Supplemental Information—Data Supporting the Disease Course of SARS and MERS

SARS Disease Course

Some of the best epidemiological data on SARS comes from an article which constructed an integrated database of 1,425 cases of SARS from an outbreak in Hong Kong.[1] Epidemiological, demographic, and clinical information was collected on all cases and used to create gamma distributions for the incubation period, time from disease onset to hospital admission, and time from hospital admission to death or discharge. These distributions are summarized in Table S1 and Figures S1-S4, along with other pertinent information on the disease course of SARS.

Table S1. SARS Disease Course Parameters.

Parameter	Value/Distribution	Notes
Incubation period	Mean = 5.29 d. Variance = 12.33 d.	• Based on 209 probable SARS cases with documented periods of exposure, using a nonparametric method.[2]
	Gamma (mean = 6.37 d.; variance = 16.69 d.)	• Based on 57 SARS cases with documented periods of exposure, fitted to gamma distributions using maximum likelihood estimation methods (see Figure S1).[3]
Contagious period[4]	≥ 5 d after the onset of disease, up until around the third week of disease (~10 d after the resolution of fever)	• ≥ 5 d after the onset of disease. • No reported instance of transmission before the onset of disease. • It is difficult to isolate the virus after the third week of disease, and no transmission has been documented more than 10 d after the resolution of fever.
Time from onset to hospital admission[5]	First time period: gamma (mean = 4.85 d.; variance = 12.19 d.); Second time period: gamma (mean = 3.83 d.; variance = 5.99 d.); Third time period: gamma (mean = 3.67 d.; variance = 10.71 d.)	• Based on 1,425 cases. The authors constructed several distributions which differed based on the week of clinical onset during the studied outbreak (see Figure S2).
Time from hospital admission to death[6]	Gamma (mean = 35.9 d.; variance = 572.9 d.)	• See Figure S3. • Based on 1,425 cases.
Time from hospital admission to discharge[7]	Gamma (mean = 23.5 d.; variance = 62.1 d.)	• See Figure S4. • Based on 1,425 cases.

[1] Donnelly CA *et al* (2003) Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *The Lancet* 361**:** 1761-1766

[2] Cai QC *et al* (2006) Refined estimate of the incubation period of severe acute respiratory syndrome and related influencing factors. *American journal of epidemiology* 163**:** 211-216

[3] Donnelly CA *et al* (2003) Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *The Lancet* 361**:** 1761-1766

[4] Peiris JS *et al* (2003) The severe acute respiratory syndrome. *N Engl J Med* 349**:** 2431-2441

[5] Donnelly CA *et al* (2003) Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *The Lancet* 361**:** 1761-1766

[6] Ibid.

[7] Ibid.

Table S2. SARS Incubation Period Data Found in Literature					
Source	**Number Observed**	**Mean (days)**	**Median (days)**	**Minimum (days)**	**Maximum (days)**
Donnelly et al. 2003[8]	57	6.4	-	-	16.69
Meltzer 2004[9]	17	-	4	1	18
Varia et al. 2003[10]	128	5	4	2	10
Hsu et al.[11]	19	-	4	2	8
Leung et al.[12]	81	4.6	-	-	-
Weighted	-	**5.18**	**4**	-	-

Table S3. SARS Infectious Period Data Found in Literature		
Source	**Number Observed**	**Day of Maximum Shedding**
Isakbeva et al. 2004[13]	7	14
Cheng et al. 2004[14]	1041	12-14
Peiris et al. 2003[15]	19	10

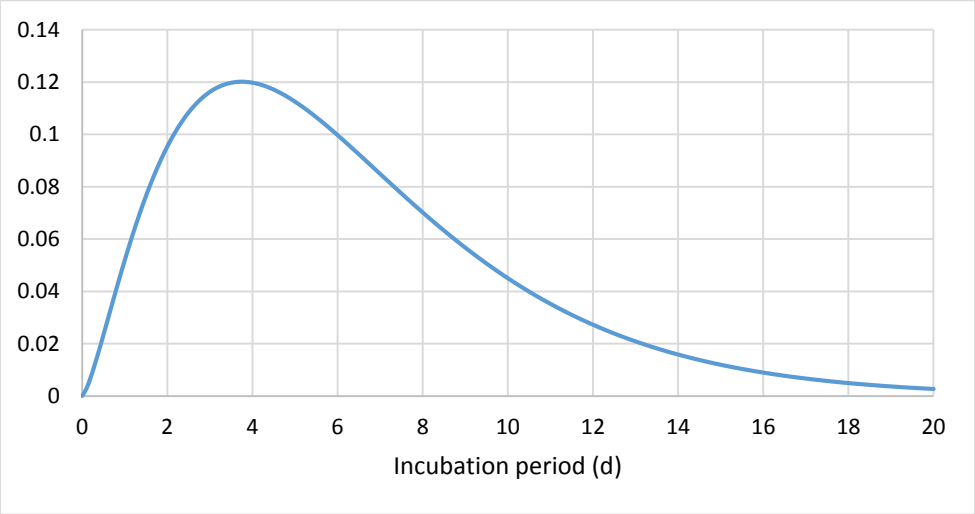

Figure S1. Gamma distribution of SARS incubation period (α = 2.43 and β = 2.62). Alpha and beta calculated with MD Anderson Cancer Center Department of Biostatistics Parameter Solver, using a mean of 6.37 d and a variance of 16.69 d.

[8] Donnelly CA *et al* (2003) Epidemiological determinants of spread of causal agent of severe acute respiratory syndrome in Hong Kong. *Lancet* 361**:** 1761-1766

[9] Meltzer MI (2004) Multiple contact dates and SARS incubation periods. *Emerg Infect Dis* 10**:** 207-209

[10] Varia M *et al* (2003) Investigation of a nosocomial outbreak of severe acute respiratory syndrome (SARS) in Toronto, Canada. *CMAJ* 169**:** 285-292

[11] Hsu LY *et al* (2003) Severe acute respiratory syndrome (SARS) in Singapore: clinical features of index patient and initial contacts. *Emerg Infect Dis* 9**:** 713-717

[12] Leung GM *et al* (2004) The epidemiology of severe acute respiratory syndrome in the 2003 Hong Kong epidemic: an analysis of all 1755 patients. *Ann Intern Med* 141**:** 662-673

[13] Ibid.

[14] Cheng PK *et al* (2004) Viral shedding patterns of coronavirus in patients with probable severe acute respiratory syndrome. *Lancet* 363**:** 1699-1700

[15] Peiris JS *et al* (2003) Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Ibid. 361**:** 1767-1772

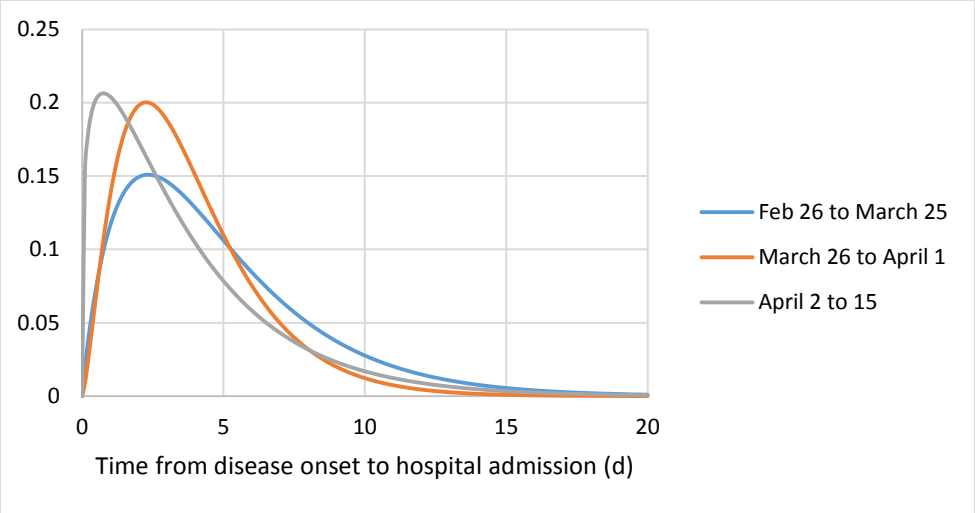

Figure S2. Gamma distributions of SARS time from disease onset to hospital admission.

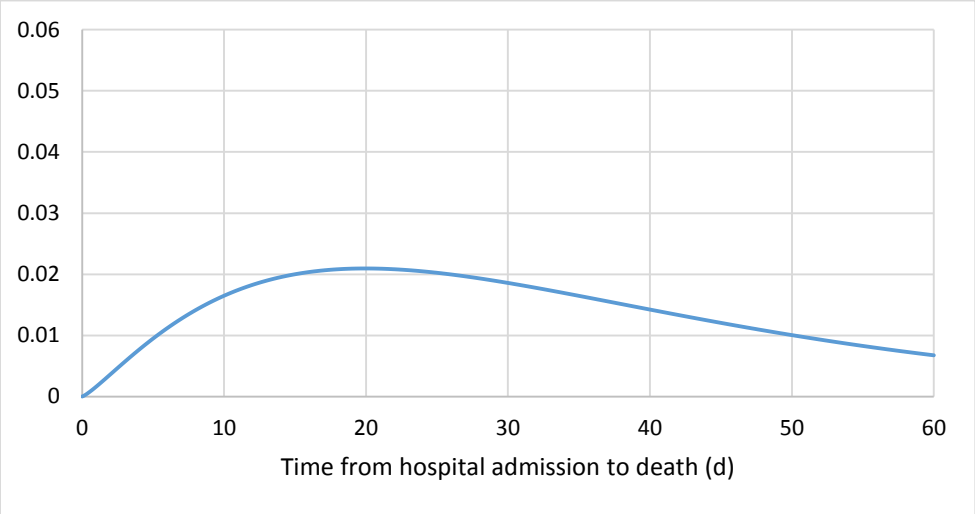

Figure S3. Gamma distribution of SARS time from hospital admission to death ($\alpha = 2.25$ and $\beta = 15.96$). Alpha and beta calculated with MD Anderson Cancer Center Department of Biostatistics Parameter Solver, using a mean of 35.9 d and a variance of 572.9 d.

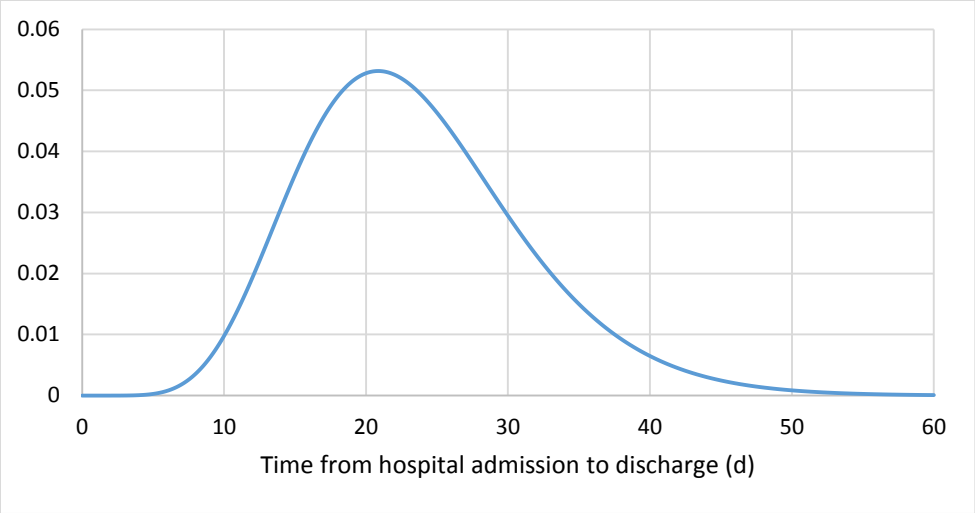

Figure S4. Gamma distribution of SARS time from hospital admission to discharge (α = 8.89 and β = 2.64). Alpha and beta calculated with MD Anderson Cancer Center Department of Biostatistics Parameter Solver, using a mean of 23.5 d and a variance of 62.1 d.

MERS Disease Course

Limited clinical data is available on the MERS disease course. Cauchemez et al. (2014) were able to construct a lognormal distribution of the incubation period with the data from seven cases. Saad et al. (2014) reported clinical data and outcomes of 70 patients with MERS in Saudi Arabia, and calculated statistics for the time from onset to hospital admission, death, and discharge. These results are summarized in Table and Figure S5.

Table S4. MERS Disease Course Parameters.

Parameter	Value/Distribution	Notes
Incubation period	Lognormal (mean = 5.5 d.; variance = 6.25 d.)	• Lognormal distribution based on data from seven cases.[16]
Contagious period		• According to a WHO Risk Assessment, patients are not contagious during the incubation period. The duration of the contagious period is unknown, but patients can shed virus after resolution of the disease.[17]
Time from onset to hospital admission[18]	Median = 5.0 d. (IQR 3.0-8.5)	• Based on data from 70 patients with confirmed MERS at a center in Saudi Arabia, for the patients who acquired MERS from outside the hospital. • The median time from illness onset to diagnosis for all patients was 7 d. (IQR 3.0-13.8).
Time from onset to death[19]	Median = 20.5 (IQR 11.8-28.0)	• Based on data from 70 patients with confirmed MERS at a center in Saudi Arabia. 42 (60%) of patients died, and all except one had severe infections requiring ICU care and mechanical ventilation.

[16] Cauchemez S *et al* (2014) Middle East respiratory syndrome coronavirus: quantification of the extent of the epidemic, surveillance biases, and transmissibility. *The Lancet Infectious Diseases* 14**:** 50-56

[17] World Health Organization (2003) Consensus document on the epidemiology of severe acute respiratory syndrome (SARS).

[18] Saad M *et al* (2014) Clinical aspects and outcomes of 70 patients with Middle East respiratory syndrome coronavirus infection: a single-center experience in Saudi Arabia. *International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases* 29**:** 301-306

[19] Ibid.

Parameter	Value/Distribution	Notes
Time from onset to hospital discharge[20]	Median = 27.0 (IQR 20.0-31.5)	• Based on data from 70 patients with confirmed MERS at a center in Saudi Arabia.

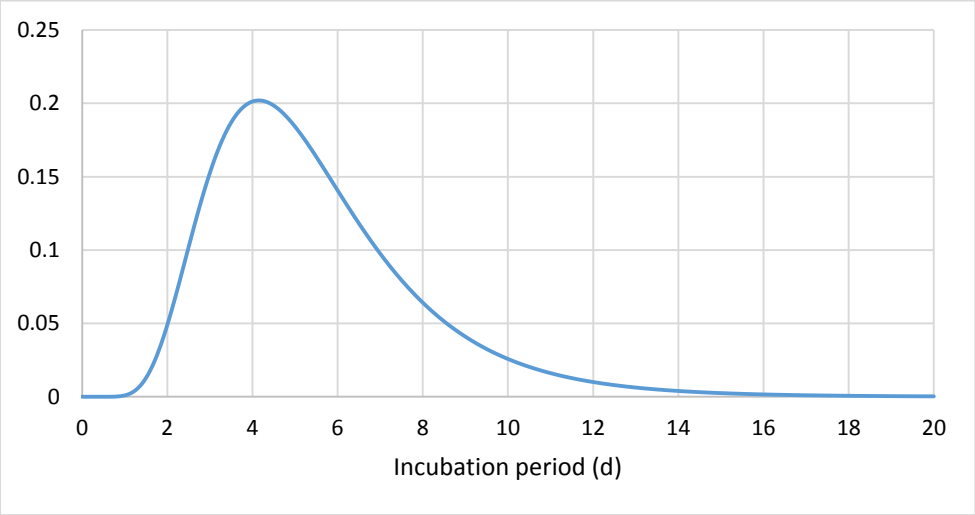

Figure S5. Lognormal distribution of MERS incubation period (μ = 1.61 and σ = 0.43).

Table S5. MERS Incubation Period Data Found in Literature

Source	Number Observed	Median (days)	Minimum (days)	Maximum (days)
Cowling et al. 2015[21]	99	6.3	-	12.1
Assiri et al. 2013[22]	23	5.2	2.2	12.4
Park et al. 2015[23]	37	6	2	15
Weighted	-	**6.07**	-	-

[20] Ibid.
[21] Cowling BJ *et al* (2015) Preliminary epidemiologic assessment of MERS-CoV outbreak in South Korea, May–June 2015. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin* 20**:** 21163
[22] Assiri A *et al* (2013) Hospital outbreak of Middle East respiratory syndrome coronavirus. *N Engl J Med* 369**:** 407-416
[23] Park HY *et al* (2015) Epidemiological investigation of MERS-CoV spread in a single hospital in South Korea, May to June 2015. *Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin* 20**:** 1-6