Surveillance of carbapenem-resistant organisms at VDH

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PUBLIC HEALTH SURVEILLANCE

Acronyms

CRE	Carbapenem-resistant Enterobacteriaceae
CRPA	Carbapenem-resistant *Pseudomonas aeruginosa*
CRO	Carbapenem-resistant Gram-negative organism (includes carbapenem-resistant Enterobacteriaceae, *Pseudomonas aeruginosa*, *Acinetobacter* spp.)
CP-CRE	Carbapenemase-producing carbapenem-resistant Enterobacteriaceae
CP-CRPA	Carbapenemase-producing carbapenem-resistant *Pseudomonas aeruginosa*
CPO	Carbapenemase-producing organism
MDRO	Multidrug-resistant organism

Carbapenem-Resistant Gram-Negative Organisms

Bacteria

Gram-positive organisms

Gram-negative organisms

Carbapenem – class of ß-lactam antibiotics effective against Gram-/+ organisms -- Doripenem, Ertapenem, Imipenem, Meropenem

Carbapenem-susceptible organism

Carbapenem-resistant organism (CRO)
(often susceptible to polymixins and tigecycline)

- Enterobacteriaceae (CRE)
  - *Klebsiella* spp.
  - *Enterobacter* spp.
  - *E. coli*
  - Others
- *Pseudomonas* spp., including *Pseudomonas aeruginosa* (CRPA)
- *Acinetobacter* spp. (CRA)
- *Citrobacter* spp.
- Other CROs

Carbapenemase – a beta-lactamase enzyme – inactivates carbapenems, can transfer resistance across genera and species via plasmids

Non-carbapenemase-producing organism

Carbapenemase-producing organism (CPO)

- CP-CRE
- CP-CRPA
- CP-CRA

CDC MDRO response tiers

Tier 1 organisms

- Novel mechanisms in U.S.
- Pan-resistant organisms

Tier 2 organisms

- Carbapenemase-producing (CP) CRE or CRPA with the following known resistance mechanisms:
  - **KPC** (*Klebsiella pneumoniae* carbapenemase) until more information available
  - **NDM** (New Delhi metallo-ß-lactamase)
  - **IMP** (imipinemase metallo-ß-lactamase)
  - **OXA-48** (oxacillinase-48-type carbapenemase)
  - **VIM** (Verona integron-encoded metallo-ß-lactamase)
- Any *mcr*-type genes

Tier 3 organisms

- Established MDROs identified in region, but not endemic

CRE Epidemiology

- High mortality rates (~50%)
- Risk factors
  - Invasive medical devices or procedures
  - Prior use of broad spectrum antibiotics
  - Critically ill
  - Immunocompromised
  - International healthcare exposure
- Transmission
  - Contact with infected/colonized people
  - Contact with wounds or stool
  - Contaminated devices/hands
  - Often in healthcare settings

Sources: CDC Antibiotic resistance threats in the US (2013); WHO Guidelines for the prevention and control of CRE, CRAB and CRPA in health care facilities (2017); WHO Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug-resistant bacterial infections (2017); CDC 2015 CRE Toolkit; UpToDate: Overview of carbapenemase-producing gram-negative bacilli (accessed: 2/20/18)

CRE Surveillance Background

From January 2018 onward, CDC requests

- Quarterly updates on all non-KPC CP-CRE cases
- Quarterly updates on all CP-CRPA

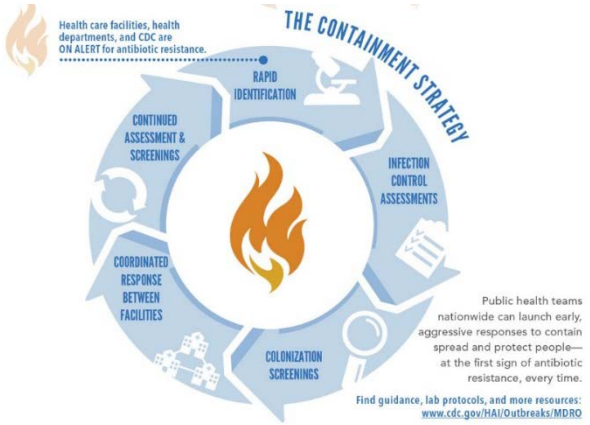
Case counts as of December 2017

Enzyme	Virginia	U.S.	Year identified in U.S.
KPC	Yes	Yes (all states)	2001
NDM	4	379 (34 states)	2009
OXA-48	2	146 (27 states)	2010
VIM	0	57 (11 states)	2009
IMP	0	36 (13 states)	2009

Source: https://www.cdc.gov/hai/organisms/cre/trackingcre.html

Objectives of CRO Surveillance

- Rapidly detect CRO
- Respond to a single case, cluster or outbreak
- Contain and control → STOP TRANSMISSION of CPOs
- Monitor for ongoing transmission



Source: CDC Interim Guidance for a Health Response to Contain Novel or Targeted MDROs; CDC Antibiotic Resistance Solutions Initiative; CDC Vital Signs, April 2018: Containing Unusual Resistance

Role and Responsibilities of Healthcare Facility and Providers

1. Reporting
2. Infection control
3. Communication
4. Coordination

1. When and What to Report

VDH VIRGINIA DEPARTMENT OF HEALTH
Protecting You and Your Environment
www.vdh.virginia.gov

VIRGINIA REPORTABLE DISEASE LIST

Reporting of the following diseases is required by state law (Sections 32.1-36 and 32.1-37 of the *Code of Virginia* and 12 VAC 5-90-80 and 12 VAC 5-90-90 of the Board of Health *Regulations for Disease Reporting and Control* - http://www.vdh.virginia.gov/surveillance-and-investigation/division-of-surveillance-and-investigation/commonwealth-of-virginiastate-board-of-health/). Report all conditions when suspected or confirmed to your local health department (LHD). Reports may be by computer-generated printout, Epi-1 form, CDC or VDH surveillance form, or upon agreement with VDH, by means of secure electronic transmission.

BOLD – Laboratories must submit initial isolate or other initial specimen to the Division of Consolidated Laboratory Services (DCLS) within 7 days of identification. All specimens must be identified with patient and physician information, and the LHD must be notified within the timeframe specified below.

