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# Super-spreading events of SARS in a hospital setting: who, when, and why?

**Key Messages**

1. Factors related to the ward environment/administration were important in nosocomial outbreaks of SARS.
2. With the current threat of avian influenza and other respiratory infections such as tuberculosis, hospital wards have to be re-designed and the daily operation reviewed to minimise environmental factors associated with nosocomial infections.

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## Introduction

It is believed that the SARS coronavirus originated from wild animals and that human-to-human transmission first occurred in Guangdong Province, China. A resident of Guangzhou, who stayed in a Hong Kong hotel in February 2003, was identified as the index case for the spread of SARS to at least five countries.[1] In the resulting epidemic, 1567 and 1755 probable cases occurred in Guangzhou and Hong Kong, respectively.[2]

A super-spreading event (SSE) is defined as a cluster of SARS infections in which one or more individuals infected many more individuals than did an average SARS patient. About 71% and 75% of the infections were attributable to SSEs in Hong Kong and Singapore, respectively.[3] The transmission efficiency of the disease was quite low in the community, with the exception of the Amoy Gardens SSE in Hong Kong.[3] Most SSEs occurred inside hospitals, but the underlying causes have not been well studied. The World Health Organization attributed the SSEs to the lack of stringent infection control measures in hospitals during the early days of the epidemic.[4] A study of four super-spreaders in Beijing found that they were likely to be older, associated with a higher fatality rate and a larger number of close contacts than non–super-spreaders.[5] Other studies focused on the risk factors at the individual level of the secondary cases among health care workers or in-patients, or were simply anecdotal reports based on personal observations and speculations. To better understand why nosocomial outbreaks of SARS occurred and to provide guidance for the prevention of SSEs in the future, we systematically analysed the risk factors associated with nosocomial outbreaks in hospital wards in Guangzhou and Hong Kong through a case-control study.

## Aims and objectives

1. To identify SSEs for SARS that occurred in public hospitals in Hong Kong and Guangzhou; and
2. To explore the factors that result in the development of SSEs in a hospital setting.

## Methods

### *Study design and population*

A case-control study was designed with individual hospital wards as the units for data collection and analysis. Cases were hospital wards with SSEs for SARS, whereas controls were hospital wards that admitted SARS patients but did not have SSEs. We defined an SSE in a ward as three or more than three new cases occurring within 2 to 10 days after admission of the first patient or an identifiable index case, or within 8 days without any known sources. There is no universally accepted critical (cut-off) number for defining an SSE, but as the basic reproductive number in the community was 2.721, we adopted a more conservative operational definition with a critical number of three or more than three new cases.

Super-spreading events were identified through two means: (1) reports of known nosocomial outbreaks from the infection control units of all hospitals, (2) plotting the date of symptom onset of each case among health care workers and in-patients for each ward to identify clustering, as well as the date of admission of all new cases (including known cases transferred from other wards or hospitals).

Efforts were made to document evidence of contact between the index case and 'secondary cases'. It was possible that a definite index case could not be identified.

All hospital wards in Guangzhou and the New Territories East Cluster of Hospitals in Hong Kong that admitted at least one case of SARS were included. Paediatric wards were excluded, as the characteristics of SARS in children were quite different from those of adults. Designated wards for treating known SARS patients were also excluded, because of possible multiple contacts with multiple-source cases.

### *Data collection*

Data related to environmental/administrative factors (including physical factors, procedural/situational factors and administrative factors during the 10 days immediately after admission of the index case [for case wards] or the first new case [for control wards and case wards without an identifiable index case]) and host factors (including symptoms, severity/dependency, treatment/intervention and comorbidity of the known index case in a case ward, or the first-admitted case in a control ward) were collected.

Ward managers or nursing officers of the included wards were interviewed in person using a structured questionnaire between September 2004 and November 2005; data were verified using staff rosters. Distances between beds were measured with a measuring tape. Medical records of all SARS patients in the included wards were reviewed to extract information related to the hosts.

### *Statistical analysis*

All data were double-keyed into a pre-designed database and analysed using the SAS software. Univariate analysis was first conducted for each risk factor. Risk factors with a P value of <0.15 were included in a multiple logistic regression analysis using the stepwise approach. This analysis was done separately for environmental/administrative factors and host factors because of the smaller usable numbers of cases and controls related to the host (resulting from unidentified index patients in some case wards or missing data). The odds ratio (OR) and the 95% confidence interval (CI) of various risk factors for the nosocomial outbreak or SSE in a ward were then estimated.

