Epidemiology, medical outcomes and costs of catheter-related bloodstream infections in intensive care units of four European countries: literature- and registry-based estimates

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Summary Despite high incidence rates, little information is available on the burden of illness of catheter-related bloodstream infections (CRBSIs) in Europe. A review of the available data was performed to estimate the clinical outcomes and costs associated with CRBSIs during intensive care unit (ICU) stays in four European countries (France, Germany, Italy and the UK). Based on these data we have estimated the CRBSI-related mortality and the annual costs associated with CRBSIs in the aforementioned countries. Results show large variation between countries: 1.12–4.2 CRBSI per 1000 catheter days, 8400–14 400 CRBSIs episodes per year, 1000–1584 deaths per year, 15 960–201 600 ICU days caused by CRBSIs and €35.9 to €163.9 million associated costs. Discrepancies are mainly explained by the heterogeneous quality of epidemiological studies, as well as the variety of national clinical practices.

Introduction

Bloodstream infections, which include catheter-related bloodstream infections (CRBSI), are a costly subset of nosocomial infection (NI) associated with a poor prognosis and high costs.1 Approximately
80% of primary bacteraemia are related to the positioning of central venous catheters (CVCs) that are commonly used in modern medicine. CRBSIs burden-of-illness data are relatively scarce and heterogeneous from one country to another. Our objective was to estimate the epidemiology, clinical outcomes and costs associated with CRBSIs in four European countries (France, Germany, Italy and the UK) based on recent information.

Methods

We performed a Medline literature review of published epidemiological studies, economic evaluations and cost studies in the field of CRBSIs. The review combined the following terms: 'nosocomial infections' or 'bloodstream infections' or 'CRBSI' and 'epidemiology' or 'incidence' or 'costs' or 'outcomes' or 'mortality' and 'France' or 'United Kingdom' or 'Germany' or 'Italy' and was performed in November 2007. The terms were searched in all fields of the summary and no restriction was used on the year of publication.

Grey literature and local surveys published in non-referenced national journals or by local or national networks involved in NIs were identified by local experts.

Available data were then used to calculate, for each country, an estimate of the total number of CRBSIs per year, the number of deaths related to CRBSIs, the total number of days spent in ICUs and the associated costs for the healthcare systems.

Results

More than 50 articles and documents were identified for the four countries and were extensively analysed. In a second step, we rejected references considered outdated as more recent data were identified during the literature search process. The estimates and references were reviewed and validated by national experts and used for the calculation if considered appropriate.

Table I summarises the key findings of this analysis. Figure 1 presents the minimum and maximum estimates per country for the additional costs of CRBSIs per implanted CVC.

Epidemiology

Epidemiology of CRBSIs is usually estimated by the number of cases per 1000 days of implanted CVCs. In 2001, more than 1500 hospitals were enrolled in this programme. The most recently available information on CRBSIs comes from a dedicated survey. This study, performed in 2005, used the HELICS (Hospital in Europe Link for Infection Control through Surveillance) definition of a CRBSI. The 38 participating centres included 5260 patients hospitalised in ICUs for more than 48 h. A CVC was implanted in 47.9% of the patients and the average duration of CVC implantation was 11.7 days. Incidence rate of CRBSI rate was estimated at 1.23 per 1000 catheter days. Other French epidemiological estimates were considered too old to be included in the analysis.

In order to estimate the total number of CRBSIs per year in France, we assumed that the number of implanted CVCs and arterial catheters was approximately 1 750 000 central venous and arterial catheters per year (source: Ethicon market research), leading to an average of 8400 infections per million catheter days in ICUs. In 1999, Gastmeier et al. provided an estimate of 6 million patient days spent in German ICUs (Krankenhausstatistik Grunddaten, Statistisches Bundesamt, Zweigstelle Bonn, 1999). Recent hospital statistics (2006) showed a 14% increase in the number of hospitalisation days in ICUs to reach 6.8 million. KISS recorded a CVC utilisation rate of 82.2%, leading to ~5.6 million catheter days in ICUs.

