Other potential reservoirs (eg, shaving cream, povidone-iodine solution, water supplies, and an alcohol-based mouthwash) were culture negative for *B. cepacia*.

Samples were obtained from unopened bottles of mouthwash distributed around the hospital that belonged to different batches, and the samples were cultured. Batches distributed from August 2004 through September 2004 were not contaminated. Batches distributed from April-2005 through July 2005 were highly contaminated. No other samples were available for analysis. The distribution of contaminated batches matched the substantial increase in the incidence of *B. cepacia* infection or colonization.

Strains from 5 patients and 6 mouthwash samples were submitted for identification to our reference center (National Center of Microbiology, Health Institute Carlos III, Majadahonda, Madrid, Spain). Pulsed-field gel electrophoresis of *Xba*I-digested genomic DNA was performed with a Chief DR-III system (Bio-Rad) according to conditions described elsewhere,[10] with several modifications. Briefly, electrophoresis was carried out in a 1.2% agarose gel for 22 hours at 6 V/cm with pulse times ranging from 5 to 35 seconds. Molecular mass markers were concatameters of phage λ New England (Biolabs, UK). Electrophoretic patterns showed that all the strains were identical (Figure).

On July 18, the use of the mouthwash product in our hospital was discontinued, and the last isolate of *B. cepacia* was obtained on July 22, 2005. The methods of production and distribution and the extent of use of this mouthwash in other hospitals are now being investigated by the Spanish Department of Health. At the moment, no information is available on the rate of *B. cepacia* infection or colonization at other hospitals that used the same product distributed by the same company as at our hospital.

Our findings strongly suggest that intrinsically contaminated alcohol-free mouthwash solution was the source of this large outbreak involving predisposed adults in ICU. To date, 2 similar outbreaks in which *B. cepacia* was isolated from culture of respiratory tract specimens from patients without cystic fibrosis have been traced to intrinsically contaminated alcohol-free mouthwash in North America.[7,8]

More-thorough surveillance of microbiological contamination of alcohol-free products used in adults predisposed to infection should be mandatory. These findings highlight the importance of hospital surveillance and investigation of unusual clusters of infection and colonization to promptly identify unexpected sources of pathogens and to protect patients at risk.

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Infect Control Hosp Epidemiol 2006; 27:1281-1282

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Analysis of Costs Attributable to an Outbreak of Severe Acute Respiratory Syndrome at a French Hospital

TO THE EDITOR—Severe acute respiratory syndrome (SARS), which is caused by the SARS-associated coronavirus

(SARS-CoV), has infected at least 8,500 people in 30 countries and claimed the lives of 765.[1] SARS-CoV is one of the latest in a series of emerging pathogens to challenge our global society.[2] Institutions will be increasingly involved in managing the outbreaks of infection caused by these pathogens. This will generate costs for the implementation of outbreak control measures and the diversion of resources towards managing these outbreaks. Few analyses of the economic burden of the SARS outbreak have been published.[3,4]

In France, after the World Health Organization alert about the SARS outbreak, a SARS surveillance system was implemented.[5] All persons suspected of having SARS were transported to the closest of 9 university departments of infectious diseases that were designated as referral centers for SARS management.[5,6] Three of the 7 patients with SARS were admitted to the infectious disease department and the intensive care unit (ICU) of our hospital (Tourcoing Hospital, Tourcoing), which had been designated as referral centers for SARS management in the Nord Pas-de-Calais and Picardie regions of France. The objective of this study was to estimate, from the perspective of Tourcoing Hospital, the additional direct medical costs and missed opportunity costs attributable to SARS outbreak management.

During the SARS outbreak, specific quarters isolated from other parts of the hospital were set up in Tourcoing Hospital for the evaluation and care of patients with suspected SARS (sectors in the infectious diseases ward and the ICU and a renovated specific sector for outpatients). A 24-hour telephone service was set up, which was staffed by a physician that patients and other physicians were asked to call. Patients were classified as having suspected SARS or no suspected SARS and as inpatients or outpatients. Outpatients were examined by the physician in the isolated outpatient sector. On the basis of this evaluation, the physician either discharged or admitted the patient to the inpatient isolation sector.[5] Patients requiring intensive care were admitted to the ICU. A dedicated nurse cared for the hospitalized patients with SARS. Patients fulfilling the criteria for a probable case had respiratory tract specimens and blood specimens collected to detect SARS-CoV (by means of reverse-transcriptase polymerase chain reaction and SARS-CoV serologic tests).