REPORT IMMEDIATELY

Anthrax [a]
Botulism [a]
Brucellosis [a]
Cholera [a]
Coronavirus infection, severe (e.g., SARS-CoV, MERS-CoV) [a]
Diphtheria [a]
Disease caused by an agent that may have been used as a weapon
***Haemophilus influenzae* infection, invasive** [a]
Hepatitis A [a]
Influenza-associated deaths <18 years of age
Influenza A, novel virus [a]
Measles (Rubeola) [a]
Meningococcal disease [a]
Outbreaks, all (including but not limited to foodborne, healthcare-associated, occupational, toxic substance-related, and waterborne)
Pertussis [a]
Plague [a]
Poliovirus infection, including poliomyelitis [a]
Psittacosis [a]
Q fever [a]
Rabies, human and animal [a]
Rubella [a], including congenital rubella syndrome [a]
Smallpox (Variola) [a]
Syphilis, primary and secondary [a]
Tuberculosis (TB), active disease [a,b]
Tularemia [a]
Typhoid/Paratyphoid fever [a]
Unusual occurrence of disease of public health concern
Vaccinia, disease or adverse event [a]
***Vibrio* infection** [a]
Viral hemorrhagic fever [a]
Yellow fever [a]

REPORT WITHIN 3 DAYS

Acquired immunodeficiency syndrome (AIDS)
Amebiasis [a]
Arboviral infections (e.g., CHIK, dengue, EEE, LAC, SLE, WNV, Zika) [a]
Babesiosis [a]
Campylobacteriosis [a]
Chancroid [a]
Chickenpox (Varicella) [a]
Chlamydia trachomatis infection [a]
Creutzfeldt-Jakob disease <55 years of age [a]
Cryptosporidiosis [a]
Cyclosporiasis [a]
Ehrlichiosis/Anaplasmosis [a]
***Escherichia coli* infection, Shiga toxin-producing** [a,c]
Gi
Gra loma inguinale
Hantavirus pulmonary syndrome [a]
Hemolytic uremic syndrome (HUS)
Hepatitis B (acute and chronic) [a]
Hepatitis C (acute and chronic) [a]
Hepatitis, other acute viral [a]
Human immunodeficiency virus (HIV) infection [a]
Influenza [a,d]
Lead, reportable levels [a]
Legionellosis [a]
Leprosy (Hansen's disease)
Le spirosis [a]
Ly
Lymphogranuloma venereum
Malaria [a]
Mumps [a]
Ophthalmia neonatorum

Voluntary – to DCLS

- Submission of all CRE/CRPA isolates with ordering lab's AST results for further characterization

Required – to the local health department *immediately*

- Any Tier 1 or Tier 2 organism, including CP-CRE or CP-CRPA as an "unusual occurrence of disease of public health concern"
- Any suspected or confirmed cluster or outbreak of any CRO

CDC MDRO Response Tiers

Tier 1

- Pan-resistant organisms, novel resistance mechanisms

Tier 2

- Any carbapenem-producing CRE or CRPA with known resistance mechanism (KPC, IMP, NDM, OXA-48, VIM), or any organism with *mcr*-type gene

Source: CDC Interim Guidance for a Health Response to Contain Novel or Targeted MDROs

2. Infection Control: *VDH Checklist for Acute and Long-Term Care Facilities*

- Adapted from the 2015 CDC CRE Toolkit
- Core measures
- Supplemental measures
- Know your baseline CRE
- When to call the health department
- Recommended infection control measures for acute and long-term care settings
- Screening fast facts

Source: http://www.vdh.virginia.gov/content/uploads/sites/13/2018/03/Attach_E3-CRE-Checklist-for-Acute-and-LTCF_2018-1.pdf

Infection Control: Core and Supplemental Measures

8 Core Measures for All Facilities (from CDC 2015 CRE Toolkit)

1. Hand Hygiene
2. Healthcare Provider Education
3. Contact Precautions
4. Patient and Staff Cohorting
5. Minimize Use of Invasive Devices
6. Promote Antimicrobial Stewardship
7. Timely Notification from Laboratories
8. Screening

Supplemental measures if transmission ongoing

- Active surveillance testing
- Chlorhexidine bathing

3. Communication

Intrafacility

- Timely notification of CRO results from micro lab to IP and unit
- To those providing direct care
- Flagging medical record for any condition requiring infection control

Interfacility – ordering facility is responsible for communication of patient's CRO status when:

- Transferring patient: alert IP/director of nursing at receiving facility
- Patient is discharged home: alert PCP, home health agency

Patient

- Ordering facility to educate patient (or guardian), provide a letter if necessary

VDH

- Report clusters/outbreaks and Tier 1 and 2 organisms, request for any support including for screening
- Encourage intra- and inter-facility communication

4. Coordination with Public Health

- Submission of CRO isolate to DCLS →
- LHD contacts IP
  - Aware of CRO case
  - Patient on contact precautions, in private room
- LHD receive final results
  - Contacts IP to close the loop
  - If CPO:
    - Complete case report form
    - Start investigation
      - Lab lookback >3 months
      - Forward CRO isolates to DCLS
      - Contact screening

Role and Responsibilities of Healthcare Facility and Providers

- Reports cases, clusters or outbreaks as required per Virginia law and regulations
- If the facility has a laboratory, ideally voluntarily reports CRE/CRPA and submits isolates to DCLS within 24–48 hours of reporting
- Implements infection control measures
- Notifies and educates the patient (or guardian) if CRO colonization or infection is detected
- Performs intrafacility communication to appropriate staff (e.g., those providing direct patient care and infection control staff) about the patient's colonization or infection status; documents and flags this information in the patient's medical record
- Performs appropriate interfacility communication (regardless of geographic location) if CRO colonization or infection is detected and when infected or colonized patient/resident is transferred
- Performs appropriate communication with the patient/resident's primary care provider if discharged to home about his/her colonization or infection status
- Coordinates response with local and state health departments

CRE 2017 Lab Survey

- Preparation for CRE testing implementation
- Estimate burden of CRE in 2016
- Understand lab capacity to identify CRE, detect carbapenemase, and test for resistance mechanism
- REDCap survey sent to 51 sentinel laboratories via DCLS November 9, 2017

RESULTS

- 78% response (40 of 51 sentinel labs)
- 26 labs - 369 CRE isolates in 2016, 10% of isolates (from 9 labs) sent to reference lab
- 10 labs - phenotypic testing capability
- 5 labs – molecular resistance testing capability

CRE/CRPA Testing at DCLS

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Bioterrorism/Special Pathogens Response Coordinator
Division of Consolidated Laboratory Services

