

Risk factors for SARS infection among hospital healthcare workers in Beijing: a case control study

Wei Liu¹, Fang Tang¹, Li-Qun Fang¹, Sake J. de Vlas², Huai-Jian Ma³, Jie-Ping Zhou⁴, Caspar W. N. Looman², Jan Hendrik Richardus² and Wu-Chun Cao¹

1 *Beijing Institute of Microbiology and Epidemiology, State Key Laboratory of Pathogen and Biosecurity, P.R. China*

2 *Department of Public Health, Erasmus MC, University Medical Center Rotterdam, The Netherlands*

3 *Department of Infectious Disease, Anhui Provincial Corps Hospital, Chinese People's Armed Police Forces, Anhui, P.R. China*

4 *Institute of Remote Sensing Application, China Academy of Sciences, Beijing, P.R. China*

Summary

OBJECTIVE To evaluate possible severe acute respiratory syndrome (SARS) infection associated risk factors in a SARS affected hospital in Beijing by means of a case control study.

METHODS Fifty-one infected and 426 uninfected staff members were asked about risk behaviours and protective measures when attending to SARS patients. Univariate and multivariate logistic regression analyses were performed to identify the major risk and protective factors.

RESULTS Multivariate analysis confirmed the strong role of performing chest compression (or intubation, which is highly correlated), contact with respiratory secretion, and emergency care experience as risk factors to acquire SARS infection. For the studied protective measures, wearing 16-layer cotton surgical mask, wearing 12-layer cotton surgical mask, wearing multiple layers of mask, taking prophylactic medicine, taking training and nose washing turned out to be protective against infection.

CONCLUSIONS This study highlighted activities associated with increased and decreased risk for SARS infection during close contact with SARS patients. These findings may help to guide recommendations for the protection of high-risk occupational groups.

keywords SARS, healthcare worker, case control study

Introduction

Severe acute respiratory syndrome (SARS) is caused by a novel coronavirus, transmitted from human to human by droplets or by direct contact. Airborne spread of the virus also accounted for certain community outbreaks of SARS (Yu *et al.* 2004). Healthcare workers (HCW) were at the highest risk of having the disease, accounting for one fifth of the global total (World Health Organization 2003). In Hong Kong, 23% of the cases of SARS were healthcare workers. In Canada and Singapore, the proportions were higher (40% and 41%, respectively), as they had fewer SARS cases in the community than Hong Kong. Risk factors for infection in HCWs have been studied extensively, and a review on SARS infection and healthcare workers disclosed a number of risk and protective factors (Chan-Yeung & Yu 2003; Lau *et al.* 2004). For example, lack of awareness and pre-paredness when the disease first struck, poor institutional infection control measures, lack of training in infection control procedures, poor compliance with the use of personal protection equipment (PPE),

exposure to high-risk procedures such as intubation and nebulisation, and exposure to unsuspected SARS patients were associated with SARS infection. Measures to prevent nosocomial infection included establishing isolation wards for triage SARS patients; training and monitoring hospital staff in infection-control procedures; active and passive screening of HCWs; enforcement of droplet and contact precautions; and compliance with the use of PPE.

In mainland China, 1 021 HCWs became infected, accounting for 19.2% of the 5 327 SARS cases in the whole country (Feng *et al.* 2009, this issue). Several hospitals in Beijing reported that nosocomial transmission occurred among HCWs, one of which (referred to hereafter as AFH (Armed Forces Hospital)) suffered one of the most serious outbreaks: 67 confirmed cases and 16 deaths among HCWs. Several studies were conducted during the outbreak. One case control study was designed to understand how HCWs contracted the disease and how to prevent their infection (Ma *et al.* 2004). It was conducted shortly after the epidemic, but the data have never been prepared for an English language publication. We therefore

made a systematic analysis based on the data to investigate possible risk and protective factors associated with infection of SARS among the HCWs in AFH.

