

What is Lurking Beneath the Surface?

The War Against Superbugs

Monique Dodd, PharmD, PhC, MLS(AMCP)^{CM}

Clinical Solutions Specialist

TriCore Reference Laboratories

monique.dodd@tricore.org

July 27, 2018



Disclosures

**Employee of TriCore Reference
Laboratories**

Objectives

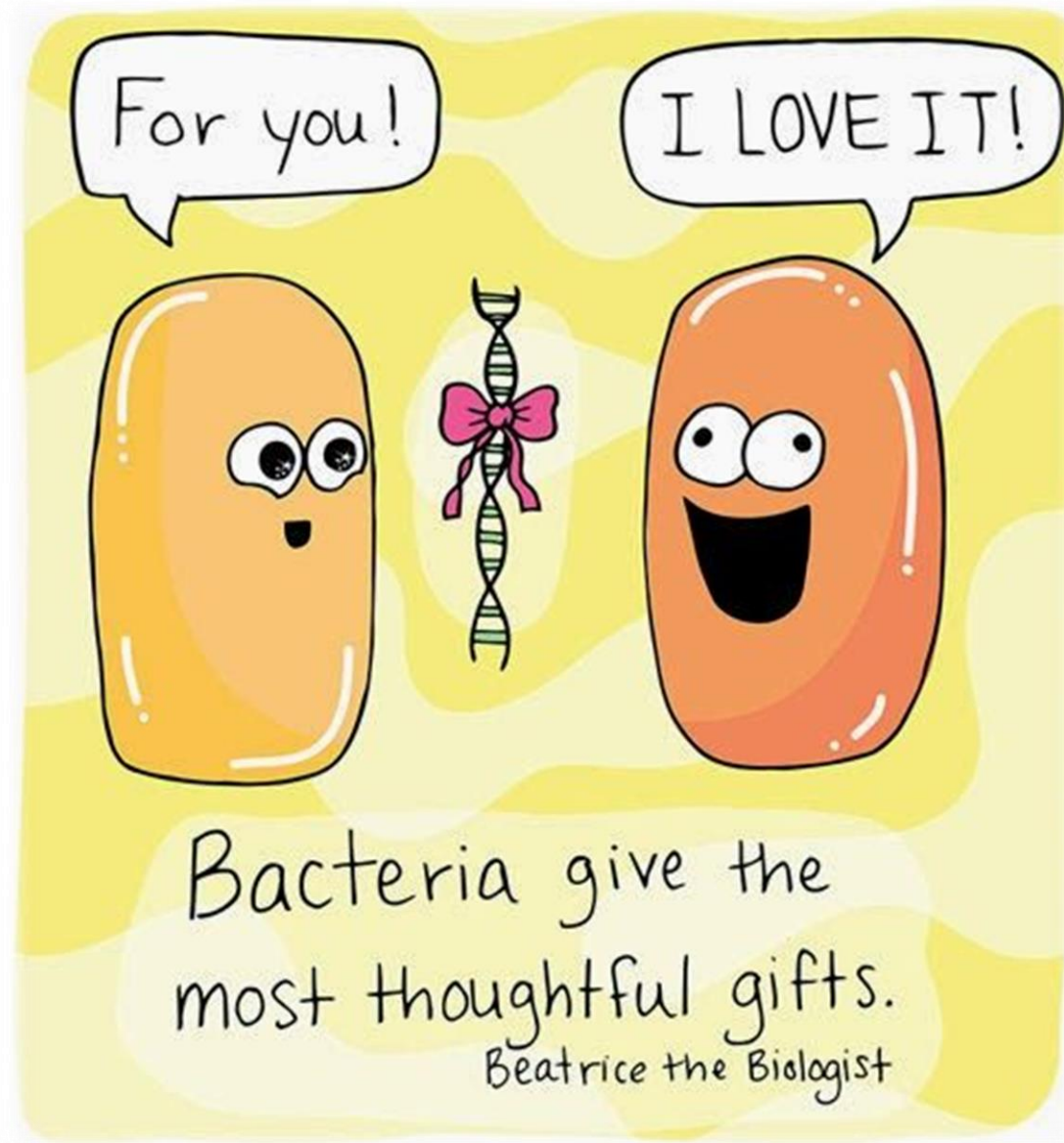
At the end of this presentation, the attendee will be able to:

1. Summarize the clinical and economic impact of the most concerning superbugs encountered in clinical practice.
2. Discuss regulatory initiatives to combat antimicrobial resistance.
3. Discuss lab initiatives and other statewide efforts targeting antimicrobial resistance in the state of New Mexico.



