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Surveillance of infection associated with external ventricular drains: proposed methodology and results from a pilot study

H. Humphreys [a,b,*], P. Jenks [c], J. Wilson [d], V. Weston [e], R. Bayston [f], C. Waterhouse [g], A. Moore [h] on behalf of the Healthcare Infection Society Working Party on Neurosurgical Infections[†]

[a] *Department of Clinical Microbiology, Royal College of Surgeons in Ireland, Dublin, Ireland*
[b] *Department of Microbiology, Beaumont Hospital, Dublin, Ireland*
[c] *Department of Microbiology and Infection Prevention and Control, Derriford Hospital, Plymouth, UK*
[d] *Richard Wells Research Centre, University of West London, London, UK*
[e] *Department of Microbiology, Nottingham University Hospitals, Nottingham, UK*
[f] *School of Medicine, University of Nottingham, Nottingham, UK*
[g] *Department of Neurosurgery, Sheffield Teaching Hospitals NHS Trust, Sheffield, UK*
[h] *Department of Neurosurgery, Plymouth Hospitals NHS Trust, Plymouth, UK*

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SUMMARY

Background: The insertion of external ventricular drains (EVDs) is necessary in some neurosurgical patients, but increases the risk of meningitis/ventriculitis. While there are well-recognized risk factors, the proportion of patients who develop meningitis/ventriculitis varies partly due to differences in definitions. A multi-disciplinary working group was established to agree definitions for EVD-associated meningitis/ventriculitis, and a surveillance system was piloted in four centres in the UK and Ireland.

Methods: Definitions were agreed based on those published previously and on clinical and microbiological criteria. An agreed dataset was developed to monitor patients after the insertion of an EVD and until the EVD was removed and the microbial aetiology was recorded.

Findings: Four neurosurgical centres participated, with 61–564 patients surveyed in each unit. The vast majority of drains were cranial. Intracranial haemorrhage was the most common indication for the EVD insertion. Between 6% and 35% of EVDs were inserted by consultants rather than junior doctors. The proportion of patients who developed meningitis/ventriculitis varied from 3% to 18% and from 4.8 to 12.7/1000 EVD-days. Coagulase-negative staphylococci were the most common microbial causes.

Conclusions: Routine and ongoing monitoring of patients with an EVD *in situ* to detect meningitis/ventriculitis presents logistical difficulties, and few units do so. This pilot study suggests that a national system of surveillance with agreed definitions and a methodology

* Corresponding author. Address: Department of Clinical Microbiology, RCSI Education and Research Centre, Beaumont Hospital, Dublin D09 YD60, Ireland. Tel.: +353 1 8093708/3710; fax: +353 1 8092871.
E-mail address: hhumphreys@rcsi.ie (H. Humphreys).

[†] Full membership of the Healthcare Infection Society Working Party on Neurosurgical Infections: H. Humphreys (Co-Chair), P. Jenks (Co-Chair), J. Wilson, V. Weston, R. Bayston, C. Waterhouse, A. Jones, J. Enstone, C. Curtis, M. Garnett and M.E. Braine.

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to enable unit-to-unit comparisons of EVD meningitis/ventriculitis is both necessary and feasible. This will, in turn, inform quality improvement processes leading to the minimization of infection.

Introduction

Patients undergoing neurosurgery are at increased risk of healthcare-associated infections (HCAIs). In the 2006 four-country prevalence survey of HCAIs, the prevalence rate in neurosurgery was 10.5%.[1] Incidence studies of neurosurgical units in Italy and Germany found that meningitis occurred in 4—8% of patients.[2,3] Postoperative meningitis/ventriculitis is a particular risk when an external ventricular drain (EVD) is inserted to monitor or control intracranial pressure.