Approximately 1 750 000 central venous and arterial catheters would be used in German ICUs per year (source: Ethicon market research), leading to an average duration of implantation of 3.2 days. The rate of 1.5 CRBSIs per 1000 catheter days from KISS (2005) then gives an estimate of 8400 infections per year in France. This number is probably underestimated and must be analysed with caution, especially regarding the implantation duration.

Italy

A national surveillance network developed by the GIVITI (Gruppo Italiano per la Valutazione degli Interventi in Terapia Intensiva) started in 2005. CRBSI rate was estimated at 2.0 per 1000 catheter days (95% CI: 1.9—2.2) in 2007 with an average
duration of implantation of 8.6 days based on 37 239 patients recruited in 124 ICUs. This estimate was in a similar range to those of other recent studies.

In Italy, 490 000 CVCs and arterial catheters are implanted every year in ICUs (Ethicon market research). Based on the previous data, this gives an estimate of 8500 CRBSIs per year.

UK
There is no surveillance system for NIs in ICUs in the UK. The most recent CRBSI study in the UK was performed by the Scottish Executive Health Department in 2005 in five hospitals (six ICUs). This pilot study using the HELICS definitions provided an estimate of 4.2 CRBSIs per 1000 catheter days (95% CI: 1.4—9.8).

Plowman estimated that there are ~4115 BSIs every year in the UK. This assumption was based on four cases in one hospital and must be analysed with caution. In the national evidence-based guidelines for prevention of hospital-acquired infections associated with the use of CVCs, an estimate of 5800 CRBSIs was given based on 210 000 implanted CVCs and arterial catheters per year. This CVC number is associated with an average duration of implantation of ~10 days and a CRBSI incidence rate of 4.2 per 1000 days, which gives an estimate of 8940 CRBSIs per year.

Mortality due to CRBSIs
Mortality attributable to CRBSIs is difficult to estimate due to the multiple confounding factors that can be identified among selected patients.

France
Published results on CRBSI-related mortality are not consistent. Soufir found no difference in mortality attributable to CRBSIs after adjusting for confounding factors collected three days prior to the infection; like several other experts, Renaud and Brun-Buisson estimated that a significant percentage of patients (11%) with CRBSIs would die because of their infection. Lastly, a study estimated the increased risk from ICU-acquired bloodstream infections at 24.8%. Therefore, based on published data (11%), CRBSI-related mortality can be estimated at 1580.

Germany
Gastmeier et al. estimated that mortality attributable to CRBSI ranges from 1000 to 1300 patients per year, i.e. 12—15%.

Italy
Mortality attributable to BSI was estimated at 17.1% by Endimiani et al.; the observed relative
risk (RR) ranged from 2.6 to 3.5 in a study by Orsi et al. This would lead to 1450 deaths associated with 8500 CRBSIs.

UK
In the UK, no information was retrieved regarding CRBSI-related mortality.

CRBSIs impact on ICU length of stay

France
The length of stay (LOS) associated with infection has been assessed by Chaix et al. for meticillin-resistant Staphylococcus aureus patients and shows a 4 days increase. Renaud et al. estimated that primary NI patients (including CRBSIs) spent 9.5 more days in the hospital than the control group; CRBSIs were responsible for an additional 14 days in LOS, but the limited sample size of the study impacts its robustness. Depending on what assumption is used (9.5 or 14 extra days in LOS), the total number of additional CRBSI-related hospital days would range between 136 700 and 201 475 days per year.

Germany
Gastmeier et al. estimated the total number of CRBSI-related ICU days at between 40 000 and 60 000 days per year, i.e. 4.8 to 7.2 (extrapolated) extra ICU days related to CRBSIs. By recalculating the total number of ICU days associated with CRBSIs based on the additional LOS per CRBSI episode (2.8 days) and the number of CRBSIs per year, the total number of CRBSI-related ICU days would be ~23 500 per year. We have decided to use published data from Gastmeier et al. in our subsequent assumptions.