Materials and methods

Cases and controls

The retrospective case control study was conducted in AFH hospital in Beijing where the nosocomial outbreak was reported. The case group were all HCWs who were diagnosed as probable SARS cases admitted between 5 March and 17 May 2003, were recruited as cases. Diagnosis was based on WHO's criteria of documented fever (temperature >38 °C), presence of cough, shortness of breath or breathing difficulty, and a significant history of exposure to a SARS patient not more than 10 days prior to onset of symptoms, plus radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome (RDS) on chest X-ray (CXR) (World Health Organization 2003). Two cases that were suspected of contracting the infection outside their hospital stay were excluded.

Eligible uninfected HCWs who worked in the same hospital and had self-reported exposure to SARS patients between March and May 2003 were identified as controls. They were subsequently confirmed following WHO vigorous criteria for close contacts: the exposure was only deemed to be definite, where there was a history of being within close physical proximity (1 m) of a patient subsequently confirmed with SARS (World Health Organization 2003). All cases and controls included were subsequently tested for Ig G antibody against SARS-CoV using ELISA method as previously described (Liu *et al.* 2006). For the case group, only one SARS patient was detected as IgG antibody negative, which was thereafter excluded from the analysis. For the control group, none of them was detected as serologically positive, thereby supporting that they had not been infected with SARS.

Epidemiological investigation and data collection

Interviews with cases and controls were carried out using a pre-tested questionnaire by a trained epidemiological group between June and July 2003. Information collected included demographic data (age, gender and ethnic group), personal medical history, coexisting conditions, work unit and ward, job description, SARS-related work behaviours, protection measures and training activities. All study participants gave oral informed consent before the interviews were conducted. Between 14 June and 19 June, the completed questionnaires were retrieved from all participants, after which they were immediately checked for validity and completeness.

Statistical analysis

Data were analysed using SPSS (version 13.0, SPSS Inc, Chicago, IL, USA) and S-plus software (version 6.0, Insightful Corp., Seattle, WA, USA). Logistic regression was performed to estimate odds ratios (ORs) and their 95% confidence intervals (CI). Univariate analyses were conducted to determine the effect of each variable separately. For variables with missing value of $>5\%$, we performed logistic regression with being missing as binary outcome and age, sex and occupation as predictors to test their non-deviance of the possibility of having missing values against the important background variables.

A multivariate logistic regression was fitted using a stepwise-forward procedure with all variables that were marginally significant ($P < 0.10$) in the univariate analyses as candidates for selection. For the multivariate analysis we performed a stepwise-forward selection procedure and took care that at each step to select a new variable we only removed observations with missing values for the variables in the model. As a result, in the final model, cases were removed with missing values for selected variables only instead of missing values for all variables that were investigated. A stepwise-forward (or backward) procedure has a disadvantage that it does not show in how far predictors are chosen at random. Thereafter we calculated all correlations between predictors and selected from the significant pairs the ones with one predictor in the final multivariate model and one not in the model. If swapping of the chosen predictor by its correlated counterpart does not seriously deteriorate the model, we conclude that we cannot tell whether one or the other predictor played a role. For all the analyses, statistical tests were based on two-tailed probability. A P -value < 0.05 was considered statistically significant.

Results

Descriptive epidemiology

Altogether 477 completed questionnaires were successfully retrieved from infected staff (51) and uninfected controls (426). The cases represent 76% (51/67) of all infected survived staff in the hospital. Sixteen infected HCWs could not be accessed or refused to be studied. The control group represents over 90% of all employees who were exposed to SARS in the hospital. The demographic and epidemiological characteristics of the two groups are listed in Table 1. The mean age was 29.5 ± 9.6 years for the cases, and 31.4 ± 8.8 years for the control group. The statistical analysis showed that the two groups were comparable in almost all of the demographic information we obtained, including age, gender, marital status, ethnicity, co-mor-

