

Why Did Outbreaks of Severe Acute Respiratory Syndrome Occur in Some Hospital Wards but Not in Others?

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Background. Most documented “superspreading events” of severe acute respiratory syndrome (SARS) occurred in hospitals, but the underlying causes remain unclear. We systematically analyzed the risk factors for nosocomial outbreaks of SARS among hospital wards in Guangzhou and Hong Kong, China.

Methods. A case-control study was conducted. Case wards were hospital wards in which superspreading events of SARS occurred, and control wards were wards in which patients with SARS were admitted, but no subsequent nosocomial outbreaks occurred. Information on environmental and administrative factors was obtained through visits to the wards and interviews with ward managers or nursing officers. Relevant information about host factors was abstracted from the medical records. Logistic regression analyses were used to identify the major risk factors for superspreading events.

Results. Eighty-six wards in 21 hospitals in Guangzhou and 38 wards in 5 hospitals in Hong Kong were included in the study. Six risk factors were significant in the final multiple-logistic regression model: minimum distance between beds of ≤ 1 m (odds ratio [OR], 6.94; 95% confidence interval [CI], 1.68–28.75), availability of washing or changing facilities for staff (OR, 0.12; 95% CI, 0.02–0.97), whether resuscitation was ever performed in the ward (OR, 3.81; 95% CI, 1.04–13.87), whether staff members worked while experiencing symptoms (OR, 10.55; 95% CI, 2.28–48.87), whether any host patients (index patient or the first patient with SARS admitted to a ward) required oxygen therapy (OR, 4.30; 95% CI, 1.00–18.43), and whether any host patients required bi-level positive airway pressure ventilation (OR, 11.82; 95% CI, 1.97–70.80).

Conclusions. Our results revealed that factors that were associated with the ward environment and administration were important in nosocomial outbreaks of SARS. The lessons learned from this study remain very important and highly relevant to the daily operation of hospital wards if we are to prevent nosocomial outbreaks of other respiratory infections in the future.

Severe acute respiratory syndrome (SARS) is the first new infectious disease of the 21st century to have attracted global attention. A Hong Kong, China, hotel was identified as the starting point for the international spread of SARS to at least 5 countries [1]. In the epidemic that affected many parts of the world, Guang-

zhou and Hong Kong were seriously affected, with 1567 and 1755 probable cases (according to the World Health Organization definition), respectively [2].

One of the intriguing characteristics of the 2003 SARS epidemic was the occurrence of superspreading events. It was estimated that 71.1% and 74.8% of the infections were attributable to superspreading events in Hong Kong and Singapore, respectively [3]. The vast majority of documented superspreading events occurred in hospitals, with few exceptions (e.g., the Amoy Gardens [4]), but the underlying causes of such events have not been well studied. The World Health Organization [5] attributed the superspreading phenomenon to the lack of stringent infection-control measures in hospitals during the early days of the epidemic. Shen

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et al. [6] identified 4 superspreading events in Beijing and found that the index patients were likely to have been older and had a higher case-fatality rate and a larger number of close contacts. Other previous studies either focused on the analysis of risk factors at the individual level, among affected health care workers [7–11] or inpatients [12], or were simply anecdotal reports based on personal observations and speculations [13–20]. To better understand why such nosocomial outbreaks occurred and to provide guidance for the prevention of superspreading events of SARS and similar infectious diseases in the future, we performed a systematic analysis of the risk factors associated with nosocomial outbreaks of SARS in hospital wards in Guangzhou and Hong Kong.

METHODS

Study design and population. A case-control study was designed with the individual hospital wards as the units for data collection and analysis. Case wards were hospital wards in which superspreading events of SARS occurred, and control wards were hospital wards in which patient(s) with SARS were admitted, but no superspreading events occurred. We defined a superspreading event as the development of ≥ 3 new cases of SARS in a ward during the period from 2 to 10 days after the admission of an identifiable index patient or as the development of a cluster of ≥ 3 new cases of SARS in a ward during a period of 8 days but without any known sources of SARS. There is no universally accepted critical (cutoff) number for defining a superspreading event, but because the basic reproductive number (R_0) in the community was 2.7 [21], we adopted a more conservative operational definition, with a critical number of ≥ 3 new cases of SARS. Superspreading events were identified through reports of known nosocomial outbreaks of SARS from the infection-control units of all hospitals and through temporal clustering (detected by plotting the date of onset of symptoms for each case of SARS that occurred among health care workers and inpatients for each ward).