A Medline literature search of ventriculitis/meningitis found that the rate of infection varied from 5% to 20%.[4] This wide variation may relate to the diagnostic criteria used. The risk factors identified included: duration of EVD; frequency of EVD manipulations; presence of intraventricular haemorrhage; and surgical technique used in inserting the device (the rate is lower when the device is tunnelled under the skin after exit from the cranium with distal skin puncture).[4] A retrospective cohort study using data from national surveillance in The Netherlands was used to develop prediction models that would assist in the detection of EVD-related meningitis.[5] Observed and predicted rates of infection were compared and the correlation was approximately 95%. Predictive factors for meningitis were abnormalities of the cerebrospinal fluid (CSF; e.g. raised white cell count), type of drain (ventricular or lumbar), and whether or not admission to an intensive care unit was required.[5]

Various criteria are used to diagnose meningitis/ventriculitis, some of which are exclusively microbiologically based (e.g. positive CSF culture), while others include microbiological findings, clinical presenting features and CSF abnormalities (e.g. increased CSF leukocyte count).[6] For surveillance purposes, it is preferable not to include a decision to treat with antibiotics because meningitis/ventriculitis may be mimicked by other conditions (e.g. intracranial haemorrhage), and antibiotics may be given to treat infection at other sites in a seriously ill patient. A further challenge for surveillance is selecting an appropriate denominator. Rates of infection are often calculated as numbers of patients with infection as a percentage of the total with an EVD. However, the use of denominators that account for the duration of the device are preferable (e.g. per 1000 EVD-days) as the risk of infection increases the longer the EVD is in situ.

Most causes of meningitis/ventriculitis are skin organisms; staphylococci (i.e. *Staphylococcus epidermidis* and *Staphylococcus aureus*) account for nearly 80%, followed by a variety of other organisms that include aerobic Gram-negative bacilli (AGNB) and, occasionally, fungi.[4] The isolation of *S. epidermidis* or other coagulase-negative staphylococci (CoNS) in the CSF needs to be interpreted with caution as this may represent contamination and can result in over-treatment.

In the absence of a national surveillance system of neurosurgical meningitis/ventricultis, a multi-disciplinary working party was established and funded under the auspices of the Healthcare Infection Society to agree definitions, identify the challenges in establishing a national surveillance system, and highlight preventative strategies. The purpose was to test the feasibility and practicality of a surveillance system to measure the incidence of ventriculitis associated with EVDs in neurosurgical patients. This article reports the agreed definitions and their use, a suggested dataset, and the results from a multi-centre pilot surveillance system in the UK and Ireland.

Methods

While the risk of infection with an EVD includes the insertion procedure, the device also provides an external route by which pathogens may gain access to the ventricles. The risk of infection is therefore likely to be influenced by the length of time that the device remains *in situ*, and the extent to which it is manipulated during this period, rather than the insertion procedure specifically. The methodology developed for this surveillance was therefore based on the methods used for central vascular catheters, rather than surgical site infection, and used device-days as a primary denominator to calculate the risk of EVD-associated ventriculitis.[7,8] The data captured were used to calculate the following metrics:

- rate of ventriculitis per 1000 EVD-days; and
- percentage of patients with EVDs who developed ventriculitis.

The number of EVD-days was determined as the number of days between device insertion and device removal for all patients included in the surveillance.

A patient-level surveillance method was employed, and each patient with a newly inserted drain was followed prospectively to identify whether or not ventriculitis occurred.[9] Table I indicates the variables captured for each patient included in the surveillance. Surveillance was continued until the device was removed or the patient was transferred/discharged or died.

The case definitions for EVD-associated ventriculitis were developed after much discussion and consideration of existing published definitions, and were adapted from Horan *et al.* to distinguish probable from definite meningitis/ventriculitis (Table II).[10] Cases of ventriculitis clearly associated with a recently removed EVD were included, and if an EVD was replaced, this was considered as a new device and a new surveillance record was commenced. A new episode of infection was recorded if a different micro-organism was isolated from the CSF, or the same micro-organism was isolated from the CSF but at least four weeks had elapsed from a previous infection and there was evidence that the first infection had resolved.[11] When definite or probable venticulitis met the definition, the causative pathogen was recorded.

Table I
Denominator data variables collected during pilot study of external ventricular drain (EVD)-related meningitis/ventriculitis

Data item	Options	Data collection
Patient demographics	Age; sex; BMI; underlying disease	On insertion
Site of insertion	Cranial; lumbar	On insertion
Date of insertion		On insertion
Reason for EVD	Intracranial haemorrhage; tumour; blocked/infected ventriculo-peritoneal shunt; trauma; other	On insertion
Type of EVD	Standard; silver coated; antimicrobial/other	On insertion
Tunnelled	Yes; no	On insertion
Emergency	Yes; no	On insertion
Surgeon	Consultant; junior doctor	On insertion
ASA score	1 to 5/unknown	On insertion
EVD access	Date and reason (CSF sampling; drugs; other)	Duration of EVD
Reason surveillance discontinued	EVD removed; EVD removed and replaced; patient transferred; patient discharged; patient died	On completion of surveillance
Date surveillance discontinued		On completion of surveillance

BMI, body mass index; ASA, America Society of Anesthesiology; CSF, cerebrospinal fluid.