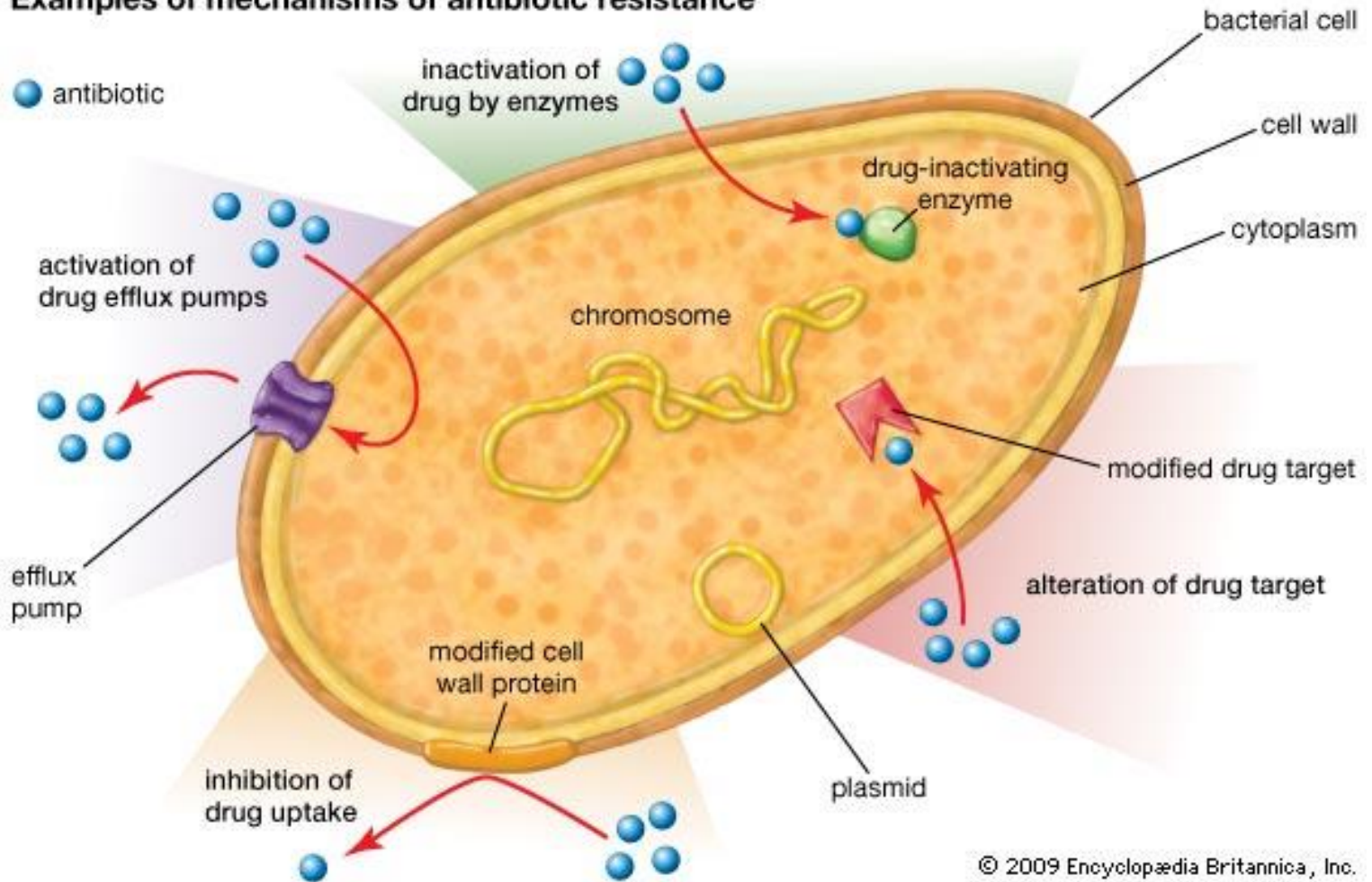
The War Against Superbugs



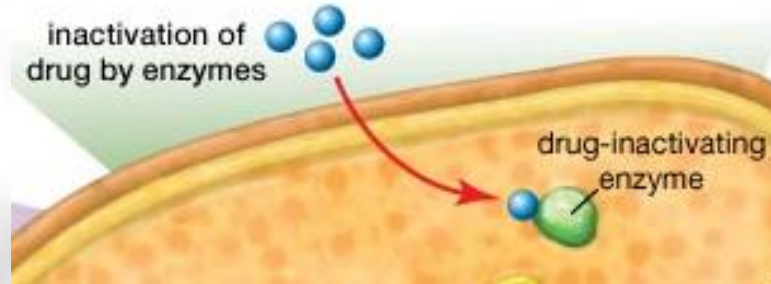


Mechanisms of Resistance

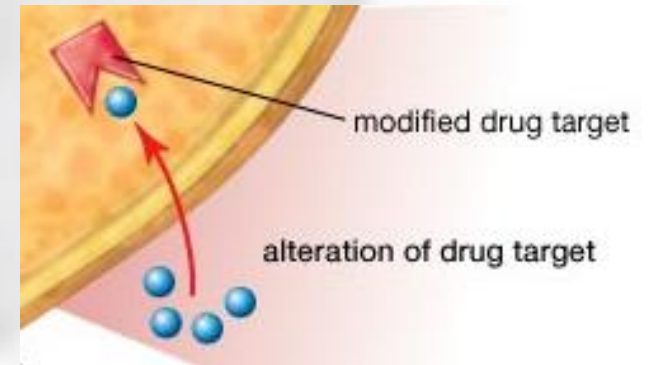
Examples of mechanisms of antibiotic resistance



