

Online Supplement

Appendix A. Compiling Taiwan SARS Outbreak Chronology

We compiled our Taiwan SARS outbreak chronology from three data sources: a SARS event list published by the Taiwanese government (<http://www7.www.gov.tw/todaytw/2005/TWtaiwan/ch08/2-8-10-0.html>; accessed on December 12, 2008), a SARS news archive released by a Taiwanese newspaper (<http://www.libertytimes.com.tw/2003/new/jul/17/Rnews-sars.htm>; accessed on December 12, 2008), and 30 journal articles relevant to the outbreak. We first relied on the government-released event list and the news archive to retrieve critical events of the outbreak and their corresponding dates. Those events were used to create a preliminary chronology. We then reviewed the 30 journal articles for the details of the events or events that were not mentioned in the first two data sources. An abbreviated version of the chronology is provided in Table A1.

Table A1. Abbreviated Version of the Taiwan SARS Outbreak Chronology

Date	Event	Date	Event
2/25	Businessman A had onset of fever and dry cough.	4/22	Hospital A reported a hospital outbreak.
3/8~ 3/13	Businessman A was hospitalized in Hospital C with general precautions.	4/23~ 4/26	A 73 year-old patient was admitted to Hospital C without revealing his prior visits at Hospital A.
3/12	WHO issued a global SARS alert.	4/24	Hospital A was segregated.
3/14	Businessman A's wife developed pneumonia and both patients were identified as SARS cases.	4/26	Healthcare workers in Hospital A held a protest for their job safety right.
3/15	WHO published a case definition for SARS surveillance.	4/27	Hospital C discovered the 73-old patient's association with Hospital A.
3/16	The public health agency in Taiwan developed a SARS control framework for response.	4/27	Taiwan government announced a compensation plan for healthcare workers.
3/21	A clinician who took care of Businessman A's wife had onset of symptoms and subsequently was reported as a SARS case.	4/29	Hospital B was segregated; A city adjacent to Taipei protested against transferring SARS patients from Hospital A to a designated facility in the city.
3/26	Four engineers of a company who had just returned from a business trip to China were detected as SARS cases in Hospital C.	5/8	The infection source of a patient in Hospital C was traced back to her prior visit at the hospital ER.
3/27	Contact tracing and home quarantine measures were implemented.	5/9	SARS Control Committee admitted difficulty processing and clarifying patients' contact history.
4/9	A 47 year-old female patient went to Hospital A ER and later was transferred to Hospital S.	5/12	Hospital C reported a hospital outbreak and suspended ER operation.
4/9~ 4/16	The public health agency in Taiwan excluded the female patient as a SARS case.	5/14~ 5/19	Hospital D and E reported outbreaks; WHO reported that Taiwan had the fastest growing outbreak.
4/12~ 4/15	A laundry worker in Hospital A has onset of symptoms and remained on duty.	5/20	More than 100 healthcare workers from Hospital A and D resigned for workplace safety reasons.
4/17	The 47 year-old female patient was confirmed positive for SARS-CoV.	5/22	Pharmacies were asked to stop selling antipyretics.
4/18	The laundry worker developed lung infiltrate and was isolated in a negative pressure room in Hospital A.	5/29~ 6/1	Taiwan launched fever clinics, fever hotline, and temperature monitoring campaign.
4/20	Taiwan government proclaimed that SARS was under control and held a SARS conference.	7/5	WHO removed Taiwan from the list of SARS affected areas.

Appendix B. Coding SARS Contact Investigation Data for Personal and Geographical Relationship

The contact investigation data used in this study were collected by public health workers in Taiwan during the timeframe of the SARS outbreak and stored in a spreadsheet. Each patient is listed as a row and described by a number of attribute columns, including name, symptom onset date, and reporting hospital. An interview note is also included to document additional information gathered during the face-to-face patient interview. Each patient was asked to recall significant interactions with people or places that might have caused the infection and to list the names of medical facilities that he/she had been since the onset of symptoms. The narrative was then compiled into a paragraph of free text. An example of the dataset is given in Table B1.