Local policies and demographic data

Local policies for the insertion and management of EVDs vary. Data were therefore captured from units participating in the surveillance related to local policies on the type of EVD used; whether or not devices were tunnelled; type of dressing; and protocols for sampling, manipulation and replacement of EVDs. For each EVD included in the surveillance, a set of patient data (age, sex, body mass index) and device data were captured (see Table I). If the EVD was manipulated, the date and reason for manipulation were recorded.

Data collection

Data were collected locally by medical microbiologists, neurosurgeons or other clinical staff by prospective surveillance of all patients who had an EVD inserted during the study period, using a standard protocol.

Ethics

As this study comprised the capture of routinely available data for the purpose of surveillance of infection, ethical approval was not required.

Table II
Definition of meningitis/ventriculitis used

1. Definite postoperative bacterial meningitis/ventriculitis
   The patient needs to meet either of the following criteria based on positive culture results:
   - A The isolation of a recognized pathogen, e.g. *Staphylococcus aureus,* Gram-negative bacilli or yeasts from at least one CSF sample
   - B The isolation of the same coagulase-negative staphylococcus, diphtheroid or other skin organism from two or more CSF specimens
2. Probable postoperative bacterial meningitis/ventriculitis
   The patient needs to meet at least two of the following criteria:
   - A Positive culture/microscopic results:
     - — The isolation of a potential skin isolate (e.g. coagulase-negative staphylococci) from only one CSF
       or
     - — The isolation of bacteria/yeast from the tip of an indwelling neurosurgical device (e.g. EVD) or a positive CSF Gram stain in the absence of positive culture
   - B Clinical features: one or more of the following: fever, change in consciousness, new onset of seizures, signs of meningeal irritation
   - C CSF inflammation: raised or increasing white cell count or low CSF glucose (i.e. CSF:blood ratio $<60\%$)

CSF, cerebrospinal fluid; EVD, external ventricular drain.
Note: a new episode of infection was recorded if (a) a different micro-organism was isolated from the CSF or (b) the same micro-organism was isolated from the CSF but at least four weeks had elapsed from the previous infection and there was clear evidence that the symptoms of the first infection had resolved (e.g. higher Glasgow Coma Scale, reduced white cell count by $>50\%$, and eradication of the organisms on Gram stain and culture in one or more follow-up CSF specimens if the EVD remained in place).

Results

Four centres participated in the pilot surveillance project, ranging in size from a unit that performed 1063 procedures per year (Unit 1) to a unit that performed 2643 procedures per year (Unit 2). EVDs were tunnelled in all of the units (Table III). There was variation in the frequency of CSF sampling between the units, although it was mainly performed as clinically indicated. However, in one unit, the frequency of CSF sampling also varied according to the individual consultant neurosurgeon. Likewise, data captured in the unit questionnaire demonstrated variations in unit protocols for the frequency of EVD manipulation from less than once per week in Unit 2 to weekly and one or more times per week in Unit 1 (Table III). The authors were not able to reliably record the reasons for EVD manipulation during prospective data capture.

The number of patients surveyed varied from 61 in Unit 3 to 564 in Unit 4 where there was already an ongoing programme of surveillance of infection following the insertion of EVDs. Also, some patients had more than one EVD inserted due to the need to remove and replace an EVD because of blockage. The duration of EVDs *in situ* varied (Table IV) from five days or less to more than 10 days. The vast majority of drains were inserted cranially. In Unit 3, only cranial EVDs were surveyed. Antibiotic-impregnated devices accounted for 73.7% (660/895) of EVDs, whilst silver-coated EVDs were used in two units and accounted for 0.44% (4/895). However, two units (1 and 4) frequently used both standard and antibiotic-impregnated devices.