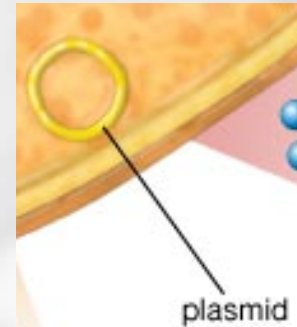
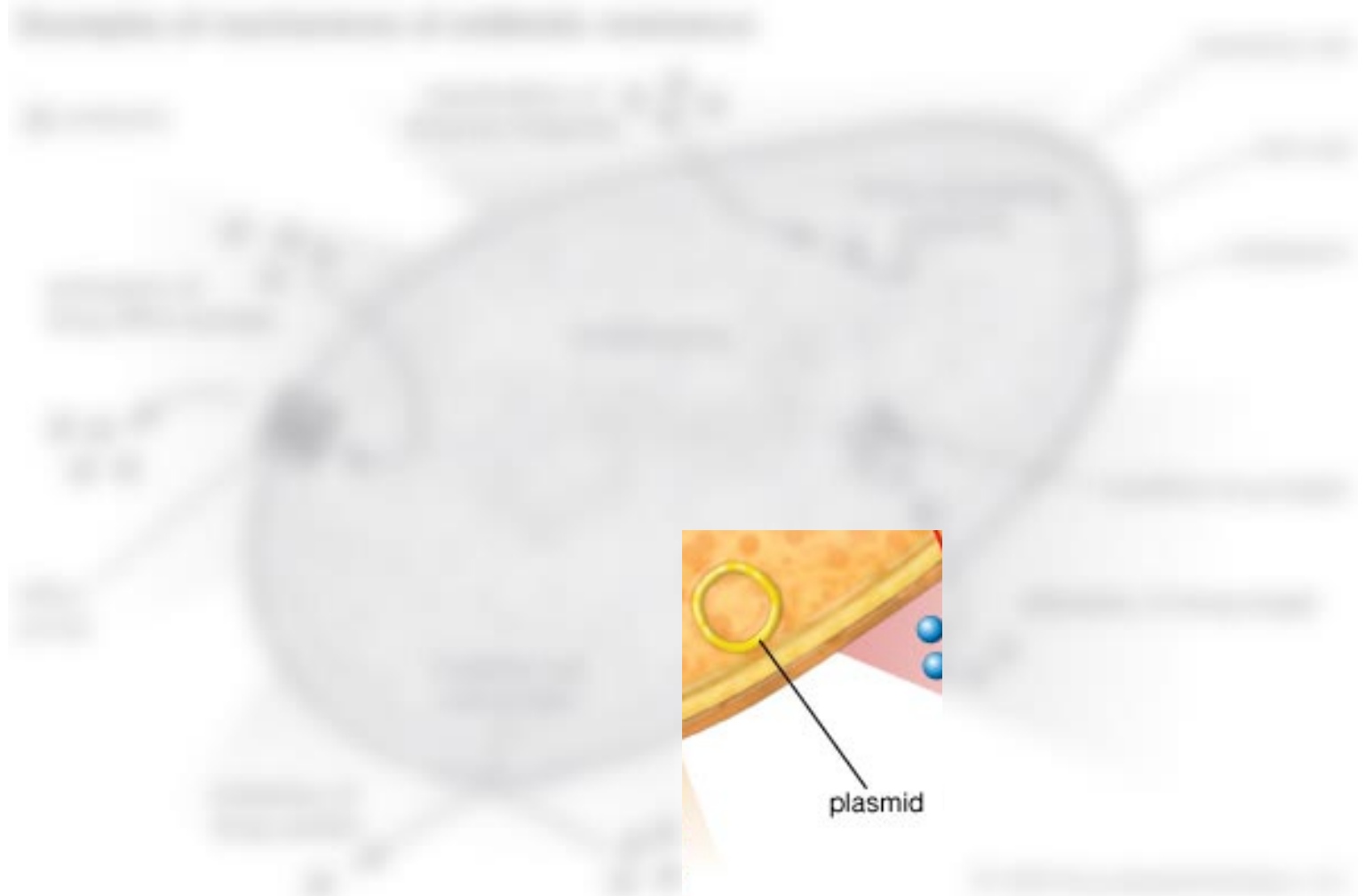
Mechanisms of Resistance



