

# WEST VIRGINIA CARBAPENEM-RESISTANT ENTEROBACTERIACEAE (CRE) SURVEILLANCE REPORT

January 1, 2017—December 31, 2017

## INTRODUCTION

Enterobacteriaceae are a family of bacteria that commonly colonize the human digestive tract. These organisms are capable of causing a wide range of infections, including urinary tract infections, blood infections and sepsis, respiratory infections, and wound infections. Carbapenem-resistant Enterobacteriaceae (CRE) are organisms in this family that have developed resistance to a last line antibiotic class, the carbapenems. Infections with these organisms are often extremely difficult to treat and are associated with a high mortality rate, up to 50% in some studies.<sup>1</sup> Carbapenem resistance is spreading, making surveillance of CRE an important aspect of prevention and control efforts.

Since August 2013, laboratories testing specimens from West Virginia residents have been required to report cases of CRE to the local health department of the patient's county of residence within 1 week of detection (see 64CSR7 <http://apps.sos.wv.gov/adlaw/csr/readfile.aspx?DocId=25071&Format=PDF>). The following surveillance report summarizes data from CRE cases between January 1, 2016, and December 31, 2016.

## METHODS

For 2017 surveillance purposes, a case of CRE was defined as an Enterobacteriaceae isolate that is resistant to at least 1 carbapenem antibiotic OR a documented carbapenemase producer. There are 4 exceptions to this case definition: *Proteus* spp., *Providencia* spp., *Morganella* spp., and *Stenotrophomonas* spp. These organisms are intrinsically resistant to imipenem, and must be resistant to 1 carbapenem other than imipenem OR be a documented carbapenemase producer.

In previous years, a case of CRE had been classified as a case if the organism was an Enterobacteriaceae that was nonsusceptible to 1 of the following carbapenems: doripenem, meropenem, or imipenem and resistant to all of the following third-generation cephalosporins that were tested: ceftriaxone, cefotaxime, and ceftazidime. In 2015, the Centers for Disease Control and Prevention (CDC) adjusted its surveillance case definition in order to alleviate some confusion, and to catch any potentially missed carbapenemase producing organisms. West Virginia adjusted its case definition to align with that suggested by the CDC for 2016.

Two types of cultures are described, clinical and surveillance. Clinical cultures were taken in an effort to diagnose active infection, and surveillance cultures were rectal or fecal cultures taken to establish whether or not a patient was colonized with CRE.

Case counts are based on date of report. Each individual case is only counted 1 time regardless of how many lab results are received for each individual, the exception being a single individual reported as infected or colonized with more than 1 type of CRE organism.

The data were analyzed 2 ways: at the organism level (see Organism data) and at the patient level (see Demographics). Data were analyzed at the state, county, and regional levels. Variables with 0-4 cases are indicated with a value of "<5" in order to protect patient confidentiality. When variables have missing data, the number of cases included in the analysis is noted beside the variable name.

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<sup>1</sup> CDC, 2012 CRE Toolkit - Guidance for Control of Carbapenem-resistant *Enterobacteriaceae* (CRE)

As per the West Virginia Department of Health and Human Resources (DHHR), Bureau for Public Health, Division of Infectious Disease Epidemiology CRE Notification Protocol,<sup>2</sup> local health departments are expected to conduct an initial assessment of long term care facilities whose residents test positive for CRE. The assessment is typically conducted over the phone using the “CRE in Long Term Care Facilities Initial Assessment” questionnaire.<sup>3</sup> The intent of the interview is to assess the number of residents in the facility who either have active infections or are colonized, infection control measures in place, and whether they are using or have access to the CDC CRE Toolkit. From this assessment, local health departments and/or regional epidemiologists can gauge the knowledge of the facility’s staff and decide whether to proceed with additional interviews or site visits.

All analyses were conducted in SAS Version 9.4 and Microsoft Excel.