Characteristics	Cases (%) <i>n</i> = 51	Controls (%) <i>n</i> = 426	<i>P</i> -value
Age (mean ± SD, range)	29.5 ± 9.6 (range: 17–69)	31.4 ± 8.8 (range: 19–74)	0.15
Gender			0.98
Male	16 (31.4)	134 (31.5)	
Female	35 (68.6)	291 (68.5)	
Marital status			0.42
Single	24 (47.1)	164 (38.5)	
Married	26 (51.0)	257 (60.3)	
Divorced or widowed	1 (2.0)	5 (1.2)	
Ethnic group			0.34
Han	48 (94.1)	412 (96.7)	
Non-Han	3 (5.9)	14 (3.3)	
Educational level			0.10
Doctor and master	10 (19.6)	75 (17.6)	
College and equal	35 (68.6)	333 (78.2)	
High school or lower	6 (11.8)	18 (4.2)	
Staff Category			0.33
Registered	32 (64.0)	301 (70.7)	
Non-registered	18 (36.0)	125 (29.3)	
Co-morbidity			0.38
Yes	3 (5.9)	41 (9.6)	
No	48 (94.1)	385 (90.4)	
Smoking			0.32
No	40 (78.4)	366 (86.7)	
<5/day	7 (13.7)	26 (6.2)	
5–10/day	3 (5.9)	25 (5.9)	
11–20/day	1 (2.0)	4 (0.9)	
>20/day	0 (0)	1 (0.2)	
Drinking alcohol			0.52
Never	23 (52.3)	169 (46.2)	
Occasionally	21 (47.7)	190 (51.9)	
Frequently	0 (0.0)	7 (1.9)	
Contact date			<0.001
Before 2 April	37 (74.0)	173 (44.9)	
After 2 April	13 (26.0)	212 (55.1)	
Employment duration in years (mean ± SD)	7.91 ± 8.94	9.09 ± 8.41	0.38
Occupation			0.29
Medical staff	16 (31.4)	155 (36.4)	
Nursing staff	25 (49.0)	220 (51.6)	
Other occupation	10 (19.6)	51 (12.0)	
Working department			
Medical ward	37 (74.0)	303 (75.9)	
Emergency department	9 (18.0)	78 (19.5)	
Outpatient clinic	3 (6.0)	14 (3.5)	
Other location	1 (2.0)	4 (1.0)	
Average number of contacts with SARS patients per day (mean ± SD)	5.0 ± 5.9	4.5 ± 6.3	0.67
Maximum number of contacts with SARS patients per day (mean ± SD)	8.5 ± 9.0	8.2 ± 10.9	0.91
Average hours working in isolation wards for SARS patients per day (mean ± SD)	6.0 ± 3.0	6.1 ± 2.8	0.88
Maximum hours working in isolation wards for SARS patients per day (mean ± SD)	7.8 ± 5.0	9.4 ± 7.6	0.26
Number of beds (mean ± SD)	9.4 ± 9.1	12.4 ± 10.1	0.17

Table 1 Demographic and epidemiological characteristics in cases and controls

SARS, Severe acute respiratory syndrome.

W. Liu *et al.* Risk factors for SARS infection

bility, occupation, educational level, job category, smoking and drinking habit, etc. The factor of close contact with SARS patients before 2 April was over-represented in the case group compared to the control group (74% *vs.* 45%, $P < 0.001$). Work load was expected to be an important factor for infection occurrence and was measured by the maximum (or average) number of contacts with SARS patients per day, and the maximum (or average) working hours in the SARS-designated isolation/contagious area per day. Statistical analysis showed that none of the factors mentioned above was significantly different between the two groups (Table 1).

Univariate analysis

Altogether we included 28 variables to test their association with disease occurrence, of which 17 gave significant results ($P < 0.10$), including seven risk factors and 10 protective factors. For example, among the healthcare

workers who reported emergency care experience (i.e. over a mean of 1 h) 21% got SARS infection, while only 8% of those without emergency care experience acquired SARS, reflecting a highly significant difference between both groups. Detailed information on the contact with SARS patients were identified. Contact with respiratory secretions, sputum, pathological specimens and deceased significantly increased the ORs of SARS infection. But this was not seen for other types of contact, i.e. with faeces, blood, urine, pulmonary lavage, medical waste, nursing contact or equipment contacts (Table 2).