Subgroup analyses by geographic location (Guangzhou and Hong Kong) were also carried out to examine the consistency of risk factors between the two cities. All risk factors selected into any of the separate multivariate models (P<0.15) for environmental/administrative factors and host factors were then included in a combined model using the stepwise approach. As the number of case wards was small and the number of risk factors examined large, some individual risk factors were grouped into composite variables by counting/scoring (the number of positive responses in the group), re-coding (any positive response in the group coded as positive for the composite variable), or ranking according to hierarchy for the statistical analyses. Composite variables by counting or ranking were re-scaled from 0 to 1 in order to equalise their weights in the logistic models. A relatively large alpha error of 0.15 was adopted in the logistic regression analyses in order not to miss potentially important risk factors, as the number of cases included was small. The 95% CI of the OR was used for assessing the statistical significance at the level of P=0.05.

## Results

In Guangzhou, 87 wards in 21 hospitals were included. In Hong Kong, 40 wards in five hospitals were enrolled. Two paediatric wards were excluded. We failed to obtain relevant information in only one ward in Guangzhou and two wards in Hong Kong.

Of the 86 wards in Guangzhou, 35 (41%) were classified as case wards, 26 (74%) of which were identified with an index patient. Of the 38 wards in Hong Kong, 13 (34%) were classified as case wards, five (39%) of which were identified with an index patient. The male-to-female ratio was 1.4:1 among index patients and 1.1:1 among first-admitted patients in control wards. The index patients in the case wards were slightly older (mean age, 51 vs 49 years) and had a longer lag time from symptom onset to hospital admission (8 vs 6 days) than the first-admitted patients in the control wards.

In the univariate analysis, environmental/administrative factors that significantly associated with an SSE included the minimum distance between beds being ≤1 m, the lack of washing/changing facilities for staff, exhaust fan never used, the use of a high flow rate $O_2$ mask, performance of resuscitation, staff working with symptoms, and high workload (with a patient/health care workers ratio of >2). Contamination events and infection-control training were not significant factors (P=0.05-0.15). Significant host factors included pulmonary congestion, resorting to oxygen therapy, higher severity of disease, the use of nebuliser, and the use of bi-level positive airway pressure ventilation (BIPAP). Respiratory symptoms (cough and phlegm), systemic symptoms (myalgia, chills, rigor, malaise, headache and dizziness) and dependency (for activities of daily living and behaviour changes) were not significant factors (P=0.05-0.15).

In the analysis combining data from Guangzhou and Hong Kong, three factors were significant: the minimum distance between beds being ≤1 m (OR=3.36), the lack of washing/changing facilities for staff (OR=0.21), and staff working with symptoms (OR=5.50). Performance of resuscitation was not a significant factor (P=0.10). The minimum distance between beds being ≤1 m was the only factor present in both the Guangzhou and Hong Kong models, though for the latter, it was only of borderline significance (P=0.07).

In the multiple logistic regression analysis for host factors, the use of oxygen therapy and systemic symptoms were significant in the Guangzhou model but not in the Hong Kong model. In the analysis for combined data, only resorting to oxygen therapy was significant (OR=3.59). The use of BIPAP had a P value of 0.06.

Four environmental/administrative factors and two host factors resulted from the final model combining data from Guangzhou and Hong Kong were significant: the minimum distance between beds being ≤1 m (OR=6.94, 95% CI=1.68-28.75), the lack of washing/changing facilities for staff (OR=0.12, 95% CI=0.02-0.97), performance of resuscitation (OR=3.81, 95% CI=1.04-13.87), staff working with symptoms (OR=10.55, 95% CI=2.28-48.87), resorting to oxygen therapy (OR=4.30, 95% CI=1.00-18.43), and the use of BIPAP (OR=11.82, 95% CI=1.97-70.80). Two environmental/administrative factors emerged consistently in the three models: the minimum distance between beds being ≤1 m and staff working with symptoms. Two environmental factors (the lack of washing/changing facilities for staff and performance of resuscitation) did not emerge in the separate models for Guangzhou and Hong Kong, but were significant in the overall model. Exhaust fan never used and systemic symptoms emerged only in the model for Guangzhou (P=0.05-0.15), but not Hong Kong or the overall model.