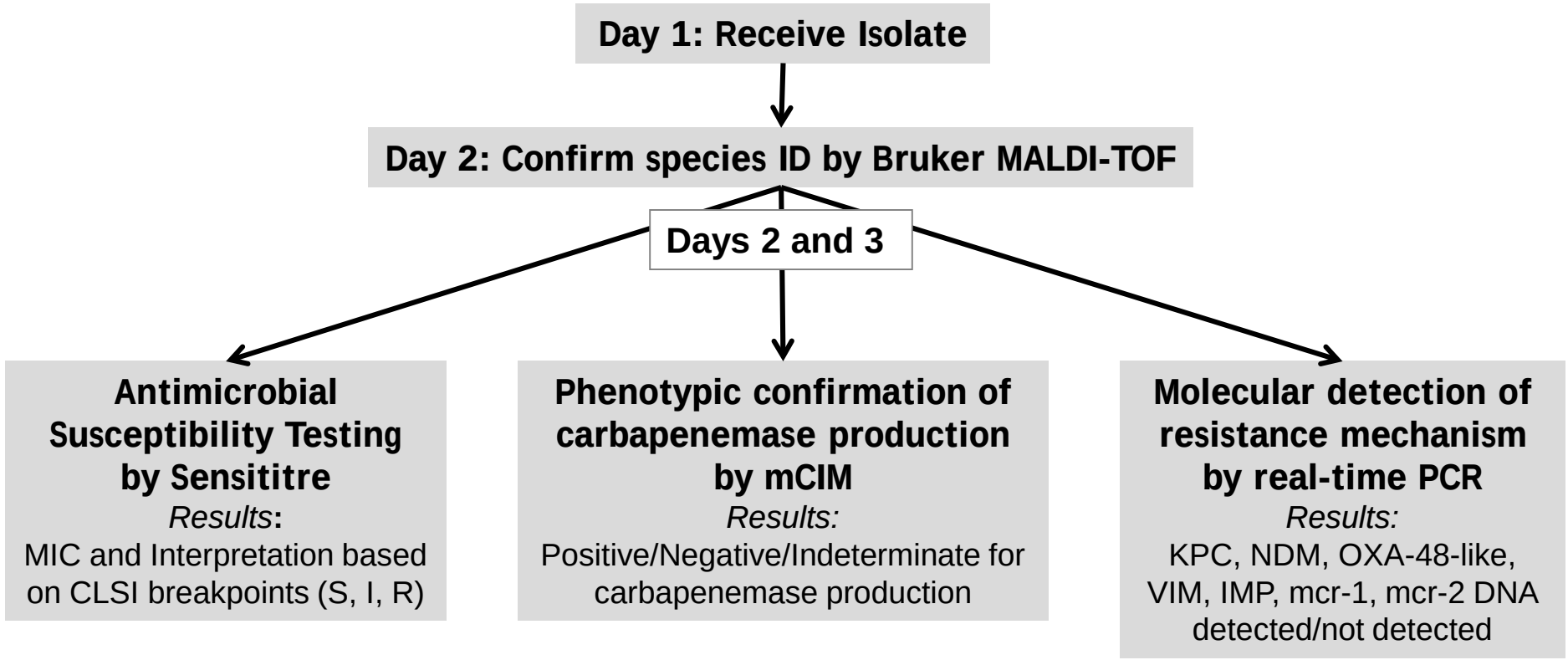
CRE/CRPA Testing: A National Effort

- DCLS part of the CDC Antibiotic Resistance Laboratory Network (ARLN)
  - ARLN provides support to 55 state and local labs and 7 regional labs to build capacity for CRE and CRPA testing
  - Virginia part of Mid-Atlantic regional lab
  - Regional lab provides free CRE colonization screening, targeted surveillance of *Acinetobacter* spp.
  - Regional lab and/or CDC can provide further characterization of certain isolates with alert values

CRE/CRPA Testing Objectives

- Identify isolates that produce a carbapenemase and classify the kind of carbapenemase present
- Effective identification of alert values
  - *E.g.*, pan-resistance, non-KPC CP-CRE, any CP-CRPA, *mcr*-type resistance
  - Immediate notification to CDC
  - Greater emphasis on screening
  - Possible submission of isolate to regional lab or CDC for additional testing
- 3-6 day turnaround time

DCLS CRE/CRPA Testing Algorithm



DCLS guidance for isolate submission

1. Pure, suspected CRE or CRPA isolate on slant or plate media
   - CRE
     - Isolate belongs to Enterobacteriaceae family
     - Resistant to at least one carbapenem
       - MIC of >4 µg/mL for imipenem, meropenem, or doripenem
       - MIC of >2 µg/mL for ertapenem
   - CRPA
     - Isolate identified as *P. aeruginosa*
     - Resistant to at least one carbapenem
       - MIC of >8 µg/mL for imipenem, meropenem, or doripenem
2. DCLS Clinical Microbiology/Virology Test Request Form
3. Copy of submitting clinical laboratory AST results
   - Required for DCLS to confirm that the isolate meets the CRE/CRPA definition for testing
   - To obtain preliminary indication that isolate may be pan-resistant

Source: https://dgs.virginia.gov/globalassets/business-units/dcls/documents/hot-topic-and-updates/final_cre-crpa-testing-instructions.pdf

CRE/CRPA Reporting and Turnaround Time

Results will be reported using secure communications:

Within **1 working day** of results:

- Report by phone any alert values to the submitting clinical laboratory and VDH, alert email sent to CDC ARLN
  - Further testing may be warranted and will be determined by the CDC
  - Isolate may be sent to ARLN Regional Lab and/or CDC for additional characterization (WGS analysis, additional AST, additional resistance mechanism testing)

Within **2 working day** of results:

- Report by phone all non-alert results to submitting clinical laboratory and VDH

Monthly:

- All CRE and CRPA testing results reported to CDC electronically

Disclaimer: Results are for surveillance purposes only and should be used to support infection prevention measures. Results should not be a substitute for diagnostic procedures or used to guide clinical decisions.

ARLN CRE Screening

- Mid-Atlantic regional lab performs free screening
- VDH submits request for screening
- Coordinate with VDH
- Swab kits available from DCLS
- Follow normal procedures
- Labs → DCLS → regional lab
- Point prevalence, admission or contact screening for index patient

Key Resources

CDC. Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE) – November 2015 Update CRE Toolkit. https://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html

CDC. Interim Guidance for Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs) (2015). https://www.cdc.gov/hai/outbreaks/mdro/index.html

CDC. Vital Signs: Containing Unusual Resistance. https://www.cdc.gov/vitalsigns/containing-unusual-resistance/index.html

HICPAC. 2007 Guidelines for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings https://www.cdc.gov/infectioncontrol/pdf/guidelines/isolation-guidelines.pdf

VDH CRE Website. http://www.vdh.virginia.gov/surveillance-and-investigation/hai/organisms/#tab-carabapenem-resistant-enterobacteriaceae-cre

DCLS CRE/CRPA Testing. https://dgs.virginia.gov/globalassets/business-units/dcls/documents/hot-topic-and-updates/final_cre-crpa-testing-instructions.pdf

Key Points

1. STOP TRANSMISSION (especially of CPOs)

2. VDH and DCLS are here to help

3. Review the VDH Checklist for Acute and Long-Term Care Facilities

http://www.vdh.virginia.gov/content/uploads/sites/13/2018/03/Attach_E3-CRE-Checklist-for-Acute-and-LTCF_2018-1.pdf

2018 National Healthcare Safety Network (NHSN) Updates

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Healthcare-Associated Infections and Antimicrobial Resistance Program
Virginia Department of Health

April 13, 2018

Patient Safety Component Protocol Changes for 2018

Throughout the Patient Safety Component Manual:

- "*i.e.*" replaced with "specifically"
  - List is all inclusive
  - Things not on the list are excluded
- "*e.g.*" replaced with "for example"
  - List may be a partial list
  - Other things not on list may be included

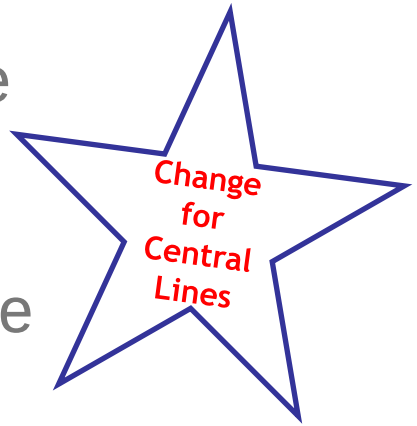
Patient Safety Component Protocol Changes for 2018