## RESULTS

### Organisms

From January-December 2017, 207 organisms were reported from 206 patients. One individual was diagnosed with infection with 2 or more different CRE organisms. The most frequently identified organism was *Enterobacter cloacae*, with 77 (37.2%) isolates. *Klebsiella pneumoniae* and *Escherichia coli* followed, each with 42 (20.3%) isolates (Table 1). The focus of the remainder of this report will be on *Enterobacter* species, *K. pneumoniae*, and *E. coli*. Any isolate not characterized to the species level is reclassified into the “Other” category as it cannot be grouped with any specific species.

Table 1. CRE Isolates 2017 West Virginia

Organism (N = 207)	Number (%)
<i>Enterobacter cloacae</i>	77 (37.2)
<i>Klebsiella pneumoniae</i>	42 (20.3)
<i>Escherichia coli</i>	42 (20.3)
<i>Enterobacter aerogenes</i>	18 (8.7)
<i>Proteus mirabilis</i>	9 (4.4)
<i>Serratia marcescens</i>	7 (3.4)
<i>Citrobacter freundii</i>	5 (2.4)
<i>Enterobacter species (spp.)</i>	4 (1.9)
<i>Klebsiella oxytoca</i>	2 (1.0)
<i>Morganella morganii</i>	1 (0.5)

Urine was the most common specimen to test positive for CRE, with 165 (79.7%) (Table 3). Two hundred and six cultures (99.5%) were clinical, and 1 (0.5%) was reported as surveillance. One case was reported to be epidemiologically linked to another CRE case; however, further investigation did not uncover evidence of transmission within the facility. Review of information entered into the West Virginia Electronic Disease Surveillance System (WVEDSS) and 2017 outbreak data did not reveal any evidence of outbreak related CRE cases in 2017. Data for cases that were not marked “No” for “Outbreak Related” were either missing or entered incorrectly.

<sup>2</sup> DIDE, 2016 CRE Notification Protocol. <http://www.dhhr.wv.gov/oeps/disease/AtoZ/documents/cre/cre-protocol.pdf>

<sup>3</sup> DIDE, 2016 CRE LTCF Initial Assessment. <http://www.dhhr.wv.gov/oeps/disease/AtoZ/Pages/CRE.aspx>

Table 3. CRE Isolates by Surveillance Region, West Virginia, 2017; N=207

CRE Isolates by Surveillance Region, West Virginia, 2017; N = 207						
	Northwest (N=23)	Northeast (N=44)	East (N=11)	South (N=54)	West (N=31)	Central (N=44)
<b>Organism Cultured</b>						
<i>Enterobacter cloacae</i>	9 (39.1%)	20 (45.5%)	4 (36.4%)	15 (27.8%)	11 (35.5%)	18 (40.9%)
<i>Enterobacter aerogenes</i>	0 (0%)	3 (6.8%)	0 (0%)	4 (7.4%)	7 (22.6%)	4 (9.1%)
<i>Escherichia coli</i>	3 (13.0%)	10 (22.7%)	4 (36.4%)	12 (22.2%)	3 (9.7%)	10 (22.7%)
<i>Klebsiella pneumoniae</i>	7 (30.4%)	7 (15.9%)	2 (18.2%)	12 (22.2%)	6 (19.4%)	8 (18.2%)
Other	4 (17.4%)	4 (9.1%)	1 (9.1%)	11 (20.4%)	4 (12.9%)	4 (9.1%)
<b>Type of Culture</b>						
Clinical	22 (95.7%)	44 (100%)	11 (100%)	54 (100%)	31 (100%)	44 (100%)
<b>Specimen Source</b>						
Urine	16 (69.6%)	40 (90.9%)	9 (81.8%)	45 (83.3%)	22 (71.0%)	33 (75.0%)
Respiratory	1 (4.4%)	2 (4.6%)	0	1 (1.9%)	4 (12.9%)	6 (13.6%)
Wound	4 (17.4%)	1 (2.3%)	1 (9.1%)	4 (7.4%)	3 (9.7%)	2 (4.5%)
Blood	1 (4.4%)	1 (2.3%)	0	4 (7.4%)	1 (3.2%)	1 (2.3%)
Tissue	0	0	1 (9.1%)	0	0	1 (2.3%)
Other	0	0	0	0	1 (3.2%)	1 (2.3%)
Rectal	1 (4.4%)	0	0	0	0	0
<b>Outbreak Related*</b>						
No	21 (91.3%)	40 (93.0%)	10 (90.9%)	53 (98.2%)	28 (93.3%)	44 (100%)
<b>Epi Linked to other CRE*</b>						
No	19 (82.6%)	39 (88.6%)	8 (72.7%)	50 (94.3%)	29 (96.7%)	42 (95.5%)

