CDC Update on Food Safety: Whole Genome Sequencing and Other Advances

123rd Association of Food and Drug Officals
Annual Education Conference
Atlanta, Georgia

June 26, 2019

Robert Tauxe, MD, MPH, Director
Division of Foodborne, Waterborne, and Environmental Diseases

Foodborne illnesses in the United States

- 48 million people become sick, 128,000 are hospitalized, and 3,000 die
- Estimated annual cost of foodborne illness: $15.6 billion
- Prevention: Understanding transmission well enough to prevent it
- Result of actions by regulators, public health, industry, consumers
- Progress often driven by foodborne outbreaks, that changes in industry practices and regulatory policies
- 1996-2007: Important progress made

- Little further progress has been made since in reducing incidence

Selected 2018 Multi-state Outbreaks

Kratom linked to multistate Salmonella outbreak

By Joseph James Whitworth
21-Feb-2018 - Last updated on 21-Feb-2018 at 09:17 GMT

Shredded coconut causes widespread salmonella outbreak

SNACK FOODS · January 17th

By Holly Van Hare | The Daily Meal

Jimmy John's sprouts linked to multistate salmonella outbreak

'Do Not Eat' Kellogg's Honey Smacks Cereal, CDC Warns

100+ News : NPR by Patrick Jarenwattananon / 53min // keep unread // hide

CDC: Five states hit by Salmonella outbreak linked to chicken salad

By Joseph James Whitworth
23-Feb-2018 - Last updated on 23-Feb-2018 at 10:44 GMT

BRIEFING • RECALLS

Pre-Cut Melon in 10 More States Link Salmonella Outbreak

By MONICA RODRIGUEZ June 15, 2018

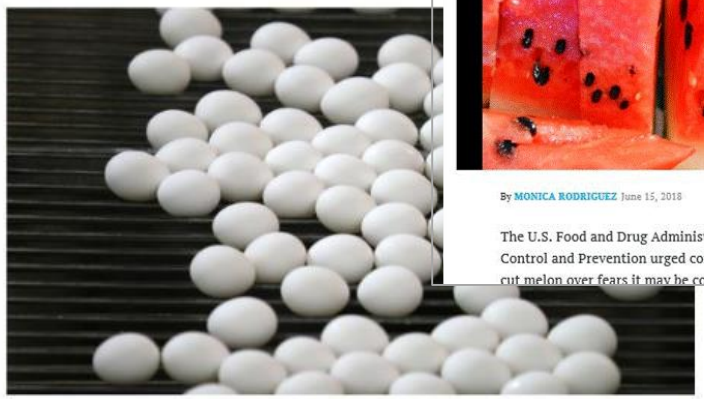
The U.S. Food and Drug Administration along with the
Control and Prevention urged consumers in 10 more sta
cut melon over fears it may be contaminated with salm

AMERICA

207 Million Eggs Are Recal Salmonella Fears

April 16, 2018 · 10:44 AM ET

BILL CHAPPELL



Eggs from Rose Acre Farms, one of the largest suppliers in the U.S., have been recalled after investigators linked them to a number of salmonella-related illnesses.

Vibrio outbreak linked to crab meat imported from Venezuela

Close-up of steamed crab meat. / GETTY IMAGES/ISTOCKPHOTO

Share / Tweet / Reddit / Flipboard / Ema

Health officials are warning U.S. consumers not to eat c
Venezuela after linking it to a dozen cases of illness in th

Salmonella outbreak in 26 state

USA TODAY NETWORK Brett Molina, USA TODAY Published 10:03 a.m.

CONNECT TWEET

(Photo: Getty Images)

Public health offic
outbreak in 26 sta

According to the
Prevention, 90 pe
outbreak strain.

No deaths have b
been sent to the hospital.

The 26 states where cases were reported are Alaska, California, Colorado, Florida, Georgia, Hawaii, Iowa, Illinois, Indiana, Kansas, Kentucky, Massachusetts, Michigan, Minnesota, New Jersey, New York, North Carolina, Ohio, Oregon, Pennsylvania, South

OUTBREAKS

Multistate E. coli outbreak traced to romaine lettuce from Arizona

Fox News

The outbreak has been traced to the Yuma, Ariz., growing region, but has not been pinned down to a specific grower, supplier, distributor or brand. (iStock)

A multistate E. coli outbreak has sent at least 22 people to the hospital prompting health

More from Fox News




Outline of Food Safety Activities at CDC

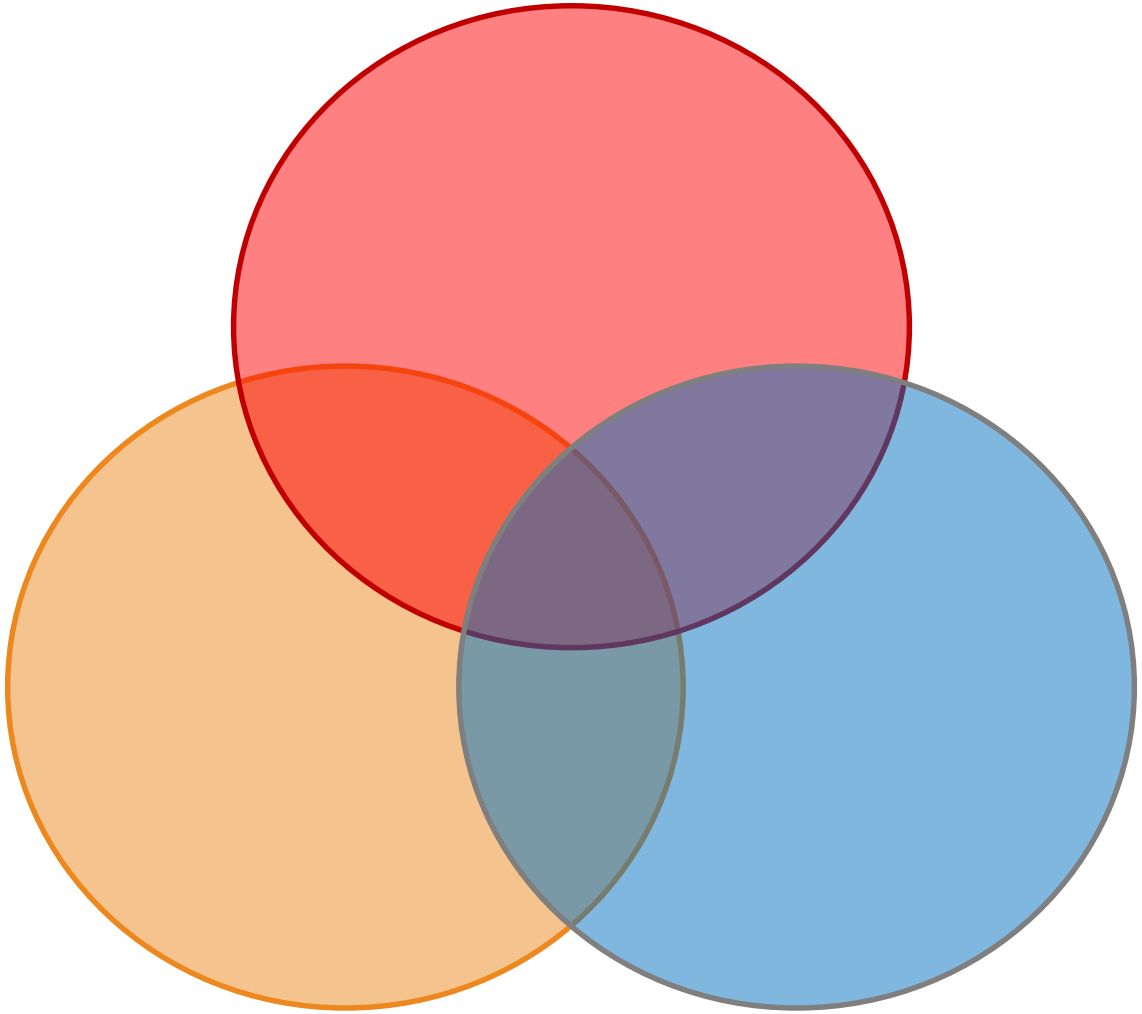
- Conduct national surveillance for infections often transmitted by food
- Investigate and control outbreaks to stop them and prevent future illness
- Drive illness prevention policy with data, analyses, and partnerships
- Innovate by applying advanced technologies to improve surveillance and to address diagnostic challenges
- Support state and local health departments, global and other partners to fulfill their primary roles in addressing the above goals

Surveillance and investigation are multi-agency efforts

- Caregivers and clinical labs
  - Make the diagnoses, and report the specific illnesses
- State and local health departments: epi, lab, and food safety officials
  - Receive reports of specific diseases
  - Interview people
  - Subtype pathogens in the public health labs
  - Traceback, assess and control within state events
- CDC is lead national public health agency
  - National disease surveillance and multistate outbreak detection
  - Epidemiologic investigation
- FDA (most foods) and USDA/FSIS (meat and poultry), as regulatory agencies
  - Trace suspected foods back to source
  - Assess production and processing facilities

How do we determine a food is the source of an outbreak?