The main indications for the insertion of EVDs were haemorrhage (47.3% 473/895) and tumour (21.6% 193/895). A minority of EVDs were inserted by consultants (21%, range 6–35%). A total of 45 patients with an EVD developed an infection (5.02%), ranging from 3% in Unit 4 to 18% in Unit 1. The latter unit also appeared to perform the most manipulations of EVDs. The rates per 1000 EVD-days were: 12.7 in Unit 1, 5.17 in Unit 2, 4.8 in Unit 3 and 5.9 in Unit 4. The median duration of EVD use for patients with an infection compared with patients without an infection was: 19 vs 10 days in Unit 2, 9.6 vs 13.67 days in Unit 3, and 10.5 vs 2 days in Unit 4. The corresponding data for Unit 1 were not available. All nine infections in Unit 1 were definite, seven of eight infections were definite in Unit 2 (other was probable), all three infections in Unit 3 were definite, and the 17 EVD infections in Unit 4 were not categorized as either definite or probable. In total, 47 isolates from EVD infections were recorded. Of these, 24 (52.2%) were *S. epidermidis* and 16 (37.8%) were AGNB.

Discussion

This pilot study was designed to look at the feasibility of the ongoing collection of data following the insertion of EVDs in neurosurgical units. Currently, this occurs in only a minority of units. The Working Group spent a considerable amount of time reviewing previously published definitions, and then drafted definitions for use in this pilot study that were felt to be robust for routine use. In particular, this study did not allow the inclusion of a decision to start antibiotics empirically for the treatment of meningitis/ventriculitis as a criterion for definite or probable infection.

The data were collected by whoever was available in each particular unit. However, the number of units involved, the number of patients surveyed and the details collected were less than had originally been intended, indicating the resources necessary for ongoing surveillance of these patients. Any future national surveillance system would need to provide guidance on logistics, such as when and who is best positioned to collect data, how it will be analysed and shared, and what actions will ensue. For many units, this would need some additional resources to ensure the regular and comprehensive collection of data.

Not unexpectedly, there were variations in practice between the units, such as how often EVDs were manipulated and the types of EVDs used (i.e. standard, silver-coated or antibiotic-impregnated catheters). Despite using defined criteria to identify infections, the proportion of patients with meningitis/ventriculitis associated with an EVD varied between units from 3% to 18% and from 4.8 to 12.7/1000 EVD-days, although the type of microbes responsible was largely similar throughout.

Ventriculitis/meningitis following EVD insertion is a relatively common healthcare-acquired infection in neurosurgical patients, although it is less prevalent than respiratory tract, urinary tract and bloodstream infections.[12–14] Recent studies have found variation in the proportion of patients with meningitis/ventriculitis after EVD insertion, and also the actual incidence per 1000 catheter-days. In a study from New York of 343 patients, the proportion of patients who developed ventriculitis was 3.5%, and 10 of 12 patients with positive CSF cultures also had infections elsewhere. The most common pathogens associated with EVD infection were skin flora, and in terms of risk factors, patients developing ventriculitis were more likely to have a prolonged duration of EVDs *in situ*.[15] In a Brazilian study of 119 patients, the proportion of patients who developed infection was 18.3% or 22.4 per 1000 catheter-days, but the majority of infections were due to AGNB.[16]

Table III
General details of neurosurgical units involved in pilot surveillance project

	Unit 1	Unit 2	Unit3	Unit 4
No. of neurosurgical procedures/year	1063	2643	2493	2274
No. of EVDs inserted/year	82	131	90	74
Whether or not EVDs are tunnelled	Yes	Yes	Yes	Yes
Sampling protocol	Daily and as clinically required[a]	As clinically indicated	As clinically indicated	As clinically indicated
Frequency of EVD manipulation	≥1/week	<1/week	Weekly	Weekly

EVD, external ventricular drain.
[a] Varied according to consultant.