Throughout the Patient Safety Component Manual:

- Clarification: Specimens in patients awaiting organ harvest
  - "If the date of specimen collection is on or after the date of documentation of evidence of consent *AND* the patient is being supported for organ donation purposes, an event identified using the specimen culture result or microbiologic non-culture based diagnostic test result should not be reported as an HAI. The patient should, however, still be included in device and patient day denominator data collection."
  - No limitation to "brain dead" patients

Device Day Count for Determination of Device-Associated Infections in 2018

- Clarification:
  - Device Days for Denominator Counts: If the device was **in place prior to admission to the inpatient location**, the device day count begins with the admission date to the inpatient location.
  - Central Line Days for Device Attribution: For patients **admitted with a central line**, the number of days of device used to determine if the bloodstream infection (BSI) is a CLABSI are counted beginning with the first day of access in an inpatient location.



Counting Denominator Days for CLABSI Surveillance

Date	Admit	HD 2	HD 3	HD 4	HD 5	HD 6	HD 7
CL Status Any Type	CL in	CL in	CL in	CL in	CL in	CL in	CL in
Accessed	No	No	**Yes**	Yes	No De-accessed	No	No
Eligible for CLABSI Event	No	No	No	No	**Yes-Eligible CL**	Yes-Eligible CL	Yes-Eligible CL
CL Day			**CL Day 1**	CL Day 2	**CL Day 3**	CL Day 4	CL Day 5
Device Day	**Device Day 1**	Device Day 2	Device Day 3	Device Day 4	Device Day 5	Device Day 6	Device Day 7

HD = Hospital day
CL Day = Central line day count for making device-associated determinations (CLABSI event)
Device Day = Central line count for reporting device days as denominators in summary data

Scenarios where “Central Line” Field Should be Marked “No”

- Patient self-injection - Observed or suspected **injection** into their vascular access lines
  - **Within the BSI infection window period** of the positive blood culture
  - Documented specifically!
- Presence of extracorporeal membrane oxygenation/life support (ECMO) or ventricular assist device (VAD)
  - Device must be in place > 2 consecutive calendar days on the BSI date of event and is still in place on the date of event or the day before
  - Optional fields in 2018; Required in 2019/2020

Scenarios where “Central Line” Field Should be Marked “No”

- Epidermolysis bullosa (EB)
  - During current admission
  - Optional field in 2019; Required in 2020
- Munchausen Syndrome by Proxy (MSBP) – “Factitious Disorder Imposed on Another”
  - Confirmed or suspected
  - During current admission
  - Optional field in 2019; Required in 2020
- Group B *Streptococcus* identified from blood
  - Date of event during the first 6 days of life

Scenarios where “Central Line” Field Should be Marked “No”

- Pus at vascular site
  - Patient with both a central line and another vascular access device has pus at the other access site
    - Arterial catheters • Arteriovenous fistulae • Arteriovenous grafts • Atrial catheters (also known as transthoracic intra-cardiac catheters) • Hemodialysis reliable outflow (HERO) dialysis catheters • Intra-aortic balloon pump (IABP) devices • Non-accessed CL (those neither inserted nor used during current admission) • Peripheral IV or Midlines
  - Organism found in pus matches at least one organism found in blood
  - Pus specimen collected in the LCBI infection window period

Scenarios where "Central Line" Field Should be Marked "No"

- In the instances listed before, NHSN users should mark the "Central Line" risk factor field as "No"
- Meeting LCBI criteria in all of the situations noted result in setting a BSI repeat infection timeframe (RIT) and any associated central line days should be included in device counts for denominator summary data

Risk Factors	
*If ICU/Other locations, Central line: Yes No	Any hemodialysis catheter present: Yes No
*If Specialty Care Area/Oncology,	Extracorporeal life support present (e.g. ECMO): Yes No
Permanent central line: Yes No	Ventricular assist device (VAD) present: Yes No
Temporary central line: Yes No	
*If NICU,	
Central line, including umbilical catheter: Yes No	Location of Device Insertion: _____
Birth weight (grams):	Date of Device Insertion: ___/___/_____

BSI Event Form

Determining Catheter-association for UTI Surveillance

- Clarification:

Criterion	Urinary Tract Infection (UTI)
	Symptomatic UTI (SUTI) Must meet at least ***one*** of the following criteria:
SUTI 1a **Catheter-associated Urinary Tract Infection (CAUTI) in any age patient**	Patient must meet 1, 2, and 3 below: 1. Patient had an indwelling urinary catheter that had been in place for **> 2 days** on the **date of event** AND was either: • Present for any portion of the calendar day on the date of event†, **OR** • Removed the day before the date of event‡ 2. Patient has at least ***one*** of the following signs or symptoms: • fever (>38.0°C): To use fever in a patient > 65 years of age, the indwelling urinary catheter needs to be in place > 2 calendar days on **date of event**. • suprapubic tenderness* • costovertebral angle pain or tenderness* • urinary urgency ^ • urinary frequency ^ • dysuria ^

Multi-Step *Clostridium difficile* Testing

- Clarification:
  - When using a multi-testing methodology for *C. difficile* identification, the final result of the **last** test finding will determine if the CDI positive laboratory assay definition is met.
- Examples:
  - Example 1. EIA GDH Antigen (+), toxin (-) followed by PCR (+) for discrepant results. Report as a LabID event determined by the final test finding of PCR (+).
  - Example 2. PCR (+) followed by EIA GDH Antigen (+), toxin (-) for toxin confirmation. NOT a LabID event as final test finding is toxin (-).

Coming Down the Pipeline from CDC

- NHSN Infection Checklists
  - For each infection type
  - Modeled after the Tennessee HAI Checklists
- 2018 HAI Internal Validation Toolkit
  - Will include a data quality checklist for review prior to data submission
- Neonatal Component
- NICU Standardized Antimicrobial Administration Ratios (SAARs)
- Outpatient Procedure Component for Ambulatory Surgery Centers
- Educational Roadmap for New IPs

Key Resources

2018 NHSN Patient Safety Component Manual.
https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf

NHSN Training Materials.
https://www.cdc.gov/nhsn/training/patient-safety-component/index.html

NHSN Internal and External Validation Guidance/Toolkit.
https://www.cdc.gov/nhsn/validation/index.html

CDC NHSN Newsletters.
https://www.cdc.gov/nhsn/newsletters/index.html

VDH HAI/AR Program Newsletters.
http://www.vdh.virginia.gov/surveillance-and-investigation/hai/communication/

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http://community.apic.org/virginia/home

VDH HAI/AR Program

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Thank you – any questions?

