Public Health Agency of Canada | Agence de la santé publique du Canada

Canadian Nosocomial Infection Surveillance Program (CNISP)

Surveillance Protocol for Vancomycin Resistant *Enterococcus* Bloodstream Infections in CNISP Hospitals

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We would like to express our sincere appreciation to Jessica Bartoszko and Robyn Mitchell of our team, whose significant contributions were instrumental in the development of this protocol.

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BACKGROUND

Vancomycin resistant *Enterococcus* (VRE) causes significant morbidity and mortality in hospitalized patients with immunocompromised conditions and intensive care needs, with few effective antimicrobial interventions available[1]. In Canada, the incidence of VRE bloodstream infections has been increasing steadily over the past several years. Divergence in infection prevention and control practices – including cessation of screening and isolation of hospitalized patients in some hospitals – has been postulated as the main driver of these changes[2]. In addition, a novel strain of vancomycin resistant *Enterococcus faecium*, which was previously "non-typeable" by multi-locus sequence typing (MLST) due to the loss of the *pstS* gene was first described in Australia and was identified in CNISP hospitals in 2013. In Canada, this novel strain was assigned the sequence type ST1478. An increase in ST1478 (from <5% of isolates in 2013 to 38.7% in 2018) coincides with an increase in VRE BSI rates. This strain is also associated with non-susceptibility to daptomycin and high level gentamicin resistance.

OBJECTIVES

1. To determine the incidence of VRE BSIs among CNISP hospitals.
2. To provide a Canadian benchmark for VRE BSIs rates.
3. To describe the epidemiology of VRE BSIs.
4. To characterize the susceptibility profile and molecular subtype of VRE BSI isolates.

METHODS

Site Eligibility

All CNISP hospitals are eligible to participate.

Case Eligibility

Inclusion Criteria

Criterion 1: Isolation of *Enterococcus faecalis or faecium* from blood

AND

Criterion 2: Vancomycin MIC ≥ 8 ug/ml

AND

Criterion 3: Patient must be admitted to the hospital

AND

Criterion 4: Is a **"newly identified VRE BSI"** at a CNISP hospital at the time of hospital admission or identified during hospitalization.

- **A newly identified VRE BSI** is defined as a positive VRE blood isolate > 14 days after completion of therapy for a previous infection and felt to be unrelated to previous infection in accordance with best clinical judgement by Infection Control physicians and practitioners

Exclusion Criteria

Emergency, clinic, or other outpatient cases who are **not admitted** to the hospital.

Numerators

Case Identification

For each **VRE BSI** that meets the above criteria, APPENDIX 3 - VRE BSI Patient Questionnaire should be completed by reviewing the patients' chart and reported to the Public Health Agency of Canada (PHAC).

IMPORTANT: For patients with more than one VRE BSI during the same calendar year, **NEW** infections are to be identified by entering as a new case and 'linking' to the patient's original VRE BSI by entering the original unique patient identifier at the end of the patient questionnaire. This will enable the identification of duplicate patients.

Exposure Classification

Once the patient has been identified with a VRE BSI, they will be classified as healthcare-associated acquired in your acute-care facility, healthcare-associated any other healthcare exposure or community-associated based on the following criteria and in accordance with the best clinical judgement of the healthcare and/or infection prevention and control practitioner (ICP).

Healthcare-associated acquired in your acute-care facility (HA-YAF)

- Patient is on or beyond calendar day 3[1] of their hospitalization

OR

- Has been hospitalized in your facility in the last 7 days or up to 90 days[2] depending on the source of the infection

OR

- Has had a healthcare exposure at your facility that would have resulted in this bacteremia (using best clinical judgement)

Healthcare-associated any other healthcare exposure (HA-OTHER)

Any patient who has a bacteremia not acquired at your facility that is thought to be associated with any other healthcare exposure (e.g. another acute-care facility, long-term care, complex continuing care (i.e. chronic care), rehabilitation facility or exposure to a medical device).