The previously reported high-risk activities were also identified in the studied subjects: Endotracheal intubation and chest compression were behaviours significantly associated with high risk for infection. The other activities, including post-mortem, intensive care unit (ICU) nursing, sample collection and chest physiotherapy, patient transferring etc. did not achieve significant results, all with $P > 0.10$.

Table 2 Univariate analysis of factors associated with SARS infection in health-care workers

Variable	Number <i>yes</i> (number observed)	% SARS cases for <i>yes-no</i> group	<i>P</i> -value for difference
Contact: nursing	176 (477)	10.6–10.8	0.96
Contact: physical contact	341 (474)	11.3–10.3	0.75
Contact: injection	193 (476)	10.8–11.4	0.82
Contact: intubation	12 (477)	50.0–9.7	<0.001
Contact: chest compression	15 (477)	33.3–11.1	0.02
Contact: respiratory secretion	115 (477)	18.3–9.0	0.004
Contact: sputum	122 (477)	18.0–8.2	0.004
Contact: faeces	102 (477)	12.7–10.1	0.45
Contact: urine	110 (477)	11.8–10.4	0.66
Contact: pulmonary lavage	2 (431)	0.0–11.9	1
Contact: equipment	61 (477)	13.0–10.6	0.83
Contact: pathological specimens	8 (477)	37.5–10.2	0.04
Contact: deceased	18 (477)	27.8–10.0	0.04
Contact: medical waste	113 (477)	11.5–10.4	0.75
Emergency care experience	90 (471)	21.1–8.4	0.001
Wearing 12-layer cotton surgical mask	123 (477)	6.5–12.1	0.07
Wearing 16-layer cotton surgical mask	274 (477)	5.5–17.7	<0.001
Wearing N95 mask	33 (477)	6.1–11.0	0.37
Wearing disposable mask	95 (477)	11.6–10.5	0.76
Layers of masks	–	–	0.002
One layer of masks	22 (477)	27.3–14.8	–
Multiple layers of masks	286 (477)	7.0–14.8	–
Wearing glasses	212 (432)	7.5–15.9	0.006
Multiple layers of protective clothes	221 (306)	6.8–14.1	0.052
Wearing gloves	364 (376)	7.4–33.3	0.011
Protective eyewear (goggle)	221 (477)	7.7–13.3	0.046
Taking prophylactic medicine	384 (473)	8.6–20.2	0.003
Performing nose wash	193 (477)	4.7–14.8	<0.001
Total number of sleeping hours per day	–	–	0.12
No change	222 (407)	11.3–11.4	–
Increase	52 (407)	7.7–11.4	–
Taking training	267 (400)	5.6–19.5	<0.001

W. Liu *et al.* Risk factors for SARS infection

Two kinds of personal protective equipment were studied, face protection and body protection. Six categories of most often used masks were identified from the participating staff: disposable mask, surgical mask, 12-layer cotton surgical mask, 16-layer cotton surgical mask, N95, and higher-level protective respirator. When evaluated individually, 12-layer cotton surgical mask and 16-layer cotton surgical mask displayed significant difference of distribution between the two groups. Healthcare workers who wore glasses had about half the risk of SARS compared to those not wearing glasses ($P = 0.006$) (Table 2). A similar reduction in ORs was achieved by wearing a protective goggle when attending to patients ($P = 0.046$), and washing the nose after attending to patients showed an even stronger effect ($P = 0.0002$) (the nose wash was performed as a nasopharyngeal rinse for cleansing). Wearing gloves and multiple layers of protective gowns also each reduced the ORs of infection significantly ($P = 0.011$ and $P = 0.052$, respectively). Among the administrative factors, taking training in infection control before contact with patients and taking prophylactic medicine (including anti-viral medicine and supplemental nutrition to enhance immunity) were shown to be protective ($P < 0.001$ and 0.003 , respectively).