- **Three types of evidence:**
  - **Epidemiologic:** association between illness and exposure
  - **Traceback:** suspected food item traced back to a common source of contamination
  - **Microbiologic:** same pathogen found in the food, farm or facility as in the ill people



Methods for all three are evolving

PulseNet 1996-2018: National network for molecular surveillance of bacterial enteric infections

Links with:

- PulseNet Canada
- PulseNet International

Standard PFGE method
Results in CDC database
All participants can use

87 labs participate:

- All state heath departments
- City health departments
- FDA laboratories
- USDA laboratories

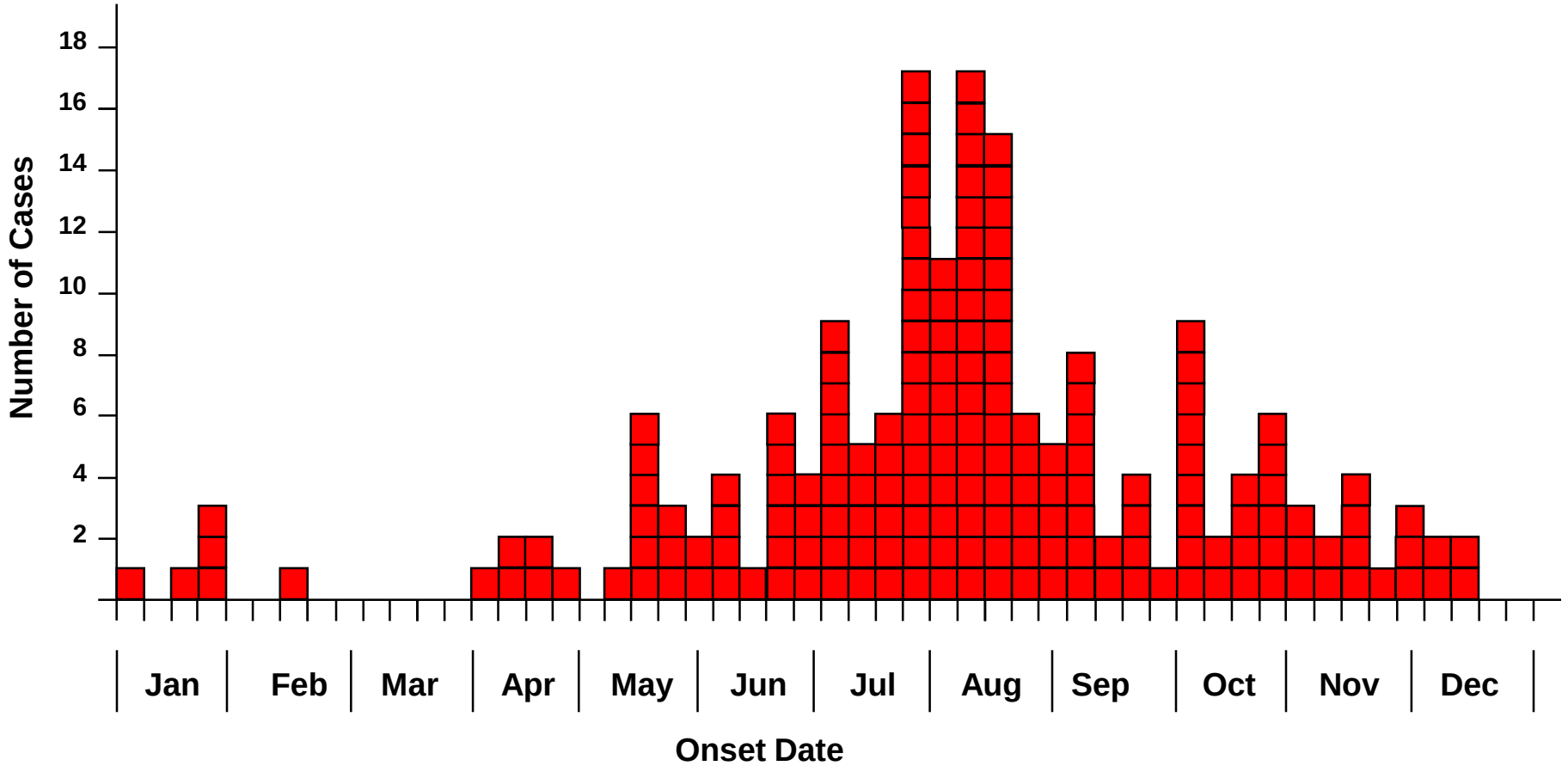
50,000 bacteria/year from

- ill people
- foods
- animals

The PulseNet surveillance network combines strain subtyping and patient interviews

- Detecting and investigating a dispersed outbreak can
  - Stop an ongoing hazard
  - Identify food safety gaps early in food production chain
  - Drive improvements in prevention across the system
- Detection depends on finding a signal in the background noise
  - Subtyping clinical strains in state and local public health labs
  - Sharing subtype data with all participants
  - Interviewing patients
  - Detailed follow-up of clusters of related isolates
- Subtyping food and animal isolates, combined in same database
- Focus on STEC, *Salmonella*, *Listeria*

Onset dates of *Escherichia coli* O157:H7 cases submitted to MDH Clinical Laboratory Section, Minnesota, 1995 (n=183)



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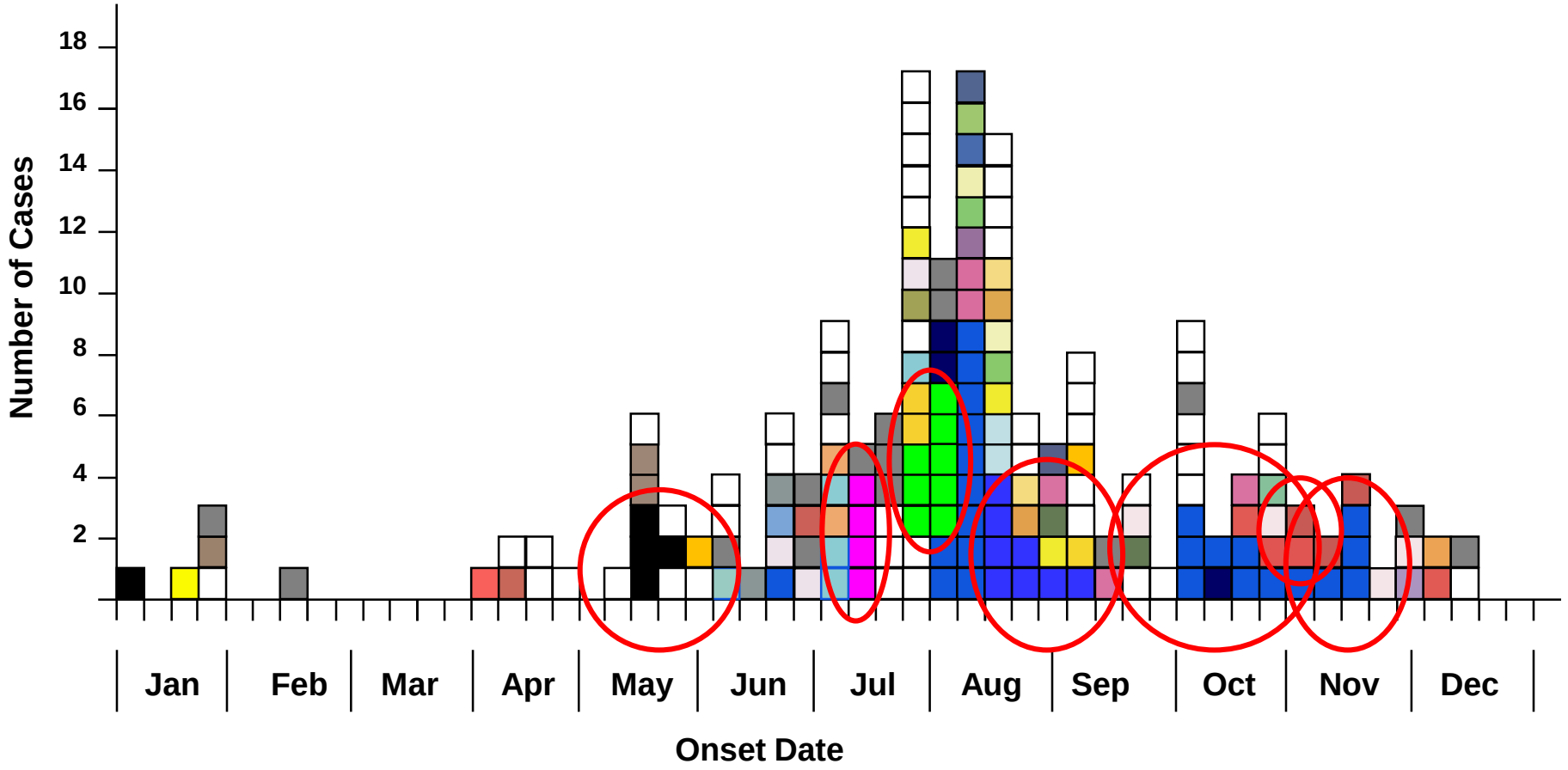
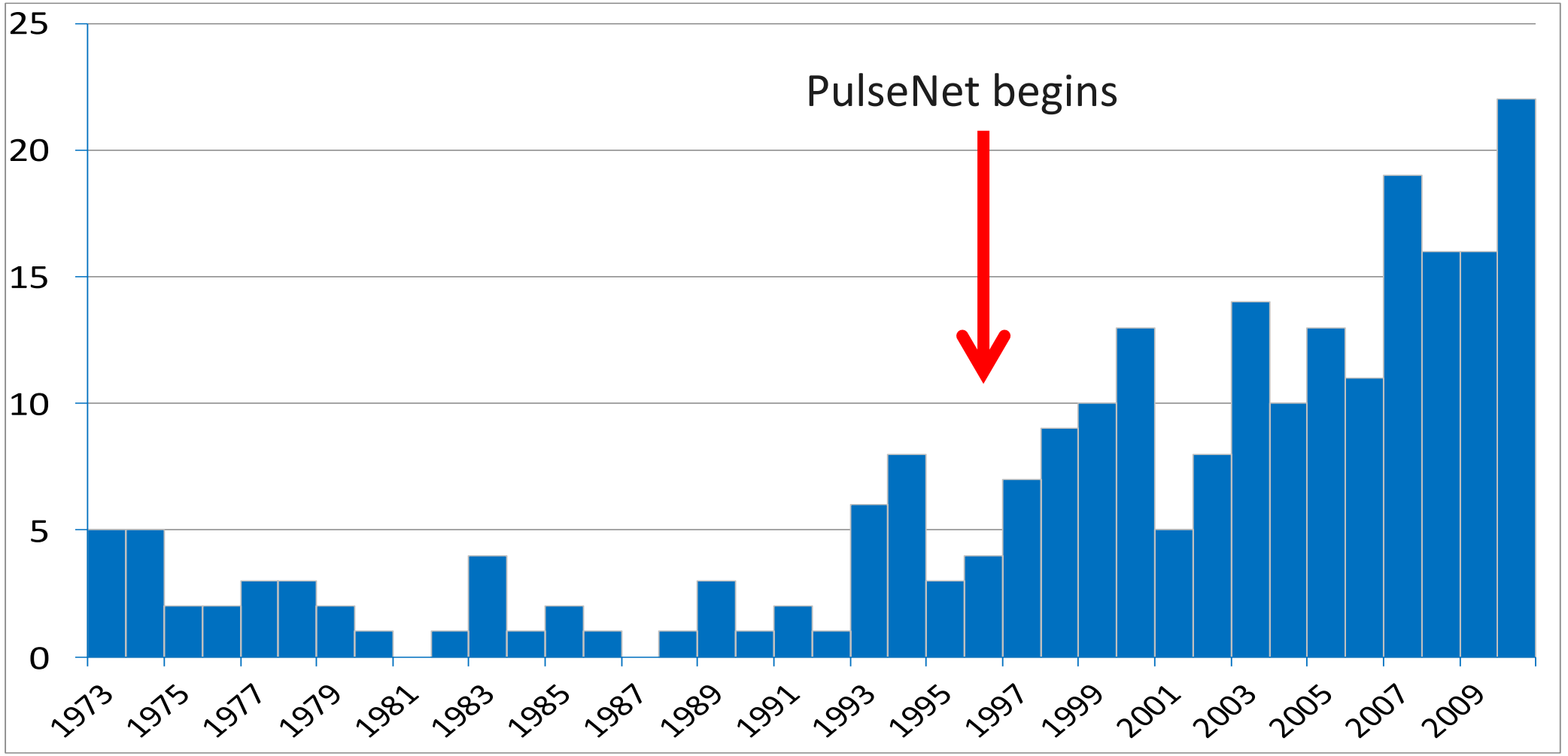
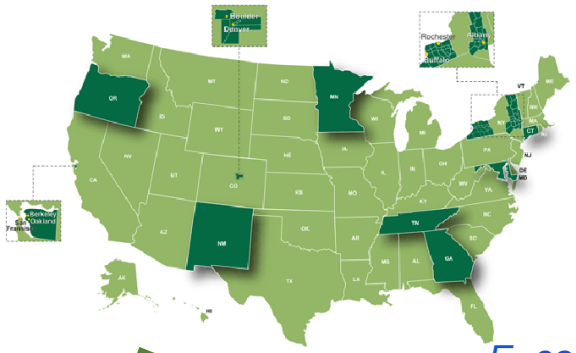