Attempts were made to collect information from all hospital wards in Guangzhou and the New Territories East Clusters of Hospitals in Hong Kong that admitted at least 1 patient with SARS during the 2003 epidemic. Pediatric wards were excluded, because the characteristics of SARS in pediatric patients are quite different from those in adult patients [22, 23]. Designated wards for treating patients who were known to have SARS were also excluded because of possible multiple contacts with multiple source patients.

Data collection. Information related to 2 factors was collected: (1) environmental and administrative factors and (2) host factors. Environmental and administrative factors included physical factors, procedural or situational factors, and administrative factors pertaining to each ward. Host factors included symptoms, severity or dependency (for activities of daily living

and behavior changes), treatment or intervention, and comorbidity of the identified index patient in a case ward or in the first patient with SARS admitted in a control ward. The details are shown in tables 1 and 2.

Ward managers or nursing officers of all of the eligible wards were interviewed in person by 1 of the 3 medically qualified coauthors (Y.L.C., S.W.L., and Z.H.X.) using a structured questionnaire. Interviews were conducted in the hospitals during the period from September 2004 through November 2005. Environmental and administrative factors referred to the situation during the study period for each ward, which was defined as the 10 days immediately after the admission of the index patient (for case wards) or the first new patient (for control wards and case wards without an identifiable index patient). Distances between beds were measured with measuring tape. Staff rosters and relevant documents were inspected and reviewed to verify and supplement information provided by the ward managers. Medical records of all patients with SARS were reviewed to abstract relevant information related to the host patient.

Statistical analysis. All data were double-keyed into a predesigned database and analyzed using SAS software, version 9.1 (SAS Institute). Logistic regression was used to estimate the ORs and 95% CIs of various possible risk factors. Because there had been no prior documented risk factors for such outbreaks, univariate analysis was first conducted for each risk factor. Risk factors with $P < .15$ were included in a multiple logistic regression model and analyzed using the stepwise approach, with the inclusion/exclusion criterion of $P < .15$. This analysis was performed separately for the environmental or administrative factors and for host factors, because there were smaller usable numbers of case wards and control wards with information of host factors, which resulted from unidentified host patients in some case wards or from missing data.

Subgroup analyses by location (Guangzhou and Hong Kong) were also performed to examine the consistency of risk factors identified in the 2 cities. All risk factors selected in any of the separate multivariate models ($P < .15$) for environmental or administrative factors and for host factors were then included in a combined, final model, using the stepwise approach. Because the number of case wards was small and the number of risk factors examined was large, we had to group some individual risk factors in composite variables by counting or scoring (the number of positive responses in the group), recoding (any positive response in the group, which was coded as positive for the composite variable), or ranking (according to hierarchy) (tables 1 and 2) for the statistical analyses. Composite variables that were counted or ranked were rescaled from 0 to 1 to equalize their weights in the logistic models. A relatively large α error of .15 was adopted in the analyses so as not to miss potentially important risk factors, because the number of case wards included in this study was small. The 95% CI of the OR

Table 1. Potential environmental or administrative risk factors for nosocomial outbreaks of severe acute respiratory syndrome.

Type of risk factor, factor	Measurement	Composite variable
Physical		
Isolation in side ward	Yes or no	Isolation/segregation ^a
Segregation of contaminated areas	Yes or no	Isolation/segregation ^a
Minimum distance between adjacent beds ^b	≤1 m or >1m	...
Sink or basin for hand-washing for staff	Yes or no	Washing or changing facilities for staff ^a
Shower for staff	Yes or no	Washing or changing facilities for staff ^a
Changing room for staff	Yes or no	Washing or changing facilities for staff ^a
Use of natural ventilation	Always/sometimes or never	...
Use of air conditioning	Always/sometimes or never	...
Use of exhaust fans	Always/sometimes or never	...
Procedural and situational		
Use of nebulizer	At least once or never	...
Use of high-flow-rate O ₂ mask ^c	At least once or never	...
Performance of resuscitation	At least once or never	...
Performance of endotracheal intubation	At least once or never	...
Performance of suction (respiratory tract)	At least once or never	...
Oral feeding of patients by staff	At least once or never	...
Occurrence of contamination event with excretions or excreta	At least once or never	...
Administrative		
Infection-control training for staff ^d	Yes or no	...
Written guidelines for infection control ^d	Yes or no	...
Designated person for infection control	Yes or no	Infection-control practice ^a
Infection risk assessment	Yes or no	Infection-control practice ^a
Cleaning of ward more frequently	More vs. same, or less	Infection-control practice ^a
Provision of respiratory protection ^e	Yes or no	...
Provision of other personal protective equipment ^f to staff	Yes or no	...
Staff working while experiencing symptoms	Yes or no	...
Work load of health care workers ^g	≤2 or >2	...