Five significant univariate variables (contact date, wearing glasses, layers of protective clothes, wearing gloves and taking training) had missing values of $>5\%$. The only significant difference between individuals with and without missing values is that the probability for not answering the question about wearing gloves is smaller for nurses (data not shown). So it is not very likely that missing of values will have caused important bias.

Multivariate analysis

The final multivariate model (Table 3) contains a total of nine variables, three variables concerning masks and none

concerning glasses, gloves etc. We have tried to exchange the mask-variables for the other protection variables, but this dramatically worsened the model, so we conclude that wearing masks, of whatever design, is of the utmost importance to prevent infection. Also, emergency care experience and not taking training were selected as important predictors of getting SARS infection. Nose wash and taking prophylactic medicine turned out to be useful. Regarding contacts with patients, we found respiratory secretion and performing chest compression as important predictors.

The correlations between seven predictor pairs are listed in Table 4. Training and contact date were shown to be correlated. Supplementary analysis showed that given taking training, contact date is not significant ($P = 0.11$), and given contact date, taking training is not significant. We therefore conclude that we cannot distinguish between these two variables. Contact with respiratory secretion was correlated with contact with sputum, but here we found that given secretion, sputum is not significant ($P = 0.63$), but given sputum, contact with secretion is clearly significant ($P = 0.027$). We therefore conclude that these variables are non-interchangeable: contact with respiratory secretion is the dangerous event. Chest compression and intubation were also highly correlated and we found that distinction between those two is not possible.

Discussion

The investigation was carried out in a hospital with a nosocomial outbreak of SARS. A total of 477 staff was recruited into the study, representing about 90% of HCWs exposed to SARS patients. The multivariate logistic regression finally disclosed three factors to be significantly associated with disease occurrence (i.e. performing chest compression or intubation, contact with respiratory secretion, emergency care experience), whereas six actions

Variable	OR	95% CI	P-value
Not wearing 16-layer cotton surgical mask	6.04	2.43–15.00	<0.001
Not wearing 12-layer cotton surgical mask	4.54	1.62–12.74	0.004
Emergency care experience	2.97	1.26–6.96	0.013
Not performing nose wash	2.41	0.98–5.93	0.056
Contact: respiratory secretion	3.27	1.41–7.57	0.006
Not taking prophylactic medicine	2.77	1.10–6.98	0.031
Not taking training	2.40	1.08–5.31	0.039
Not wearing multiple layers of masks	2.44	1.03–5.77	0.026
Contact: chest compression	4.52	1.08–18.81	0.031

The variables are shown in order of selection. No variables were excluded after selection, which means that a variable like '(Not) performing nose wash' is in the table, although it has a P -value > 0.05 (it was <0.05 when it was selected).

Table 3 Multivariate analysis of factors significantly associated with SARS infection in healthcare workers

Table 4 Correlation analysis of significant factors in the univariate analyses of Table 1 and 2. Only the significant correlations are shown

Variable 1	Variable 2	Correlation coefficient	P-value
Contact: intubation†	Contact: chest compression†	0.201	<0.001
Contact: respiratory secretion	Contact: sputum‡	0.512	<0.001
Contact: pathological specimens	Contact: deceased	0.091	0.047
Contact date†	Taking training†	0.167	0.001
Performing nose wash	Taking training	0.144	0.004
Wearing 12-layer cotton surgical mask	Wearing 16-layer cotton surgical mask	-0.510	<0.001
Wearing glasses	Protective eyewear (goggle)	0.101	0.036

†Factors that cannot be distinguished within the model.

‡Factor excluded from the multivariate model, due to insignificant contribution in the presence of the correlating factor.

turned out to be protective (i.e. wearing 16-layer cotton surgical mask, wearing 12-layer cotton surgical mask, wearing multiple layers of masks, taking prophylactic medicine, nose wash and taking training). However, the effect of taking training cannot be distinguished from having been in contact with SARS patients late in the epidemic (after 2 April). Similarly, contact through performing chest compression and contact through intubation are interchangeable.