Community–associated (CA):

No exposure to healthcare that would have resulted in this bacteremia (using best clinical judgement[3]) and does not meet the criteria for healthcare-associated BSI

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[1] *Calendar day 1 is the day of hospital admission*

[2] *For example, a VRE bacteremia from a surgical wound that occurs 3 weeks after a surgical procedure completed in your facility should be considered HA – your acute-care facility (up to 90 days after procedure if implant). A VRE bacteremia secondary to UTI occurring >7 days after discharge from your facility should not be considered HA – your acute-care facility.*

[3] *Consideration should be given to the frequency and nature of exposure to a medical device, procedure and/or facility. For example, pediatric patients with clinic visits for otitis media, asthma, well-baby etc., may or may not be considered as HA while pediatric patients with clinic visits that involved invasive procedures or day surgery may be more likely to be considered HA. Adult patients attending dialysis, receiving chemotherapy, attending outpatient visits involving invasive procedures, attending a complex continuing care hospital or undergoing day surgery may also be more likely to be considered HA.*

Denominator Data

Denominator data will be collected on the quarterly denominator form and submitted in CNPHI.

The data collected will include:

1) total number of patient admissions per year

2) total number of inpatient-days per year

Data Management and Reporting

Case Reporting

All denominator and patient questionnaire data (SEE APPENDIX 3 - VRE BSI Patient Questionnaire) should be submitted online through the Canadian Network for Public Health Intelligence (CNPHI) at www.cnphi-rcrsp.ca.

Laboratory Reporting

Blood Isolates: One blood isolate is required for every eligible VRE BSI and submitted to the NML. For patients with more than one VRE BSI in a calendar year, please indicate the patient's previous unique patient ID on the Laboratory Shipping Form (Appendix 2).

Mandatory Shipping Form: Each shipment of eligible VRE blood isolates must be accompanied by a Laboratory Shipping Form. Please complete the template found in the Laboratory Shipping Form and ensure it is included in the shipment. Please note that the Laboratory Shipping Form must also be emailed to the NML at nml.arni-rain.lnm@phac-aspc.gc.ca in excel format.

Instructions for submitting laboratory specimens:

- Vancomycin-resistant *E. faecium* and *E. faecalis* isolated from a blood infection will be identified by the submitting lab's preferred methods (e.g. grows on a VRE screen plate and identified by phenotypic methods).
- The isolate in pure culture and properly labelled with a CHEC number (in indelible ink/marker) should be stored by an appropriate method (i.e. swab at 4°C, cryobeads or glycerol stock at-20°C). Isolates can be stockpiled for bulk shipment to the NML.
- Unique patient ID must use the following syntax: Site number (alphanumeric) e.g. 99Z, year (2 digits) e.g. 22, strain number (3 digits) e.g. CHEC #, would be 99Z22001.
- If your hospital is shipping MRSA and VRE isolates in the same batch, please indicate on the swabs/tubes which isolates are MRSA and which are VRE.

Note: The unique patient ID for the isolate must match the unique patient ID on the corresponding submitted VRE questionnaire.

Surveillance Algorithm

The surveillance algorithm (Appendix 1) has been provided to assist in surveillance activities.