^a Data were combined by counting.

^b Measured from side-to-side.

^c Flow rate >6 L/min.

^d Both infection-control training and written guidelines included the following items separately: isolation of suspected patients, disinfection, decontamination, personal hygiene, use of gloves, use of masks, use of goggles or face shield for eye protection, use of gown, and reporting of new cases. Data were combined by counting.

^e A hierarchy ranking was used to combine 4 variables: surgical or cotton mask, 1; N95 mask, 2; N95 mask with fit testing, 3; and positive air-powered respirator, 4.

^f Surgical cap, goggles, face shield, gown, gloves, and shoe covers. Data were combined by counting.

^g No. of patients per health care worker.

was used to assess statistical significance at the conventional level of .05.

RESULTS

With 2 pediatric wards having been excluded, 87 wards in 21 hospitals in Guangzhou and 40 wards in 5 hospitals in Hong Kong admitted patients with SARS in 2003. One ward in Guangzhou and 2 wards in Hong Kong did not participate, and they were excluded from the analysis. The nature of the case and control wards included is shown in table 3.

Of the 86 wards studied in Guangzhou, 35 (40.7%) were

classified as case wards, and an index patient was identified in 26 of these wards (74.3%). For Hong Kong, 13 (34.2%) were classified as case wards, and an index patient was identified in 5 (38.5%). The ratio of male to female patients was 1.38:1 among index patients and 1.09:1 among the first patients admitted in the control wards. The index patients in the case wards were slightly older than the first patients admitted with SARS in the control wards (mean age, 51.3 vs. 48.6 years), and they also experienced a longer duration from symptom onset to hospital admission (8.3 days vs. 5.7 days). However, these differences were not statistically significant.

Table 2. Potential risk factors associated with the host patient (index patient or the first patient with severe acute respiratory syndrome [SARS] admitted to a ward) for a nosocomial outbreak of SARS.

Type of risk factor, factor	Measurement	Remarks (regrouping method)
Symptoms		
Respiratory	Yes or no	Cough and sputum (combined by counting)
Gastrointestinal	Yes or no	Vomiting and diarrhea (combined by counting)
Systemic	Yes or no	Myalgia, chills, rigor, malaise, headache, and dizziness (combined by counting)
Severity or dependency		
Pulmonary congestion	Yes or no	Congestive heart failure, excessive pulmonary secretion, and pulmonary edema (combined by counting)
Requiring oxygen supply	Yes or no	...
Severity	Yes or no	Shortness of breath, breathing difficulty, respiratory distress syndrome, admission to ICU, and death (combined by counting)
Dependency	Yes or no	Dependent for activities of daily living and behavior changes (combined by counting)
Treatment or intervention		
Use of nebulizer	Yes or no	...
Use of mechanical ventilation	Yes or no	...
Use of BIPAP ventilator	Yes or no	...
Comorbidity		
Diseases affecting immunity	Yes or no	Chronic renal failure, cirrhosis, chronic hepatitis, active pulmonary tuberculosis, influenza, pneumonia, and malignancies (combined by recoding)
Cardiovascular diseases	Yes or no	Ischemic heart disease, congestive heart failure, hypertension, and stroke (combined by recoding)
Respiratory diseases	Yes or no	Active pulmonary tuberculosis, chronic obstructive airway disease, and asthma (combined by recoding)
Infections	Yes or no	Chronic hepatitis, active pulmonary tuberculosis, influenza, and pneumonia (combined by recoding)

NOTE. BIPAP, bi-level positive airway pressure ventilation; ICU, intensive care unit.