Table B1. Example of SARS Contact Investigation Data

ID	Name	Symptom Onset Date	Diagnosis Date	Reporting Hospital	Type	Interview Note
092001	Patient A	02/25/2003	03/10/2003	Hospital C	Patient	The patient went to Guangdong China for business between 2/8 and 2/21. He came back to Taiwan and had fever on 2/25. He developed a dry cough 2 days later and went to Clinic A for medical care. He went to Clinic B and was transferred to Hospital C. His chest X-ray showed pulmonary edema. He was treated in an intensive-care unit and his symptom improved.
092002	Patient B	03/07/2003	03/14/2003	Hospital C	Patient	The patient's husband (092001) had been to Guangdong China for business. They lived together and interacted daily. She developed symptoms on 3/7. She was admitted to Hospital C and is under treatment. She was confirmed positive for SARS CoV.
092011	Patient C	03/21/2003	03/27/2003	Hospital C	Healthcare worker	The patient is a physician in Hospital C who took care of Patient B. He performed a chest ultrasound on her on 3/14. He also stayed with Patient B for an hour on 3/17 during intubation procedure. He became ill on 03/21.

In order to retrieve relations (or contacts) between patients or between a patient and a place from the interview note, we coded it as follows. First, if the interview note of a patient mentions another SARS patient (e.g., the patient's husband (092001) had been to Guangdong China for business), we insert an entry denoting their relationship into a

personal mapping table as illustrated in Table B2. If a calendar date associated with their interaction is available, we insert the date.

Table B2. Example of Personal Mapping Table

Patient 1	Patient 2	Relationship	Contact Date	Refined Category
092002	092001	Wife-Husband		Family member
092011	092002	Physician-Patient	03/14/2001	Close Contact
092011	092002	Physician-Patient	03/17/2001	Close Contact

Second, if the interview note of a patient mentions a place or hospital that he/she had visited (e.g., the patient went to Guangdong China for business between 2/8 and 2/21), we insert an entry denoting this connection into a geographical mapping table as illustrated in Table B3. If a calendar date associated with the visit is available, we insert the date.

Third, if a patient is indicated as a healthcare worker in the dataset, we insert an entry showing his/her hospital into the geographical mapping table. Since the exact date that might have caused a hospital infection for a healthcare worker is not available, we use the patient's symptom onset date for approximation.

Table B3. Example of Geographical Mapping Table

Patient	Place	Connection	Start Date	End Date	Refined Category
092001	Guangdong, China	Business Trip	02/08/2003	02/21/2003	Overseas Travel
092001	Clinic A	Hospital Admission	02/27/2003	02/27/2003	Hospital Admission
092001	Clinic B	Hospital Admission	03/10/2003	03/10/2003	Hospital Admission
092001	Hospital C	Hospital Admission	03/10/2003		Hospital Admission
092002	Hospital C	Hospital Admission	03/14/2003		Hospital Admission
092011	Hospital C	Working at Hospital	03/21/2003	03/21/2003	Hospital Workplace
092011	Hospital C	Hospital Admission	03/27/2003		Hospital Admission

After all the interview notes were coded into personal and geographical mapping tables, we reviewed the entries and created broader categories as shown in Table 2 to group similar relations or connections. For example, we consolidated the relations of wife-husband, son-parent, and niece-aunt into a family member category. Furthermore, we removed entries of those places that had been visited by only one patient from the geographical mapping table because those places were not considered important potential disease pathways. For the date of a contact or visit that is unavailable in the interview note, we approximate it with patients' symptom onset date.

Appendix C. Assessing SARS Dissemination Patterns with Vector Autoregression Models

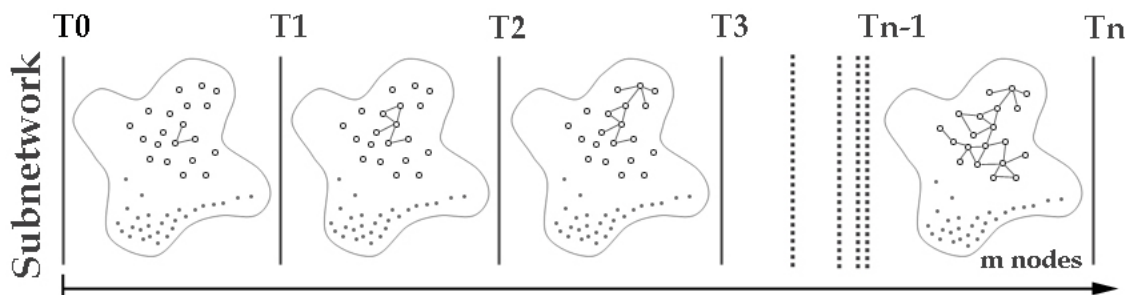
To quantitatively explore how the three important social contexts of infection (i.e., overseas travel, personal contact, and hospital infection) interacted and fostered SARS dissemination, we derived a procedure from social network analysis that incorporates vector autoregression (VAR) models. The procedure has four main steps: constructing contact subnetworks, creating subnetwork movies, extracting the magnitude of changes in linkage, and specifying VAR models.