\*Percent < 100 indicates missing or incomplete data

## Demographics

The mean age of cases in 2017 was 65.0 years, with a range of 10 months to 98 years. One hundred and forty-five (70.4%) were female. The majority of cases were white, with 159 (79.1%). One hundred and sixty-five (80.1%) were identified as not Hispanic or Latino, and for 38 (18.9%), information about ethnicity was missing.

The highest number of cases was identified in Kanawha County with 28 (13.5%), followed by Raleigh County residents with 15 (7.3%). When analyzed by surveillance region, the Southern region reported 54 (26.1%) cases, followed by the Central and Northeast regions each with 44 (21.3%). Figure 3 shows the distribution of CRE cases by surveillance region.

Sixty-five (31.6%) cases were hospitalized at the time of specimen collection, and 14 (6.9%) died. Fewer than 5 deaths occurred in any surveillance region. Of the 33 (15.9%) cases who resided in long term care facilities, assessments were performed for 28 (84.9%). An assessment was not performed for 4 (12.1%) cases, and 1 (3.0%) result was missing.

Table 4. CRE Cases by Demographic Variable and Surveillance Region, West Virginia, 2017; N=206

CRE Cases by Demographic Variable and Surveillance Region, West Virginia, 2017; N=206						
	Northwest (N=23)	Northeast (N=44)	East (N=11)	South (N=53)	West (N=43)	Central (N=44)
<b>Age, years (Avg. or N (%))</b>	66.6	67.3	66.8	66.1	66.7	68.3
0-18	0	0	<5	<5	<5	0
19-35	<5	<5	0	<5	0	<5
36-53	5 (21.7%)	8 (18.2%)	<5	11 (20.8%)	5 (16.1%)	6 (13.6%)
54-71	5 (21.7%)	12 (27.3%)	<5	17 (32.1%)	8 (25.8%)	21 (47.7%)
≥72	12 (52.2%)	21 (47.7%)	5 (45.5%)	22 (41.5%)	17 (54.8%)	15 (34.1%)
<b>Sex</b>						
Female	18 (78.3%)	31 (70.5%)	10 (90.9%)	35 (66.0%)	20 (64.5%)	31 (70.5%)
<b>Race</b>						
White	20 (90.9%)*	37 (90.2%)*	8 (72.7%)*	38 (71.7%)*	29 (93.6%)*	27 (62.8%)*
<b>LTCF Resident</b>						
Yes	9 (39.1%)*	6 (13.6%)*	<5	8 (15.1%)*	<5*	5 (11.4%)*
<b>Hospitalized</b>						
Yes	7 (30.4%)	17 (38.6%)*	<5*	14 (26.4%)*	11 (35.5%)*	12 (27.3%)*
* indicates Missing or Unknown data						

CRE incidence rates for the 6 surveillance regions were calculated per 100,000 population using 2010 Census data. Statewide, the rate of new CRE cases identified was 13.4 per 100,000 persons. The Southern region of the state saw the highest incidence with 16.8 new CRE cases per 100,000 persons (Table 5).

Table 5. CRE Incidence by Surveillance Region, West Virginia, 2017

CRE Incidence by Surveillance Region, West Virginia, 2017			
	Population (2010 Census)	2017 Cases (No. of Organisms)	2017 Incidence (per 100,000 population)
<b>South</b>	322,213	54	16.8
<b>Northeast</b>	296,912	44	14.8
<b>Central</b>	312,852	44	14.1
<b>West</b>	313,985	31	9.9
<b>Northwest</b>	309,445	23	7.4
<b>Eastern</b>	297,587	11	3.7
<b>State Total</b>	<b>1,540,142</b>	<b>207</b>	<b>13.4</b>

Incidence was also calculated for each county and is shown per 10,000 population to more accurately reflect the average population size of West Virginia counties. Figure 2 shows CRE case counts by county.