Email us at:

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Extra Slides

2017 CRE LAB SURVEY RESULTS

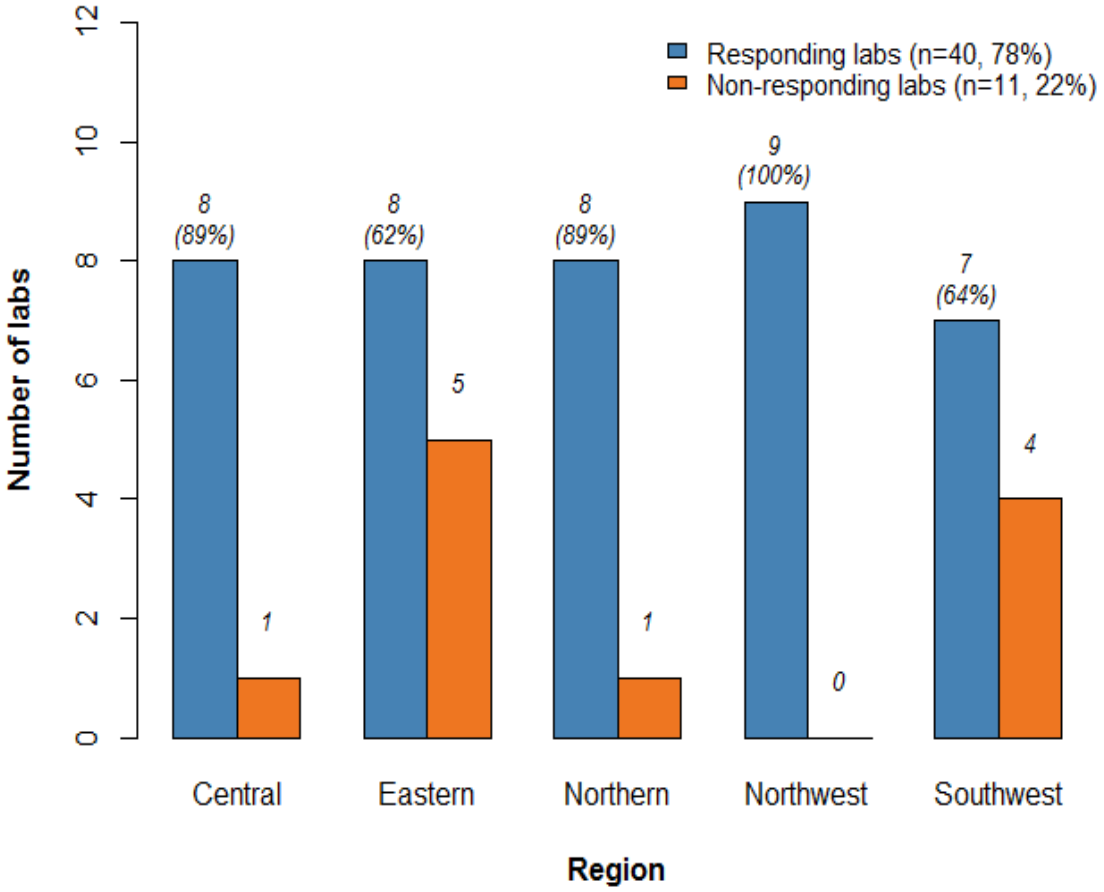
Purpose

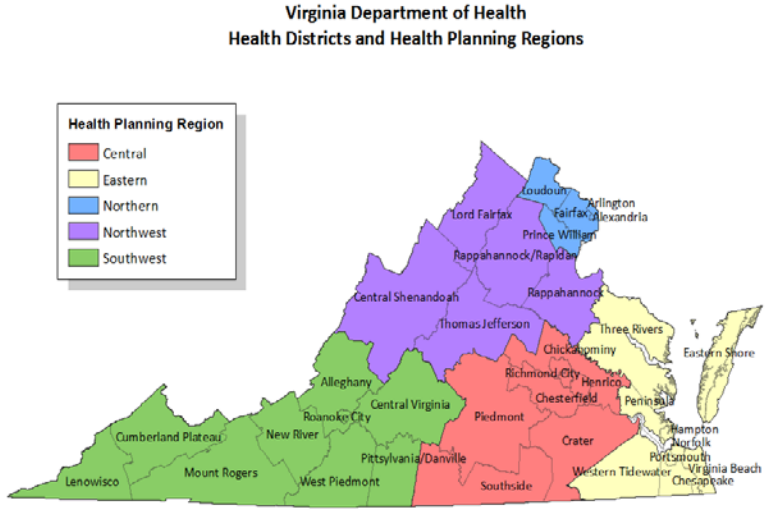
- Preparation for CRE testing implementation
- Estimate burden of CRE in 2016
- Understand lab capacity to identify CRE, detect carbapenemase, and test for resistance mechanisms

Methods

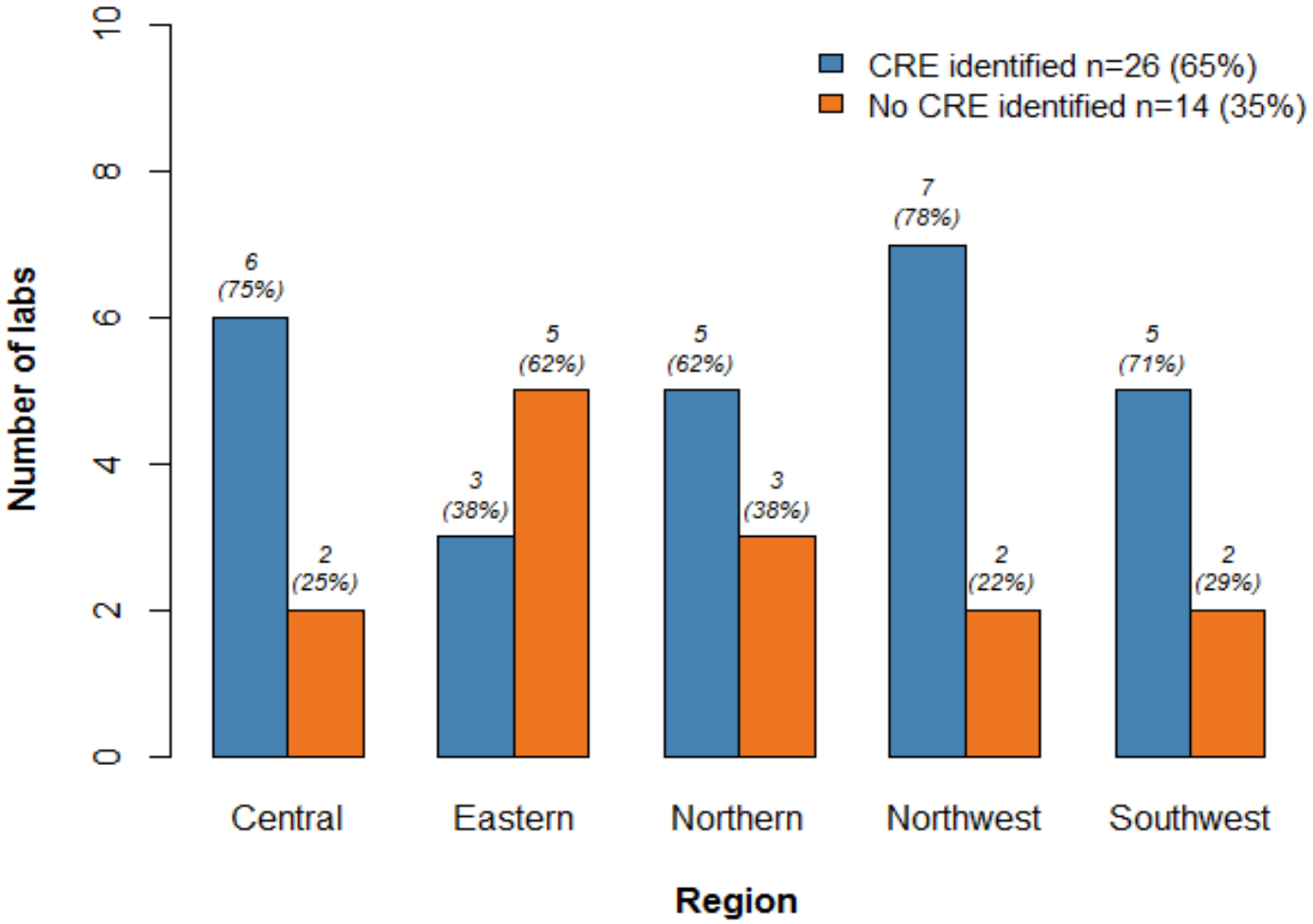
- REDCap survey sent to 51 sentinel laboratories via DCLS November 9, 2017