Italy
Orsi and Di Stefano estimated the average additional LOS associated with BSI at between 19.1 and 19.9 days in their case—control study. A more recent analysis using the Ministry of Health discharge database on hospitalisation gave 12.7 days LOS for the ICD9 Diagnosis Code ‘996.62 – Infection due to intravascular device ...’. The total number of CRBSI-related hospital days per year can then be estimated by multiplying the number of CRBSIs (8500) by the average duration of hospitalisation (12.7 days) for vascular device-related septic caemia, i.e. 107 900 days.

UK
Plowman carried out a study based on four cases and focused on the outcomes and cost of NIs in one district general hospital. This analysis estimated (through modelling) that CRBSIs might be responsible for an extra LOS of 4.0 days (1.9 days based on observed, not modelled, data). The extra LOS was considered to be low but associated with a significant use of medical resources. This translates into an estimate of 16 980 to 35 750 days caused by CRBSIs, i.e. 1.9–4 days extra LOS multiplied by the 8940 CRBSIs in the UK.

Estimated costs for the healthcare systems

The cost of a CRBSI episode can be calculated by multiplying the additional LOS related to CRBSI by the daily ICU cost.

France
Extra costs related to CRBSIs were not directly estimated. Chaix et al. estimated that MRSA patients cost €6,884 (S9,275: exchange rate = €1, 35) more than controls. Adrié et al. estimated that a severe sepsis acquired during an ICU stay would cost three times more than the control. We estimated ICU daily costs based on an estimate of €745 in 1999 from the Assistance Publique des Hôpitaux de Paris, which reached €813 per day in 2005 [cf. inflation rate for health services published by the national institute for statistics and economic studies (INSEE)]. The cost of a CRBSI episode would then range between €7,730 (9.5 × €813) and €11,390 (14 × €813) with a total cost for the healthcare system between €100.0 and €131.0 million.

Germany
No estimate of extra costs due to CRBSIs was identified in the literature. Beyersmann et al. found that catheter-related sepsis was responsible for 2.8 extra ICU days. The cost per ICU day was estimated by the Ministry of Health at €1,500 (University Hospital of Tübingen). Therefore, the cost of a CRBSI episode would be ~€4,200 (€1,500 × 2.8). Total costs for the German Sickness Fund might then range from €59.6 to €78.1 million.

Italy
Italian ICU daily cost can be estimated at €1,026 according to national statistics. Knowing that the average LOS for medical device-related infections is 12.7 days, the average cost of a CRBSI can then be estimated at €13,035 (12.7 days × €1,026). The total costs for the Italian healthcare system would then be estimated at circa €81.6 million annually.

UK
Plowman provided an estimate of additional costs per BSI of ~€9,251 (€6,209) (exchange rate: £1 = €1.49) when modelled versus €4,392 (£2,949) when
observed. Overall, based on our assumptions, the costs for the NHS (National Health Service) could be estimated between £19.1 and £36.2 million (£28.5 to £53.9 million).

Discussion

One limit of our study is explained by the literature review method, which only searched in the Medline database. We attempted to control this bias by interviewing clinical experts, who would be aware of grey literature and articles that were initially not retrieved.

Overall, the analysis confirms that CRBSI is a serious medical issue that creates significant medical and economic burden for the healthcare systems.

From a medical standpoint, the large variation of CRBSI rates across countries (Table I) is mainly driven by the heterogeneity of available data such as epidemiology, number of patients at risk, medical outcomes and costs. This partly reflects the diversity of practices across Europe and the efficacy of global public health programmes to prevent infections. Experts also highlighted that local practices, especially the type of ward where CRBSIs are treated, could have huge consequences on the estimates, especially for ICU length of stay, mortality rates and costs.