Univariate analysis showed that environmental or administrative factors significantly associated ($P < .05$) with the occurrence of superspreading events included minimum distance between beds of ≤ 1 m, lack of washing or changing facilities for staff, no use of an exhaust fan, use of high-flow-rate O_2 mask, performance of resuscitation, staff working while experiencing symptoms, and a workload of >2 patients per 1 health care worker (table 4). Occurrence of a contamination event and infection-control training had P values between .05 and .15. Significant host factors identified included pulmonary congestion, host patient requiring oxygen therapy, higher severity of disease, use of a nebulizer, and use of bi-level positive airway pressure (BIPAP) ventilation (table 4). Three other host factors with P values between .05 and .15 were respiratory symptoms (cough and phlegm), systemic symptoms (myalgia, chills, rigor, malaise, headache, and dizziness), and dependency (for activities of daily living and behavior changes).

Multiple logistic regression models for environmental or ad-

ministrative factors are shown in table 5. In the model combining data from Guangzhou and Hong Kong, 3 significant factors ($P < .05$) emerged: minimum distance between beds of ≤ 1 m (OR, 3.36), availability of washing or changing facilities for staff (OR, 0.21), and staff working while experiencing symptoms (OR, 5.50). A possible environmental or administrative factor was performance of resuscitation ($P = .10$). Minimum distance between beds of ≤ 1 m was the only factor present in both the Guangzhou model and the Hong Kong model, although it was only of borderline significance ($P = .07$) in the latter.

Multiple logistic regression models for host factors are shown in table 6. Two factors—use of oxygen therapy and systemic symptoms—stood out to be significant ($P < .05$) in the Guangzhou model. None of the factors studied was significant in the Hong Kong model. In the model with combined data, only host patient requiring oxygen therapy was significant ($P < .05$), and use of BIPAP ventilation had a P value of .06.

Table 3. Types of case and control wards in Guangzhou and Hong Kong.

Type of ward	Guangzhou		Hong Kong		Total
	No. of case wards	No. of control wards	No. of case wards	No. of control wards	
Medical	10	7	12	15	44
Surgical	0	6	1	4	11
ICU	5	8	0	2	15
Infectious disease	5	3	0	0	8
Respiratory	3	5	0	0	8
Accident and emergency	2	6	0	0	8
Chinese medicine	4	1	0	0	5
Fever cohort	0	0	0	1	1
Other	6	15	0	3	24
Total	35	51	13	25	124

NOTE. ICU, intensive care unit.

The logistic models that combine environmental or administrative factors and host factors are shown in table 7. Four environmental or administrative factors and 2 host factors were significant in the final model that combines data from Guangzhou and Hong Kong ($P < .05$): minimum distance between beds of ≤ 1 m, washing or changing facilities for staff, performance of resuscitation, staff working while experiencing symptoms, host patient requiring oxygen therapy, and use of BIPAP ventilation. Two environmental or administrative factors emerged consistently in the 3 models: minimum distance between beds of ≤ 1 m and staff working while experiencing symptoms. No use of an exhaust fan and systemic symptoms appeared only in the model for Guangzhou ($P = .05-.15$).

Sensitivity analysis was conducted by varying the critical number for defining a superspreading event. When a cutoff value of 4 cases was used, 5 factors emerged in the final combined model, including 3 significant factors in the model with a cutoff value of 3 cases (minimum distance between beds of ≤ 1 m, staff working while experiencing symptoms, and host patient requiring oxygen therapy). Systemic symptoms in the host patient became a significant risk factor, and use of a high-flow-rate O₂ mask in the ward was included in the model ($P = .12$). When a cutoff value of 5 cases was used, 5 significant factors were present in the final combined model: minimum distance between beds of ≤ 1 m, staff working while experiencing symptoms, host patient requiring oxygen therapy, systemic symptoms, and use of a high-flow-rate O₂ mask (table 8).

DISCUSSION

This is the first study to analyze, in a systematic manner, risk factors associated with nosocomial outbreaks of SARS, using an analytic, epidemiological design. We found that significant environmental risk factors associated with the occurrence of a

superspreading event (clustering of ≥ 3 cases) included minimum distance between beds of ≤ 1 m and performance of resuscitation in the ward. Use of BIPAP ventilation and use of oxygen were the significant risk factors associated with the host patient. Of the administrative factors, allowing staff with symptoms to work also increased the risk. Providing adequate washing or changing facilities for staff was protective. Sensitivity testing by applying more stringent cutoff points (4 or 5 clustered cases) suggested that our results were quite robust, with 3 significant risk factors being identified consistently: minimum distance between beds of ≤ 1 m, staff working while experiencing symptoms, and host patient requiring oxygen therapy.