Our study was subjected to a number of limitations. First, as in all retrospective surveys, recall bias was a concern. However, it is unlikely that ORs of this magnitude could result primarily from recall bias, since the associations shown are clear. The study was conducted shortly after the outbreak, thus minimising the information bias to which retrospective studies are otherwise susceptible. Another possible bias is that the case group attributed their infection to some high risky performance (e.g. performing intubation) and less efficient protection (wearing only one layer of mask while attending patients), while the control group did the opposite.

During SARS epidemic in mainland China, all healthcare staff working in hospitals had been required to follow the recommended personal protection procedures. However, the risk of SARS infection, the level of precaution taken and the compliance with the standard largely depended on multiple factors, including the different time phases of patient contacts, different working areas and the various types of procedures performed. The outbreak in the hospital could be divided into two phases. In the early phase, there was a general lack of familiarity and training regarding infection-control measures among hospital staff. Medical wards and equipment were not adequately set up for the strict infection control standard. While in the later phase, after a super spreading event (SSE) occurred in the hospital, HCWs became more vigilant about protecting

themselves from SARS transmission, which together with adequate training and infection control measures led to significant differences in the infection rate between subjects from before and after 2 April 2003, when the institutional infection control measures were established and enforced. We defined two phases of contact with SARS using the date of 2 April as the divide. As found in univariate analysis, early contact with SARS patients increased the ORs of SARS infection significantly. For the different working areas the univariate analysis did not show significant difference of the distributions between the case and control group.

In multivariate analysis, history of contact with respiratory secretion from an infected patient was associated with 3.27-fold increased ORs of infection for the attending HCWs. This is consistent with previous findings (Teleman *et al.* 2004), thus adding to the evidence that contact with respiratory secretions is an important risk factor. Certain types of procedures have been shown to be high-risk because they can lead to extensive spreading of droplets from the patient, for example, the use of the jet nebulizer and intubation and assisted ventilation (CDC 2003a; Ofner *et al.* 2003; Fowler *et al.* 2004). Our study found a significant association of infection with performing chest compression; while performing intubation showed significant correlation with the former, we cannot distinguish between these two variables given multivariate logistic regression, so both might act as factors that enhance the probability of SARS infection. However, Lau *et al.* (2004) showed that performing particular high-risk procedures on SARS patients was not considered to increase the disease risk. This might be due to the different types of procedures considered and inadequate sample size.

Severe acute respiratory syndrome (SARS)-CoV infection is thought to occur primarily by either contact or large respiratory droplet transmission (CDC 2003b; Ruan *et al.*

2003). The effectiveness of protective measures of using masks, gloves, gowns, and hand-washing, recommended under 'droplet precautions' when caring for SARS patients, was also investigated for their protection effect. Some studies show that use of any mask was associated with lower ORs of infection in healthcare-related clusters (Ruan *et al.* 2003; Seto *et al.* 2003; Nishiura *et al.* 2005). One study showed that consistent use of an N95 mask was more protective than not wearing a mask or consistent use of a surgical mask (Loeb *et al.* 2004). In our study, wearing a 16-layer cotton surgical mask or 12-layer surgical mask, as well as multiple layers of masks, reduced the risk of infection. However, this does not mean that the higher-level protective masks, e.g. the N95 mask, cannot cause effective protection. The counting of N95 mask use was not large enough to give a significant *P*-value. This might pose an important limitation leading to the failure to detect an effect, even though it may be there. The factor using more than one layer of masks was shown to be more protective than a single layer, which presents strong evidence that necessary and appropriate face protection should be advised to diminish the risk of droplet infection. The adoption of 16-layer and 12-layer cotton surgical masks individually was shown to be highly effective on risk reduction and therefore should be recommended accordingly.

Wearing glasses is not intended as protection, yet it indeed showed significant protective effect in univariate analysis. This, together with the significant results of wearing goggles as shown in univariate analysis, might confirm the crucial role of eye protection, although both factors were not confirmed in the subsequent multivariate analysis. These findings fit well with droplets transmission because droplets are generated at the face level, making the mask and eye protection necessary for protection.

The finding that wearing of gowns and gloves achieved statistical significance in univariate, but not in multivariate analysis, differs from the previous studies, where neither gloves nor gowns were found to be protective (Varia *et al.* 2003; Teleman *et al.* 2004). In the study by Seto *et al.* (2003) in Hong Kong, however, gowns were found to be protective, although protection from gloves also failed to achieve statistical significance. In our final multivariate model, we explicitly tested the hypothesis that inclusion of mask over gowns and gloves was due to change but were strengthened in confidence by the fact that exchange of one set of predictors for the other seriously distorted the model. So the failure of inclusion of gowns and gloves was due to their insufficient contribution to the multivariate logistic model. However, wearing of gloves or gowns should never be downplayed because of the insignificant *P*-value in multivariate analysis. It should be noted that the effect of protective measures might be enhanced by beforehand

training on infection control knowledge. In both univariate and multivariate analysis, the infection control training was significantly associated with lower risk of infection and also showed significant interaction with wearing multiple layers of masks. The latter finding had also been suggested in a previous study (Lau *et al.* 2004).

Although several risk factors and protective measures have been identified, we should judge them in relation to the two exposure phases. During the early phase, HCWs in the hospital did not fully acknowledge the risk of the exposure to patients, and adequate personal protective equipments were not applied. The performance of endotracheal intubation and chest compression also helped to disseminate infected aerosol widely to a large number of patients and staff on the ward. This happened a lot during emergency care. During the latter phase, when the workers realised that they were dealing with a high risk infectious disease, they started to use personal protective equipment; however, due to general lack of familiarity and training regarding infection-control measures among the working staff, the protective measures were not administered adequately while dealing with SARS patients. This might explain to some extent that even after protective measures were implemented, there remained hospital workers that contracted the infection.

The high degree of correlation in the risky and protective procedures makes it difficult to ascertain which type of activity is most important for SARS infection, e.g. performing chest compression and performing intubation cannot be distinguished for their contribution to the multivariate model. The same applies to taking training and contact data (after 2 April). Thus, we should be aware that these types of personal risk and protective activities definitely played role in the disease occurrence, although they could not be identified as such in the stepwise multivariate model. We also believe that, whereas this study accepted the current factors as significant using a *P*-value < 0.05, other risk and protective factors for disease infection exist, which we failed to elucidate in this study.

In summary, this study identified exposure to high-risk procedures (such as chest compression), and contact with respiratory secretions to be significant risk factors for SARS infection among HCWs in a hospital in Beijing. These results also provide confirmation that personal protective measures against droplet spread, such as wearing multiple layers of mask, are effective against the nosocomial spread of SARS. This knowledge may help prepare public health officials and clinicians for a reappearance of SARS, should it occur, or for the emergence of another comparable infectious disease. All HCWs should remain vigilant to evaluate and improve their infection-control practices to limit possible future outbreaks of SARS and SARS-like

W. Liu *et al.* **Risk factors for SARS infection**

other nosocomial outbreaks). From the administrative point of the hospital, teaching and training of the medical profession in infectious diseases and the capacity of the public health sector to deal with these diseases must be strengthened.

Acknowledgements

This study was supported by the Commission of the European Community under the Sixth Framework Program Specific Targeted Research Project, SARS Control 'Effective and Acceptable Strategies for the Control of SARS and new emerging infections in China and Europe' (Contract No. SP22-CT-2004-003824), and Grants from National Natural Science Foundation of China for Excellent Young Scientists (No. 30725032), and National Natural Science Foundation of China (No. 30590374).

Conflicts of interest

The authors have declared no conflicts of interest.