Sensitivity analysis was conducted by varying the critical number for defining an SSE. With a cut-off value of four cases of nosocomial spread of SARS in a single ward, five factors emerged in the final combined model, including three significant factors in the model with a cut-off value of three cases (minimum distance between beds being ≤1 m, staff working with symptoms, and resorting to oxygen therapy). Systemic symptoms in the host became a significant risk factor and the use of a high flow rate $O_2$ mask in the ward was included in the model (P=0.12). Using a cut-off value of five cases, five significant factors were present in the final combined model: minimum distance between beds being ≤1 m, staff working with symptoms, resorting to oxygen therapy, systemic symptoms, and the use of a high flow rate $O_2$ mask in the ward.

## Discussion

We analysed risk factors associated with nosocomial outbreak of SARS in a systematic manner, using an analytic epidemiological design. Significant environmental risk factors associated with the occurrence of SSE (clustering of three or more cases) included minimum distance between beds being ≤1 m and performance of resuscitation. The use of BIPAP and oxygen therapy were significant risk factors related to the host. Administratively, allowing staff with symptoms to work also increased the risk. Providing adequate washing/changing facilities for staff was protective. Sensitivity testing by applying more stringent cut-off points (four or five clustered cases) suggested that our results were quite robust, with three significant risk factors being identified consistently: minimum distance between beds being ≤1 m, staff working with symptoms, and host resorting to oxygen therapy.

Environmental and administrative factors were important in the prevention of nosocomial outbreaks of SARS. These factors have also been identified as risks for nosocomial spread of other respiratory infectious diseases and they should be rectifiable. Inadequate bed spacing and overcrowding in hospital wards increases the risk of nosocomial infection outbreaks.[6-9] Unfortunately, it is a usual practice to increase the number of hospital beds to meet with the increasing demand, especially during an epidemic. This practice is against the original design of the hospital ward and infection control policy. When the distance between beds is reduced, droplet can spread from one patient to the adjacent patients and ventilation (natural or mechanical) can also be jeopardised. A place for medical treatment and care then becomes a hazardous environment, both for the patients and staff.

Staff working with symptoms could spread SARS in hospital wards and this risk factor is consistently found in all three models in the current analysis. The SARS coronavirus load in patients is highest in the first week of the infection and the patient is most contagious when febrile.[10] Therefore, staff working with symptoms might account for some nosocomial outbreaks where no index patients could be identified.

Provision of washing/changing facilities in hospital ward for staff helped to reduce the risk of nosocomial outbreak. This also suggested that health care workers could act as passive carrier of the SARS coronavirus leading to nosocomial transmission of the infection.

The use of oxygen and BIPAP in patients with infectious respiratory diseases has been a subject for debate since the SARS outbreak. The high flow rate of oxygen/air and/or the positive pressure resulting from such treatment procedures might accentuate the spread of potentially infectious exhaled/expelled air from such patients.[11] Exhaled air from a mask can travel to 0.4 m on each side of the patient.[12] In the present study, the use of oxygen therapy and BIPAP both imposed a significant risk for nosocomial spread of SARS in the model with combined data from Guangzhou and Hong Kong with a cut-off value of three cases and the use of oxygen therapy also significantly increased the risk of nosocomial outbreaks in models with higher cut-off values. We did not have enough detail about the oxygen therapy modalities to the index cases to allow a more refined analysis regarding the types of mask/cannula and the flow rate of oxygen supply. Proper capturing (enclosure/containment/local exhaust) and filtering (high efficiency particulate air filter) of exhaled/expelled air should be implemented if oxygen therapy and BIPAP must be used on clinical grounds. The mechanical manoeuvres associated with resuscitation can potentially generate large amounts of aerosols that are infectious, especially during intubation of the airway and manual bagging to support ventilation of the patient. 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.[13]

Higher occurrence of systemic symptoms in the index or first case emerged as a significant risk factor when SSE was defined by clusters of 4+ or 5+ cases. It is not known if this could be related to a higher viral load. Higher viral loads had been reported to be associated with oxygen desaturation, diarrhoea, hepatic dysfunction, mechanical ventilation and death. However, clear relationships with systemic symptoms have not been reported.