Table IV
Data collected on external ventricular drain (EVD)-associated ventriculitis in four neurosurgical units[a]

	Unit 1	Unit 2	Unit 3	Unit 4
No. of patients surveyed	82	131	61	564
Duration of EVD *in situ* (days)				
≤5	39 (26%)	36 (26%)	16 (20%)	348 (62%)
6–9	71 (47%)	23 (16%)	41 (51%)	99 (17%)
≥10	40 (27%)	82 (58%)	23 (29%)	117 (21%)
Site of insertion				
Cranial	80	129	61	515
Lumbar	7	2	—[b]	49
Type of EVD				
Standard	10	0	0	209
Silver-coated	0	0	2	2
Antimicrobial-impregnated	127	131	49	353
Other	2	0	10	0
Indication for EVD				
Haemorrhage	43 (41%)	66 (50%)	26 (43%)	370 (66%)
Tumour	40 (38%)	17 (13%)	11 (18%)	125 (22%)
Blocked shunt	12 (12%)	8 (6%)	0	13 (2%)
Trauma	8 (8%)	2 (2%)	1 (2%)	53 (9%)
Other	1 (1%)	38 (29%)[c]	23 (37%)	3 (1%)
Status of operator				
Consultant	8 (6%)	25 (19%)	14 (24%)	202 (35%)
Junior doctor	123 (94%)	106 (81%)	43 (76%)	362 (65%)
Frequency of EVD Access				
≤5 times	36 (60%)	124 (95%)	57 (92%)	N/A
6–9 times	19 (32%)	6 (4%)	4 (6%)	N/A
≥10 times	5 (8%)	1 (1%)	1 (2%)	N/A
No. (%) of infections	17 (18%)	8 (6%)	3 (5%)	17 (3%)
Rate/1000 EVD-days	12.7	5.17	4.8	5.9
Microbiology aetiology[d]				
CoNS	10	3	3	8
Staphylococcus aureus	1	0	0	1
AGNB	4	4	0	4
Yeasts	1	0	0	1
Others	1	1	0	1

EVD, external ventricular drain; CoNS, coagulase-negative staphylococci; AGNB, aerobic Gram-negative bacilli; N/A, not available.
[a] For some data, the denominator is number of patients; for other data, the denominator is the number of EVDs. Some patients had more than one EVD, and data were incomplete for some parameters.
[b] Only cranial drains surveyed.
[c] For this centre, includes 27 for whom infection was an indication.
[d] For some infections, ≥1 isolate was recovered.

Many of the studies reported in the literature are limited by being single-centre studies or involving relatively small numbers of patients. There are logistical difficulties in conducting multi-site studies and in collecting data over a prolonged period of time unless adequate resources are in place, as this study also highlights. However, in an Italian study of 13 intensive care units where each unit recruited 10 or more patients over a period of six months or more, data were collated on 271 patients involving a total of 311 catheters.[17] Fifteen patients (5.5%) had confirmed ventriculitis/meningitis and 15 patients (5.5%) had suspected infection. Gram-negative bacteria were equally as likely to be the cause of infection as Gram-positive bacteria, and risk factors for infection included placement of the EVD outside the operating room, a co-existing extracranial infection, and a combination of both an EVD and a lumbar drain *in situ*.[17] This study included more sites than the present study, but collected data on fewer patients. Nonetheless, the overall proportion of patients with meningitis/ventriculitis was similar even if there were fewer infections due to AGNB in the present study. The British Neurosurgical Trainee Research Collaborative (BNTRC) is in the process of completing a multi-centre audit of EVDs throughout the UK and Ireland, including rates of infection but using different definitions; the results may further inform ongoing surveillance systems and how they can best be delivered.

The collection of local data and its comparison with other centres facilitates the identification of those factors which may be contributing to infection, and what measures are necessary to manage infection. This requires agreed definitions for infection. The present authors reviewed previously published definitions, and decided on the definitions above as they were considered to be feasible and to allow for the variables involved. Unlike those from the Centers for Disease Prevention and Control (CDC) and the National Healthcare Safety Network in the USA, this study included categories (i.e. definite and probable infections), and the definitions require two culture-positive CSFs for microbes that can colonize the skin to be deemed probable meningitis. Also, meningitis/ventriculitis in the newborn was not included specifically in this pilot study.[18] Nonetheless, it is likely that a similar protocol, albeit with some modifications, could be used in children and neonates.

As with measures to reduce bloodstream infection and ventilator-associated pneumonia, there is increasing use of a healthcare bundle to minimize EVD-associated infection, including the prevention of EVD-associated ventriculitis/meningitis.[19–23] A bundle consisting of education, meticulous EVD handling, CSF sampling only when clinically necessary and routine replacement of an EVD on the seventh day was instituted in an intensive care unit in Greece.[19] This resulted in a decrease in the proportion of patients infected from 28% to 10.5%, with *Acinetobacter baumannii* being the most common cause. In another study of 2928 EVDs inserted over a six-year period, a comprehensive protocol or bundle for EVD placement was developed and its efficacy evaluated.[20] The protocol included the use of pre-operative prophylactic antibiotics, use of antimicrobial catheters, and CSF sampling only when infection was suspected. Following implementation of the bundle, the proportion of patients infected decreased from 1.5% to 0.46%, with the highest incidence between days 4 and 14 after EVD insertion. Gram-positive bacteria such as CoNS were more common than Gram-negative bacilli as the cause of infection.[20] In a Dutch study where a very high baseline proportion of patients were infected (i.e. 37%), a comprehensive bundle was implemented aggressively between 2004 and 2006. This included measures to reduce infection following the insertion of both EVDs and lumbar drains.[21] This led to a significant decrease in the infection rate to 11.3%, but even after the intervention, the proportion of patients receiving antibiotic prophylaxis at the time of EVD insertion only increased from 31% to 56%.[20] One of the possible reasons for the relatively high background rate of EVD-associated infections in this

centre was that catheters were often inserted at the bedside, but this was changed to insertion in a separate room dedicated to this procedure.

There is significant variation in the proportion of patients who developed infection and the rate per 1000 catheter-days as well as the causative organisms between studies, and for reasons that are not always obvious. Nonetheless, the collection of data, its analysis and comparison with similar units is useful in identifying where improvements can be made. As these are difficult-to-treat infections, sometimes causing death but often causing prolonged length of hospital stay and impaired intellectual capacity in some patients, there is a significant clinical need to improve practice and to improve the safety of patient care.

Practice varies in terms of using standard, antibiotic-impregnated or silver-coated EVDs; two of the four units did not use standard EVDs. A recent meta-analysis of the impact of silver-impregnated EVDs only found one randomized controlled trial (RCT) and six prospective or retrospective non-RCTs.[24] There was a significantly lower infection rate associated with silver-impregnated EVDs in the RCT but not in the pooled non-RCTs. However, infections caused by Gram-positive bacteria were lower in patients with silver-coated EVDs. In a recent post-hoc analysis from The Netherlands involving two units, with plain EVDs and EVDs impregnated with rifampicin and clindamycin, there was no significant difference in the rate of EVD-associated infection using both CDC and culture-based definitions.[25] However, many studies in this clinical area are hampered by insufficient numbers of patients or by flawed design. Data from comprehensive surveillance performed at national level may indicate whether silver-coated or antibiotic-impregnated EVDs should be used routinely or only after other infection prevention measures have failed to reduce infection rates.

The purpose of this pilot study was to investigate the feasibility of ongoing surveillance in neurosurgical units of infective complications following the insertion of EVDs, with a view that such a system or a variation of it could be routinely implemented nationally with an acceptable protocol. Furthermore, not all aspects of infection prevention were surveyed, such as the use of antibiotic prophylaxis and whether or not antibiotics were administered before insertion and/or throughout the duration of EVD placement. However, the study was not large enough to make recommendations on preventative measures, which was one of the original objectives of the Working Group. As a pilot study, the study has limitations, including being able to collect data from only four neurosurgical units and deficiencies in the data collected (e.g. one unit did not distinguish between definite and probable cases). Also, the number of patients varied between the units, as did practices such as the type of EVD used. The authors were not able to investigate risk factors for infection given the lower number of units involved than had been expected, but they would probably be similar to those published previously.[4,16,26,27] However, the study emphasizes the need for regular and comprehensive surveillance of patients at the time of EVD insertion until removal using agreed and robust definitions to help explain differences in infection rates and microbial aetiology. The data collected and the difference in the proportion of patients infected highlights the need for ongoing surveillance, the sharing of data with comparisons allowing for differences in case mix and, ultimately, the identification of factors that can be modified to reduce infection.

In conclusion, the results of this pilot study and the BNTRC study confirm the need for, and the feasibility of, a national surveillance programme which would require some support locally. The use of an agreed set of definitions, a practical dataset and the sharing of data would identify risk factors, increase awareness and subsequently lead to the development of a set of guidelines, all contributing to reducing these important infections.

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