PulseNet increased the number of multistate foodborne outbreaks reported to CDC: 1973-2010

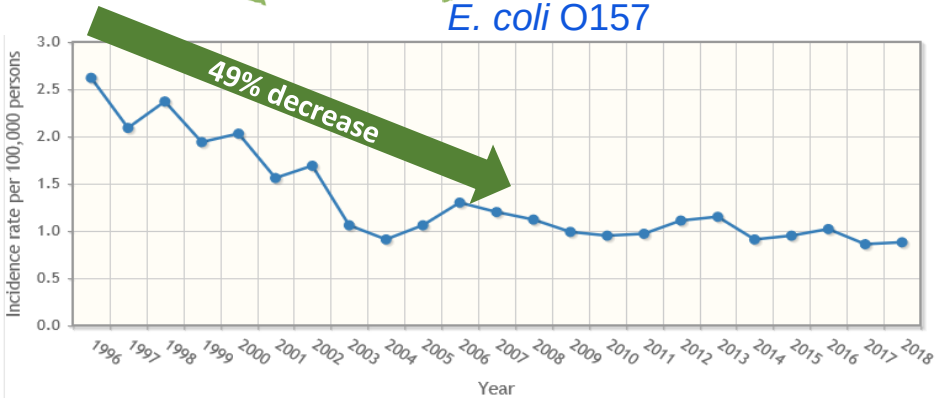


Incidence of diagnosed cases, by pathogen — FoodNet, 2018

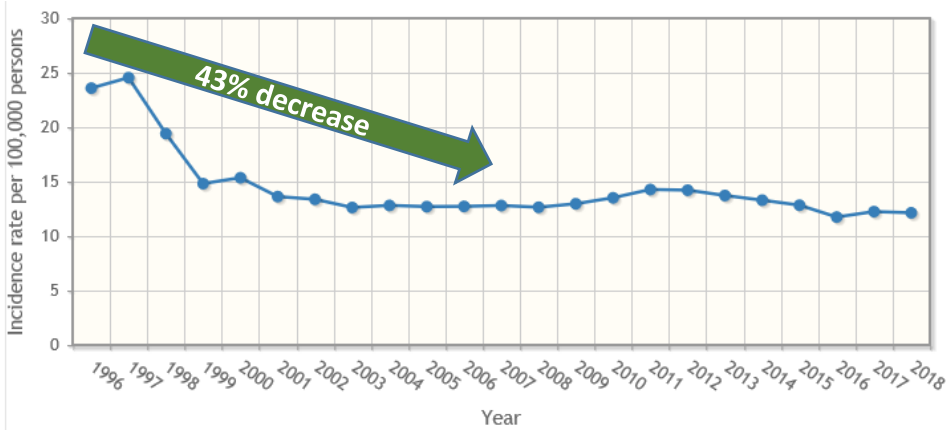


- Active surveillance, part of Emerging Infections Program
- Collaboration among CDC, 10 FoodNet sites, FDA, USDA/FSIS
- 8 infections often spread through food
- Reliable and up-to-date data on illness trends

E. coli O157

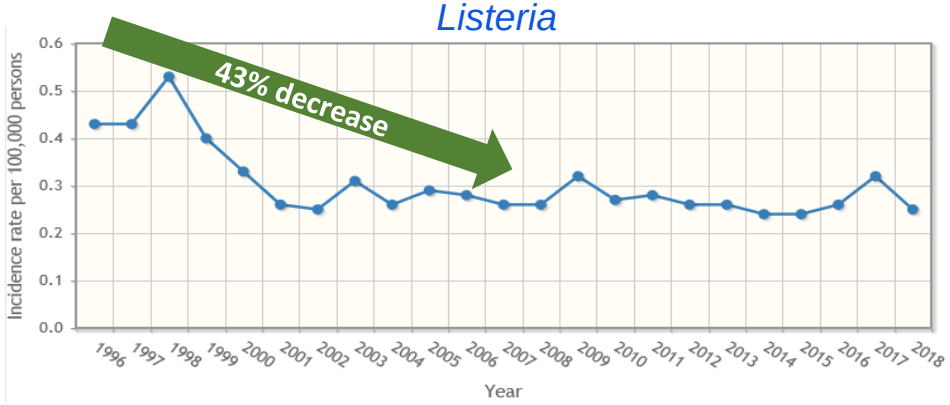


Campylobacter

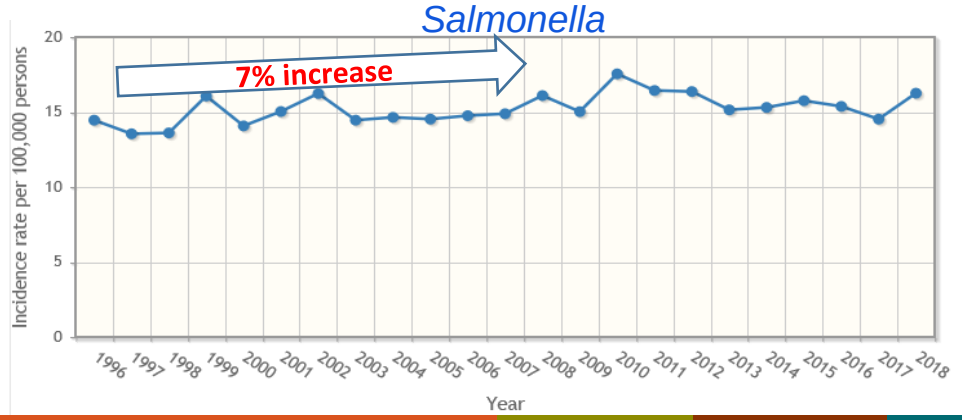


Confirmed only

Listeria



Salmonella



Food Safety Goals for 2020 and 2030

- Healthy People 2020: From baseline in 2006-2008:
  - 33% reduction in *Campylobacter* infections
  - 50% reduction in *E. coli* O157 infections
  - 33% reduction in *Listeria monocytogenes* infections
  - 25% reduction in *Salmonella* infections
  - 33% reduction in *Vibrio* infection
  - 50% reduction in hemolytic uremic syndrome in children <5 years of age