Figure 1. CRE Incidence per 10,000 Population by County, West Virginia, 2017

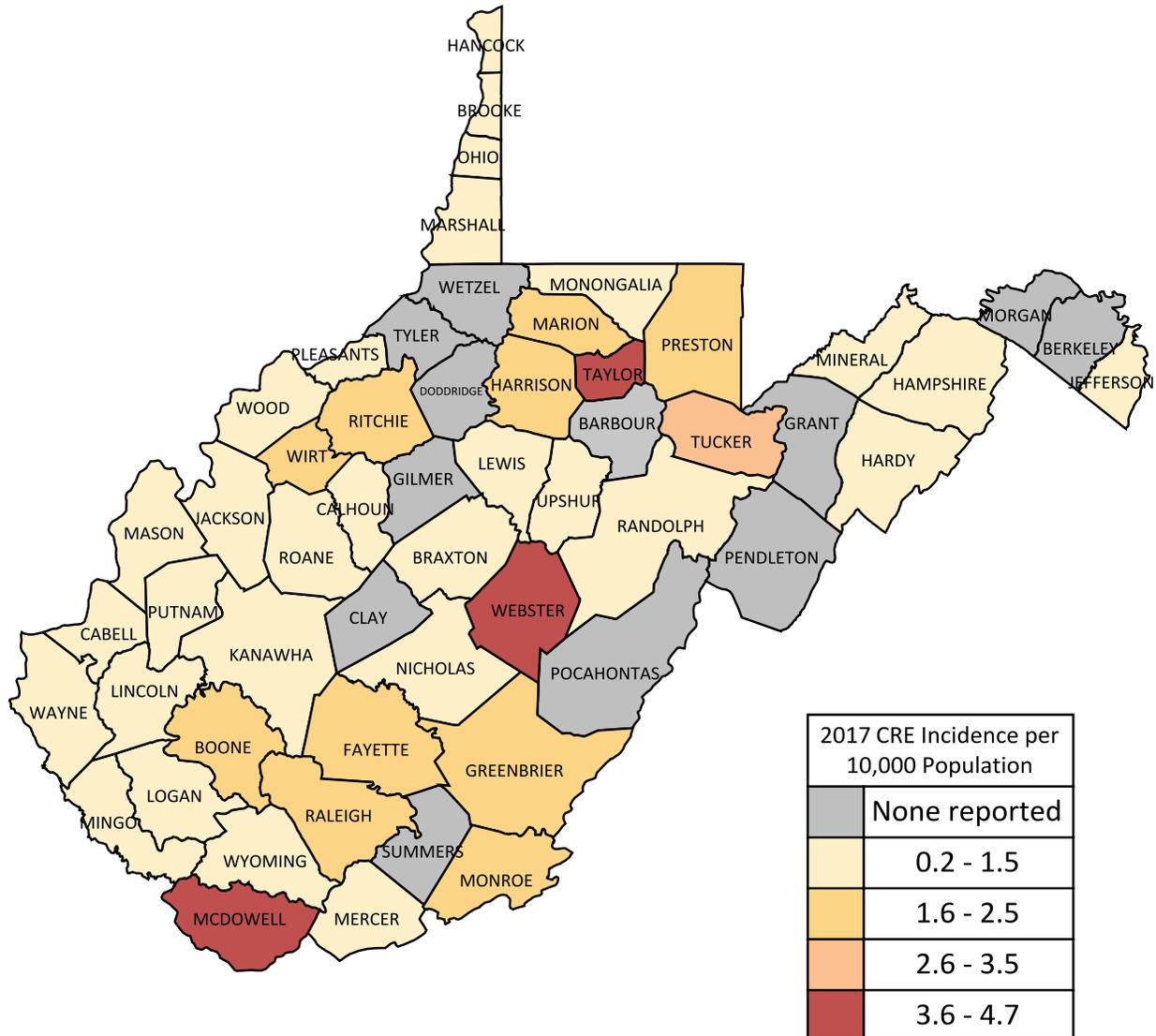
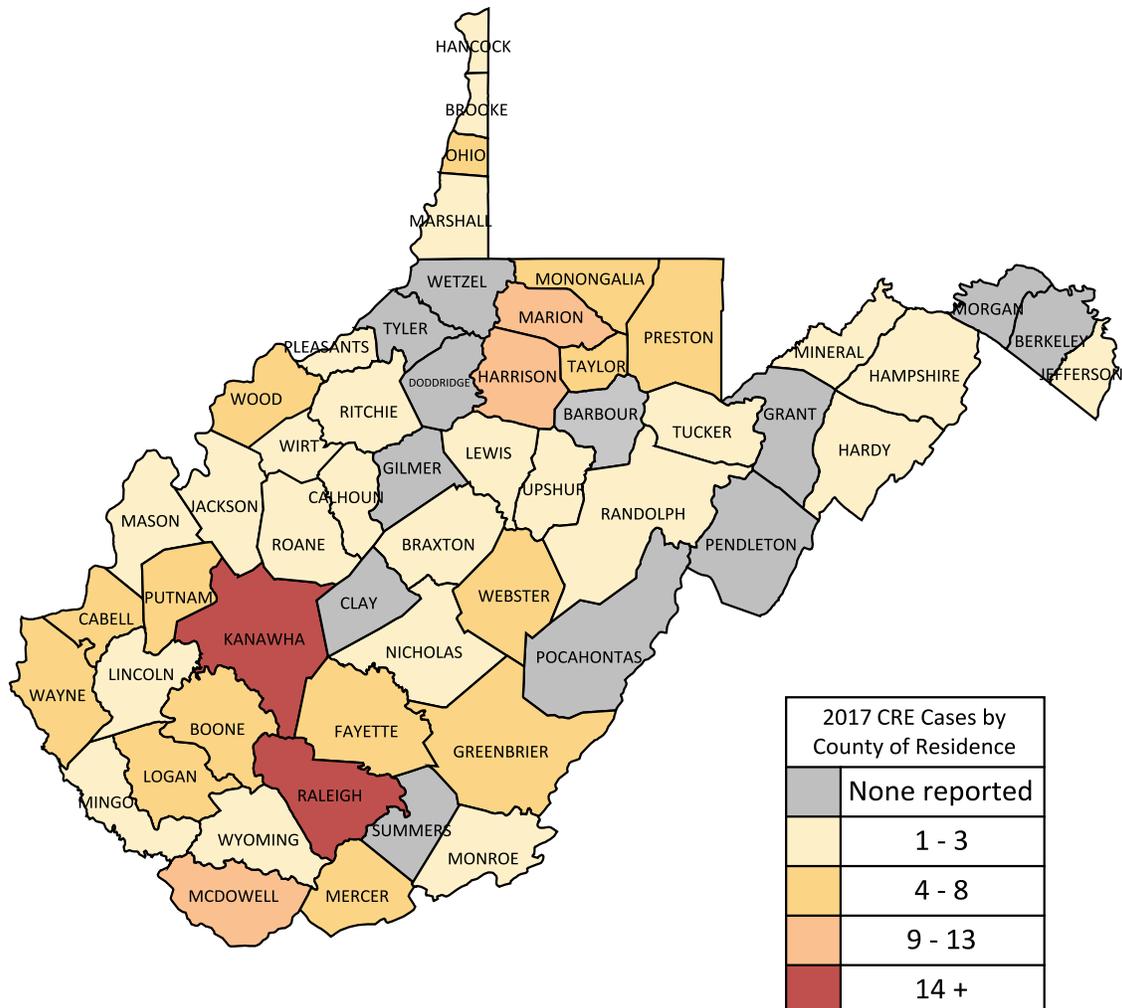


Figure 2. CRE Case Counts by County, West Virginia, 2017; N=207

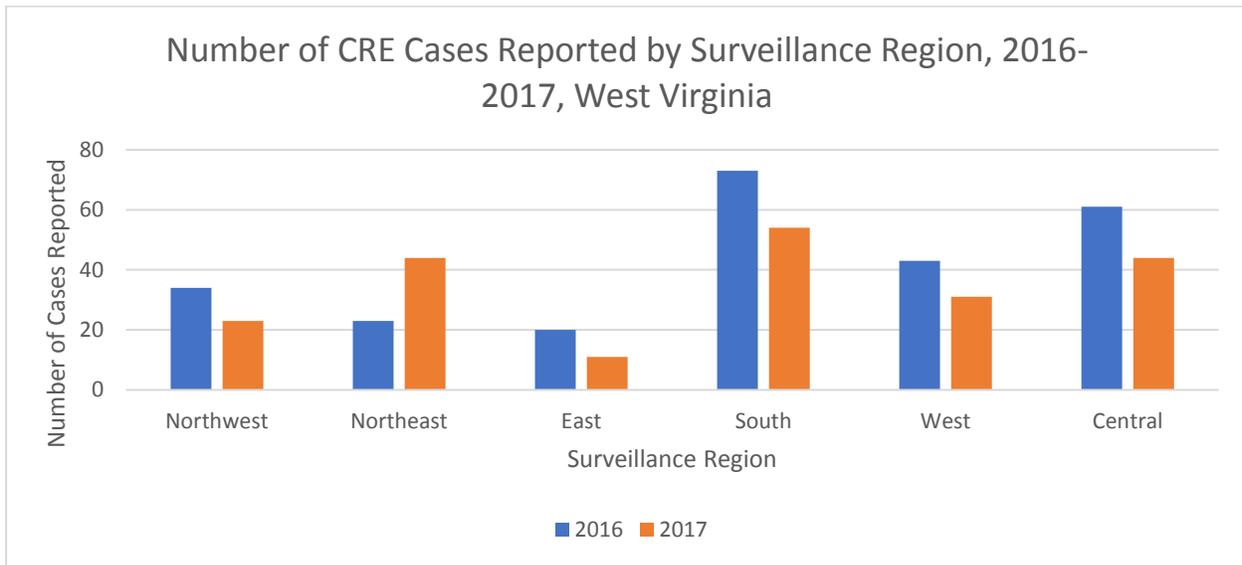


## DISCUSSION

The spread of carbapenem resistance among Enterobacteriaceae is considered an urgent public health threat by the CDC. The data presented in this report paint a concerning picture of CRE’s foothold on West Virginia. Although there are still counties not yet reporting cases, health facilities throughout the state should implement the CDC CRE prevention and control plan as no health facility is likely to remain unaffected.

Comparison to previous years was not possible for 2016 due to a major change in case definition. Such a comparison is possible between 2016 and 2017. Overall, West Virginia saw an 18.5% decrease in reports of new CRE cases. Four of 5 surveillance regions experienced a decrease, with the exception of the Northeast Region. CRE reports increased by 91.3% for the Northeast Region following the implementation of electronic laboratory reporting (ELR) for a major university medical system.

Figure 3. Number of CRE Cases Reported by Surveillance Region, West Virginia, 2016-2017



A small portion of CRE cases identified during 2017 reported hospitalization at the time of specimen collection, and review of investigation details showed that many cases did not report extensive health care exposures. In order to better assess potential sources of infection and/or transmission, several variables were added to the CRE case investigation forms for 2018. These variables were selected based on literature review, review of protocols and investigation forms used in other states where CRE is reportable, and West Virginia's own population characteristics. Additional variables include homelessness, admission to intensive-care units (ICU), home health care utilization, antibiotic prescriptions, and indwelling devices in place 2 calendar days prior to culture.

There are 61 licensed home health agencies providing services to patients across the State. In 2015, home care professionals made 1,152,305 visits to 51,153 clients.<sup>4</sup> To date, there is very little literature available regarding the impact of home health services on the spread of multi-drug resistant organisms. West Virginia has not developed any educational materials or resources specifically targeting home health care providers. The purpose for adding home health care utilization to CRE case investigation is to assess the need for educational intervention with these agencies, and to identify whether exposure to home health care services is a risk factor for CRE infection.