In absolute value, CRBSI numbers are also very different across countries. In France, one catheter per 60 inhabitants is used; this ratio is one per 285 in the UK. This discrepancy translates into a strong heterogeneity in CRBSI numbers regardless of other parameters such as variations in medical practices. Ultimately, this might artificially affect the economic impact of CRBSIs.

Nevertheless, observed gaps between European countries cannot be explained only by the aforementioned parameters. Thus, epidemiological and economic studies focusing on NIs and CRBSIs often use different designs and are performed in different settings. Therefore, evidence generated by these studies needs to be interpreted with caution, especially when nationwide extrapolations are performed based on data coming from a limited number of centres.

German, French and Italian epidemiological estimates might be more accurate as they are based on national surveys that better reflect the variability in practices and medical processes in place to control NIs. British estimates come from a pilot study involving five centres, which makes the findings less robust and more difficult to interpret at a national level. The LOS parameter can be used to illustrate our difficulty in comparing outcomes from healthcare systems in which data are not collected in a similar manner; for example, if patients in a country stay longer – on average – in the hospital compared to another country, the additional LOS caused by CRBSIs might be shorter for those patients. In other words, the smaller increase in LOS due to CRBSI could be the consequence of a longer baseline average LOS. Overall, a European initiative like 'HELICS' can certainly provide more homogeneous epidemiological data that would facilitate comparisons between different countries.

Mortality rates associated with CRBSIs are mainly based on assumptions because the results of published studies are not consensual. Indeed, a few studies highlighted a correlation between mortality and CRBSIs whereas others did not. This confirms that longer term studies with a larger sample size are required to estimate more precisely the impact of CRBSIs on mortality and LOS, and are therefore useful to control for confounding factors.

From an economic perspective, CRBSIs are known to generate substantial expenditures at the hospital level. The cost for a CRBSI episode is very dependent on the 'location' of the patient in the hospital. As CRBSI is considered as a life-threatening condition that is usually managed in specialised wards and requires immediate intensive care, this will automatically impact CRBSIs treatment costs. Even though patients mainly stay in ICUs at the beginning of their episode and are rapidly transferred as their health status improves, significant costs have been generated by intensive care. Consequently, estimates based on a longer ICU LOS will translate into a high cost. Furthermore, as the differences in medical practices and the variability of therapeutic strategies preventing CRBSIs lead to longer hospitalisation and additional expenditures, CRBSI-related ICU costs increase, regardless of medical specialties and geographic areas.

Discrepancies in average CRBSI costs between countries can also be explained by the methods used for the estimates. The UK estimate is a cost model based on four patients. The French estimate is based on a case–control study whereas German and Italian estimates are mainly based on assumptions and not on dedicated studies.

Countries’ costs associated with CRBSIs are high and mainly dependent on the estimate of the number of hospitalisation days related to CRBSIs. This parameter is influenced by the differences in medical practices and therapeutic strategies implemented once the infection has appeared. Additionally, even though new technologies are
less invasive, the need for catheters is still growing. Therefore, the risk of infection has mechanically increased along with patient exposure to catheters. Moreover, the huge differences in the number of catheters used in ICUs favoured a more consistent data collection regarding catheter usage nationwide. In our review, we restricted the analysis to the ICU environment. Nevertheless, as CRBSIs occur in multiple hospital locations, their true medical and economic impact might be much higher than estimated.

Consequences of CRBSIs on healthcare systems were also estimated for the USA, The Netherlands, Argentina and Belgium. All these studies highlighted the consequences of CRBSIs or nosocomial BSIs on mortality, costs and length of stay and described the variability of estimates depending on the study design, the population considered and the country.

Overall, there is an increasing need for prevention in order to better control the incidence of CRBSIs. More and more countries develop national programmes and guidelines to promote and increase the use of preventive therapies to fight against CRBSIs. These actions will also help to reduce the significant costs related to these infections, which is a critical secondary objective.

Conflict of interest statement
None declared.

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