- Healthy People 2030 goals: From baseline in 2016-2018: Under development
  - Fewer targets for reducing incidence
  - More modest reductions in incidence

2020: https://www.healthypeople.gov/2020/

Expanding efforts at CDC to meet Food Safety Goals

- Make surveillance and investigations more powerful
  - Implement whole genome sequencing for routine PulseNet subtyping
  - Detect and control outbreaks we may be missing now
  - To identify emerging problems

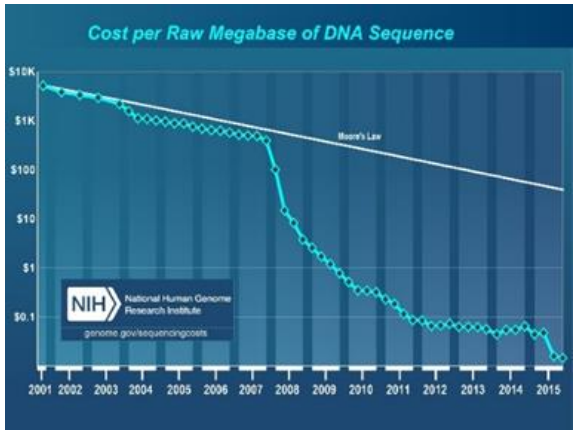
- Use our surveillance to target interventions
  - Attribute illnesses to specific food categories
  - Account for changing diagnostic tests that affect surveillance

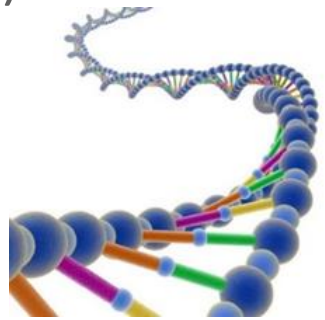
- Stay on the cutting edge as new laboratory diagnostic methods arise.
  - The challenge of culture–independent diagnostic tests
  - Metagenomic tools for public health are coming

2020: https://www.healthypeople.gov/2020/

Whole genome sequencing and routine public health surveillance – Big data meets microbiology

- PulseNet: National subtyping network since 1996, using pulsed-field gel electrophoresis (PFGE). 50,000 strains/yr
- Cost and speed of sequencing bacteria has dropped
- Reading and interpreting sequence faster
- 3M base pairs = 1800 pages of text (2 Moby Dick volumes)
- Comparing whole genomes give vastly more information
  - Strains are closely related (same source?)
  - Strains from patients related to strains from foods
  - Predict antibiotic resistance, many other features
- What happens if we try it in PulseNet?





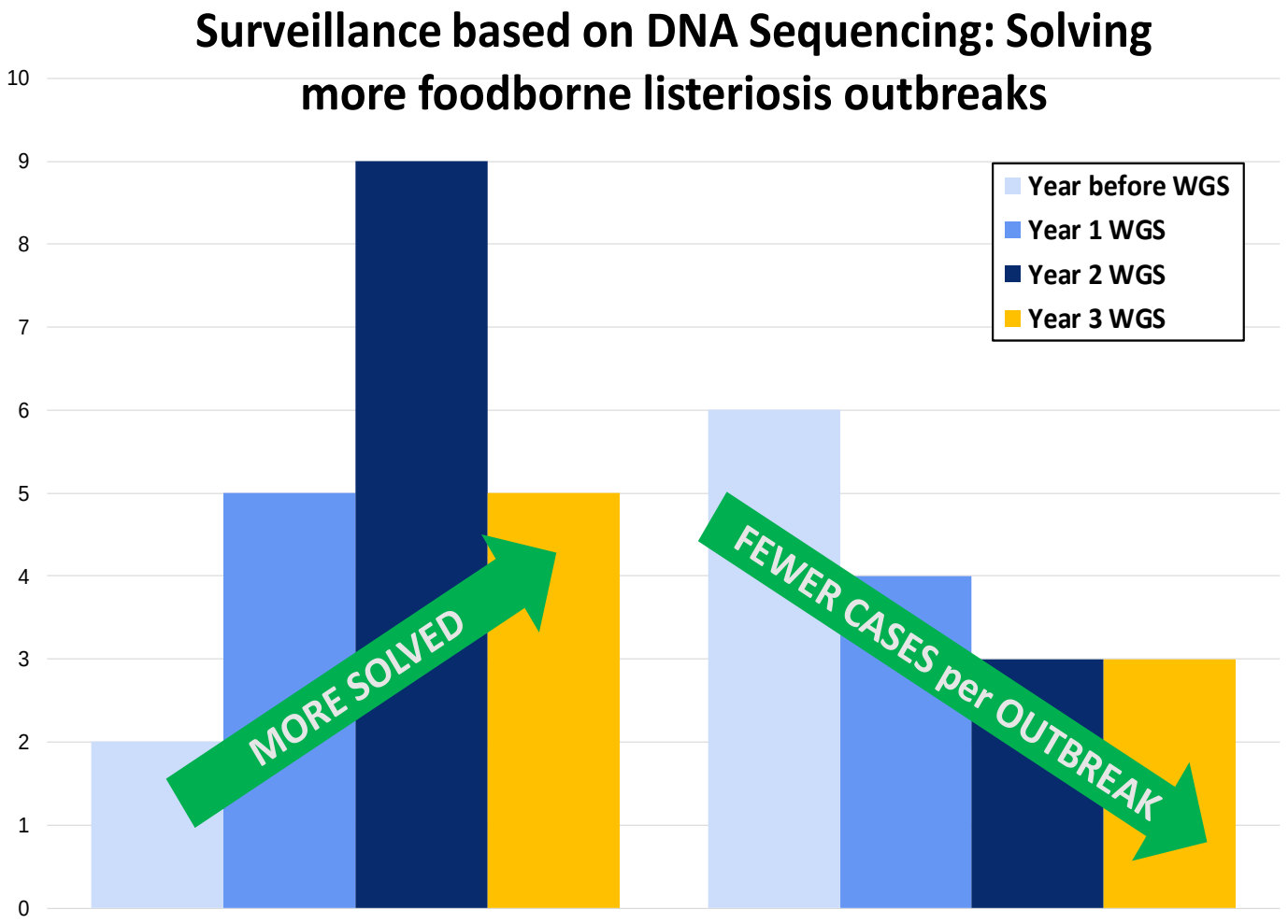
20 years of PulseNet USA
1996 - 2016

Applying whole genome sequencing to surveillance Listeriosis Pilot Project 2013- 2016

- *Listeria*: severe, but rare illness in elderly, immunocompromised or pregnant (800 cases/year)

- 2013: Pilot project with WGS
  - Began sequencing all clinical, food, and environmental *Listeria* isolates
  - FDA, and FSIS/USDA partners

- Solved outbreaks increased 3x
- Size of outbreaks decreased
- Identified new and unsuspected risks



Jackson 2016. Clin Infect Dis 63:380-6

Salmonella Enteritidis (SE) and frozen stuffed breaded raw chicken products – Minnesota, 2015

- For SE: PFGE has too few types to easily find clusters
- Minnesota DOH began sequencing SE in 2015
- Found 2 clusters in summer of 2015

- **Cluster #1**: 5 illnesses
- Ate one brand of frozen stuffed breaded raw chicken entrée
- Same strain found in product
- Product distributed to many states
- 2.4 M pounds recalled

- **Cluster #2**: 15 illnesses (including 7 in other states)
- Ate a different brand of frozen stuffed breaded chicken products
- Same strain found in frozen product
- Product distributed to many states
- 1.7 M pounds recalled

- Most knew the product was raw, and followed cooking instructions
- Some checked the internal temperature
- UDSA now considering further standards for products like this

www.cdc.gov/salmonella/outbreaks/

Salmonella Enteritidis (SE) and eggs from a small farm – Tennessee, 2016

- For SE: PFGE has too few types to easily find clusters
- 2016: TDOH began sequencing SE, found an outbreak
- 6 cases from Restaurant A: Steak with Bernaise sauce, made with raw eggs
- Eggs from local Farm X (<3000 hens)
- Env cultures on Farm X negative for SE

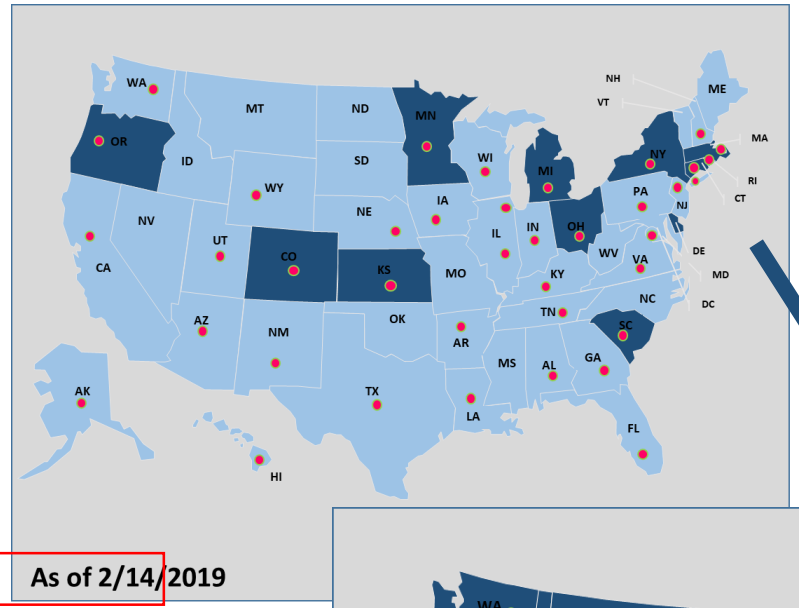
- A month later, found a 2nd outbreak. WGS, within 3 SNPs of first outbreak
- 9 cases from Restaurant B: ate mayo made with raw eggs at Restaurant B;
- Eggs also from farm X
- Reinvestigation of farm X: SE in chicken litter
- Restaurant B changed egg suppliers
- All receiving eggs educated not to use them raw