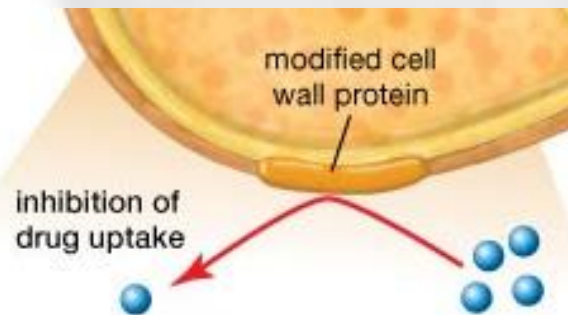
Mechanisms of Resistance



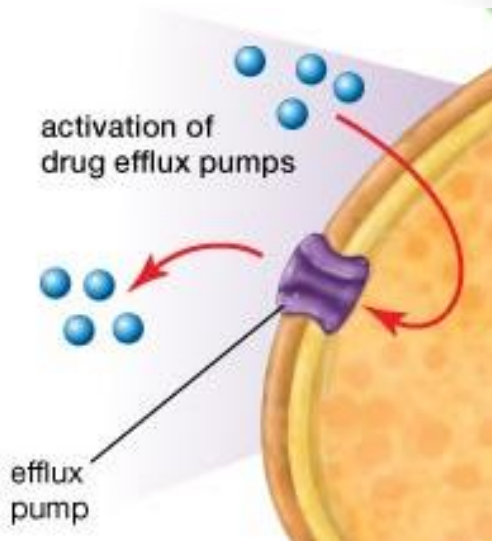
Mechanisms of Resistance



Mechanisms of Resistance



Mechanisms of Resistance



Other Factors of Antibiotic Resistance



Infection control



Bacterial population density



High risk patient populations



Global travel

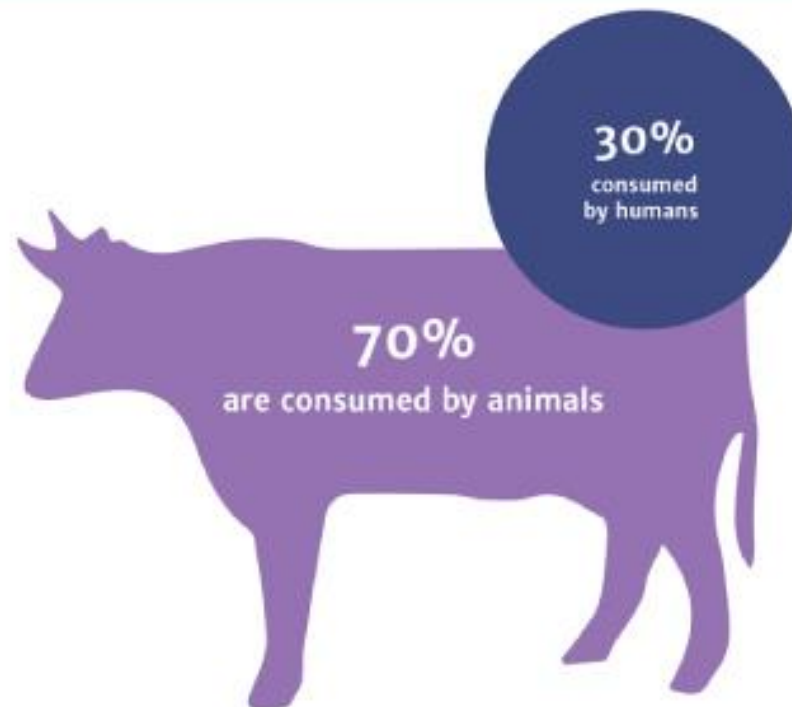


Limited rapid diagnostics



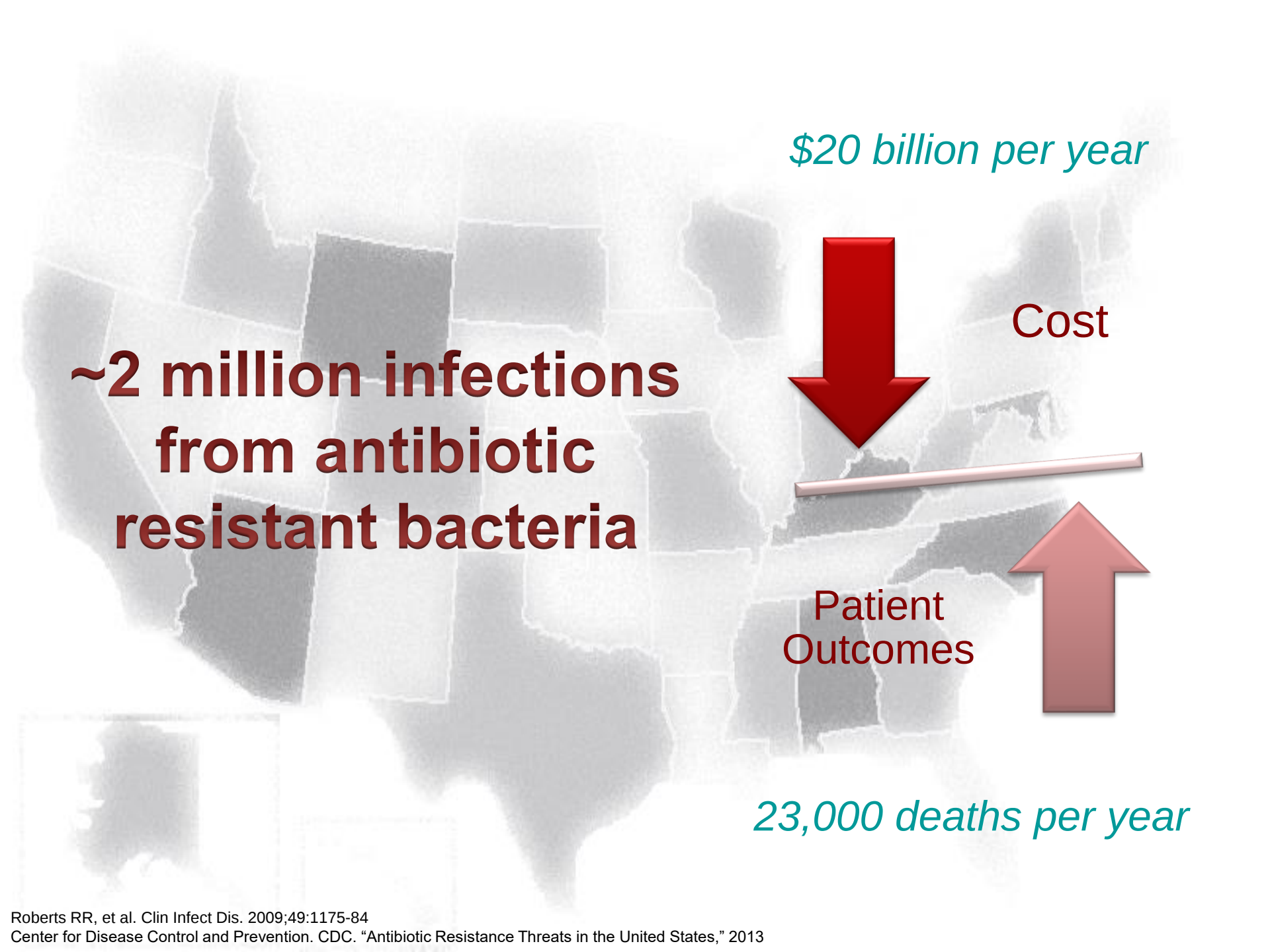
Lack of vaccines

ANIMALS IN THE USA CONSUME MORE THAN TWICE AS MANY MEDICALLY IMPORTANT ANTIBIOTICS AS HUMANS



Source: Animal consumption figure of 8,893,103kg from FDA, 2012. Human consumption of 3,379,226kg in 2012 based on calculations by IMS Health. The figures are rounded from 72.5% used in animals and 27.5% used in humans.

 Review on
Antimicrobial
Resistance



**~2 million infections
from antibiotic
resistant bacteria**

\$20 billion per year

Cost

Patient
Outcomes

23,000 deaths per year

Total Number of New Antibacterial Agents

0 2 4 6 8 10 12 14 16



**ANTIBIOTIC
DEVELOPMENT
IS DWINDLING**

Source: *The Epidemic of Antibiotic-Resistant Infections*, CID 2008;46 (15 January)
Clin Infect Dis. (2011) May 52 (suppl 5): S397-S428. doi: 10.1093/cid/cir153

2014

- Dalvance (dalbavancin)
- Orbactive (oritavancin)
- Sivextro (tedizolid)
- Zerbaxa (ceftolozane/tazobactam)

2015

- Avycaz (ceftazidime/avibactam)

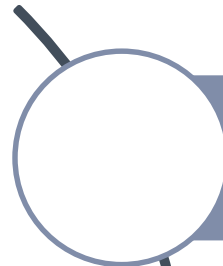
2017

- Baxdela (delafloxacin)
- Vabomere (meropenem/vaborbactam)

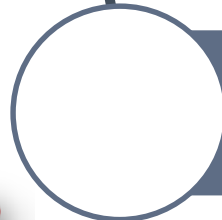
Post-antibiotic Era?

Antibiotic-resistant Organisms of Most Concern

Urgent:



Clostridium difficile

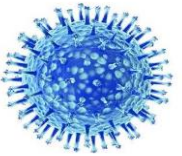


Carbapenem-resistant
Enterobacteriaceae



Drug-resistant *Neisseria
gonorrhoeae*

Clostridium difficile



250,000 infections



14,000 deaths



\$1M in excess medical costs



Key Recommendations



Unexplained and new-onset ≥ 3 unformed stools in 24 hours