West Virginia maintains the highest rate of antibiotic prescription in the country. Outpatient providers cited numerous barriers to appropriate prescribing during a 2016-2017 knowledge, attitudes, and practices survey. Patient satisfaction surveys and a general lack of knowledge among patients were the most frequently described challenges, regardless of practitioner level (physician, nurse practitioner, or physician's assistant). The State intends to collect data regarding antibiotic exposure within the 6 months prior to positive culture to establish a correlation between CRE incidence and antibiotic consumption in the regions most affected by both high rates of antibiotic prescription and new CRE case identification. These data may be used to further emphasize the importance of antibiotic stewardship efforts in outpatient settings.

<sup>4</sup> West Virginia Health Care Authority, 2016 Annual Report. <https://hca.wv.gov/data/Reports/Documents/AnnualRP2016>

These data should be interpreted with some caution. West Virginia conducts passive surveillance of CRE and relies on laboratory or facility reporting of cases. Although CRE is a reportable condition for laboratories in West Virginia, some cases may go unreported. Determining the true cause for hospitalization is not possible during the analysis of these data as the information gathered pertains only to patient status at the time of specimen collection. True cause of death is similarly unclear.

There are some limitations to determining an accurate CRE incidence, chief among them assessing the population actually at risk. While some CRE infections may be acquired in the community, the majority have historically been associated with exposure to health care facilities and prolonged use of broad spectrum antibiotics. Hospital populations are not stable, making it difficult to ascertain who is most at risk. Though somewhat more stable, nursing home populations change over the course of a year as well. The number of people residing in nursing homes is also relatively small, despite a generally older population in West Virginia. According to the Kaiser Family Foundation,<sup>5</sup> the population residing in West Virginia certified nursing facilities was 8,852 in 2014—a mere 0.5% of the estimated total state population in 2014. As the rates for this report were calculated using the West Virginia population as a whole, the results should be interpreted with some caution, and may be much higher than stated here. Additional studies would need to be conducted to accurately discern the most important risk factors for developing an infection with a carbapenem resistant organism in West Virginia.

West Virginia does not currently track which laboratories perform resistance mechanism testing, such as modified Hodge testing, to detect carbapenemase production among CRE isolates. This type of testing is not necessary to direct clinical care of patients, but it is useful in planning aggressive infection prevention efforts in areas with a high prevalence of carbapenemase producing CRE organisms (CP-CRE). Carbapenemases, enzymes that inactivate carbapenem and many other classes of antibiotics, are typically located on mobile bits of genetic material called plasmids. These plasmids are easily exchanged between different bacteria, thus facilitating rapid spread of carbapenem resistance. The CDC recommends more stringent infection prevention practices in areas where CP-CRE are prevalent as these organisms are suspected to be responsible for much of the spread throughout the country.<sup>6</sup>

Despite the limitations, these data have implications for important infection prevention activities. Health care facilities of all types in all regions of the state should adhere to recommendations for standard and contact precautions for patients who are either infected or colonized with any multi drug resistant organism (MDRO), and especially CRE organisms. Special attention must be paid to hand hygiene practices and personal protective equipment (PPE) usage among health care facility staff, and facilities should be conducting regular audits of personnel hand hygiene and PPE compliance. Tools to facilitate the implementation of these audits are available from DHHR's Division of Infectious Disease Epidemiology (DIDE). A robust infection prevention program also includes antibiotic stewardship implemented facility wide. These programs should include appropriate use guidelines for first line treatments of common conditions that are supported by evidence-based practices. Educating providers, patients, and the general public on the dangers of overusing antibiotics remains an important investment of time and effort on the part of state and local health departments.

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<sup>5</sup> Kaiser Family Foundation, 2016 Total Number of Residents in Certified Nursing Facilities. <http://kff.org/>

<sup>6</sup> CDC, Healthcare-associated Infections (HAIs)-FAQs about Choosing and Implementing a CRE Definition.