- *Salmonella* Enteritidis is about 20% of all salmonellosis
- Limited number of PFGE types makes cluster detection difficult
- WGS looks promising in finding small outbreaks, and undetected sources
- Regulations for SE in eggs covers farms with ≥ 3000 hens

https://cste.confex.com/cste/2017/webprogram/Paper7567.html

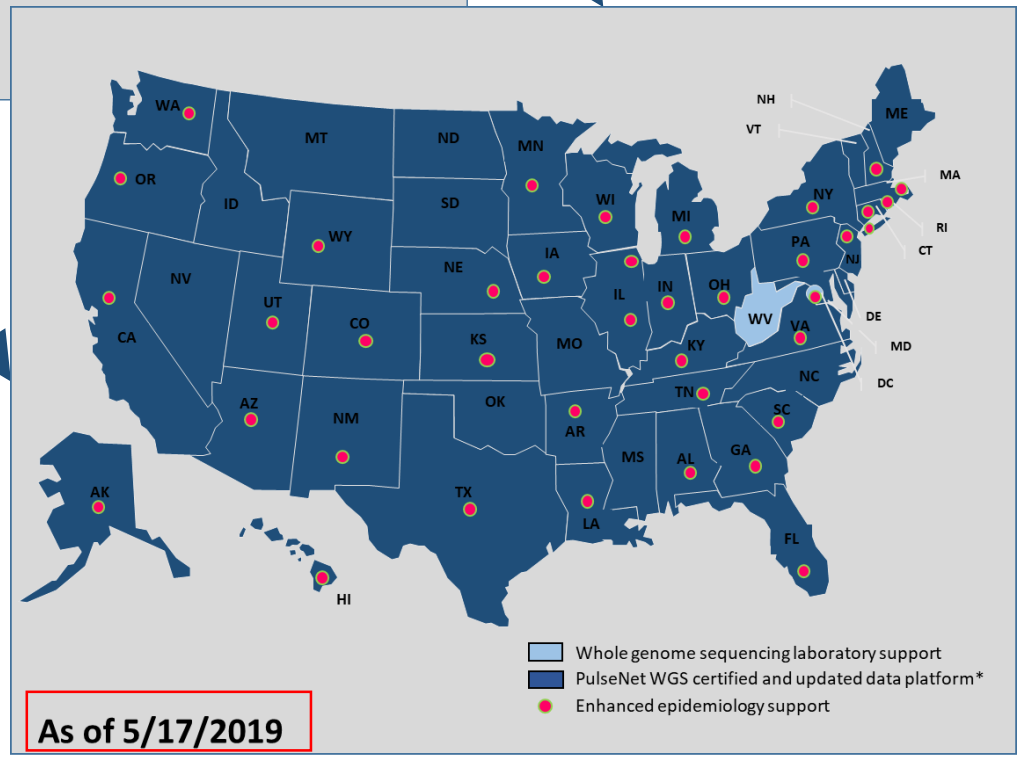
Implementing whole genome sequencing as PulseNet standard – 2017-2019

- **2017-2019**
  - Built state lab and epi capacity
  - Trained and certified staff in all 50 states
  - Built data infrastructure
  - Partner with FDA Genome TrakR labs, and FSIS labs
  - PulseNet transition to WGS (end of June 2019)



PulseNet USA
The National Molecular Subtyping Network for Foodborne Disease Surveillance

PFGE ▶▶ WGS
Pulsed-Field Gel Electrophoresis || Whole Genome Sequencing



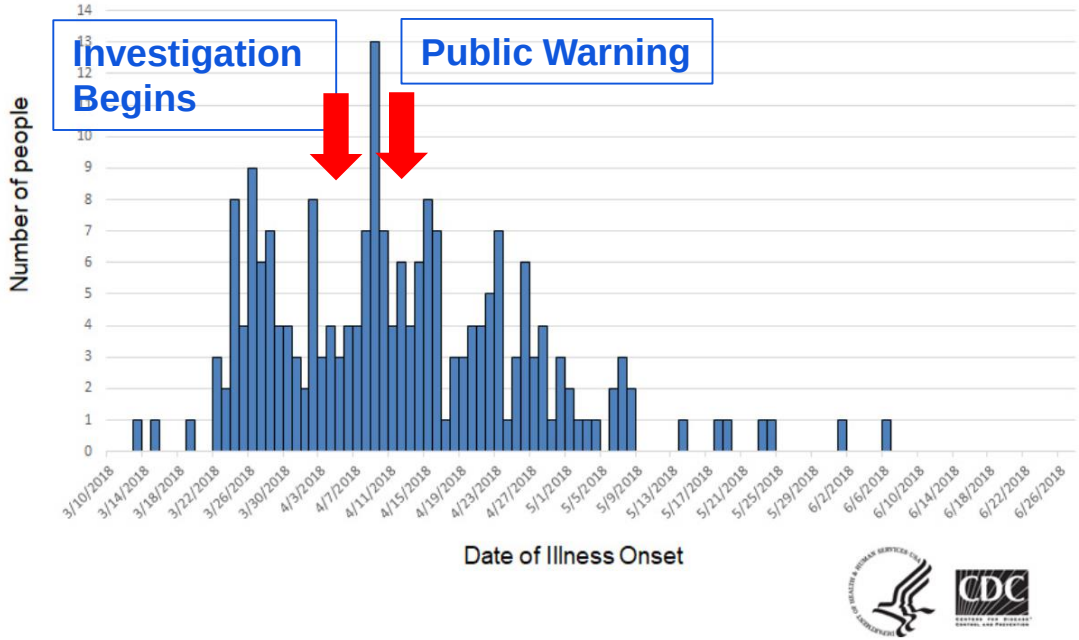
- **Expect PulseNet with WGS to find more:**
  - Clusters that are truly genetically related
  - Successful epidemiologic investigations
  - Gaps in food safety and targets for prevention

“Clade of concern”: MDR *E. coli* O157:H7 and Romaine

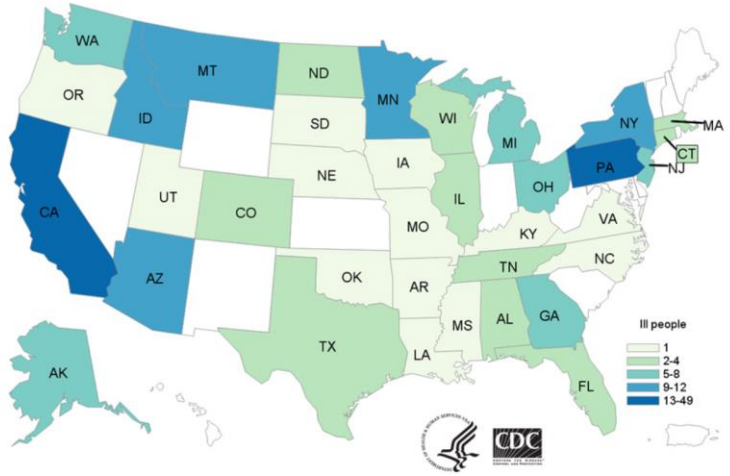
- Large outbreak in spring of 2018, linked to Romaine
- 210 cases, 36 states, 96 hospitalized, 27 HUS, 5 deaths
- Largest O157 outbreak in last decade
- 87% said they ate Romaine lettuce, more than baseline
- Traced to ~ 23 fields, across span of ~ 50 miles

  in Yuma Growing area
- Ended after repeated warnings, end of harvest

People infected with the outbreak strain of *E. coli* O157:H7, by date of illness onset*



People infected with the outbreak strain of *E. coli* O157:H7, by state of residence, as of June 27, 2018 (n=210)



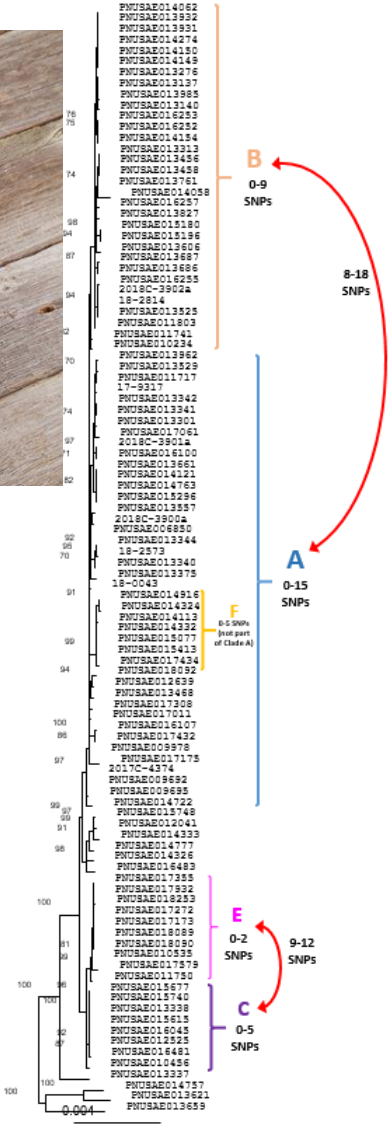
- WGS defined one main clade, one second clade
- WGS: Main clade has a history:
  - Mid 2017: 11 cases, Lake Wildwood in California
  - Late 2017: 17 cases, salad suspected in Midwest
- **Need heightened surveillance, prevention research**

