The changing epidemiology of *Staphylococcus aureus* bloodstream infection: a multinational population-based surveillance study

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Abstract

Although the epidemiology of *Staphylococcus aureus* bloodstream infection (BSI) has been changing, international comparisons are lacking. We sought to determine the incidence of *S. aureus* BSI and assess trends over time and by region. Population-based surveillance was conducted nationally in Finland and regionally in Canberra, Australia, western Sweden, and three areas in each of Canada and Denmark during 2000–2008. Incidence rates were age-standardized and gender-standardized to the EU 27-country 2007 population. During 83 million person-years of surveillance, 18 430 episodes of *S. aureus* BSI were identified. The overall annual incidence rate for *S. aureus* BSI was 26.1 per 100 000 population, and those for methicillin-sensitive *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) were 24.2 and 1.9 per 100 000, respectively. Although the overall incidence of community-onset MSSA BSI (15.0 per 100 000) was relatively similar across regions, the incidence rates of hospital-onset MSSA (9.2 per 100 000), community-onset MRSA (1.0 per 100 000) and hospital-onset MRSA (0.8 per 100 000) BSI varied substantially. Whereas the overall incidence of *S. aureus* BSI did not increase over the study period, there was an increase in the incidence of MRSA BSI. Major changes in the occurrence of community-onset and hospital-onset MSSA and MRSA BSI occurred, but these varied significantly among regions, even within the same country. Although major changes in the epidemiology of community-onset and hospital-onset MSSA and MRSA BSIs are occurring, this multinational population-based study did not find that the overall incidence of *S. aureus* BSI is increasing.

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Background

Staphylococcus aureus is the second most common cause of bloodstream infection (BSI), and is the most important cause of BSI-associated death [1–3]. Population-based studies conducted in many regions around the world have identified incidence rates of 15–40 per 100 000 population per year,

with case-fatality rates of approximately 15–25% [4–16]. The epidemiology of *S. aureus* BSI appears to be changing. Many regions worldwide have witnessed increases in the overall incidence of *S. aureus* BSI, and there have been increases in the number and severity of BSIs caused by methicillin-resistant *S. aureus* (MRSA), associated with the emergence of community-associated strains in many areas [11,14,15,17–25]. However, it is unclear whether these increases in MRSA BSI may be replacing or adding to the burden of disease caused by methicillin-sensitive *S. aureus* (MSSA) [6,13,22–24,26–28]. In addition, it is not known to what extent changes in the occurrence of both MSSA and MRSA BSI may be attributable to shifts in incidence between community-based and hospital-based patients.

In order to best establish the distribution and determinants of an infectious disease, population-based studies are optimal. This is because, in these designs, selection bias is minimized by inclusion of all cases of disease occurring among residents of a defined population. Furthermore, by virtue of the fact that all cases are identified among a known population, shifts between subpopulations such as community and hospital can be evaluated, and comparisons among different populations and time periods are facilitated. With the exception of one study that specifically compared MRSA incidence rates between the UK and the USA [29], population-based studies investigating the epidemiology of invasive or bacteraemic *S. aureus* disease to date have been limited to single regions or one country. The objective of this study was therefore to define the occurrence of all MSSA and MRSA BSIs within a large multinational population and to evaluate temporal and regional differences. We were specifically interested in determining whether the overall incidence of *S. aureus* BSI has been changing, and whether MRSA may be replacing or adding to the burden of disease caused by MSSA.

Methods

Study protocol

This study utilized a multicentre population-based cohort design. Active surveillance was conducted nationally in Finland and in eight other regions within Australia, Canada, Denmark and Sweden under the auspices of the International Bacteremia Surveillance Collaborative [30]. All incident episodes of *S. aureus* BSI as defined by the growth of this organism from one or more blood cultures from residents of the surveillance populations during 1 January 2000 to 31 December 2008 were identified. Study laboratories were estimated to identify ~99% of all positive blood cultures from residents of the surveillance regions, and were equipped with electronic information systems to allow complete retrieval of recorded data. Patient age and gender were recorded, and isolates were determined to be MSSA or MRSA with standard methodology, according to the protocols established in each of the participating centres. Cases were classified as hospital-onset if the first culture was obtained more than 2 days after admission to hospital or within 2 days of discharge, and as community-onset otherwise. The Conjoint Health Research Ethics Board at the University of Calgary approved this study, and each centre complied with their local specific scientific and ethical review requirements.

Surveillance populations

The Canberra Region (population 370 000) includes the city of Canberra within the Australian Capital Territory and the satellite city of Queanbeyan and several small surrounding rural towns within the state of New South Wales [31]. The three Canadian centres included Sherbrooke (Quebec), Victoria (British Columbia), and Calgary (Alberta). Sherbrooke has a population of 152 000 residents, and is served by a single microbiology laboratory located in the Centre Hospitalier Universitaire de Sherbrooke [13]. Data from the Victoria area included the south local health area of the Vancouver Island Health Authority (population 364 000), and cases were identified at the regional microbiology laboratory [30]. Laboratory-based surveillance in the Calgary Health Region (population 1.2 million) was conducted at Calgary Laboratory Services [32]. The Danish surveillance regions included the North Denmark Region and two areas within the Capital Region of Denmark. The North Denmark Region surveillance was conducted using the previous boundaries of the North Jutland County (population 495 000). Surveillance from the Capital Region of Denmark was conducted within the boundaries of the two prior regions of Copenhagen City (population 640 000) and Copenhagen County (population 620 000). Surveillance data from Finland (population 5.3 million) was obtained from the National Infectious Disease Register, to which all Finnish clinical microbiology laboratories report all bacterial isolations from blood [33]. The Swedish surveillance region included the Skaraborg County Health Region located in western Sweden (population 256 000), where cases occurring in the community and among patients admitted to all four hospitals were identified [8].

Data management and statistical analysis

Data were analysed with Stata 11.2 (StataCorp, College Station, TX, USA). For purposes of analysis, MSSA and MRSA were considered independently. Only the first isolate per type per patient per year was included in analysis. The incidence of *S. aureus* BSI was calculated by dividing the number of incident cases by the surveillance population as deter-