References

- Centers for Disease Control and Prevention (2003a) Cluster of severe acute respiratory syndrome cases among protected health-care workers—Toronto, Canada, April 2003. *Morbidity and Mortality Weekly Report* **52**, 433–436.
- Centers for Disease Control and Prevention (2003b) Outbreak of severe acute respiratory syndrome—worldwide. *Morbidity and Mortality Weekly Report* **52**, 226–228.
- Chan-Yeung M & Yu WC (2003) Outbreak of severe acute respiratory syndrome in Hong Kong Special Administrative Region: case report. *BMJ* **326**, 850–852.
- Feng D, Vlas SJ, Fang LQ *et al.* (2009) The SARS epidemic in mainland China: bringing together all epidemiological data. *Tropical Medicine of International Health* **14** (Suppl. 1), 4–13.
- Fowler RA, Guest CB, Lapinsky SE *et al.* (2004) Transmission of severe acute respiratory syndrome during intubation and mechanical ventilation. *American Journal of Respiratory and Critical Care Medicine* **169**, 1198–1202.
- Lau JT, Fung KS, Wong TW *et al.* (2004) SARS transmission among hospital workers in Hong Kong. *Emerging Infectious Diseases* **10**, 280–286.
- Liu W, Fontanet A, Zhang PH *et al.* (2006) Two-year prospective study of the humoral immune response of patients with severe acute respiratory syndrome. *J Infect Dis* **193**, 792–795.
- Loeb M, McGeer A, Henry B *et al.* (2004) SARS among critical care nurses, Toronto. *Emerging Infectious Diseases* **10**, 251–255.
- Ma HJ, Wang HW, Fang LQ, Jiang JF, Wei MT, Liu W, Zhao QM, Ma J, Cao WC (2004) A case-control study on the risk factors of severe acute respiratory syndromes among health care workers. *Zhonghua Liu Xing Bing Xue Za Zhi* **25**, 741–744.
- Nishiura H, Kuratsuji T, Quy T & Anderson RM (2005) Rapid awareness and transmission of severe acute respiratory syndrome in Hanoi French Hospital, Vietnam. *American Journal of Tropical Medicine and Hygiene* **73**, 17–25.
- Offer M, Lem M, Sarwal S, Vearncombe M & Simor A (2003) Cluster of severe acute respiratory syndrome cases among protected health care workers—Toronto 2003. *Canada Communicable Disease Report* **29**, 93–97.
- Ruan YJ, Wei CL, Ee AL *et al.* (2003) Comparative full-length genome sequence analysis of 14 SARS coronavirus isolates and common mutations associated with putative origins of infection. *Lancet* **361**, 1779–1785.
- Seto WH, Tsang D, Yung RW *et al.* (2003) Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* **361**, 1519–1520.
- Teleman MD, Boudville IC, Heng BH, Zhu D & Leo YS (2004) Factors associated with transmission of severe acute respiratory syndrome among health-care workers in Singapore. *Epidemiology and Infection* **132**, 797–803.
- Varia M, Wilson S, Sarwal S *et al.* (2003) Investigation of a nosocomial outbreak of severe acute respiratory syndrome (SARS) in Toronto, Canada. *CMAJ* **169**, 285–292.
- World Health Organization (2003) Case definitions for surveillance of severe acute respiratory syndrome (SARS). WHO, Geneva. (<http://www.who.int/csr/sars/casedefinition/en/>). Accessed June 2003.
- Yu IT, Li Y, Wong TW *et al.* (2004) Evidence of airborne transmission of the severe acute respiratory syndrome virus. *New England Journal of Medicine* **350**, 1731–1739.

Corresponding Author Wu-Chun Cao, Beijing Institute of Microbiology and Epidemiology, State Key Laboratory of Pathogen and Biosecurity, 20 Dong-Da Street, Feng Tai District, 100071 Beijing, P.R. China. E-mail: caowc@nic.bmi.ac.cn

Correction added after online publication <July 13 2009>: Reference Ma *et al* reference added.