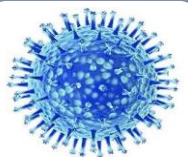


Oral vancomycin or fidaxomicin is recommended over metronidazole



Repeat testing (within 7 days) during same episode of diarrhea

Carbapenem-resistant Enterobacteriaceae



140,000 infections



Mortality of 26-44%



\$147M-\$553M in
excess medical costs



Case Definitions

Carbapenem-resistant enterobacteriaceae (CRE)	Enterobacteriaceae that have resistance to antibiotics in the class of carbapenems
---	--

Carbapenamase-producing CRE

Resistant to at least one carbapenem

And one of the following:

Positive for carbapenemase production by a phenotypic test
(e.g. Modified Hodge, Carba NP positive)

OR

Positive for known carbapenemase resistance mechanism
(e.g., Carba-R positive)

Carbapenemase genes are commonly transmitted on plasmids

KPC	Klebsiella pneumoniae carbapenemase
NDM	New Delhi metallo-beta-lactamase
IMP	Imipenemase metallo-beta-lactamase
VIM	Verona integron-encoded metallo-beta-lactamase
OXA-48	Oxacillinase-48

KPC is the most widespread in the US

How to Treat?

Discuss with your antimicrobial stewardship team

Infection Source	Core Drugs	Possible Adjunct Drugs
Blood	High dose meropenem + polymyxin B	aminoglycoside, tigecycline, fosfomycin, rifampin
Lung	High dose meropenem + polymyxin B	tigecycline, aminoglycoside, fosfomycin, rifampin
GI	High dose meropenem + polymyxin B + tigecycline	fosfomycin, rifampin
Urine	High dose meropenem + fosfomycin or aminoglycoside	colistin

Potential treatment options for CRE KPC-Producing *Klebsiella pneumoniae*

Drug-resistant *Neisseria gonorrhoeae*



246,000
infections



\$235M in excess
medical costs

UK man has world-first case of super-strength gonorrhoea

Public Health England say case is first global report of strand resilient to main antibiotic care



▲ Gonorrhoea bacteria. The man, who has a partner in UK, contracted the infection in south-east Asia. Photograph: Alamy