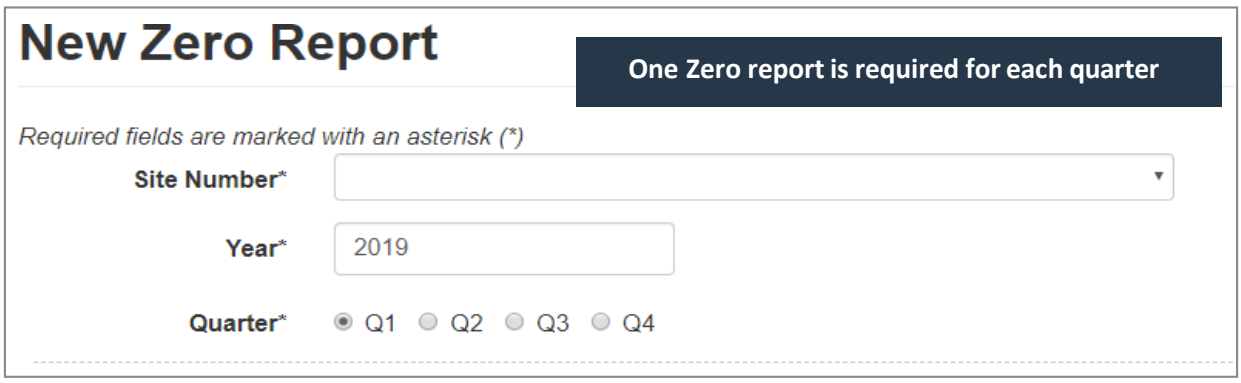
Submission Timeline

Please submit VRE BSI data and isolates according to the following timeline:

Numerator (cases)	Data and isolates due by June 30th	Data and isolates due by September 30th	Data and isolates due by December 31st	Data and isolates due by March 31st of following surveillance year
Isolates				
Denominator data				
Zero Report (if no cases)				

Zero report

For any quarter with no cases at your site, a zero report must be made in the CNPHI VRE module so that quarters with zero counts can be differentiated from missing data. If no cases are submitted and you are missing zero reports for a surveillance year, your hospital data will not be included in the rates.



Analysis

Regional and national BSI rates (per 1,000 admissions and per 10,000 inpatient-days), descriptive epidemiology, sequence type and resistance data will be calculated each year by PHAC and NML staff. Data will be reported through PHAC surveillance reports, presentations, publications, and published on the Agency and/or AMMI website.

