Severe acute respiratory syndrome (SARS) is a newly described, deadly, communicable disease, first manifested in an epidemic that started in November 2002 in Guangdong Province, China (1). A medical professional who had worked with SARS patients in Guangdong visited Hong Kong on 21 February 2003. The disease quickly spread to 26 countries with local transmission in Singapore, Hanoi, Hong Kong and Toronto. The agent of SARS is an RNA coronavirus, not seen before in humans, known as SARS-CoV (1). The virus has been isolated from specimens (2); the genome has been sequenced (3); and infectivity in monkeys has been demonstrated. At the end of the 2003 epidemic, 8098 possible cases and 774 deaths were reported to WHO (4).

Although SARS has been controlled, the potential evolution of this virus is not well understood. This paper reviews the epidemiological characteristics of the epidemic; inconsistencies in transmissibility and mortality, the molecular epidemiology of SARS-CoV (4), the results of mathematical modelling, and evidence of evolution towards virulence in pathogens in similar settings.

Transmission

The epidemic probably started in mid-November 2002 in Fushan City in southern China’s Guangdong Province (4, 5) where at least two patients had atypical pneumonia of unknown cause. Immediately, similar cases were reported in five cities in Guangdong. A 35-year-old male patient who worked in Shenzhen as a chef was transferred to Heyuan People’s Hospital in Heyuan City where he infected at least 11 people. In Guangdong, there was no official recognition of a possible public health problem, and limited containment measures were implemented. On 11 February 2003 the provincial health department held a news briefing and stated that 305 cases had been reported and five people had died; these statistics were later revised to 792 cases and 31 deaths.

A 64-year-old male physician who had been treating SARS patients in hospital in Guangdong travelled to Hong Kong on 21 February 2003, having experienced symptoms five days earlier (6). He checked into the Metropole Hotel, and the following day he was admitted to an intensive care unit. He died on 4 March (7). Before being admitted to hospital, he infected his brother-in-law and 10 people in the hotel (8). A 27-year-old Shanxi businesswoman travelled to Guangzhou on 18 February; she became ill on 22 February and was admitted to hospital in Beijing, infecting many health-care workers. A doctor at this hospital wrote to Time magazine in early April to alert the public to the fact that Beijing had many unreported cases of SARS, prompting the government to implement control measures in Beijing (9). A 72-year-old Beijing man became ill in Hong Kong, and on 15 March he took a flight back to Beijing, spreading the virus into Inner Mongolia, Hebei and Tianjin (9). A person infected at the Amoy Garden Apartments later spread the virus to the Taiwan Peace Hospital in early April.

Several themes have become apparent in tracing the spread of this disease:

• health workers comprised the majority of cases (10), the remainder were members of the same household as an infected person;
• close and/or repeated contact was required for the disease to be transmitted from person to person;
• people who infected more than 10 people spread the disease into new geographical areas;
• the number of people who became ill after exposure varied greatly, from 0 to >30;
• the transmission of the virus from Beijing to Shanghai and between Guangdong and Hong Kong was unexpectedly limited (occurring three months after the first cases), despite the large amount of travel that occurs between these areas (11).

Mortality

Mortality rates are calculated as:

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\text{Mortality rate} = \frac{\text{people infected with SARS who died/probable cases}}{100}.
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Mortality rates varied widely among the outbreak areas, ranging from 0% to 17.1%, with the majority of regions first affected, such as Guangdong, experiencing mortality rates ranging from 4% to 10% and others that were affected later, such as Singapore, ranging from 13% to 17%.
Mortality rates were similar among areas affected later: Toronto, 17.1/100 000 people; Jilin, China, 17.1/100 000; Hong Kong, 17.0/100 000; Singapore 13.9/100 000; and Hanoi 8.0/100 000. The younger average age of the populations in Hong Kong and Toronto may account for minor differences in mortality rates between these two areas and rates in Hanoi and Singapore; the overall mortality rate in patients aged older than 75 years was 38% compared with 0% in children and people younger than 24 years despite an equal incidence of 1.0–4.0 cases/10 000 population (9). Differences in standards of living and health-care systems are unlikely to have caused the differences in mortality because these factors are similar in Hong Kong, Toronto and Singapore. Although health-care standards are lower in Hanoi, thus raising mortality, the younger average age of the population there accounts for the slightly lower mortality. It is possible that cold weather may affect the communicability of SARS as well as mortality owing to a seasonal increase in respiratory illnesses and greater exposure to the disease within sealed buildings. However, this is unlikely since the cities affected by the outbreak vary greatly in climate.