Treatment Options

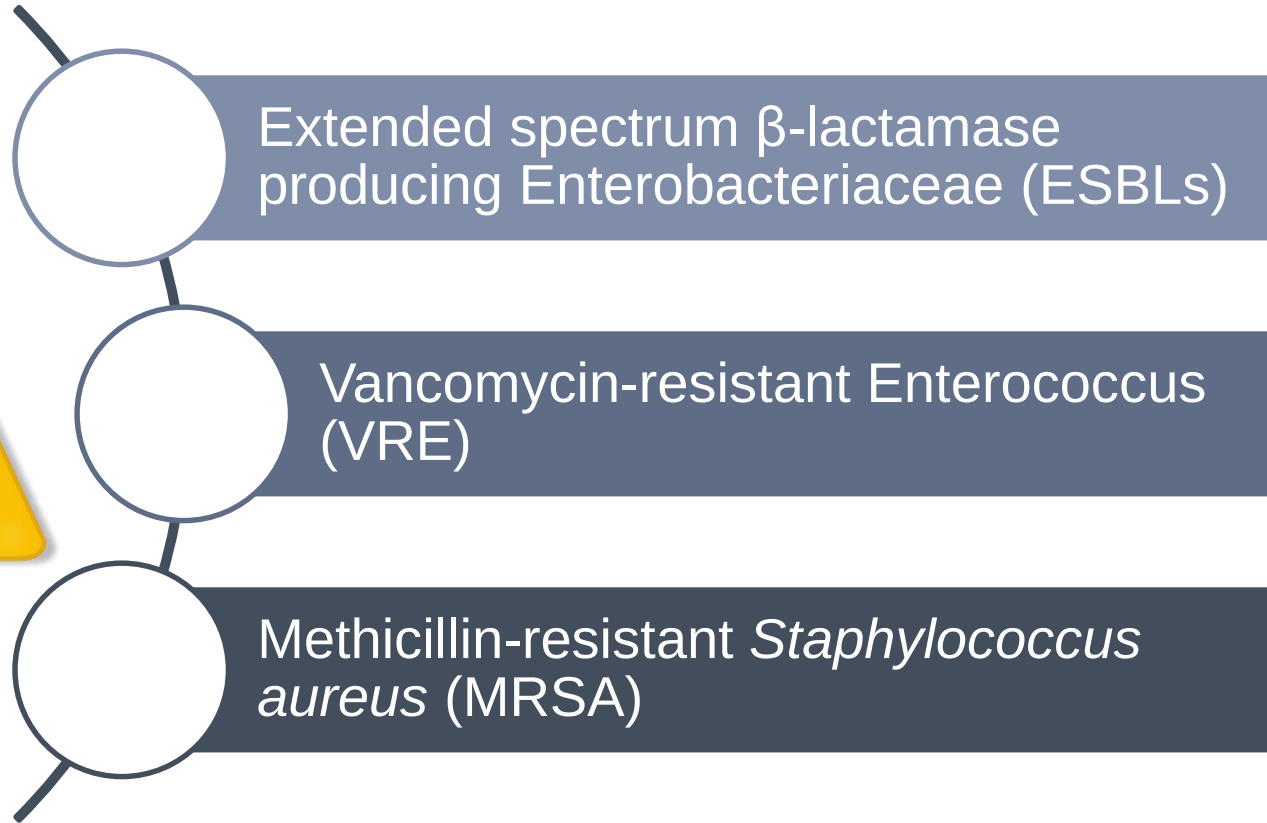
Theory of Dual Therapy

Ceftriaxone (or cefixime) + azithromycin or doxycycline

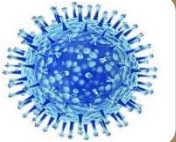
	Percentage	Estimated number of cases
Gonorrhea		820,000
Resistance to any antibiotic	30%	246,000
Reduced susceptibility to cefixime	<1%	11,480
Reduced susceptibility to ceftriaxone	<1%	3,280
Reduced susceptibility to azithromycin	<1%	2,460
Resistance to tetracycline	23%	188,600

Source: The Gonococcal Isolate Surveillance Project (GISP)—5,900 isolates tested for susceptibility in 2011.
For more information about data methods and references, please see technical appendix.

Serious:



ESBL Producing Enterobacteriaceae



26,000 infections



1,700 deaths



\$40K in excess medical costs

Confers resistance to:

- Most β -lactams, including 3rd and 4th generation cephalosporins and monobactams
- Hydrolyze penicillins and cephalosporins

Susceptible to carbapenems

VRE



20,000 infections



1,300 deaths

E. faecalis

ampicillin + ceftriaxone
Or
ampicillin + aminoglycoside

E. faecium

Daptomycin
+
 β -lactam

Others?

MRSA



80,461 infections



11,285 deaths



\$322M in excess
medical costs

vancomycin resistance

daptomycin

cefteroline

dalbovancin

Ortivancin

telavancin

Regulatory Initiatives

NATIONAL ACTION PLAN FOR COMBATING ANTIBIOTIC-RESISTANT BACTERIA

MARCH 2015



1. Improving surveillance

2. Developing better diagnostic tools

3. Accelerating drug development

4. Combatting global antibiotic resistance

January 1, 2017

Hospitals & Nursing Care Centers

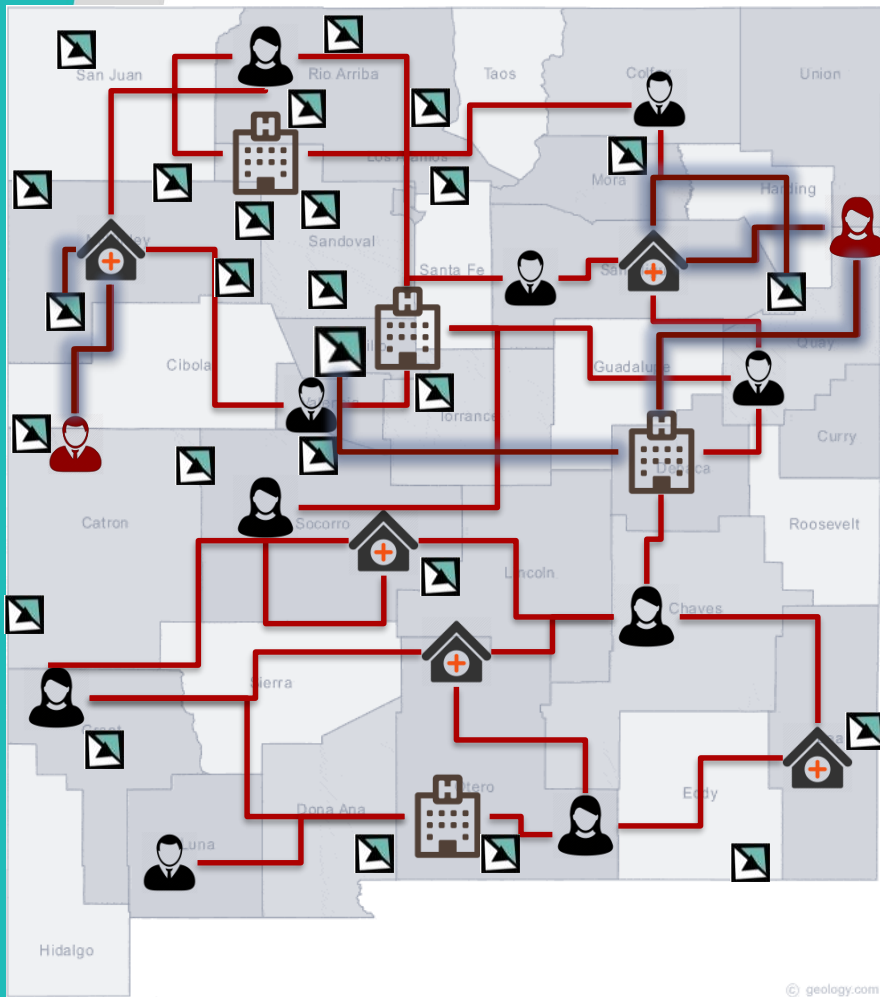
Antimicrobial Stewardship Programs

1. Organization priority
2. Provider education
3. Patient education
4. Multidisciplinary team
5. Core Elements
6. Protocols and procedures
7. Collect, analyze and report data
8. Improve program



TriCore Initiatives

Strength of a Clinical Laboratory



- Clinical labs guides 70% of medical decisions and provides significant value in patient evaluation^{1,2}
- Patients may have multiple providers
 - Clinical laboratories provide the longitudinal history
- Can Identify high risk patients using clinical labs near real-time³
- Effective care coordination relies on real-time standardization of health data⁴

Organism	Amikacin	Ampicillin	Ampicillin Sulbactam	Aztreonam	Cefazolin	Cefepime	Cefoxitin	Ceftriaxone	Ciprofloxacin	Ertapenem	ESBL
Citrobacter freundii	100.00%	1.12%	2.56%	92.93%	1.28%	97.11%	1.44%	86.06%	94.06%	99.19%	100.00%
Citrobacter koseri	99.68%	1.92%	95.83%	99.68%	87.82%	99.68%	96.79%	99.68%	99.68%	100.00%	100.00%
Enterobacter aerogenes	100.00%	5.44%	4.58%	90.96%	5.87%	98.57%	6.30%	88.67%	98.57%	98.22%	95.74%
Enterobacter cloacae	100.00%	5.39%	4.25%	86.50%	3.53%	93.46%	4.05%	78.61%	96.78%	90.65%	90.48%
Enterococcus faecalis	99.17%	99.66%	56.50%	92.70%	75.00%	93.13%	82.67%	86.46%	81.37%	99.39%	96.04%
Enterococcus faecalis, Vancomycin Resistant	80.00%	69.57%	33.33%	40.00%	66.67%	80.00%	66.67%	50.00%	80.00%	100.00%	100.00%
Enterococcus faecium	96.43%	47.93%	50.00%	88.46%	69.57%	100.00%	66.67%	95.83%	75.86%	95.65%	100.00%
Enterococcus faecium, Vancomycin Resistant	98.11%	2.89%	34.88%	74.51%	57.14%	79.25%	57.14%	58.14%	67.92%	89.29%	84.21%
Escherichia coli	99.97%	57.49%	61.93%	96.69%	91.31%	96.59%	96.00%	95.98%	84.95%	99.86%	96.84%
Escherichia coli	83.33%	100.00%	40.00%	81.82%	37.50%	83.33%	50.00%	66.67%	58.33%	100.00%	100.00%
Klebsiella oxytoca	100.00%	8.12%	57.35%	94.59%	63.98%	95.31%	96.38%	93.49%	96.14%	99.88%	94.44%

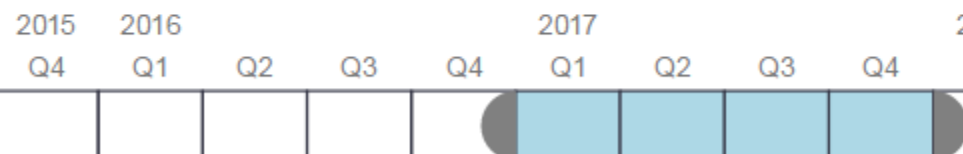
Facility	# Isolates
Commercial	30490
Presbyterian Hospital	20927
University Hospital	10892
Presbyterian Rust Medical Center	2168
Presbyterian Kaseman Hospital	1574
Clovis (Plains Regional Med Ctr.)	1456
Espanola General	1080
Lincoln County Med Ctr.	517