Our results showed that environmental and administrative factors were important in causing and preventing nosocomial outbreaks of SARS. These rectifiable factors have also been identified as risk factors for nosocomial spread of other respiratory infections. Inadequate bed spacing and overcrowding in hospital wards is well known to increase the risk of nosocomial outbreaks [24–27]. Unfortunately, it is a usual practice—against the original design of the hospital ward and infection-control policy—to increase the number of hospital beds in a ward to meet the increasing demand, especially during an epidemic. When the distance between beds is reduced, droplets can spread from a patient to the adjacent patients, and ventilation (natural or mechanical) can also be jeopardized.

Staff working while experiencing symptoms could spread SARS in hospital wards [12], and this risk factor is consistently found in all 3 models in the current analysis. The SARS coronavirus load in a patient is highest during the first week of the disease, and the patient is most contagious when he or she is febrile [28]. We believe that staff working while experiencing symptoms might account for some nosocomial outbreaks in which no index patients could be identified, although we do not have well-documented evidence to prove this hypothesis.

Table 4. Univariate analysis of the environmental or administrative factors and host factors.

Type of factor, factor	OR (95% CI)	<i>P</i>
Environmental or administrative factors		
Isolation or segregation	0.97 (0.50–1.87)	.93
Minimum distance between beds of ≤ 1 m	3.71 (1.67–8.20)	.001
Washing or changing facilities for staff	0.26 (0.08–0.88)	.03
Never used natural ventilation	0.61 (0.28–1.34)	.21
Never used air conditioning	0.81 (0.39–1.69)	.58
Never used exhaust fan	2.18 (1.03–4.59)	.04
Use of nebulizer	1.37 (0.66–2.85)	.40
Use of high-flow-rate O ₂ mask	2.42 (1.15–5.08)	.02
Performance of resuscitation	2.72 (1.27–5.81)	.009
Performance of endotracheal intubation	1.22 (0.58–2.56)	.59
Performance of suction	1.46 (0.64–3.35)	.37
Oral feeding of patients by staff	1.66 (0.67–4.00)	.26
Occurrence of contamination event	1.88 (0.83–4.24)	.13
Infection control training	0.01 (<0.01 to 1.22)	.059
Written guidelines for infection control	0.59 (0.14–2.51)	.48
Infection control practice	1.30 (0.53–3.23)	.56
Provision of respiratory protection	1.02 (0.30–3.44)	.97
Provision of other personal protective equipment to staff	0.62 (0.14–2.72)	.52
Staff working while experiencing symptoms	5.26 (1.96–14.10)	.001
Workload, >2 patients per health care worker	2.76 (1.16–6.57)	.02
Host factors		
Respiratory symptoms	2.27 (0.75–6.90)	.15
Gastrointestinal symptoms	1.05 (0.21–5.27)	.95
Systemic symptoms	3.43 (0.74–15.90)	.12
Pulmonary congestion	4.74 (1.11–20.30)	.04
Requiring oxygen therapy	4.78 (1.75–13.03)	.001
Severity	4.73 (1.23–18.14)	.02
Dependency	2.76 (0.80–9.57)	.11
Use of nebulizer	3.91 (1.42–10.78)	.006
Use of mechanical ventilation	1.56 (0.47–5.22)	.52
Use of BIPAP ventilation	5.56 (1.69–18.37)	.005
Diseases affecting immunity	1.06 (0.41–2.79)	.90
Cardiovascular diseases	1.39 (0.59–3.28)	.46
Respiratory diseases	1.46 (0.33–6.51)	.69
Infections	1.21 (0.38–3.89)	.76

NOTE. *P* values <.15 are in boldface type.

Provision of washing or changing facilities in hospital wards for staff helped reduce the risk of nosocomial outbreaks. This also suggested that health care workers could act as passive carriers of the SARS coronavirus, which would lead to nosocomial transmission.

The use of oxygen and BIPAP ventilation among patients with infectious respiratory diseases has been a subject of debate since the emergence of SARS in 2003. The high flow-rate of oxygen or air and/or the positive pressure resulting from such treatment procedures might accentuate the spread of potentially infectious air exhaled or expelled from patients [20]. In our recent study of airflow around oxygen masks during oxygen

therapy, exhaled air from the mask can travel up to 0.4 m on each side of the patient [29]. In the present study, both the use of oxygen therapy and BIPAP ventilation imposed a significant risk for nosocomial spread of SARS in the final combined model (cutoff value, 3 cases), and use of oxygen therapy also significantly increased the risk in models with higher cutoff values. We did not have enough details about oxygen therapy modalities given to the index patients to allow a more refined analysis regarding the types of masks or cannulae and flow rate of oxygen supply in this study. Proper capturing (enclosure, containment, and local exhaust) and filtering (high-efficiency particulate air filter) of exhaled or expelled air should be imple-

Table 5. Multivariate model for environmental or administrative factors.