Thanks to Matt Wise, CDC

WGS is already making investigations more powerful

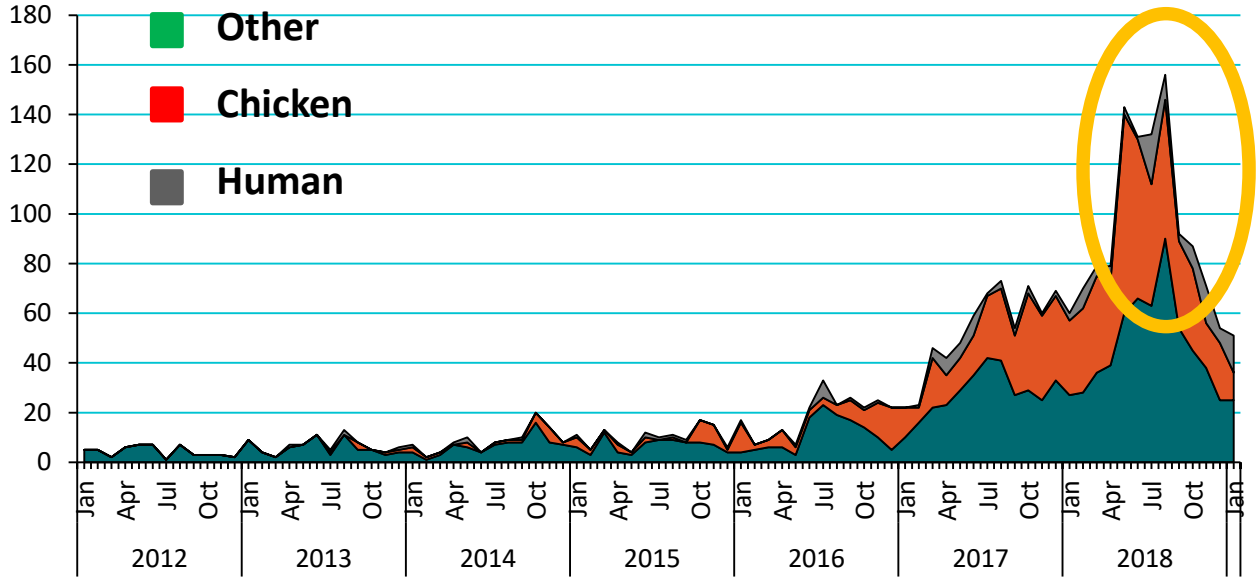
- **2018: *E. coli* O157 infections and Romaine Lettuce - Yuma Growing Area**
- WGS linked together 22 different PFGE patterns into 2 main clades
- Confidence that two dozen farms were all related, reflecting a widespread contamination
- *E. coli* O157 isolated from the irrigation canal matched the main outbreak clades
- Linked this outbreak with events in preceding year.

- **4/19/2019: Leafy Greens Marketing Agreement**
  Requires farmers to sanitize surface waters sprayed onto leafy greens

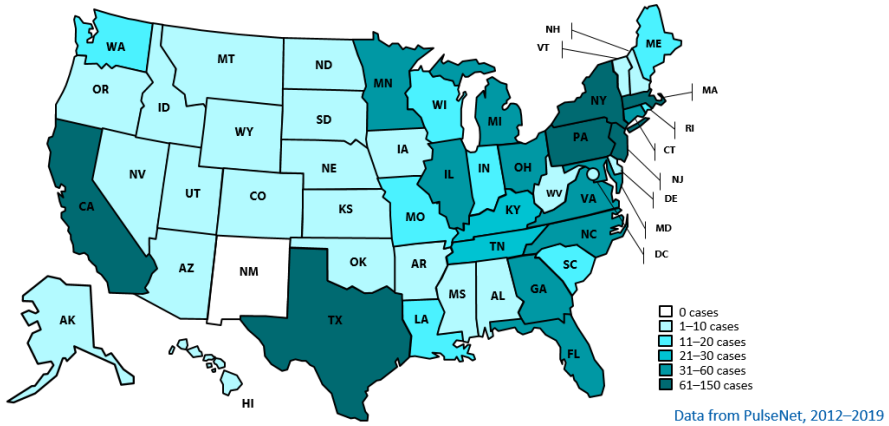


“Clade of concern”: Sustained event traced to a complex source: MDR *Salmonella* Infantis and poultry

- MDR strain first seen in travelers to Peru in 2012
- Rare ESBL resistance gene (defined by PFGE)
- Resistant/Decreased susceptibility to 10 agents, including Amp, Cipro, Ceftriaxone, and Tmp/Sxt
- Difficult to treat with commonly used antibiotics
- First non travel-associated US case in 2014
- Increasing rapidly in 2017-2018
- Multiple PFGE types – all related by WGS



Case map: *Salmonella* Infantis MDR strains 2012-2019 (n = 1246)



Data from PulseNet, 2012–2019

- Now represents 30% of all *S* Infantis in humans, 573 in 2018
- USDA/FSIS isolates: In chicken since 2013, rapid increase in 2017
- In 2018: 495 isolates from chicken, 53 isolates from turkey
- Met with National Chicken Council several times in last year, Jan 2019
- **Preharvest investigations and interventions needed**

Thanks to Louise Francois Watkins

WGS is defining “Clades of Concern”

- Groups of closely-related strains that
  - Cause repeated outbreaks
  - Emerging in people and in specific food commodities
  - May be multi-drug resistant

Greek: “Klados”

- Examples of current “clades of concern”
  - *E. coli* O157:H7 in Southwest (e.g. the “Yuma” strains) – recurrent outbreaks
  - MDR *Salmonella* Infantis, emerging in chickens from many processors
  - MDR *Salmonella* Reading , related to turkeys in many processors

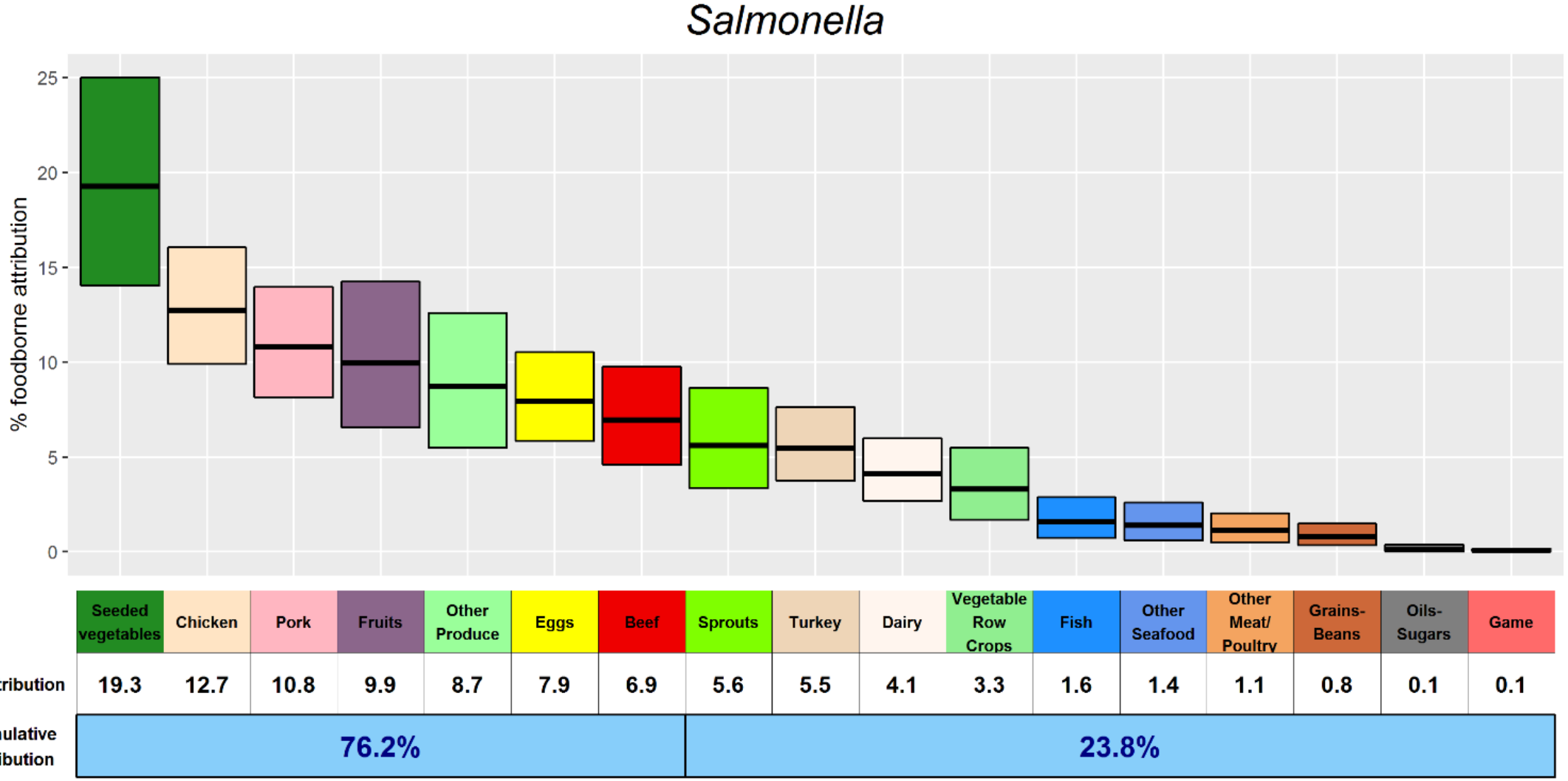
- Need to address with
  - Sustained investigation and traceback
  - Concerted broad prevention strategies