CultureSource	# Specimens
Urine	55742
Aer/Ana Culture Swab	4744
Blood Cult,Bact/Yst	2508
Aerobic Culture Swab	2103
Body Fluid	1120
Sputum	996
Tissue	971
Trach	386

CollectDate

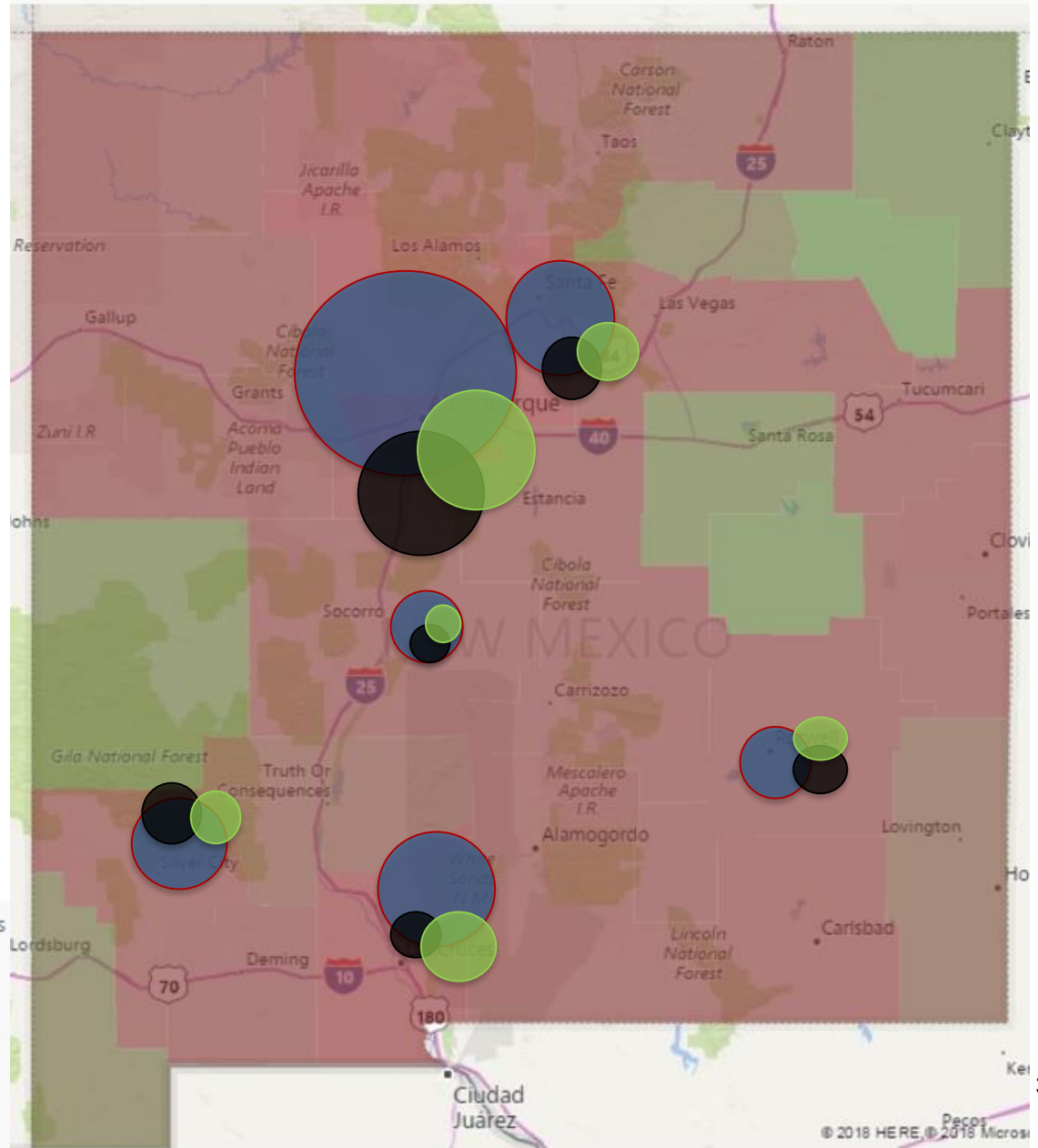
Y ☒ Q M W D
Quarter

Q1 2017 - Q4 2017



Identify hot spots

Total State Patients
2,670,538



A Peak into Antibiotic Susceptibility (2017)

Antibiotic – n(%S)

Ceftaroline – 133 (96%)

	# of Isolates	Ceftazidime- avibactam (Avycaz)	Ceftolozane- tazobactam (Zerbaxa)
Pseudomonas aeruginosa	14	79%	63.6%
Escherichia coli	1	100.0%	0.0% (Intermediate)
Klebsiella pneumoniae	2	100.0%	50.0% (1 resistant)
Klebsiella oxytoca	1	100.0%	0.0% (Intermediate)
Enterobacter cloacae	1	100.0%	0.0% (Intermediate)

Discussion



Antimicrobial resistance is both clinically and economically taxing



There are national initiatives to combat antimicrobial resistance



The laboratory can play a collaborative role in antimicrobial resistance surveillance



Monique Dodd, PharmD, PhC, MLS(AMCP)^{CM}
Clinical Solutions Specialist
TriCore Reference Laboratories
monique.dodd@tricore.org