Most provinces in China were affected earlier in the epidemic and had substantially lower mortality rates than Toronto, Hong Kong, Singapore and Hanoi. Guangdong had a mortality rate of 4%; Shanxi had a rate of 5.13%; and Hebei had a rate of 5.6%. The mortality rate in Beijing was 7.26%, which is similar to that in Taiwan, falling between the higher rate seen in Hong Kong and the lower rate of Guangdong. It is interesting that both Beijing and Taiwan had documented importation of the virus from two different sources: Guangdong and Hong Kong.

Discussion
Differences in the strain of the SARS-CoV may account for the wide variation in the number of people infected by one exposure as well as for regional differences in mortality rates. The evidence suggests that the first community-acquired strain or strains from Guangdong were less virulent and probably less infectious, given the delay in the spread of the disease to Hong Kong and the apparent lack of events in which one person infected more than 10 others. One study in May 2003 compared animal traders with three control groups in Guangdong (12). It found that 13% of animal traders tested for SARS-CoV antibodies were positive compared with 1–3% of health-care workers involved in SARS control; public health staff in Guangdong, and healthy adults having routine physical examinations. None of the study participants had been ill during the outbreak in Guangdong, suggesting that early cases in Guangdong were milder. The disease was conspicuous by its absence among the contacts of patients who had a substantial number of exposures early on in the outbreak, indicating that many of these people were immune to the virus (13).

The divergent rates of incidence and mortality are consistent with the typed strains from patients in Singapore and Toronto who were exposed to the source patient at the hotel in Hong Kong and with those from patients in Beijing and Guangdong, from whom two strains emerged (4). The first strain was associated with the spread from the hotel in Hong Kong, and a second strain was associated with other samples from Hong Kong, Beijing and Guangdong. The genes encoding the S proteins of the SARS virus, responsible for its binding to host-cell receptors, membrane fusion, pathogenesis, virulence, and cell and species tropism, differ in the two strains (4, 14) indicating selective pressure on the virus due to host immunity (15).

The strain that spread from Hong Kong to Singapore, Toronto and Viet Nam, and later to Beijing and Taipei, was more virulent, and mortality rates were higher. Evolution towards increasing virulence is favoured in circumstances in which there are reproductive advantages for the pathogen (15). Changes in the strain resulting in increased virulence may accompany increased excretion (by coughing and sneezing, for example), which enhances the evolutionary fitness of the virus by allowing it to infect and reproduce in more hosts. Also, within health-care settings, the more seriously ill a patient becomes, the more contact he or she requires with health professionals, making health professionals the vector for the infection; the virus is thus passed on to a large pool of susceptible people, in intensive care for example, who are likely to have serious pre-existing medical conditions. The deadliness of hospital-acquired group B streptococcus, as opposed to that which is acquired in the community, is an example of the ability of organisms to adapt and reproduce within health-care settings despite rigorous interventions to prevent transmission (15). The influenza pandemic of 1918 (15) during which the virus spread rapidly through people living in close proximity precluded the need for the host to travel in order for the virus to spread. This echoes the conditions in many hospitals affected by SARS-CoV and explains the success of the virus in spreading through the apartment complex in Hong Kong and the market in Singapore and its lack of success in spreading outside of those settings.

Finally, population ecologists have demonstrated that the patterns of the outbreaks in Hong Kong and Beijing could not adequately be described by a model of a virus that moves from susceptible to infected to removed individuals (an SIR model). However, a model of a pathogen that moves from susceptible to exposed to infected to protected individuals, which allows for a class of immune hosts, has been developed (11). This model described the spread of a mild virus that conferred some immunity and a second epidemic of a virulent successor strain. The results of this modelling successfully matched the incidence observed in Hong Kong and Guangdong.

Conclusion
We have compiled the early epidemiological evidence on the SARS outbreak. It generally shows that there were lower mortality rates in regions in which SARS was acquired in the community and higher rates in those areas in which hospitals played a large part in transmission. While case definitions from across the globe may not be uniform, the possibility of large variations in transmission and the microbiological evidence cannot be ignored. In addition, the implications of the mutation of SARS-CoV are so vitally important to prevention efforts that we believe all possible explanations for the data should be explored, and it should not just be ascribed to differences in case definitions. ■

Conflicts of interest: none declared.

References
Web version only, available at: http://www.who.int/bulletin
References