Response by region (N=51)

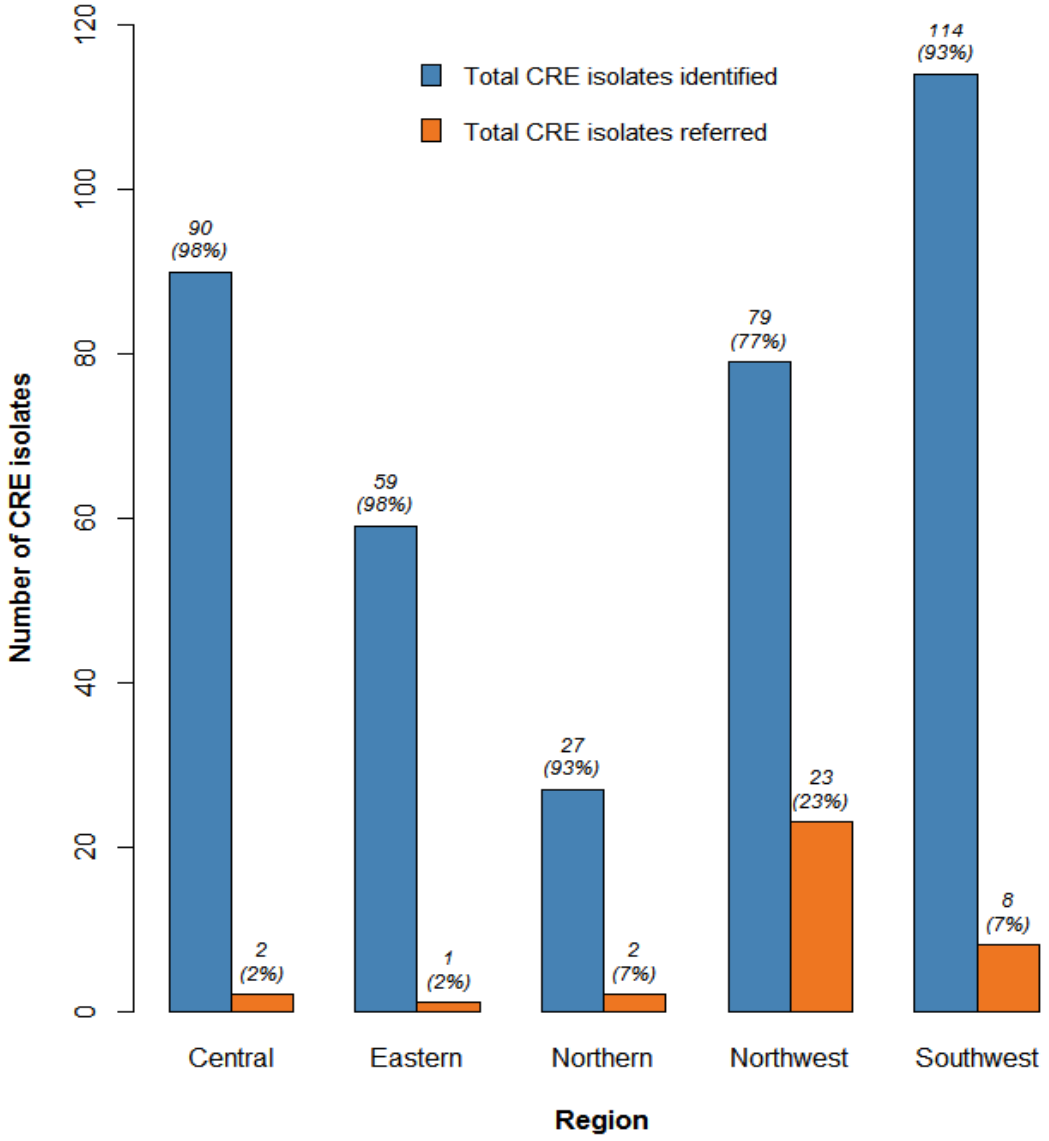




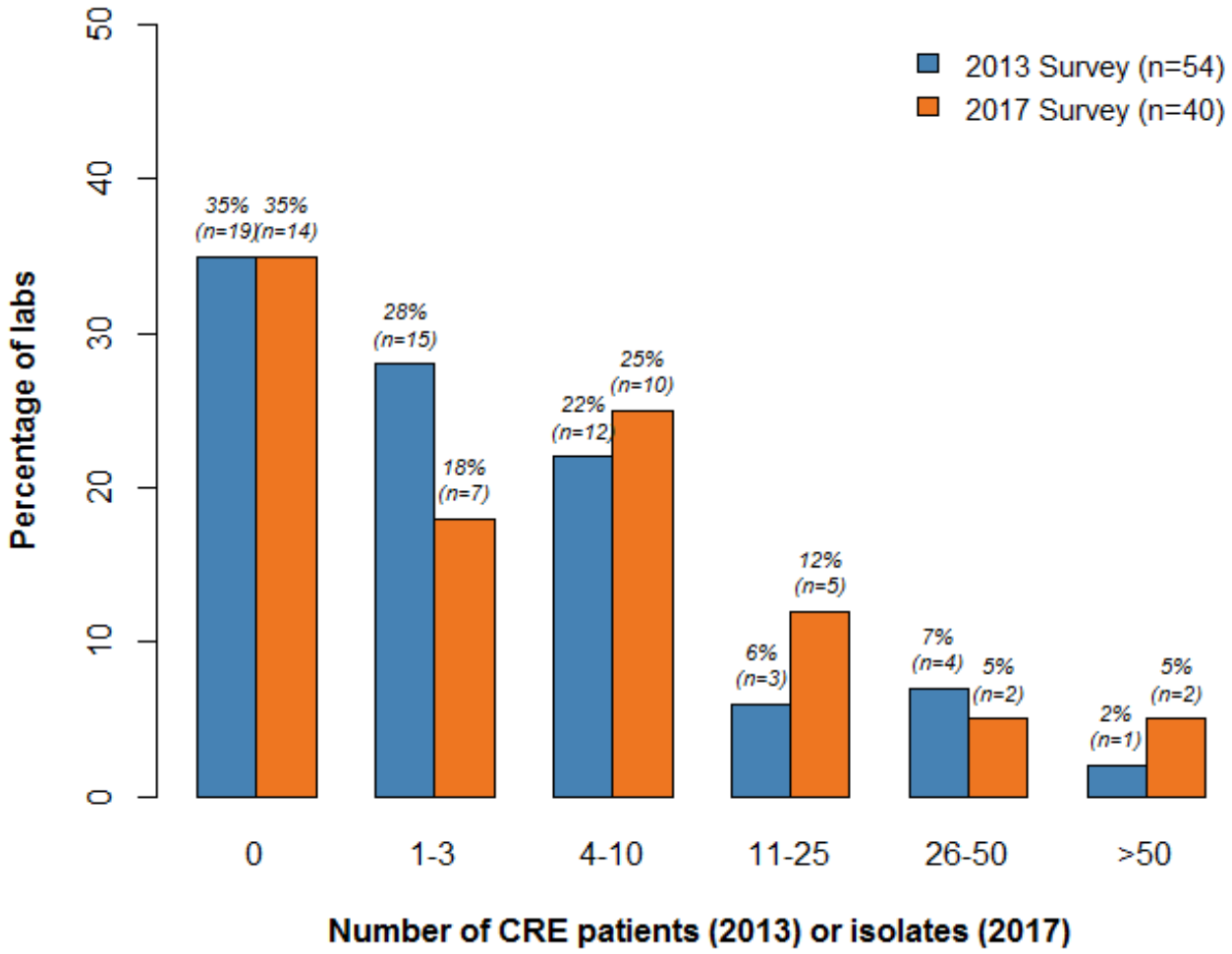
Labs reporting CRE by region in 2016 (n=40)



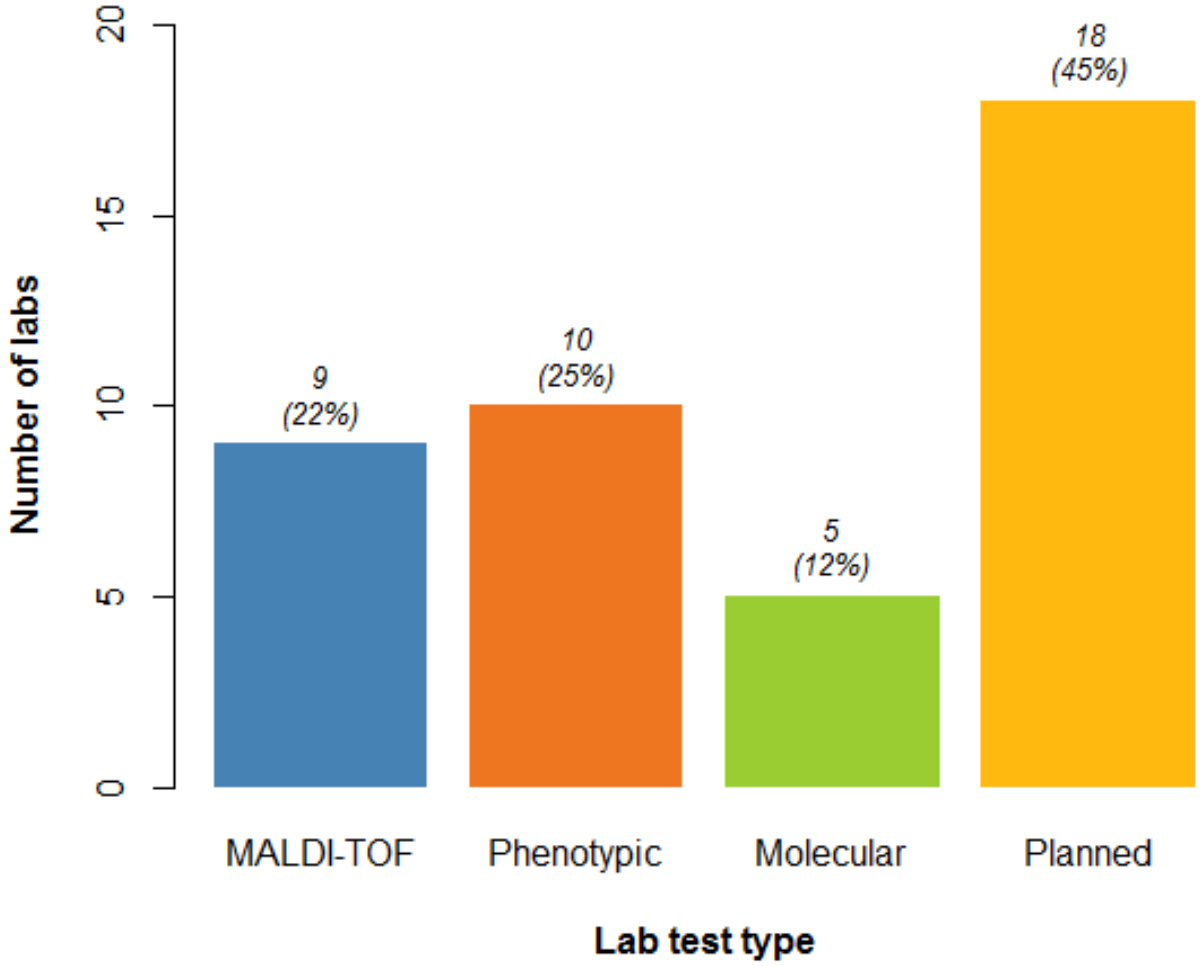
CRE isolates identified and referred by region (n=369)