Although the participation rate of this study was very high (97.6%, 124/127 of all eligible wards), the study was confined to two centres in southern China and the applicability to other countries with different hospital practices was not known. Nonetheless, our study provided evidence on risk factors for SSE in the hospital setting. The interviews were carried out more than 1 year after the outbreak and recall inaccuracies might exist. Site inspections and physical measurements were performed on various environmental risk factors and documents and staff roosters reviewed. Information bias should have been substantially reduced. Nonetheless, all host factors were extracted from original medical records and may be objective. Another intrinsic weakness was the lack of statistical power due to the small number of case wards, especially in subgroup analysis for Hong Kong. Hence, the contribution of certain risk factors (such as type of ventilation in ward, lack of appropriate personal protective equipment and infection-control training) could not be ruled out entirely. A larger international collaboration may help solve this problem. The consistent results in different subgroup analyses in Hong Kong and Guangzhou provide indirect support that our results are in general valid. Environmental/administrative factors were more important than host factors. Other than the presence of systemic symptoms (in analyses with more restrictive definitions for SSE), the two host factors identified (ie the use of oxygen therapy and BIPAP) pertained more to environmental contamination than patient characteristics. In other words, this study managed to characterise the super-spreading environment more than the so-called super-spreaders.

## Conclusions

With the current threat of avian influenza and other respiratory infections such as tuberculosis, hospital wards have to be re-designed and the daily operation reviewed to minimise environmental factors associated with nosocomial infections. Adequate spacing between beds and provision of washing/changing facilities for staff are important. Staff with symptoms of respiratory infections should refrain from working in the wards. Adequate protective devices should be provided. More work should be done on the safe use of oxygen therapy and/or ventilatory support in patients with respiratory infections.

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Yu IT, Xie ZH, Tsoi KK, et al. Why did outbreaks of severe acute respiratory syndrome occur in some hospital wards but not others? Clin Infect Dis 2007;44:1017-25.

## References

1. Centers for Disease Control and Prevention. CDC update: outbreak of severe acute respiratory syndrome – worldwide, 2003. MMWR 2003;52:241-8.
2. World Health Organization: Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003 (revised 26 September 2003). Available at: http://www.who.int/csr/sars/country/table2003_09_23/en/. Accessed 22 June 2006.
3. Yu ITS, Li Y, Wong TW, et al. Evidence of airborne transmission of the Severe Acute Respiratory Syndrome virus. New Engl J Med 2004:350:1731-9.
4. Severe Acute Respiratory Syndrome (SARS) – Multi-Country Outbreak – Update 30: Status of Diagnostic Test, Significance of "Super Spreaders", Situation in China, 15 April, 2003. World Health Organization. Available at: http://www.who.int/csr/don/2003_04_15/en/. Accessed 22 June 2006.
5. Shen Z, Ning F, Zhou W, et al. Superspreading SARS Events, Beijing, 2003. Emerg Infect Dis 2004;10:256-60.
6. Cars O. Colonisation and infection with resistant gram-positive cocci.

Epidemiology and risk factors. Drugs 1997;54:4-10.
7. Harbarth S, Sudre P, Dharan S, Cadenas M, Pittet D. Outbreak of *Enterobacter cloacae* related to understaffing, overcrowding, and poor hygiene practices. Infect Cont Hosp Ep 1999;20:598-603.
8. Andersen BM, Lindemann R, Bergh K, et al. Spread of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive unit associated with understaffing, overcrowding and mixing of patients. J Hosp Infect 2002;50:18-24.
9. Aujard Y, Fauroux B. Risk factors for severe respiratory syncytial virus infection in infants. Resp Med. 2002;96(S2):S9-14.
10. Peiris JS, Lai ST, Poon LL, et al. Coronavirus as a possible cause of severe acute respiratory syndrome. Lancet. 2003;361:1319-25.
11. Somogyi R, Vesely AE, Azami T, et al. Dispersal of respiratory droplets with open vs closed oxygen delivery masks: implications for the transmission of severe acute respiratory syndrome. Chest. 2004;125:1155-7.
12. Hui DS, Ip M, Tang JW, et al. Airflows around oxygen masks: A potential source of infection. Chest. 2006;130:822-6.
13. Thorne CD, Khozin S, McDiarmid MA. Using the hierarchy of control technologies to improve healthcare facility infection control: lessons from severe acute respiratory syndrome. J Occup Environ Med. 2004;46:613-22.