, Research Report to Environmental Protection Department, Hong Kong Government, Department of Community & Family Medicine, The Chinese University of Hong Kong, 2002.

- 16 Hajat S, Haines A, Goubet SA, et al. Association of air pollution with daily GP consultations for asthma and other lower respiratory conditions in London. Thorax 1999;54:597-605.
- 17 Hajat S, Haines A, Atkinson RW, et al. Associations between air pollution and daily consultations with general practitioners for allergic rhinitis in London, United Kingdom. Am J Epidemiol 2001;**153**:704–14.
- 18 Hajat S, Anderson HR, Atkinson RW, et al. Effects of air pollution on general practitioner consultations for upper respiratory diseases in London. Occup Environ Med 2002;59:294–9.
- 19 Xu X, Dockery DW, Christiani DC, et al. Association of air pollution with hospital outpatient visits in Beijing. Arch Environ Health 1995;50:214-20.
- 20 Xu X, Li B, Huang H. Air pollution and unscheduled hospital outpatient and emergency room visits. Arch Environ Health 1995;103:286-9
- Ostro BD, Eskeland GS, Sanchez JM, et al. Air pollution and health effects: a 21 study of medical visits among children in Santiago, Chile. Environ Health Perspect 1999;107:69-73.
- 22 Hwang JS, Chan CC. Effects of air pollution on daily clinic visits for lower respiratory tract illness. Am J Epidemiol 2002;**155**:1–10.
- 23 Wong TW, Wun YT, Yu TS, et al. Air pollution and GP consultations for espiratory illnesses. J Epidemiol Community Health 2002;56:949–50.
- 24 WONCA International Classification Committee. International classification of primary care, 2nd ed. Oxford: Oxford University Press, 1998.
- 25 Katsouyanni K, Touloumi G, Samoli E, et al. Confounding and effect modification in the short-term effects of ambient particles on total mortality: results from 29 European Cities within the APHEA2 Project. Epidemiology 2001.12.521-31
- 26 Hastie T, Tibshirani R. Generalized additive models. London: Chapman and Hall 1990
- 27 Hastie T, Tibshirani R. Generalized additive models for medical research. Stat Methods Med Res 1995;4:187-96.

- 28 Dominici F, McDermott A, Zeger SL, et al. On the use of generalized additive models in time-series studies of air pollution and health. Am J Epidemiol 2002.156.193-203
- iHAPSS, Health Effects Institute. http://www.ihapss.jhsph.edu/data/ NMMAPS/R/ (accessed 28 August 2005).
- 30 Fleiss JL. The statistical basis of meta-analysis. Stat Methods Med Res 1993;2:121-45.
- 31 Katsouyanni K, Touloumi G, Samoli E, et al. Different convergence parameters applied to the S-plus GAM function. Epidemiology 2002;13:742.
- 32 Lippman M, Ito K, Burnett RT. Association of particulate matter components with daily morbidity and mortality in urban populations, Research Report 95. Cambridge, MA: Health Effects Institute, 2000:5–72
- 33 Schwartz J, Neas LM. Fine particles are more strongly associated than coarse particles with acute respiratory health effects in schoolchildren. Epidemiology 2000.11.6-10
- 34 Schwartz J, Dockery DW, Neas LM. Is daily mortality associated specifically
- with fine particles? J Air Waste Manage Assoc 1996;46:927–39.
  Klemm RJ, Mason RM, Heilig CM, et al. Is daily mortality associated specifically with fine particles? Data reconstruction and replication of analyses. J Air Waste Manage Assoc 2000;50:1215-22
- Wallace L. Indoor particles: a review. J Air Waste Manage Assoc 36 1996;**46**:98–1269
- 37 Hedley AJ, Wong CM, Thach TQ, et al. Cardiorespiratory and all-cause mortality after restrictions on sulphur content of fuel in Hong Kong: an intervention study. Lancet 2002;360:1646-52.
- 38 Schwartz J. Is there harvesting in the association of airborne particles with daily deaths and hospital admissions? Epidemiology 2001;12:55-61
- 39 Schwartz J. Harvesting and long term exposure effects in the relation between air pollution and mortality. Am J Epidemiol 2000;151:440-8.
- 40 World Health Organization. Health aspects of air pollution: Results from the WHO Project "Systematic Review of Health Aspects of Air Pollution in Europe". Copenhagen: WHO Regional Office for Europe, 2004.

# LUNG ALERT

### Need for oral protein energy supplements in CF: fact or myth?

▲ Poustie VJ, Russell JE, Watling RM, et al and the CALICO Trial Collaborative Group. Oral protein energy supplements for children with cystic fibrosis: CALICO multicentre randomised control trial. BMJ 2006;332:632–5

ue to a multitude of causes, cystic fibrosis (CF) is characterised by poor nutrition which is an important predictor of decline in lung function. Oral protein energy supplements are used widely to improve energy intake and nutritional status in patients suffering from CF. These supplements are costly and a significant proportion of patients find them unpalatable.

The CALICO trial (Calories In Cystic Fibrosis-Oral) is a multicentre randomised control trial which evaluated the role of protein energy supplements in improving or preventing the deterioration in body mass index centile of children with CF. 102 children with CF (age 2-15 years) with suboptimal nutrition (body mass index 0.4–25th centile, no gain in weight over the previous 3 months, or 5% decrease in weight over a 6 month period) were randomised to receive protein energy supplements plus dietetic advice or dietetic advice alone. There was no difference in the mean change in body mass index between the two groups over a 12 month period (mean difference 2.9 centile points; the study was powered to detect a 10 point difference). No significant difference was observed in the other anthropometric parameters (weight and height centile and mid arm circumference), change in lung function, activity, and gastrointestinal score.

The authors concluded that there was no added benefit of protein energy supplements over regular dietetic advice in children with CF with moderate malnutrition. However, they may have a role in the treatment of malnourished children, especially during acute weight loss.

### A Gulati

Specialist Registrar in Respiratory Medicine, Ipswich Hospital, Ipswich, UK; atulgulati70@rediffmail.com