Factor	Guangzhou		Hong Kong		Overall	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Minimum distance between beds of ≤ 1 m	5.41 (1.51–19.30)	.009	5.13 (0.89–29.57)	.07	3.36 (1.38–8.16)	.008
Washing or changing facilities for staff	...	>.15	0.18 (0.02–1.58)	.12	0.21 (0.05–0.88)	.03
Never used exhaust fan	3.96 (1.30–12.04)	.02	...	>.15	...	>.15
Performance of resuscitation	2.86 (0.99–8.29)	.05	...	>.15	2.12 (0.87–5.12)	.10
Staff working while experiencing symptoms	5.38 (1.39–20.77)	.15	...	>.15	5.50 (1.74–17.40)	.004

NOTE. The inclusion criterion was $P < .15$. The ratio of case to control wards was 34:51 in Guangzhou, 10:25 in Hong Kong, and 44:76 in both combined. Ninety-five percent CIs not including 1 are in boldface type.

mented if oxygen and BIPAP ventilation must be used for clinical reasons. The mechanical maneuvers and procedures associated with resuscitation can generate large amounts of aerosols that are potentially infectious, especially during intubation of the airway and manual ventilation. More thought should be given to redesigning the procedures by engineering or administrative means to achieve effective containment of any possible contamination arising from the resuscitation process [30].

Higher occurrence of systemic symptoms in the index patient or the first patient with SARS admitted to the ward emerged as a significant risk factor when a superspreading event was defined by clusters of ≥ 4 or ≥ 5 cases. It is not known whether this could be related to a higher virus load. Higher virus loads have been reported to be associated with oxygen desaturation, diarrhea, hepatic dysfunction, mechanical ventilation, and death [31, 32], but unfortunately, clear relationships with systemic symptoms have not been reported.

The strength of this study is the very high participation rate of 97.6% (124 of 127 eligible wards). However, there are several limitations in this study. Because the study was confined to 2 cities in southern China, we are not sure if our results could be applied to other countries with different hospital practices. Nonetheless, we believe that our study has provided the best available evidence thus far on risk factors for superspreading events in the hospital setting. Another limitation might be that the interviews were conducted >1 year after the occurrence of the outbreaks of SARS, and recall inaccuracies might exist. However, we performed site inspections and physical measurements to obtain information on various physical and en-

vironmental risk factors and reviewed documents and staff rosters to complement and supplement recall and reporting by the ward managers. Therefore, information bias should have been substantially reduced. On the other hand, all host factors were abstracted from review of original medical records and should be objective. Another intrinsic weakness of the current study was the lack of statistical power because of the small number of case wards, especially in the subgroup analysis for Hong Kong. Thus, the contribution of certain possible risk factors (such as type of ventilation in the ward and lack of appropriate personal protective equipment and infection control training) could not be entirely ruled out. Certain factors that are intuitively important (e.g., presence of patient isolation or segregation and performance of mechanical ventilation or intubation among index or initial patients) unexpectedly did not have notable effects on univariate analyses. The true effects of these factors might have been subsumed by closely related risk factors that were statistically significant, such as resuscitation having been performed. The small number of study units prevents us from including these factors in multiple regression analyses that could have identified their independent effects. Perhaps a larger international collaboration would help solve this problem. All in all, the fairly consistent results of different subgroup analyses in Hong Kong and Guangzhou provide indirect support that our results are generally valid. Environmental or administrative factors were more important than host factors. Other than the presence of systemic symptoms (in analyses with more restrictive definitions for a superspreading event), the 2 host factors identified—use of oxygen therapy and use of BIPAP ventilation—pertained more to environmental

Table 6. Multivariate model for host factors.