Using surveillance to help target interventions

- Interagency Food Safety Analytics Consortium (IFSAC): CDC, FDA, FSIS work together to summarize information on sources of foodborne infections
- Have constructed a model based on reported foodborne outbreaks over the last 18 years, giving more weight to most recent 5 years
- Attributed cases of illness across 17 major food categories, by pathogen
- Most recent summary based on 1998 – 2016
- Repeat and update annually

https://www.cdc.gov/foodsafety/ifsac/annual-reports.html

Using surveillance to target interventions
IFSAC Attribution: *Salmonella* infections for 2016



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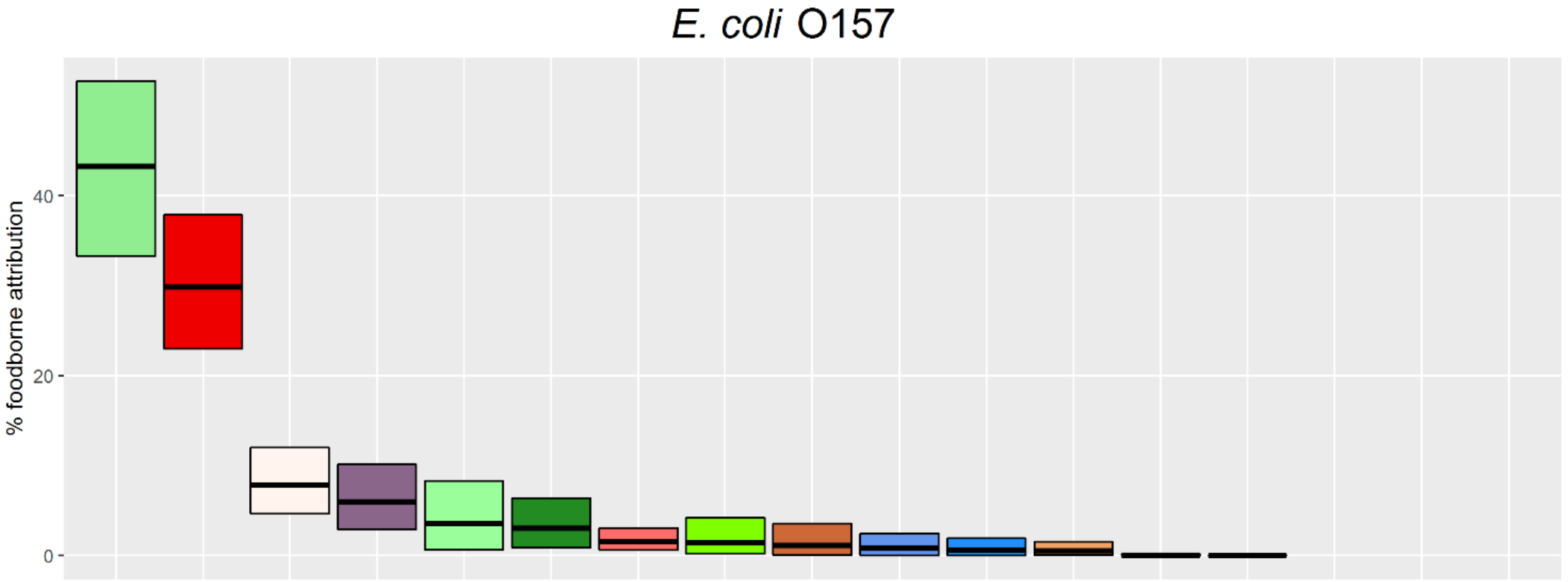
Using surveillance to target interventions
IFSAC Attribution: *E. coli* O157 for 2016



	Vegetable Row Crops	Beef	Dairy	Fruits	Other Produce	Seeded vegetables	Game	Sprouts	Grains-Beans	Other Seafood	Fish	Other Meat/ Poultry	Chicken	Turkey	Pork	Eggs	Oils-Sugars
% attribution	43.2	29.9	7.8	6.0	3.6	3.1	1.6	1.5	1.2	0.8	0.6	0.6	0.1	0.0	--	--	--
cumulative attribution	73.1%		26.9%														

https://www.cdc.gov/foodsafety/ifsac/annual-reports.html

Summary of biggest targets for prevention

- **FDA regulated foods**
- Fresh produce: *Salmonella* and STEC*
  - Leafy greens and STEC*
  - Seeded vegetables and *Salmonella*
- Eggs: *Salmonella*
- Cheese and other RTE foods: *Listeria*

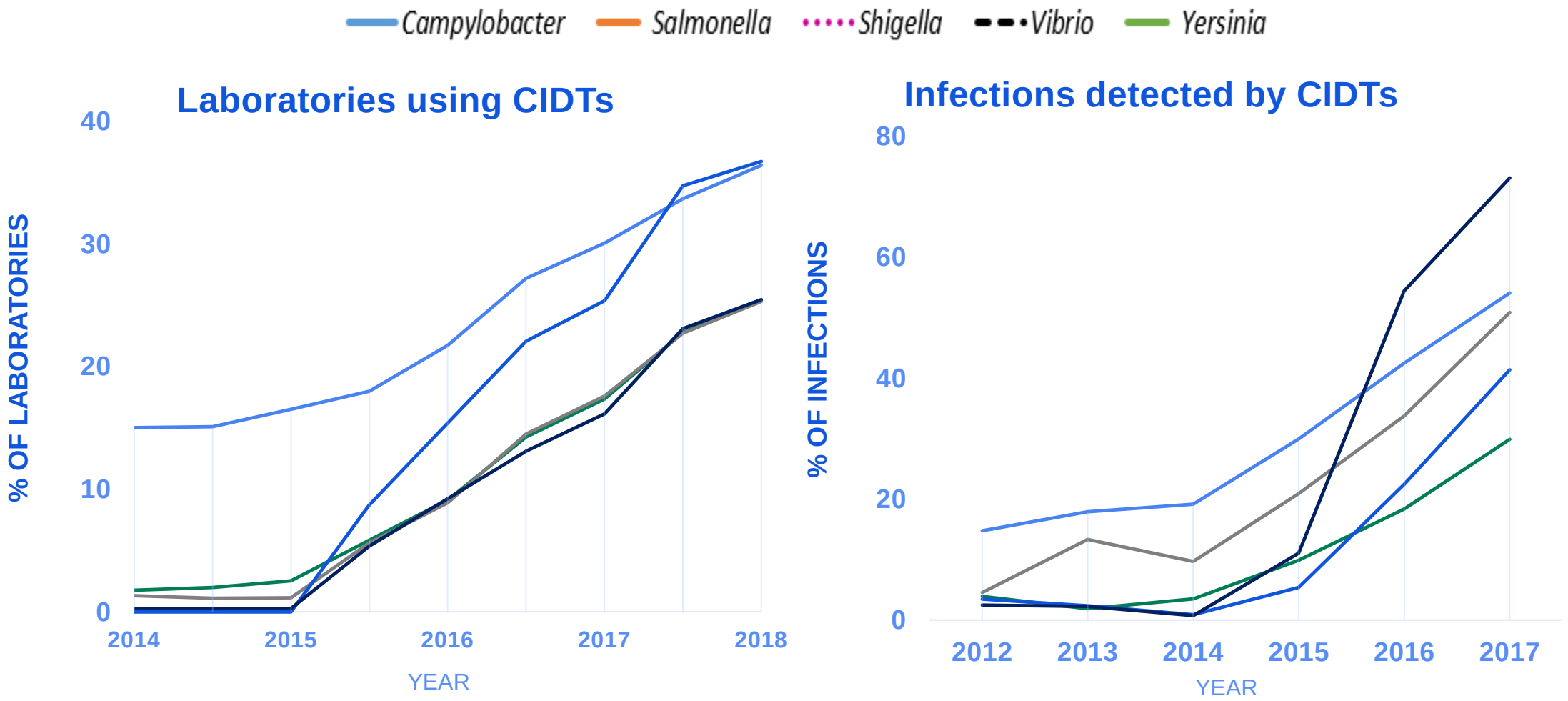
- **FSIS regulated foods**
- Chicken: *Salmonella* and *Campylobacter*
- Ground beef: *Salmonella* and STEC*
- Pork: *Salmonella* and *Yersinia*

*Shiga toxin–producing *E. coli*, such as *E. coli* O157

Accounting for impact of changing diagnostic methods on case surveillance – culture-independent diagnostic panels

- Since 2015, use of rapid multi-pathogen diagnostic panels increasing in clinical laboratories
- Can diagnose up to 22 different infections, with results available in hours
- More people are being tested for more pathogens, including some that could not be routinely diagnosed before
- Tests do not yield a living bacterial isolate, unless the specimen that was positive is then cultured for that organism. **Isolate needed for PulseNet subtyping**
- Insurance may not cover cost of doing this “reflex culture”
- Labs are starting to send the positive specimens to the public health laboratories for culture