All the above procedures necessitated the reorganization of large parts of the hospital and therefore involved additional expenses. Additional expenses were estimated from the financial, accounting, and human resources records of the hospital. The period considered was March through July 2003.[1] Costs were expressed in 2003 euros. The financial, accounting, and human resources departments routinely track records of expenses at Tourcoing Hospital. During the SARS outbreak, all additional expenses incurred by the hospital that were exclusively related to SARS management were explicitly stated in these records, especially expenses related to additional human resources and investment in materials. The human resources expenses included new staff, additional working hours for physicians and nurses, and extra work from construction workers (Table). Investment in materials included additional equipment and construction of the structures necessary to meet high isolation standards in the 3 SARS sectors (Table). These structures did not include separate rooms with negative-pressure, high-efficiency particulate air filters, which were neither available nor built at Tourcoing Hospital during the SARS epidemic. Such rooms were constructed after the SARS outbreak to prepare for future outbreaks, but their cost is not included in this analysis. Expenses also included the cost of safe transportation of samples to the laboratories where testing was done (reverse-transcriptase polymerase chain reaction analysis was done at the Institut Pasteur, Paris, France, and serologic testing was done at Erasmus University, Rotterdam, The Netherlands).

Opportunity costs were defined as those resulting from a

TABLE. Additional Direct Medical Costs of Managing the Outbreak of Severe Acute Respiratory Syndrome (SARS) in 2003 at Tourcoing Hospital, France

Resource, by category	Cost, €
Human resources	
Additional workers[a]	
Nurses	29,570
Cleaners	3,510
Subtotal, additional workers	33,350
Additional working hours	
Nurses and physicians	14,280
Radiologists	110
Physiotherapists	50
Cleaners	1,360
Construction workers	3,290
Subtotal, additional working hours	19,090
Additional duty shifts	68,060
Subtotal, all human resources	120,500
Equipment and materials	
Disposable protective equipment[b]	81,810
Patients' rooms, laboratory and radiology equipment[c]	21,020
Ribavirin[d]	26,840
Subtotal, equipment and materials	129,670
Construction work	47,340
Safe transportation of samples to laboratories	58,520
Total	356,030

[a] New staff (nurses and cleaners) who were less familiar with isolation standards and use of personal protective equipment were moved to the general infectious diseases sectors, and trained staff already working in these sectors were transferred to the isolated SARS sectors.

[b] Disposable protective equipment used was as follows: N-95 respirator masks (n = 12,770; €67,884), gowns (n = 9,000; €3,740), shoe covers (n = 10,000; €754), protective eyewear and goggles (n = 310; €766), caps (n = 10,000; €238), and other equipment (eg, aprons, gloves, biohazard pathology specimen bags, and appropriate waste bags; €8,428)

[c] Material for specific sectors set up in the hospital for the evaluation of patients with suspected SARS, including equipment trolleys, sphygmomanometers, thermometers, otoscopes, a chest X-ray machine, rayon swab sticks with plastic shafts and tubes containing viral transport medium, telephones, chairs, tables, clocks, and bed linen.

[d] 1.2 g vials of virazole (n = 26; €26,440) and 200 mg capsules of Rebetol (n = 120; €410).

https://doi.org/10.1086/508846 Published online by Cambridge University Press

decrease in the use of hospital medical services.[7] This was estimated for the period from January 1, 2000, through December 31, 2003, using the French diagnosis-related group system, which classifies patients into statistically and clinically homogeneous groups.[8] Data on use of medical services included data on inpatient care and were extracted from records of the hospital accounting department. The time-series autoregressive-moving average (ARIMA) analysis was used to determine whether the SARS outbreak was associated with changes in the use of medical services.[9] The ARIMA analysis first identified the pattern of observed sequences of medical service use before the outbreak and next extrapolated the identified pattern to predict the use of medical services after the outbreak. Then the extrapolated pattern was compared with data observed after the outbreak. We performed all analyses using Stata 8 software (Stata).

During the outbreak period, 307 phone calls were received, 30 patients were seen during outpatient visits, and 10 patients were admitted to the inpatient units, including 1 with a virologically confirmed case of SARS and 2 with probable cases. The total number of hospital days for these patients was 118 in the ICU and 78 in the inpatient isolation ward. The patient with virologically proven SARS was admitted to the hospital on March 23, 2003, and died in the ICU on July 8, 2003. The estimated costs of the additional hospital resources used are shown in the Table. The total cost of these resources reached €356,030, and can be broken down into 4 major categories: human resources (€120,500), additional materials (€129,670), construction (€47,340), and transportation (€58,520). The cost of the additional resources used was estimated to be €35,603 per suspected case and €118,677 per confirmed case. The general patterns of observed and predicted expenditures with respect to hospital medical service use for inpatient care were similar during the preoutbreak, outbreak, and postoutbreak periods, and the outbreak had no impact on hospital medical service use (Figure).