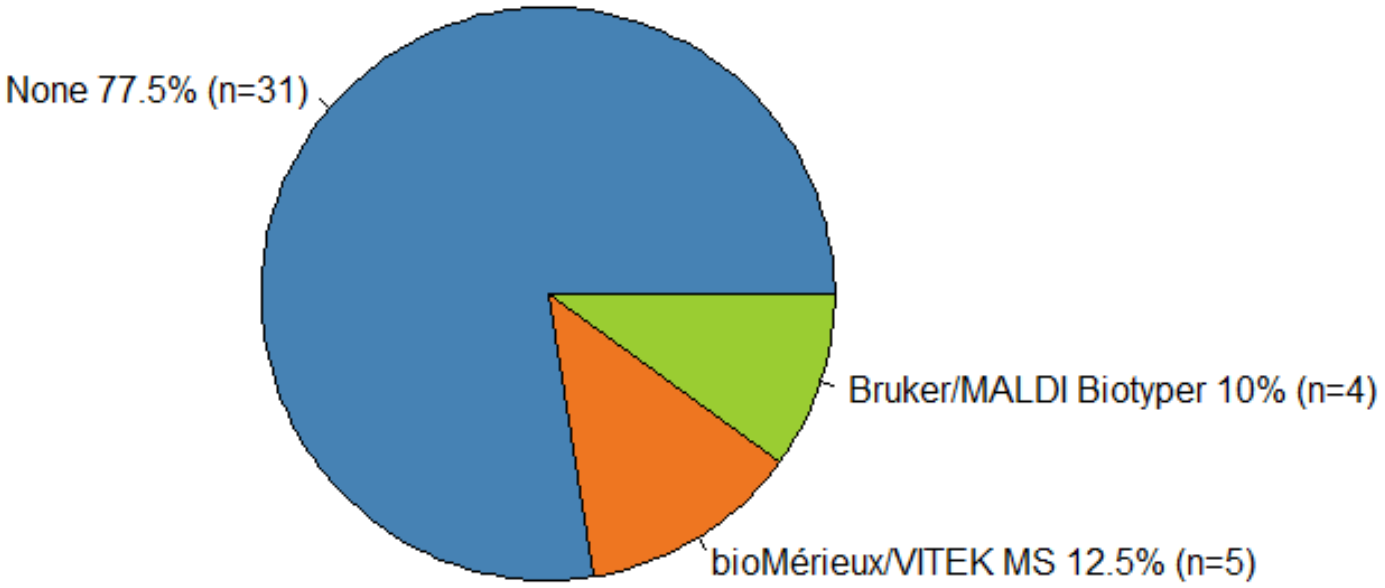
2012 v. 2016 CRE patients/isolates



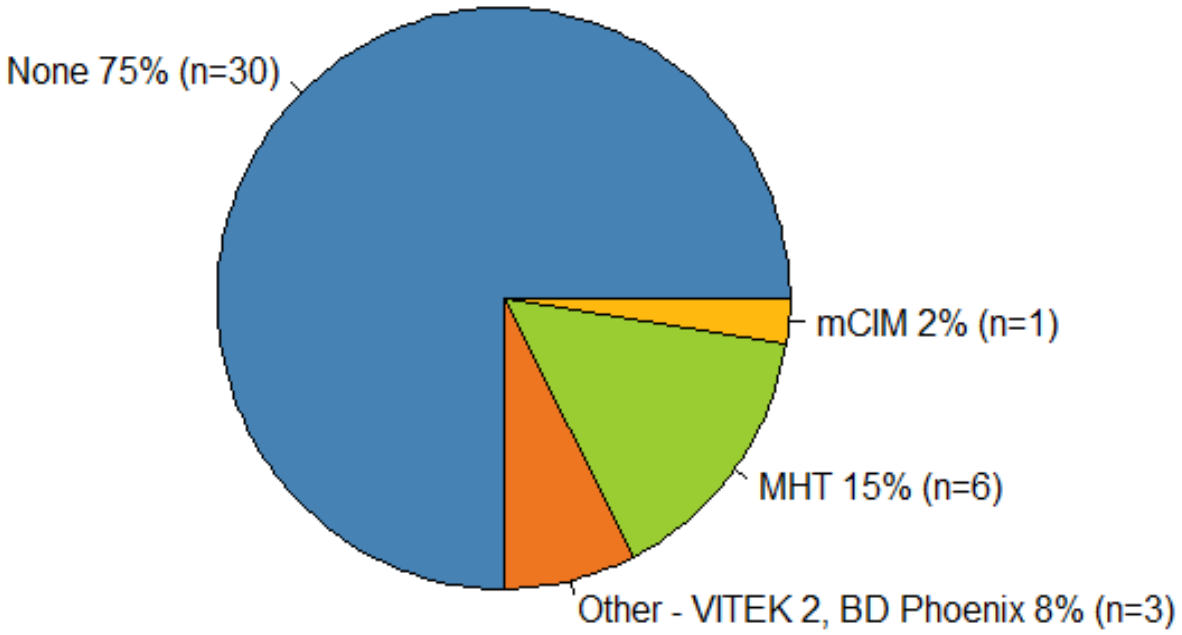
CRE testing technologies



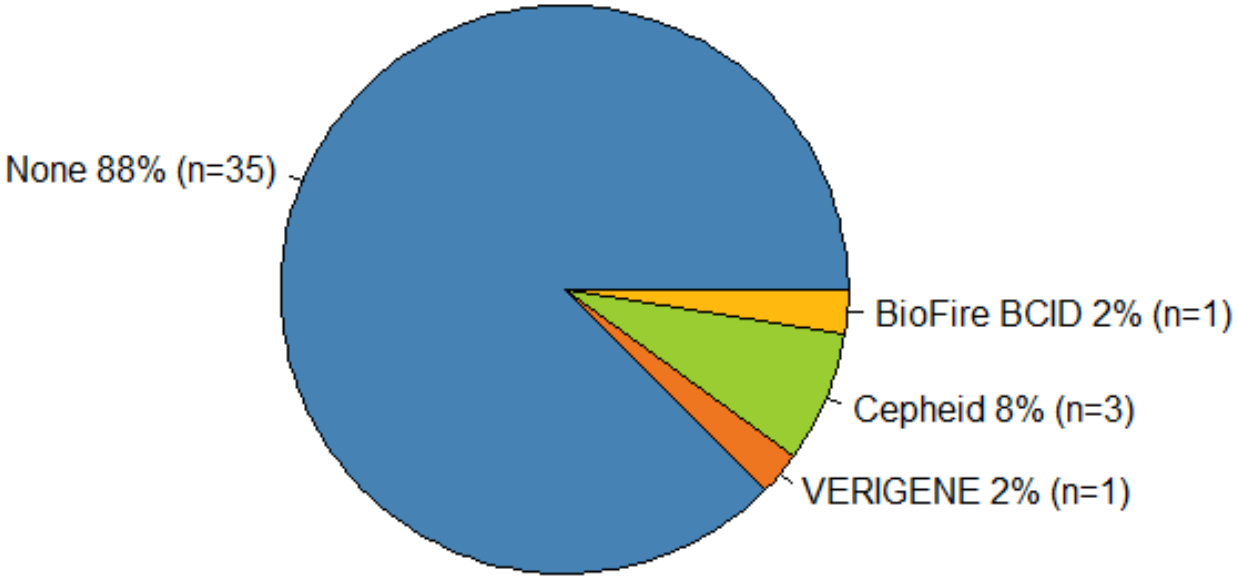
MALDI-TOF capacity (n=40)



Phenotypic testing capacity (n=40)



Molecular testing capacity (n=40)



New methods and technologies

Method/Technology	Number of labs
Antimicrobial susceptibility testing	1
Phenotypic testing • **CarbaNP** • **mCIM**	 6 5
Molecular testing • **PCR (Cepheid Xpert Carba-R)** • **BioFire**	 6 1