ETHICS

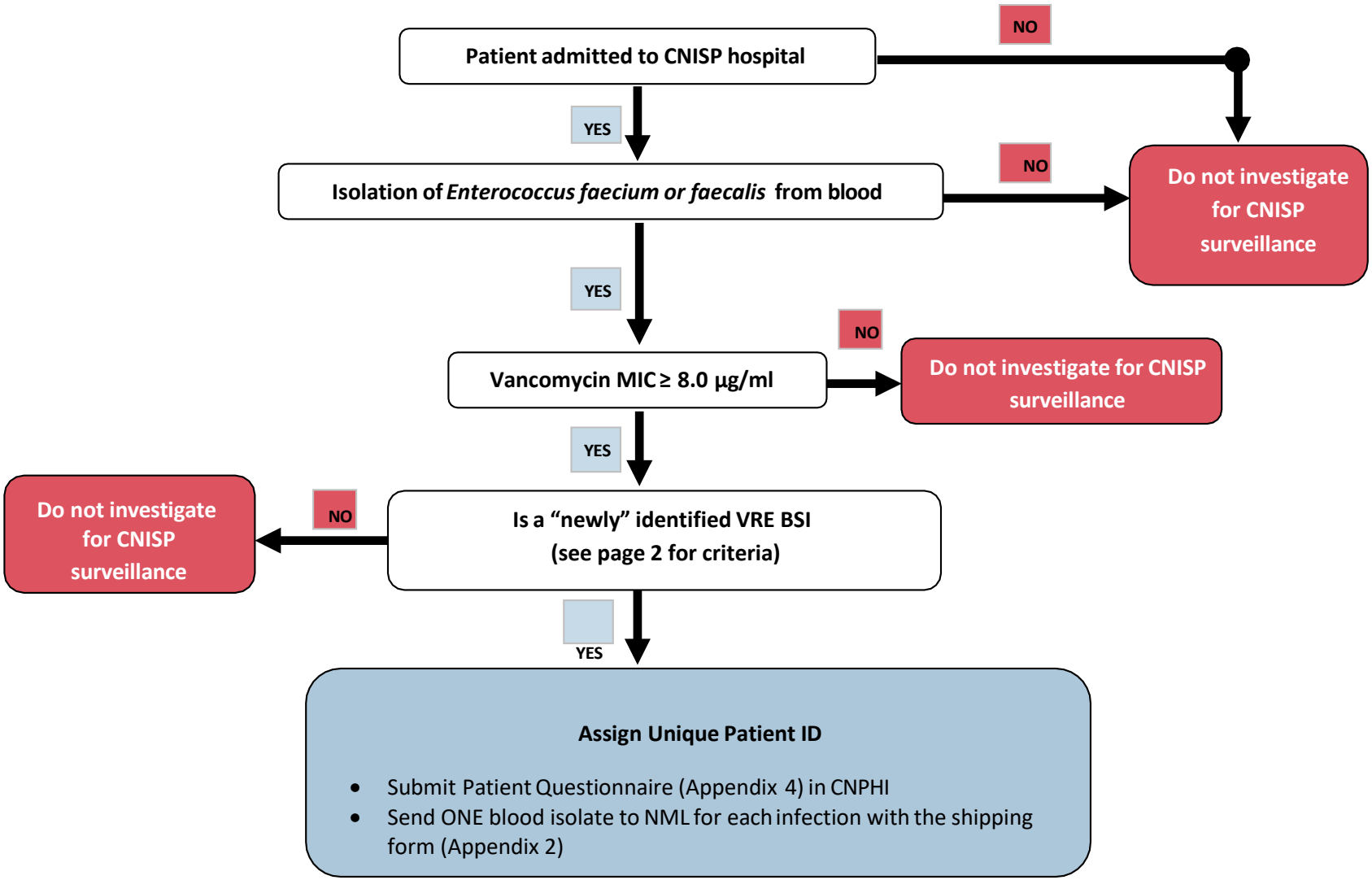
While this surveillance project is observational and does not involve any alteration in patient care, ethics approval may be sought at some hospital sites. Surveillance for healthcare-associated infections is a routine component of quality assurance and patient care in Canadian healthcare institutions and therefore informed consent is not required. A unique identifier linked to patient name will only identify patients at the local CHEC site and is not transmitted to the Agency. All data submitted to the Agency are kept strictly confidential.

PRIVACY

There is current demand for public disclosure of hospital-associated infections. Any data released by CNISP will be in summary format and will not identify individual hospitals. Hospital administrators should be made aware that national reporting of aggregate data will occur.

Appendix 1

Appendix 1 - Algorithm for VRE BSI surveillance



Appendix 2

Appendix 2 - Laboratory Shipping Form

Include the following form with the shipment **AND** email to the NML address provided.

If your hospital is shipping MRSA and VRE isolates in the same batch, please indicate on the swabs/tubes which isolates are MRSA and which are VRE.

Send isolates to:
Dr. George Golding
National Microbiology Laboratory
1015 Arlington St., Winnipeg, Manitoba R3E 3R2
Tel: 204 784 8096
Fax: 204 789 5020
Use FedEx billing number: 6327-8173-3

In addition, email the shipping form to
nml.arni-rain.lnm@phac-aspc.gc.ca

Please click on the icon below to access the excel shipping form:

Appendix 4_VRE
Standardized Shipp

Appendix 3

Appendix 3 - VRE BSI Patient Questionnaire

Please note: this form is only to be completed for bloodstream infections.

1.	Does this patient meet the criteria for a VRE bloodstream infection (refer to inclusion and exclusion criteria)? □ **Yes –** if yes, please complete the remainder of the questionnaire □ **No –** if *no*, do **NOT** complete this questionnaire.
2.	CHEC Site: _____
3.	Unique Patient ID: _____ **YY** _____ **(** e.g. 99Z22001) *(CHEC site #) (year) (case number)*
4.	Age: _____ □ **Years** □ **Months** □ **Days**
5.	Postal Code *(first 3 digits):* _____
6.	Sex: □ **Male** □ **Female** □ **Unknown**
7.	Date of admission: _____/ _____/ _____ DD MMM YYYY
8.	Date of patient's positive culture: _____/ _____/ _____ DD MMM YYYY
9.	What was the probable origin of the bacteremia? *Check one response only*:

Primary bacteremia	Secondary bacteremia
□ IV catheter-associated □ Peripheral-line □ Central-line □ Other line, *please specify*:_____ □ Primary bacteremia (source unknown/cannot determine)	□ Skin or soft tissue/burn wound □ Surgical site infection □ Endocarditis □ Urinary tract infection/urosepsis □ GI (e.g. intraabdominal abscess, peritoneal fluid, ascending cholangitis etc.) □ Mucosal barrier injury □ Other site, *specify*:

10.	Where was this VRE BSI acquired? *Check one response only:*

	□ Healthcare-associated – acquired in your acute-care facility (HA-YAF)[4] □ Healthcare-associated – acquired from any other healthcare facility or exposure[5] □ Community-associated (CA)[6] □ Unknown
11.	Was the patient receiving any of the following treatments at the time of positive blood culture? (*Check **ALL** that apply)* □ No □ Chemotherapy □ Radiation therapy □ Hemodialysis □ Peritoneal hemodialysis □ Unknown
12.	Did the patient have a central venous catheter[7] at the time of positive blood culture? □ **Yes** □ **No** □ **Unknown**
13.	Was the patient a bone marrow or stem cell transplant recipient? □ Yes, *please specify date of procedure*: _____/ _____/ _____ DD MMM YYYY □ No □ Unknown
14.	Was the patient a solid organ transplant recipient? □ **Yes**, *please specify date of procedure*: _____/ _____/ _____ DD MMM YYYY □ No □ Unknown

[4] Patient is on or beyond calendar day 3 of their hospitalization OR has had a healthcare exposure (inpatient or outpatient) at your facility that would have resulted in this infection or colonization (using best clinical judgement)
[5]Any patient who has an infection or colonization not acquired at your facility that is thought to be associated with another healthcare facility or exposure (e.g. another acute-care facility, long-term care, complex continuing care, rehabilitation facility or exposure to a medical device).
[6]No exposure to healthcare that would have resulted in this infection or colonization (using best clinical judgement) and does not meet the criteria for a healthcare-associated infection or colonization.
[7]Central Venous Catheter (CVC) include non-tunnelled (standard) CVC, coated or not, peripherally inserted CVC (PICC), tunnelled devices (e.g. Broviac, Hickman), tunnelled haemodialysisline, intra-cardiac catheters such as intra-arterial &and ventricular lines, dual function lines suchas temperature/venous catheters (e.g. Cool line catheters, Quattro catheters, introducers etc.), pulmonary catheters, umbilical artery and vein catheters and implanted

catheters (including ports).

15. Please indicate which treatment(s) the patient received for the VRE BSI **ONLY** *(please do not report treatment received for other infections)*

□ Linezolid
□ Daptomycin
□ Tigecycline
□ Other, *specify*: _____
□ Unknown
□ None

16. Please indicate which antimicrobials the patient received 30 days prior to their positive blood culture
*Check **ALL** that apply:*

□ Vancomycin
□ Fluoroquinolones
□ Cephalosporins
□ Carbapenems
□ Penicillins
□ Macrolides

□ Linezolid
□ Daptomycin
□ Other, *specify*: _____
□ None
□ Unknown

17. Was the patient admitted to an ICU within 30 days of positive blood culture?

□ Patient was already in an ICU at the time the positive blood culture was obtained
□ Yes, please indicate the date of ICU admission: _____/ _____/ _____
DD MMM YYYY
□ No
□ Unknown

18. What was the outcome at 30 days from the date of positive blood culture?

□ Patient discharged or transferred alive, please specify date: _____/ _____/ _____
DD MMM YYYY
□ Patient still alive and in hospital
□ Patient died, - please specify date of death: ____/ _____/ _____
DD MMM YYYY
- please indicate the relationship of VRE BSI to the death:
□ VRE BSI was the cause of death[8]
□ VRE BSI contributed to death[9]
□ Death is unrelated to VRE BSI[10]
□ Causality between VRE BSI and death cannot be determined
□ Unknown

19. Is this a NEW infection in a patient previously identified with a VRE BSI in this surveillance year?
□ No
□ Yes, enter the *original/previous unique Patient ID*: _____ **YY** _____ **(**e.g. 99Z22001)
(CHEC site #) (year) (case number)

[8] *The patient had no other condition that would have caused death during this admission.*
[9] *VRE BSI exacerbated an existing disease condition that led to the patient's death.*
[10] *The patient died, but death was not related to VRE BSI*

Appendix 4

Appendix 4 - Data Dictionary

Definitions and notes for completing Appendix 3- VRE BSI Patient Questionnaire **Appendix 3 - VRE BSI Patient Questionnaire**

1. **Does this patient meet the criteria for a VRE BSI infection?**

   Please refer to the inclusion and exclusion criteria under the Case Eligibility

   If the patient meets the criteria for a VRE BSI, please complete the remainder of this questionnaire. If the case does NOT meet the criteria for VRE BSI, please do **NOT** complete this questionnaire.

2. **CHEC Site #**

   This will be the **3-character** alphanumeric number assigned to your institution. It will always begin with the two digit number assigned to your CHEC member e.g., 07, 15, and a letter assigned by the CHEC member for that specific institution e.g., A, B, C, etc. The CHEC site # for each institution should always be the same for all the CHEC/CNISP surveillance projects and will always have all three alphanumeric digits reported as the CHEC site #, e.g., 07A, 15A.

3. **Unique patient ID**

   This 10 character code should consist of the 3 character CHEC site # (e.g., 09A), the surveillance year the infection occurred in (e.g., 22), and a consecutive number starting at 001 and continuing with each additional case. An example of the first case in an institution would be 09A22001. An example of the thirty-fifth case would be 09A22035, and so on.

Note: Always label the laboratory isolate with this same unique patient ID.

As a patient may have more than one VRE BSI during the same calendar year, **NEW** infections are to be identified by entering as a new case and 'linking' to the patient's original VRE BSI by entering the original unique patient ID at the end of the questionnaire.

4. **Age**

   Please enter the patient's age (in years, months or days) at the time of positive culture.

5. **Postal code (first 3 digits)**

   Please indicate the patient's residential postal code (first 3 digits). If patient does not have a postal code (e.g. homeless), please leave blank.

6. Sex

Please check male, female or unknown as appropriate.

7. Date of admission

Please indicate the date when the patient was admitted to the hospital.

8. Date of this patient's positive culture

Please indicate when the positive blood isolate for VRE was obtained.

9. Source of blood infection.

Please select the source of infection from which the positive blood culture was obtained.

The National Healthcare Safety Network (NSHN) definition of **mucosal barrier injury**:

Patient with at least one blood culture growing an eligible intestinal organism or at least two blood cultures with viridans group streptococci but no other organisms isolated who meets any National Healthcare Safety Network criteria for Mucosal Barrier Injury BSI: specifically, allogeneic hematopoietic stem cell transplant recipient who meets National Healthcare Safety Network criteria; or a neutropenic patient meeting National Healthcare Safety Network criteria.

Please refer to the National Healthcare Safety Network document https://www.cdc.gov/nhsn/PDFs/pscManual/4PSC_CLABScurrent.pdf for complete definitions (CDC, January 2022).

10. Source of acquisition

Please indicate whether the BSI was acquired in a healthcare setting or in the community according to the following definitions. If the source of acquisition cannot be determined, please report as unknown.

Healthcare-associated acquired in your acute-care facility (HA-YAF)

- Patient is on or beyond calendar day 3[8] of their hospitalization

OR

- Has been hospitalized in your facility in the last 7 days or up to 90 days[9] depending on the source of the infection

OR

[8] *Calendar day 1 is the day of hospital admission*

[9] *For example, a VRE bacteremia from a surgical wound that occurs 3 weeks after a surgical procedure completed in your facility should be considered HA – your acute-care facility (up to 90 days after procedure if implant). A VRE bacteremia secondary to UTI occurring >7 days after discharge from your facility should not be considered HA – your acute-care facility.*

- Has had a healthcare exposure at your facility that would have resulted in this bacteremia (using best clinical judgement)

Healthcare-associated any other healthcare exposure (HA-OTHER)

Any patient who has a bacteremia not acquired at your facility that is thought to be associated with any other healthcare exposure (e.g. another acute-care facility, long-term care, complex continuing care rehabilitation facility, clinic or exposure to a medical device).

Community–associated (CA):

No exposure to healthcare that would have resulted in this bacteremia (using best clinical judgement[10]) and does not meet the criteria for healthcare-associated BSI

11. Receiving treatment at the time of positive culture

Please indicate if the patient was receiving any of the following treatments: chemotherapy, radiation therapy, hemodialysis, peritoneal dialysis at the time of positive blood culture.

12. Patient with central venous catheter (CVC) at the time of positive blood culture

Please indicate if the patient had a CVC at the time of positive blood culture. Central Venous Catheter (CVC) refers to non-tunnelled (standard) CVC, coated or not, peripherally inserted CVC (PICC), tunnelled devices (e.g. Broviac, Hickman), tunnelled haemodialysis line, intra-cardiac catheters such as intra-arterial and ventricular lines, dual function lines such as temperature/venous catheters e.g. Cool line catheters, Quattro catheters, introducers etc., pulmonary catheters, umbilical artery and vein catheters and implanted catheters (including ports).

13. Bone marrow or stem cell transplant recipient

Please indicate if the patient was a bone marrow or stem cell transplant recipient. If yes, please specify the transplant date if available.

14. Solid organ transplant recipient

Please indicate if the patient was a solid organ transplant recipient. If yes, please specify the transplant date if available.

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[10] *Consideration should be given to the frequency and nature of exposure to a medical device, procedure and/or facility. For example, pediatric patients with clinic visits for otitis media, asthma, well-baby etc., may or may not be considered as HA while pediatric patients with clinic visits that involved invasive procedures or day surgery may be more likely to be considered HA. Adult patients attending dialysis, receiving chemotherapy, attending outpatient visits involving invasive procedures, attending a complex continuing care hospital or undergoing day surgery may also be more likely to be considered HA.*

15. Treatment for VRE BSI

Please indicate all of the treatments that the patient received for their VRE BSI. Please do not include treatment for other infections.

16. Antimicrobials exposure within past 30 days

Please indicate which antimicrobials the patient received 30 days prior to their positive blood culture.

17. ICU admission within 30 days

Please indicate if the patient was admitted or transferred to the ICU within 30 days following the date of positive blood culture.

18. Outcome at 30 days

Please indicate what the patient's outcome was at 30 days following the date of positive blood culture.

19. Is this a NEW infection in a patient previously identified with a VRE BSI in this surveillance year?

Please indicate whether this is a new infection in a patient previously identified with a VRE BSI in this surveillance year. If yes, please indicate the unique PID of the original/previous case

Appendix 5 - Data Uploader on CNPHI

CNPHI – UPLOAD DATA FILES

How to submit data using the uploader on CNPHI

Step 1.
Surveillance
Canadian Nosocomial Infection Surveillance Program

Step 2.
Choose an application

Step 3.
Menu

Step 4.
Upload Data

***Select surveillance year**
***Choose your file**

Step 5.
Upload Epi Data

References

1. Johnstone J, Chen C, Rosella L et al. Patient and hospital level predictors of vancomycin-resistant *Enterococcus* (VRE) bacteremia in Ontario, Canada. *Am J Infect Control* 2018; **46**(11):1266-1271.