On the basis of our results, we conclude that for cases of suspected SARS, expenditures for ambulatory or inpatient care are much higher than the average expenditures for patients with other diseases. This should be taken into account when classifying SARS or other emerging pathogens in the national systems of diagnosis-related groups. Other investigators have demonstrated that outbreaks of infection significantly increase total expenses for hospitals.[10,11] However, although we should be cautious about comparing studies directly because of differences in the methods used to calculate costs, the estimates of excess cost due to the an emerging pathogen outbreak, namely SARS, in our study were much higher than estimates reported in these studies. For example, one study found that the excess cost to the hospital per infected or colonized infant was estimated to be $16,000 during an outbreak of infection due to extended-spectrum β-lactamase–producing *Klebsiella pneumoniae* in a neonatal intensive care unit.[11]

The additional direct medical expenditure for SARS management mainly involved additional human resources and investments in materials. First, healthcare workers assigned to care for SARS patients only, to avoid even indirect contact with other patients. Second, providing care for patients with suspected SARS was less efficient than caring for those with other diseases, because of the need to use infection control measures. Third, the time devoted by each healthcare worker to patients with suspected SARS was longer than that devoted to other patients, as the workers had to deal with psychosocial issues generated by frustrations with quarantine, the regulations restricting visitors, and the fear of infection. Material investments mostly concerned purchases of disposable protective equipment.

The absence, in this study, of a significant reduction in the use of hospital medical services for inpatient care during the outbreak contrasted with data from another study of medical service use in Taiwan, which showed, at the peak of the SARS

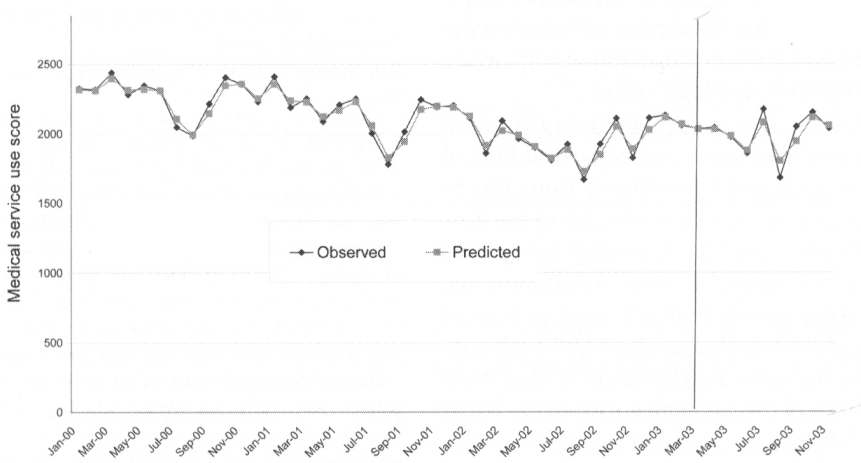

FIGURE. Observed and predicted use of hospital medical services before, during, and after the outbreaks of severe acute respiratory syndrome (SARS), from January 1, 2000, through December 31, 2003. The medical service use score was calculated according to Drummond et al.[7] and the French diagnosis-related group system.[8] The *vertical line* marks the start of the outbreak.

https://doi.org/10.1086/508846 Published online by Cambridge University Press

outbreak, a 35% reduction in inpatient care.[3] However, unlike our study, the Taiwan study was performed in a country strongly affected by the outbreak.

There are several limitations to our results. First, to estimate additional direct medical costs attributable to the SARS outbreak, we derived the necessary data from the financial, accounting, and human resources records of Tourcoing Hospital. Therefore, rather than a micro-costing approach, we used a macro-costing approach that may have lacked precision. Second, this study was conducted from a hospital perspective, and we did not estimate the costs related to resources used outside the hospital, such as visits to general practitioners, emergency services, and patients' transportation to the hospital, or the costs of surveillance of the index patient's family and other contacts. The overall costs related to SARS from a societal perspective, accounting for benefits, harms, and costs to all parties, are higher than our estimates.

The example of the SARS outbreak illustrates the global nature of the burden of emerging pathogens. Institutions in the United States and European countries will be increasingly involved in managing outbreaks of infectious disease, such as zoonotic diseases, in other parts of the world. Adequate preparations for such outbreaks require knowledge of their potential economic burden, in particular for budget allocation purposes.

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Defining Influenza-like Illness

TO THE EDITOR—We read with great interest the article by Babcock et al.[1] recently published in the journal. It was demonstrated that the most frequent symptom of influenza among hospitalized patients was cough, followed by subjective fever and fatigue. The authors commented that the finding of normal temperature in a substantial proportion of influenza patients was probably the result of medical interventions (eg, antipyretic use) for the hospitalized patients. However, Thursky et al.[2] concluded, in a study that recruited patients from sentinel general practices in Australia, that a case definition of cough, subjective fever, and fatigue had higher positive predictive value than did the definition of the Centers for Disease Control and Prevention (CDC). Despite methodological differences in the diagnostic tests used and the patients recruited, the 2 studies have similar findings: cough, subjective fever, and fatigue are the most important symptoms of influenza. Both also found that a high temperature (37.8°C or higher) was not the prime indicator of influenza, as it is regarded by the CDC.

Because influenza is "an unvarying disease caused by a varying virus,"[3(p157)] it should have a uniform case definition. In Europe, Aguilera and colleagues[4] collated a list of case definitions of influenza-like illness used by 14 different European countries. No two definitions were exactly same. Some countries used a definition with criteria that would require further explanation. For example, Denmark used the term "symptoms of respiratory infection" as one of the criteria,