Table C1. Categorization of Contact Records Using Different Contexts of Infection

Contact Category	Specific Types of Contact
Overseas Travel	Overseas Travel
Personal Contact	Family Member Roommate Colleague Close Contact
Hospital Infection	Hospital Visit Hospital Admission Hospital Workplace

Constructing Contact Subnetworks. We created three distinct contact subnetworks for these contexts in order to differentiate their respective effects on SARS dissemination. Each subnetwork was constructed with contacts pertaining to the corresponding context as listed in Table C1. For example, the hospital infection subnetwork was built with the contacts pertaining to hospital visit, admission, and workplace. Each subnetwork has the same 479 patient nodes for representing the patients in our dataset. The overseas travel and hospital infection subnetworks have additional geographical nodes to establish person-to-location relationships as indicated in the coded contacts.

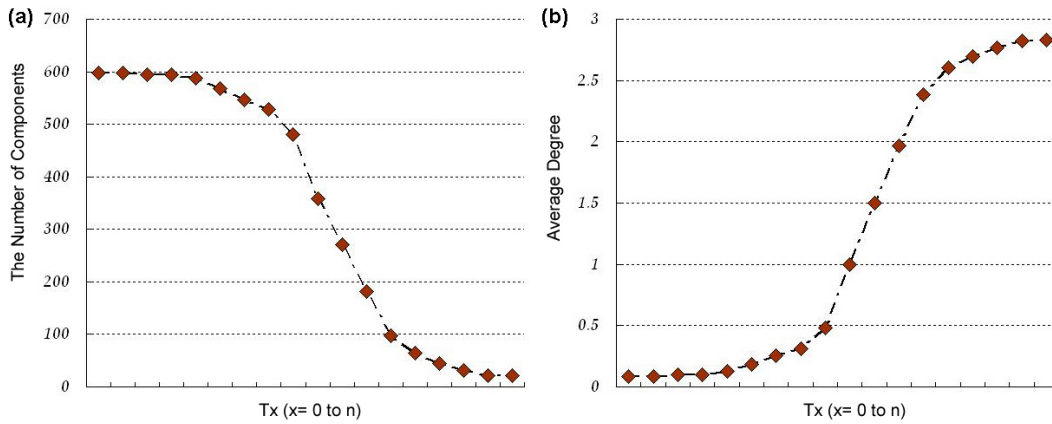
Figure C1. Segmentation of a Subnetwork



Creating Subnetwork Movies. We segmented each subnetwork with a constant interval, such as a day or a week, as shown in Figure C1. The segment of a subnetwork at T_x (where $x= 1$ to n) has the same number of nodes as the subnetwork (m nodes) but includes only the linkages that appeared between T_0 and T_x , according to the timestamps of the coded contacts. This results in a subnetwork movie with overlapping windows showing how linkage is expanding among nodes over time (Moody et al. 2005).

Extracting the Magnitude of Changes in Linkage. We used two macro network measures – the number of components and the average degree of nodes – to quantify patient linkage in each subnetwork segment. The number of components denotes the number of maximal-connected subgraphs in a social network, conceptually depicting the degree to which individuals are grouped (Scott 2000, Wasserman and Faust 1994). As the linkage expands in a subnetwork movie, the number of components decreases and exhibits a downward linkage curve as shown in Figure C2 (a). The degree of a node indicates how many ties the node has and signifies the activity or popularity of the individual it represents. Hence, the average degree of nodes reflects the overall activity or connectivity of a social network (Wasserman and Faust 1994). Since the size of subnetwork segments remains constant, as the linkage expands, the average degree of nodes increases and results in an upward linkage curve as shown in Figure C2 (b).

Figure C2. Linage Curves Extracted with the Number of Components and the Average Degree of Nodes

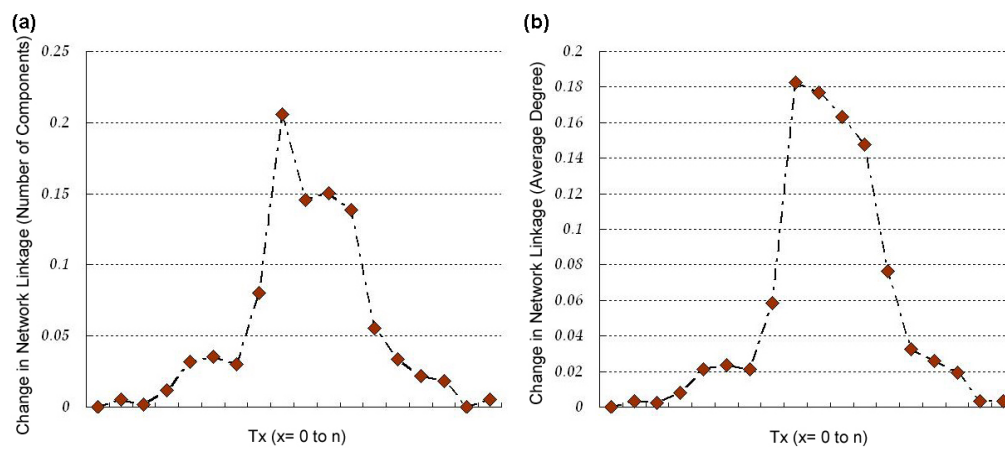


We then calculated the magnitude of changes in a linkage curve with the equation C1:

$$\Delta P_x = \frac{|P_x - P_{x-1}|}{|P_n - P_0|}, \quad (C1)$$

where $x = 2$ to n ; P_x refers to the subnetwork linkage at time T_x measured by either the number of components or the average degree of nodes; P_{x-1} is the subnetwork linkage at the interval before T_x (i.e., T_{x-1}); and the absolute value of $(P_n - P_0)$ denotes the overall change in the subnetwork linkage between time T_0 and T_n . This equation shows the relative change in the linkage between T_x and T_{x-1} , with respect to the total change observed over the entire period. The resulting ratio depicts the slope of a linkage curve in a given interval. Figure C3 shows the magnitude of changes in patient linkage converted from Figure C2.

Figure C3. Magnitude of Changes in Patient linkage by the Number of Components and the Average Degree



With these two network measures, we extracted two sets of time-series data from the subnetwork movies. To test which set of data better indicates the severity of SARS dissemination, we used two multivariate regression models as shown in Table C2. The daily number of new SARS patients was the dependent variable in both models. According to the results summarized in Table C3, the model using the average degree attains an adjusted R^2 value of 0.85, significantly higher than that derived by the model using the number of components.

To assess whether the use of time-series data anchored solely in the average degree is appropriate for describing the outbreak, we performed a joint F-test to see if the coefficients of the component variables are zero for the null hypothesis in an unrestricted model. Our results failed to reject the null hypothesis, with an F-value of 0.2185 and an associated p -value of 0.88. On the basis of our regression models and F-test results, we chose to analyze the time-series data using the average degree of nodes.

Table C2. Multivariate Regressions to Test the Fit of Time-Series Data

Multivariate Regression Model	Dependent Variable	Latent Variable	Latent Variable Definition
Model 1 (Avg. Degree)	N _{Daily}	Deg _{FT}	Change in linkage in the overseas travel subnetwork by the average degree
		Deg _{PC}	Change in linkage in the personal contact subnetwork by the average degree
		Deg _{HP}	Change in linkage in the hospital infection subnetwork by the average degree
Model 2 (Components)	N _{Daily}	Com _{FT}	Change in linkage in the overseas travel subnetwork by the number of components
		Com _{PC}	Change in linkage in the personal contact subnetwork by the number of components
		Com _{HP}	Change in linkage in the hospital infection subnetwork by the number of components

Table C3. Key Fitness Test Results of Two Multivariate Regression Models

Regression Model	Adjusted R ²	Independent Variable	Coefficient	p-Value
Model 1 (Using the average degree)	0.85	Deg _{FT}	-0.0488	0.15
		Deg _{PC}	0.0082	0.72
		Deg _{HP}	1.0952	0.00***
		Constant	-0.0002	0.74
Model 2 (Using the number of components)	0.78	Com _{FT}	0.2269	0.25
		Com _{PC}	-0.1075	0.70
		Com _{HP}	0.9714	0.00***
		Constant	0.0001	0.83

*** $p < 0.01$; ** $p < 0.05$; * $p < 0.10$.

Specifying VAR Models. VAR models were chosen as our time-series models for two reasons. First, VAR models support multiple variables so that testing the effects of these contexts of infection on one another is feasible. Second, VAR models are nonstructural and enable the exploration of dynamic structures embedded in the data without theories (Pindyck and Rubinfeld 1998). To specify a VAR model, we need to select the endogenous variables that are most likely to interact with a system and search for the largest lag to capture the influences of these variables. In this study, the changes in patient linkage under the three contexts (i.e., Deg_{FT}, Deg_{PC}, and Deg_{HP}) are our variables and the Akaike information criterion (AIC) were used for lag selection. We assessed the number of lags in increments until AIC reached a minimum value (Pindyck and Rubinfeld 1998).

Choosing the largest number of lags is a non-trivial task. Theoretically, the number of lags in our case should range from 1 to 7, as the SARS incubation period had a median value between 4 and 7. But, we only have 45 and 83

data points for the importation and hospital outbreak phases respectively. To maintain appropriate degrees of freedom, we limited the maximum number of lags to 4. It is important to note that our findings may be constrained by our choice of the largest lag number. On the basis of the analysis results (Table C4), we selected 1 and 3 as the numbers of lags for the importation and hospital outbreak phases respectively.

Table C4. Selection of the Numbers of Lags for the Respective Phases Using AIC

Number of Lags	Importation Phase	Hospital Outbreak Phase
1	-21.3967	-19.4575
2	-21.2907	-19.6223
3	-21.3757	-19.6831
4	-21.1921	-19.5810

References

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- Pindyck, R. S., D. L. Rubinfeld. 1998. *Econometric Models and Economic Forecasts*. Irwin/McGraw-Hill, New York.
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Appendix D. VAR Results for the Hospital Infection Subnetwork

To investigate how the central coupling mechanisms broke the vicious circle between personal contact and hospital infection found in the hospital outbreak phase, we constructed another VAR model by assuming that hospital visit, admission, and workplace constitute distinct self-contained subsystems. We set the number of lags to 4, based on the AIC as shown in Table D1 and report the significant coefficients in Table D2. Hospital admission (Deg_{HP_Adm}) was influenced by the lags of hospital visit (Deg_{HP_Visit}), hospital workplace (Deg_{HP_HCW}), and itself. This result supports the speculation that many patients were infected in hospitals during their visits not directly related to SARS. The VAR results show healthcare workers' infections can be partially attributed to the variation of the hospital visit at lag 1 ($Deg_{HP_Visit\ L1}$). That is, when hospital visits became an important context of infection, the likelihood that healthcare workers became infected at work increased. Surprisingly, hospital admissions (Deg_{HP_Adm}) exhibited a negative influence on hospital visit and workplace at lag 1, a finding contrary to the common intuition that sudden increases in the admission of SARS patients would exacerbate nosocomial infections. This inverse relationship supports the assertion that unrecognized patients constituted a major cause of SARS outbreaks. When more SARS patients were identified and treated clinically, fewer healthcare workers and hospital visitors were infected in hospitals.

Table D1. Number of Lags for the Hospital Infection Subnetwork

Number of Lags	AIC
1	-18.8405
2	-19.011
3	-19.098
4	-19.1602

Table D2. VAR Results for the Hospital Infection Subnetwork

Dependent Variable	Independent Variable	Coefficient	p-value
Deg _{HP_Admission}	Deg _{HP_Admission} L1	0.2721	0.01***
	Deg _{HP_Admission} L4	0.2225	0.02**
	Deg _{HP_HCW} L2	0.1265	0.01***
	Deg _{HP_HCW} L4	0.1651	0.001***
	Deg _{HP_Visit} L3	0.1778	0.004***
Deg _{HP_HCW}	Deg _{HP_Admission} L1	-0.4893	0.05*
	Deg _{HP_HCW} L1	0.4106	0.000***
	Deg _{HP_HCW} L2	0.2264	0.06*
	Deg _{HP_Visit} L1	0.2729	0.06*
Deg _{HP_Visit}	Deg _{HP_Admission} L1	-0.4497	0.02**
	Deg _{HP_Visit} L1	0.2083	0.07*
	Deg _{HP_Visit} L3	0.4510	0.000***

*** $p < 0.01$, ** $p < 0.05$, * $p < 0.10$; Deg_{HP_Admission}: hospital admission; Deg_{HP_HCW}: hospital workplace; Deg_{HP_Visit}: hospital visit.