2. Johnstone J, Policarpio ME, Lam F et al. Rates of blood cultures positive for vancomycin- resistant Enterococcus in Ontario: a quasi-experimental study. *CMAJ Open* 2017; **5**(2): E273- E280.

3. Carter GP, Buultjens AH, Ballard SA et al. Emergence of endemic MLST non-typeable vancomycin-resistant *Enterococcus faecium*. *J Antimicrob Chemother* 2016; **71**: 3367–71.

4. Van Hal SJ, Beukers AG, Timms VJ et al. Relentless spread and adaptation of non-typeable vanA vancomycin resistant *Enterococcus faecium*: a genome-wide investigation. *J Antimicrob Chemother* 2018; **73**: 1487–1491

Revision History

Date	Revisions Made
May 1, 2014	Added question 9 to the questionnaire addressing the 30-day outcome of patients with VRE bacteremia
October 30, 2014	Began making changes to homogenize CNISP protocol formatting
November 3, 2014	1. Case definition' renamed to 'inclusion criteria' 2. 'Numerator Data' moved under 'Inclusion Criteria'
November 5, 2014	1. 'Introduction' added (copied from VRE Report 'Background'). 2. 'Data Analysis' and 'Ethics' copied from the CDI protocol.
November 12, 2014	Edited 'Unique identifier code' in the Data Dictionaries
November 27, 2014	Updated protocol to reflect 2015 surveillance year
December 29, 2014	Added Q9-18 to collect additional data for blood stream infections only
October 30, 2015	1. Additional question added for blood isolates; "Did the patient have a central venous catheter at the time of positive blood culture?" 2. Question 14 was changed from 3 months to 30 days prior to the positive blood culture 'Data Analysis' and 'Ethics' copied from the CDI protocol.
December 29, 2016	Addition of antimicrobials for Q15. Addition of definitions for Surgical Wound and Urine in Data Dictionary.
November 10, 2017	The following updates were made to the 2018 protocol: 1. Surveillance of bloodstream infections only. 2. Added additional sources of blood infection (Q9). 3. Updated healthcare and community-associated definitions. 4. Update to inclusion/exclusion criteria – defined new VRE BSI in the same calendar year. 5. Added Q18 to the patient questionnaire - for patients with multiple VRE BSI in the same calendar year, indicate the original case PID.
October 15, 2018	1. Removed all references to a specific surveillance year, as protocol may not be updated annually. 2. Added the following response options to source of blood infection: mucosal barrier injury and GI 3. Added first 3 digits of postal code and removed DOB
February 7, 2019	Updated format (numbering)

September 30, 2019	In the data dictionary included in the January 2019 NHSN definition of mucosal barrier injury
January 8, 2020	1. Updated the background section 2. In the data dictionary, included the 2020 NHSN definition of mucosal barrier injury
January 2021	Added Q20 (COVID-19)
January 2022	Updated the working group member list and email addresses for CNISP and NML
November 2022	Added sub-question pertaining to attributable mortality (Q18) Deleted COVID-19 co-infection question (Q20)
November 2023	Updated the working group member list In the FR text, updated “infection du sang” to “bactériémie” because based on feedback received, that was the preferred FR translation. Provided the following clarification for shipping VRE isolates: “If your hospital is shipping MRSA and VRE isolates in the same batch, please indicate on the swabs/tubes which isolates are MRSA and which are VRE.”
November 2024	Updated the working group member list Updated wording of source of blood infection question to “probable origin of the bacteremia” (Q9), separated response options into primary and secondary bacteremia and added peripheral line, central line or other as response options under IV catheter-associated bacteremia