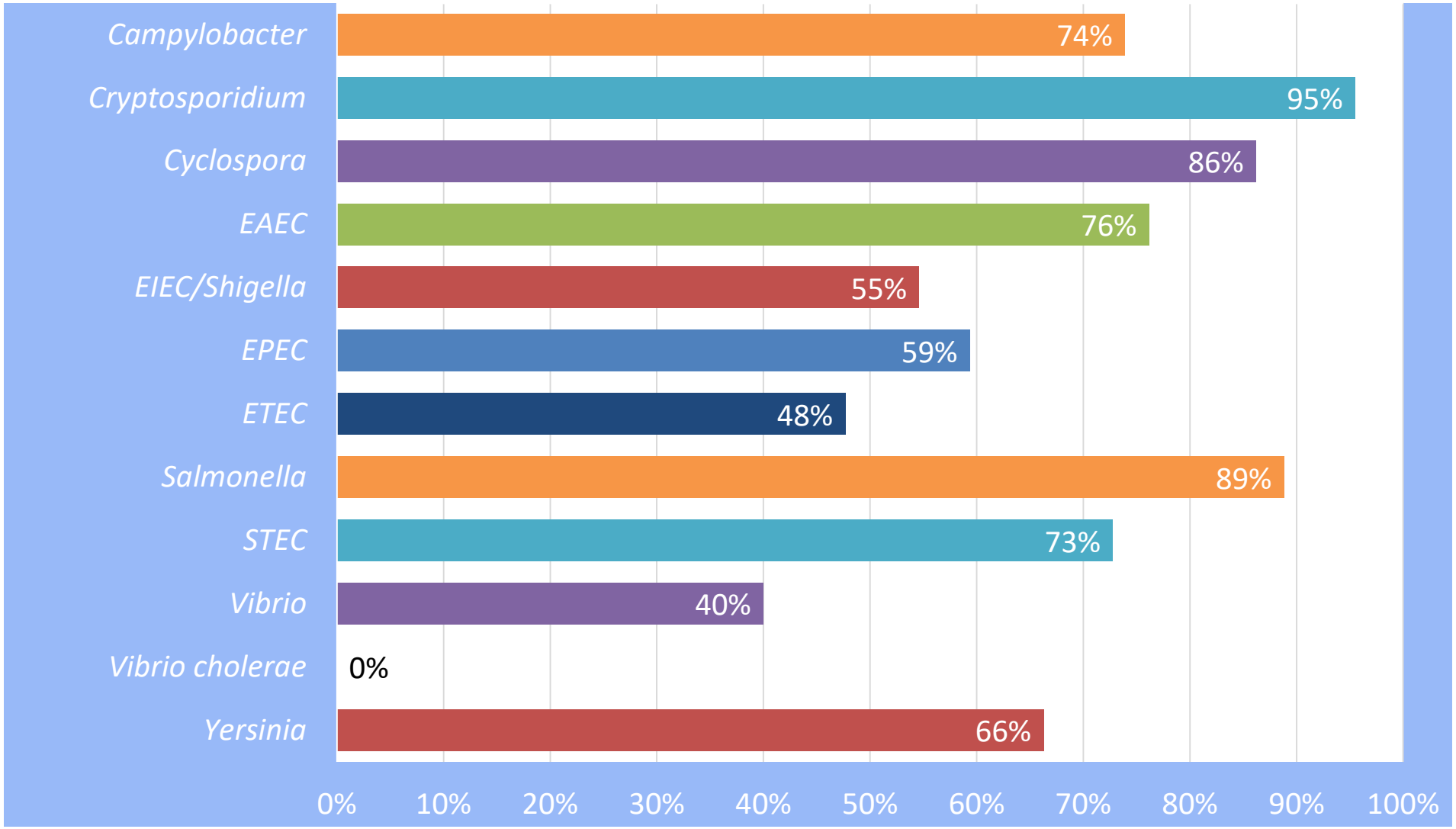
CIDT uptake and infections detected, FoodNet, 2012–2018*



*STEC excluded due to diagnostic differences, 2018 results preliminary

Dr. Aimee Geissler, CDC

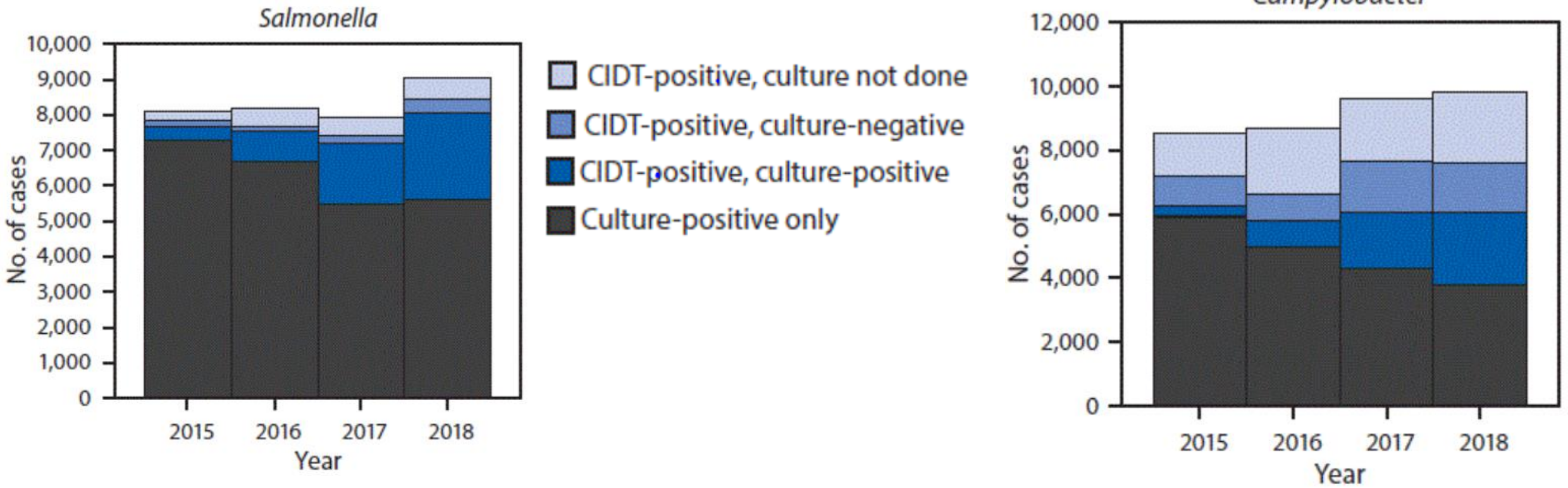
Culturing CIDT positive specimens in a state public health laboratory can recover an isolate (Minnesota)



David Boxrud, MDH

Including CIDT+ cases, cases are up. Are more infections truly happening, or they more likely to be diagnosed?

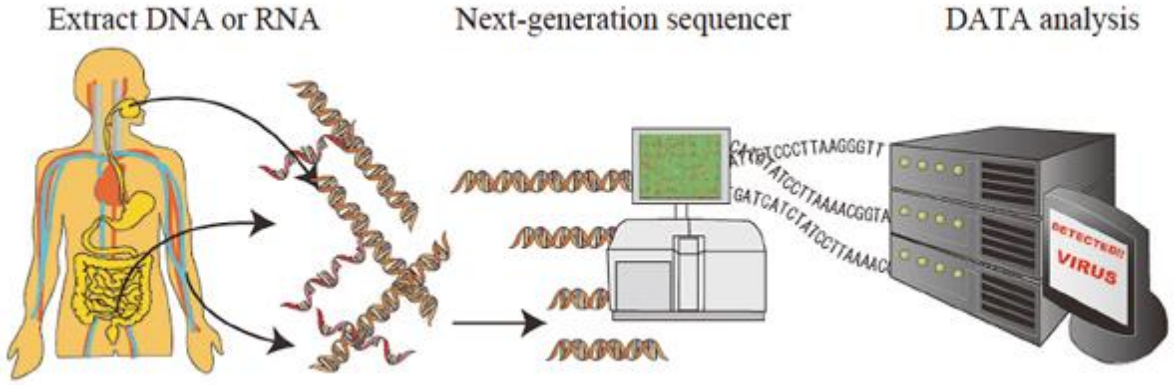
- FoodNet Active Surveillance (Collaboration of CDC, FDA, FSIS and 10 states)
- Tracking CIDTs since 2015



FoodNet Preliminary Report for 2018. MMWR 2019;68 (16):369-373

As microbiologic and diagnostic methods march forward, what will keep us on the cutting edge?

- Whole genome sequencing currently can take two weeks to turn around and requires an isolate
- Public health will need more advanced molecular diagnostic tools for direct use on clinical specimens to get results in hours and provide information public health needs
- Clinical researchers are exploring metagenomic methods now
- Work at CDC has begun as well, and will be a growing focus in the future



http://www.biken.osaka-u.ac.jp/act/act_imet-horii_e.php

Implementing whole genome sequencing - Challenges

- The clinical world is using more culture-independent diagnostic tests (CIDTs) that do not yield a living bacterial isolate.
- Sequencing requires an isolate, so need “reflex culture” on CIDT+ specimens
- “Big data” puts strain on IT infrastructure at CDC and in state health departments
- Changes in laboratory workflow and workforce
- Expecting a surge in detected clusters = more investigations (
  need more epidemiologists and environmental specialists)

Implementing whole genome sequencing - Opportunities

- Better target and accelerate prevention strategies
- Public health epi and lab on common network platform in each state
- Value beyond foodborne outbreak detection and investigation; can be used for other pathogens
- Bridge to the future – developing new metagenomic methods will depend on DNA sequence data

Foodborne disease prevention in the 21st century: An evolving public health approach

- Whole genome sequence-based surveillance is an evolutionary step forward:
  - More precise subtyping, combined with enhanced patient interviews and traceback
  - More outbreaks and sources detected and controlled
  - More food safety gaps found and corrected
  - Applicable to many other infections as well as the enteric ones
- A step towards the future, when Public Health will have culture-independent tools providing needed information rapidly
- Better approaches to defining the targets for prevention

- **Long term effect: Impact on industry, regulators, and consumers to drive down incidence of foodborne infections**

Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov