

The Toronto SARS Outbreak: Implications for Vaccine Development

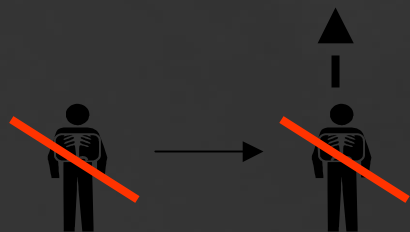
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University of Toronto, Toronto, Canada*

October 30, 2003

WHO Summary Table of SARS (Nov 1, 2002 to Aug 7, 2003)

Country	Total Probable Cases	Number of Death	Case Fatality Rate (%)
Canada	251	41	17
China, HK SAR	1765	300	17
China, Taiwan	665	180	27
Singapore	238	33	14
USA	33	0	0
TOTAL	8422	916	11



Index Case
(Mother)

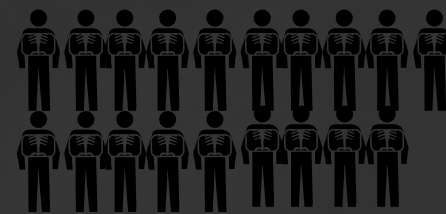
Case A
(Son)

**Family &
MD**



Mr. P

**Mr. P's
wife**

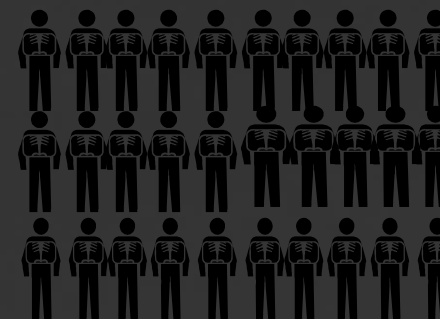
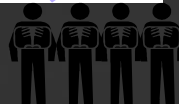


19 persons

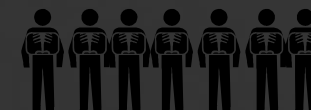
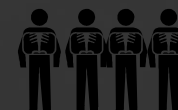


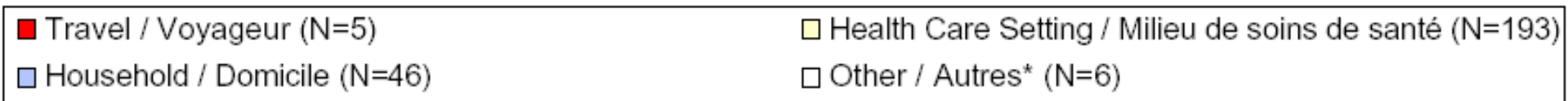
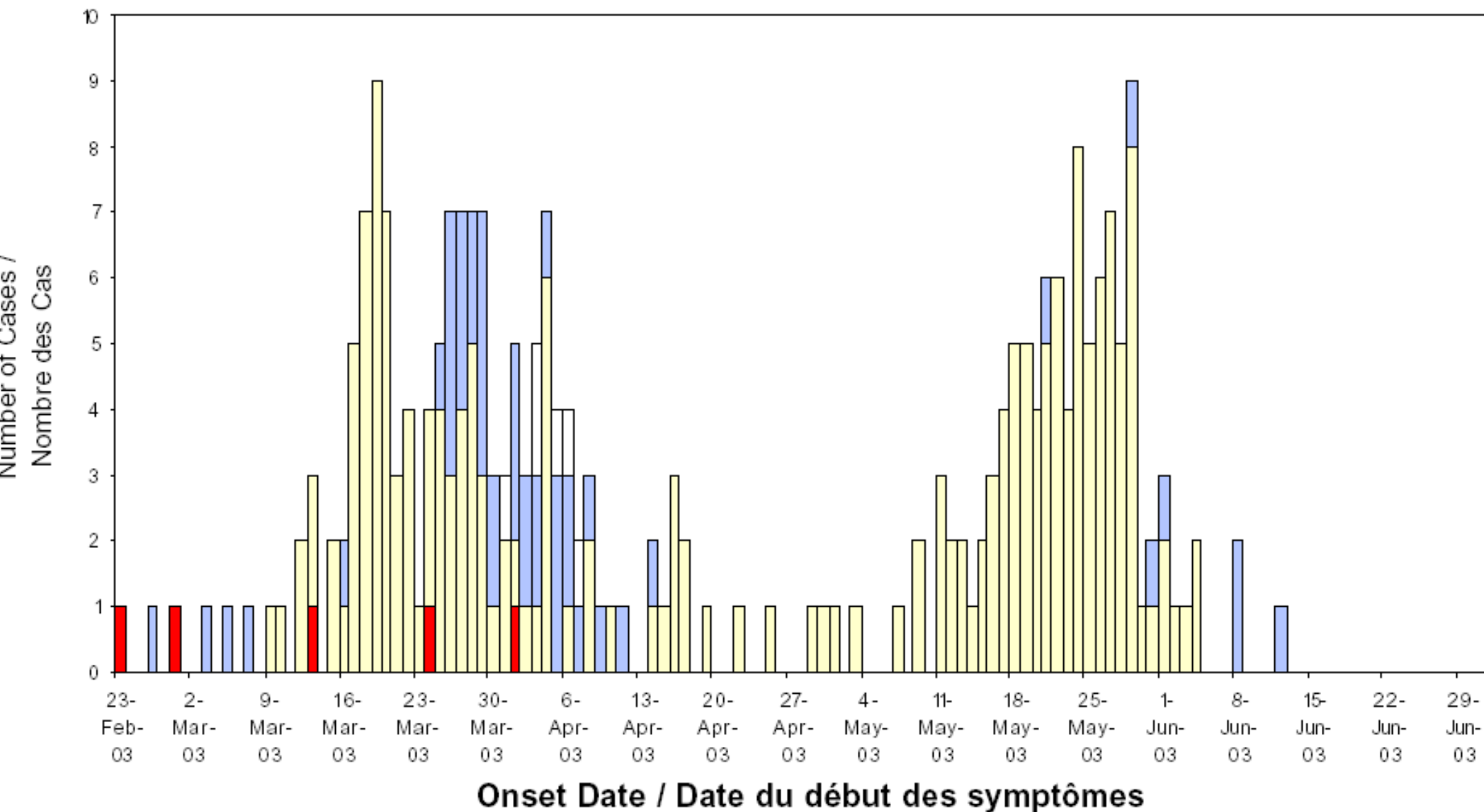
5 persons

Mr. D



Mr. R

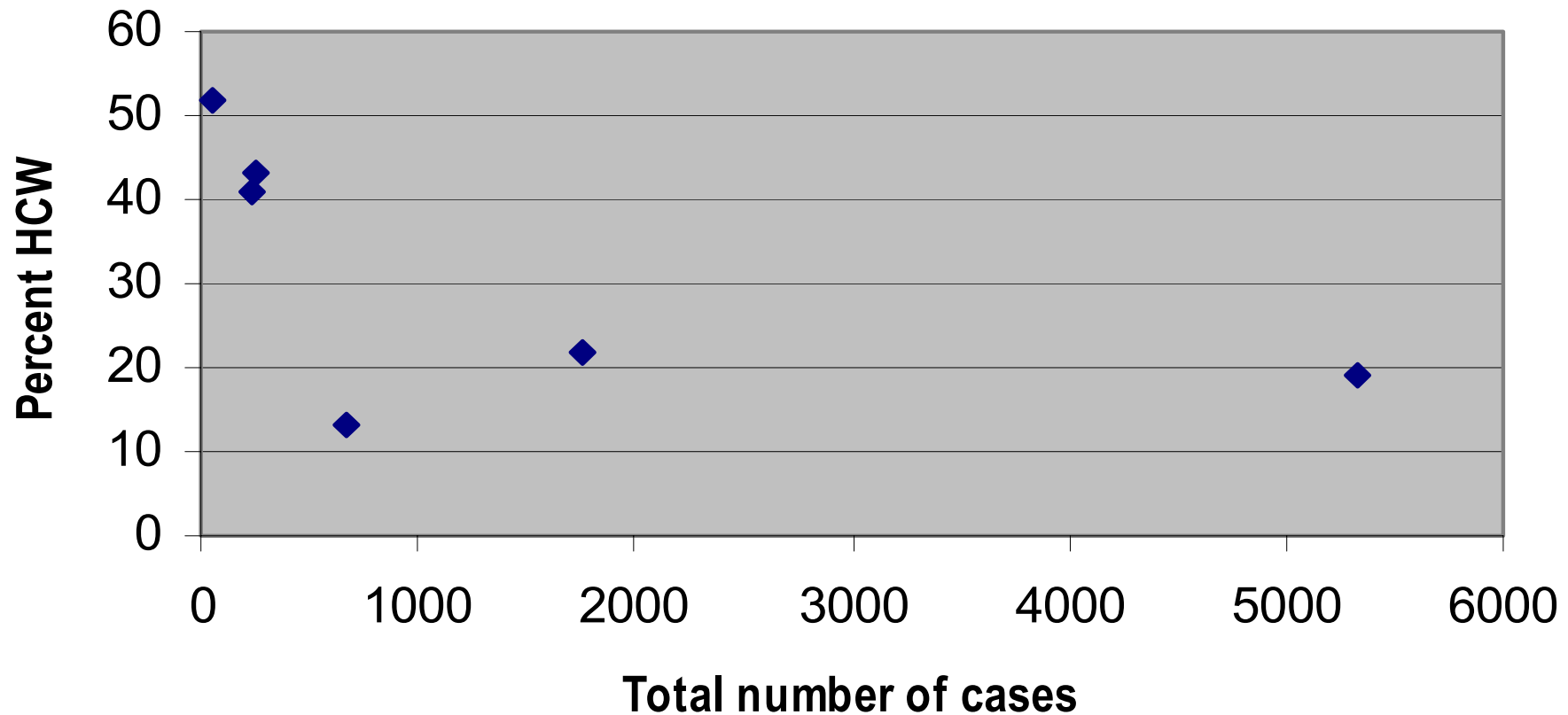




Severe Acute Respiratory Syndrome, Toronto

Exposure	No. (%)	No. (%)
Hospital - worker	91 (33%)	52 (42%)
- patient/visitor	49 (18%)	64 (51%)
Other healthcare (clinic, EMS)	8 (2.9%)	2 (1.6%)
Household contact	76 (28%)	9 (7.2%)
“Community”	16 (5.9%)	-
Travel	12 (4.4%)	-
Under investigation	21 (7.7%)	-

Relationship between size of outbreak, and proportion HCWs

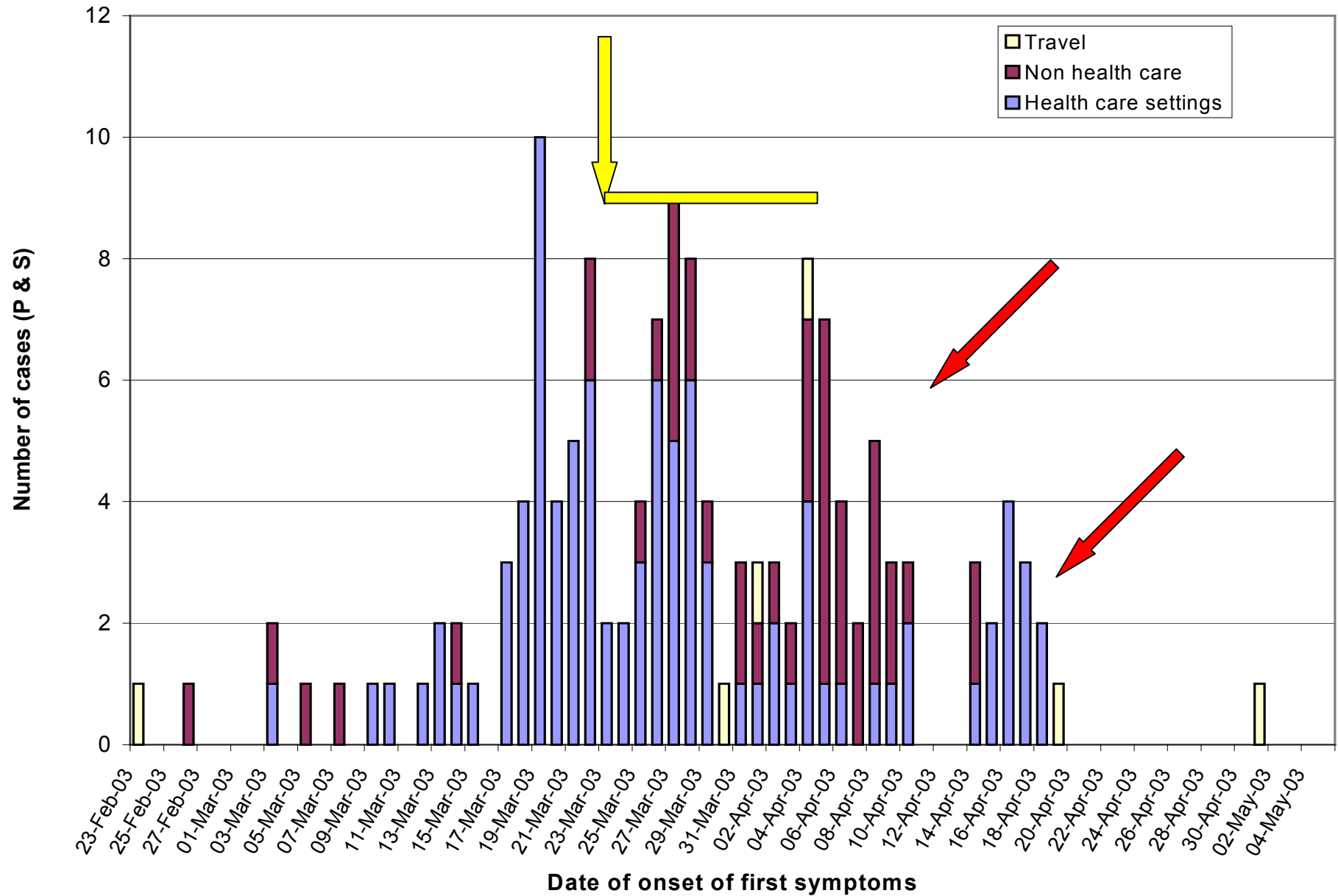


Diagnosis of LRTI (including LRTI due to SARS)

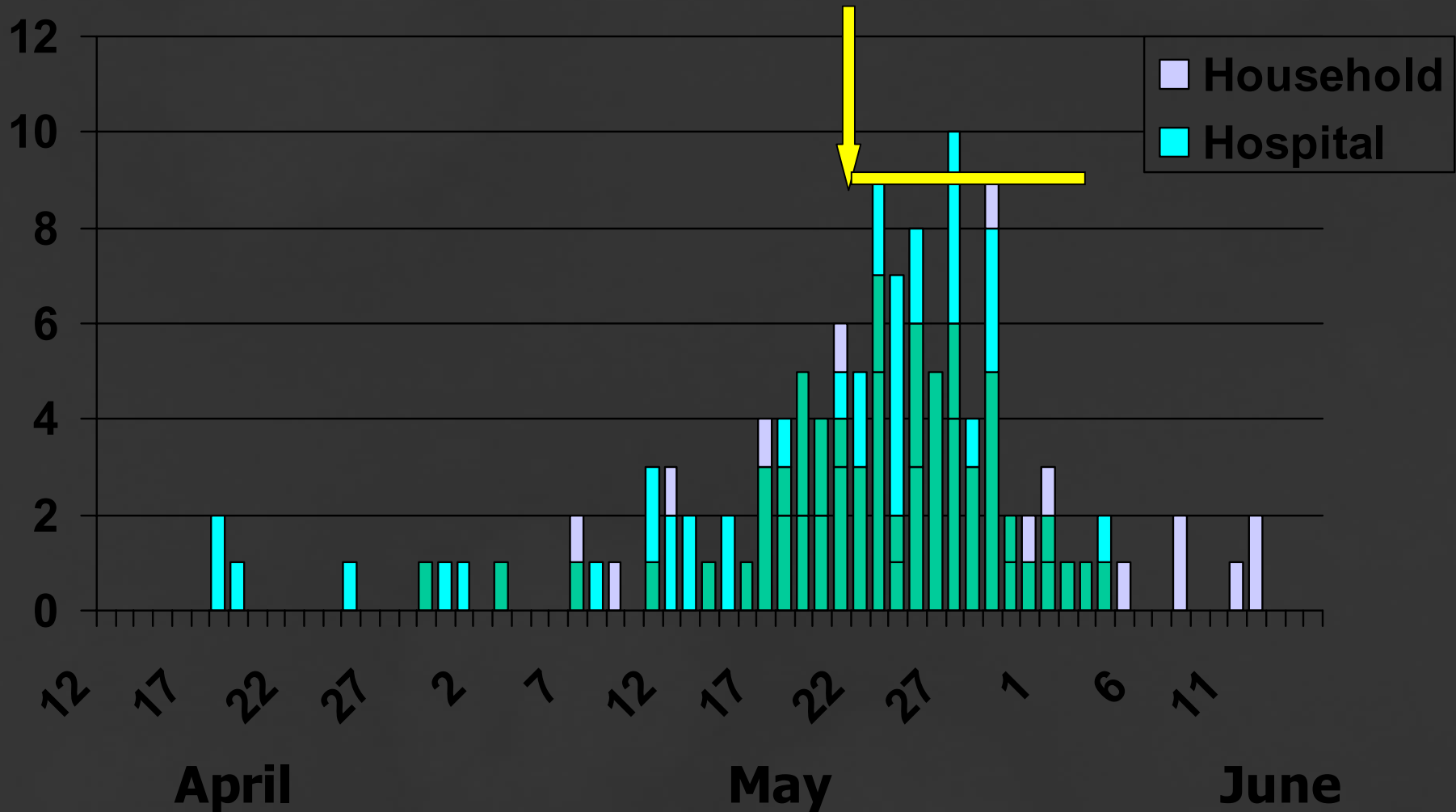
- No study has reliably shown a correlation between clinical symptoms, physical exam and/or chest radiography and etiology
- 15 - 30% may have a mixed infection
- No pathogen found in 40-60%

Metlay et al. JAMA 278:1997; Bartlett et al. N Engl J Med 333:1995; Semin Resp Infect 13:1998; Infect Dis Clin North Amer 12:1998; Taylor EL et al. Can J Infect Dis 1999; Reed et al. West J Med 1996

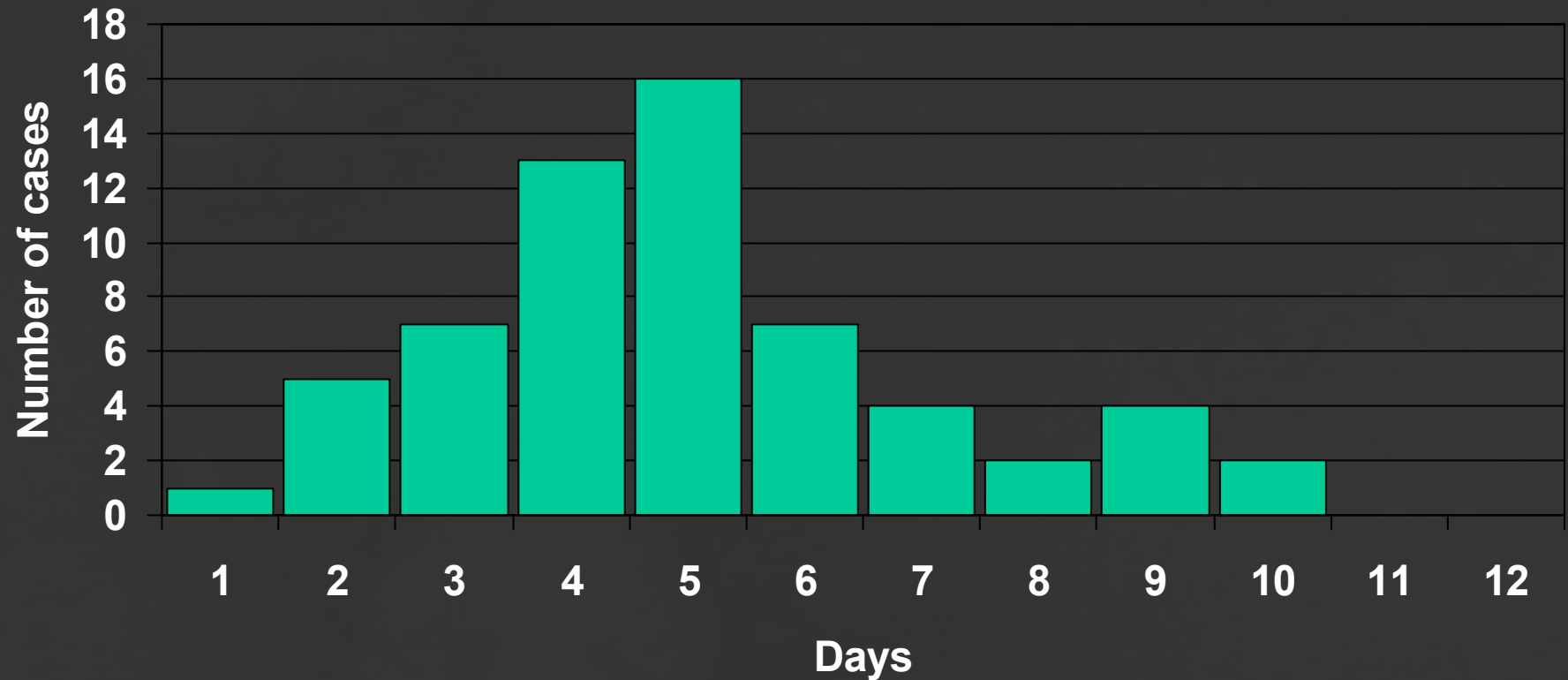
Toronto Area Probable and Suspect cases by source of infection May 5, 2003



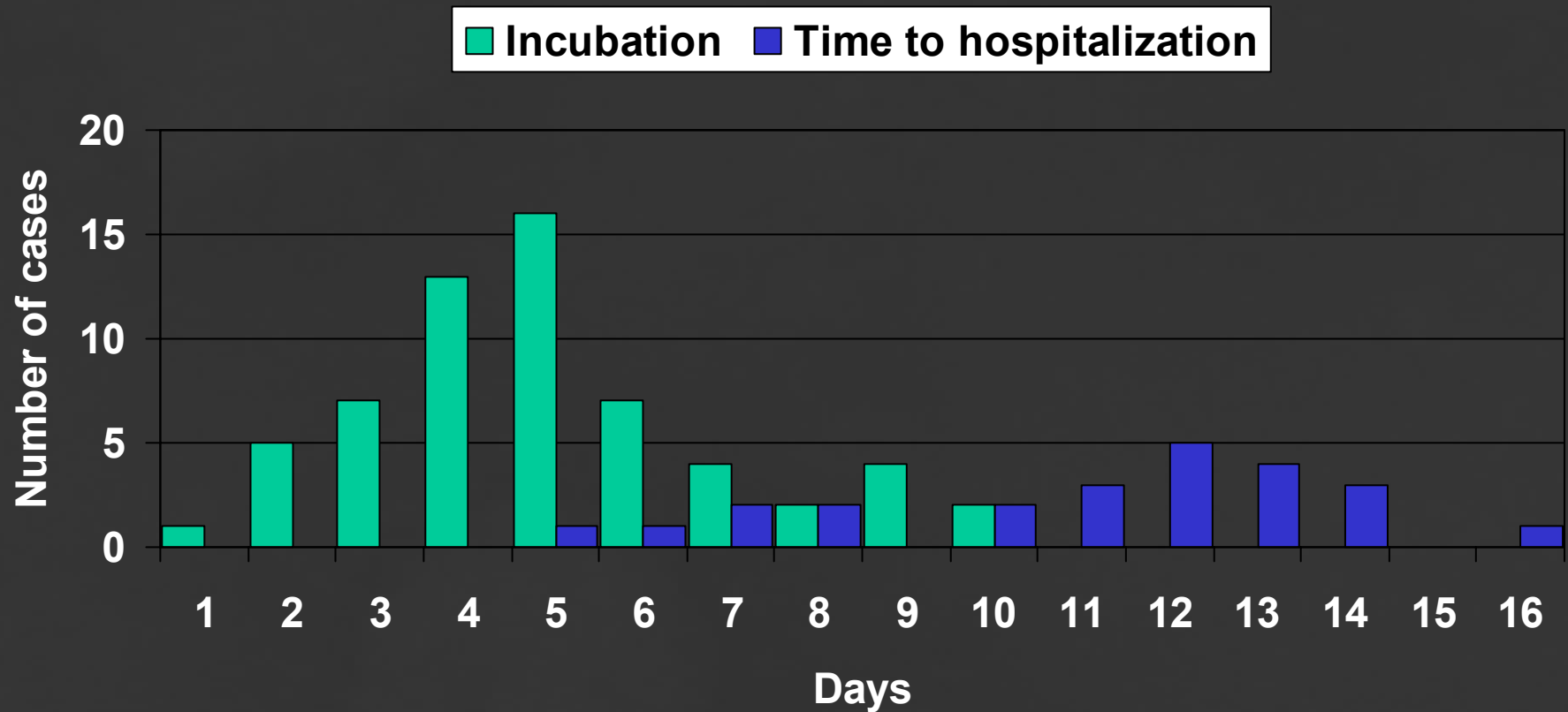
"SARS-2" - Toronto



Incubation Period SARS, Toronto, 2003



Incubation Period SARS, Toronto, 2003



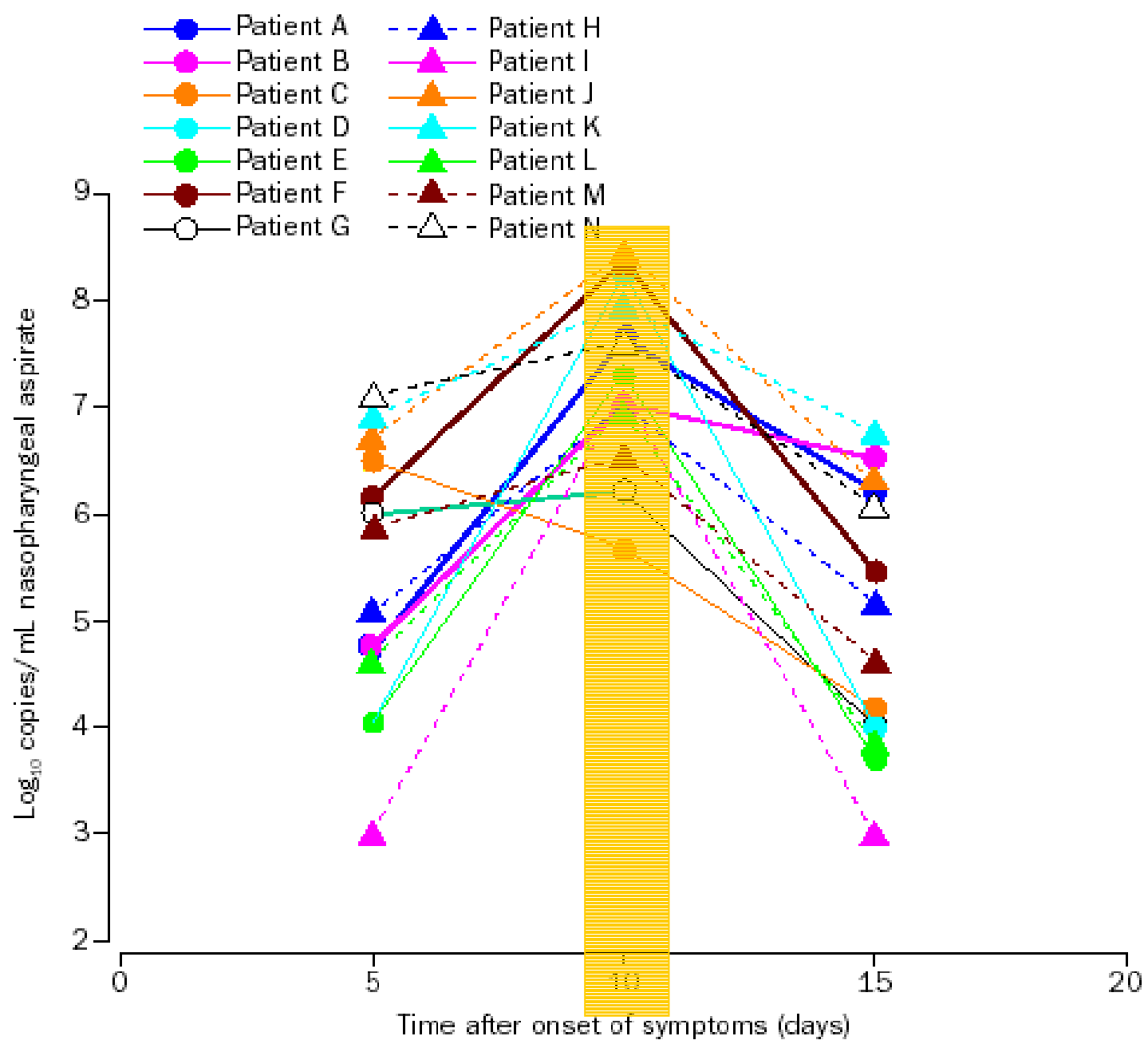


Figure 4: Sequential quantitative RT-PCR for SARS-associated coronavirus in nasopharyngeal aspirates of 14 SARS patients

Likelihood of positive test from upper resp sample, by severity of illness

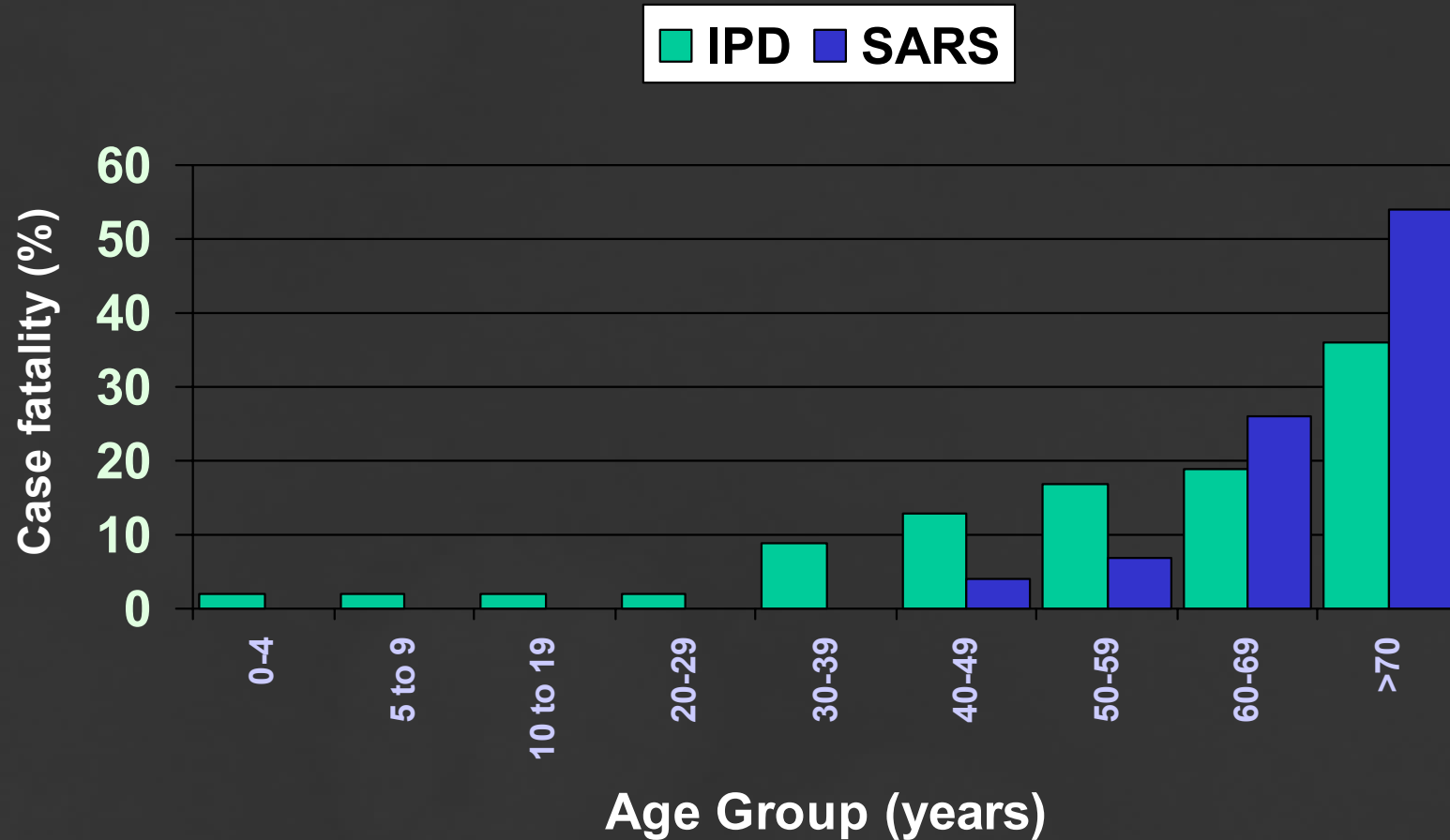
	Required intubation	Not intubated
PCR test upper respiratory sample		
Positive	11	46
Negative	2	49

OR 5.9, 95% CL 1,56; P=.03

Severe Acute Respiratory Syndrome (SARS): Case-Fatality

Age yrs)	No. cases	No. (%) deaths
<18	20	0
18-35	96	0
36-64	216	15 (7%)
≥65	60	28 (47%)
Total	392	43 (11%)

Case-Fatality Rates Invasive Pneumococcal Disease vs SARS



Preliminary Canadian Data

(from the *Canadian SARS Research
Network Pathology Group*)

Gabriella A. Farcas, Kevin C. Kain,
Susan M. Poutanen, Tony Mazzulli,
Barbara M. Willey, Donald E. Low,
Jagdish Butany, Sylvia L. Asa

Study Patients

- 44 patients have died in Canada
- $n = 20$
- M:F ratio: 9:11
- Age range: 43 – 99 years old
- Range of time from onset of symptoms to death: 5 – 51 d (one at 108 d)

Autopsy Tissue SARS-CoV RT-PCR Positivity

Tissue	Lung	Small Bowel	Large Bowel	Lymph Node	Spleen	Liver	Kidney
Proportion Positive	19/20	11/16	11/16	9/14	9/18	7/18	6/17
% Positive	95%	73%	73%	69%	53%	41%	38%
Maximum Viral Load	8.8 x 10 ⁹	1.8 x 10 ⁸	3.7 x 10 ⁸	8.9 x 10 ⁸	7.0 x 10 ⁴	1.6 x 10 ⁶	7.4 x 10 ⁵

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Highlights of Results

(EID, ICAAC Sept. 2003)

- Higher SARS-CoV viral loads in the lung were associated with multi-organ viral dissemination
- Lower SARS-CoV viral loads in lung, bowel, and liver were associated with longer durations of illness (but not with the use of ribavirin or steroids)
- Death not only due to overwhelming immune response → Viral replication likely ongoing even at death up to 51 days post symptom onset

Issues in Vaccination

- Inability to accurately make diagnosis means vaccine is essential
- Post-exposure vaccine desirable, and may be possible
- If geographically localized endemic disease, or irruptions
 - patients (need vaccine that works in 60 yo liver transplant recipients)
 - health care workers
 - travellers