Factor	Guangzhou		Hong Kong		Overall	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Requiring oxygen therapy	10.30 (2.57–41.34)	.03	...	>.15	3.59 (1.25–10.29)	.02
Use of BIPAP ventilation	...	>.15	...	>.15	3.26 (0.93–11.41)	.06
Systemic symptoms	13.35 (1.32–134.96)	.001	...	>.15	...	>.15

NOTE. The inclusion criterion was $P < .15$. The ratio of case to control wards was 26:48 in Guangzhou, 5:25 in Hong Kong, and 31:73 in both combined. Ninety-five percent CIs not including 1 are in boldface type. BIPAP, bi-level positive airway pressure.

Table 7. Multivariate model for all risk factors with $P < .15$ in the separate models for environmental or administrative factors and for host factors.

Type of factor, factor	Guangzhou		Hong Kong		Overall	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Environmental or administrative factors						
Minimum distance between beds of ≤ 1 m	11.77 (1.54–90.13)	.02	10.28 (0.58–182.10)	.11	6.94 (1.68–28.75)	.008
Washing or changing facilities for staff	...	>.15	...	>.15	0.12 (0.02–0.97)	.05
Never used exhaust fan	4.16 (0.98–17.72)	.05	...	>.15	...	>.15
Performance of resuscitation	...	>.15	...	>.15	3.81 (1.04–13.87)	.04
Staff working while experiencing symptoms	11.18 (1.99–62.81)	.006	19.27 (1.12–332.48)	.04	10.55 (2.28–48.87)	.003
Host factors						
Requiring oxygen therapy	10.14 (1.70–60.37)	.01	...	>.15	4.30 (1.00–18.43)	.05
Use of BIPAP ventilation	6.67 (0.90–49.23)	.06	...	>.15	11.82 (1.97–70.80)	.007
Systemic symptoms	12.71 (0.70–232.03)	.09	...	>.15	...	>.15

NOTE. The ratio of case to control wards was 26:48 in Guangzhou, 4:25 in Hong Kong, and 30:73 in both combined. Ninety-five percent CIs not including 1 are in boldface type. BIPAP, bi-level positive airway pressure.

contamination than to individual patient characteristics. In other words, this study managed to characterize the environment, rather than individual infected patients, during super-spreading events.

After the pandemic of SARS in 2003, only a few isolated cases of SARS, involving laboratory workers or animals, have been reported. Nevertheless, the lessons learned from this study remain very important and highly relevant to the daily operation of hospital wards if we wish to prevent nosocomial outbreaks of respiratory infections in the future. With the current threat of avian influenza and other respiratory infections, such as tuberculosis, hospital wards have to be redesigned and managed in a manner to ensure that environmental factors associated with nosocomial infections are kept to the minimum. The importance of adequate spacing between beds and provision of washing or changing facilities for staff cannot be over-emphasized. Staff with symptoms of respiratory infections

should refrain from continuing their clinical duties. Adequate complementary protective devices at the source of infection (namely, infected patients) would have to be designed. Additional work needs to be conducted with regard to the safe use of oxygen therapy and/or ventilatory support among patients with respiratory infections.

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Table 8. Multivariate models for combined data of Guangzhou and Hong Kong with different definitions of superspreading event.

Type of factor, factor	Superspreading event					
	3 cases		4 cases		5 cases	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Environment or administrative factors						
Minimum distance between beds of ≤ 1 m	6.94 (1.68–28.75)	.008	4.03 (1.16–14.05)	.03	9.41 (1.73–51.26)	.01
Use of high-flow-rate O_2 mask	...	>.15	2.52 (0.79–8.10)	.12	7.08 (1.30–38.42)	.02
Washing or changing facilities for staff	0.12 (0.02–0.97)	.0515	...	>.15
Performance of resuscitation	3.81 (1.04–13.87)	.0415	...	>.15
Staff working while experiencing symptoms	10.55 (2.28–48.87)	.003	6.75 (1.87–24.33)	.004	8.21 (1.63–41.43)	.01
Host factors						
Requiring oxygen supply	4.30 (1.00–18.43)	.05	6.56 (1.69–25.48)	.007	10.97 (1.73–69.39)	.01
Use of BIPAP ventilation	11.82 (1.97–70.80)	.0071515
Systemic symptoms	...	>.15	24.16 (2.57–227.5)	.005	213.6 (7.45–999.9)	.002

NOTE. The ratio of case to control wards was 30:73 in the group with 3 cases, 25:78 in the group with 4 cases, and 18:85 in the group with 5 cases. Ninety-five percent CIs not including 1 are in boldface type. BIPAP, bi-level positive airway pressure.

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