Gaps and Opportunities for Public Health Investments in Enteric Diseases

Heather Carleton, MPH, PhD

Chief, Enteric Diseases Laboratory Branch, DFWED, NCEZID, U.S. Centers for Disease Control

Chair, PulseNet USA

Co-Chair, PulseNet International

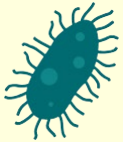
NASEM Pathogen Genomics, July 2024

Culture-BasedTestingfor Enteric Disease Surveillance in the United States

Symptoms

A person with diarrheal illness seeks medical care and is tested for bacterial infection.

Testing & Diagnostics

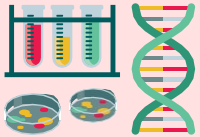


Culture-Based Testing

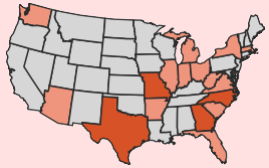
Isolating bacteria takes several days, delaying diagnosis.

The isolated bacteria is sent to Public Health Laboratories (PHL).

Outbreak Detection



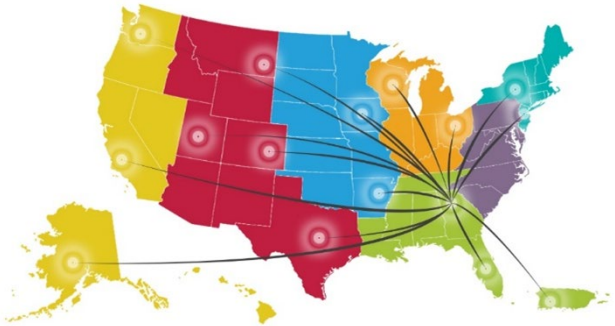
The PHL performs a Whole Genome Sequencing (WGS). This test helps detect serotype, antimicrobial resistance, and whether an isolate may be part of an outbreak.



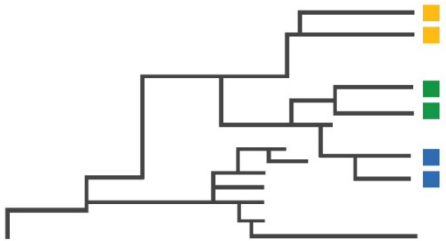
WGS data is used to detect outbreaks in PulseNet. Bacterial isolates are needed to link people that became ill from a common source.

PulseNet USA
The National Molecular Subtyping Network for Foodborne Disease Surveillance
CDC

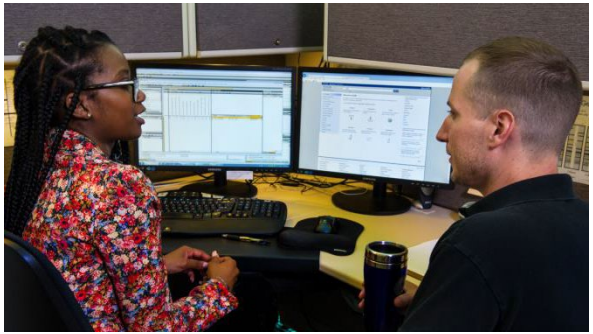
WGS in PulseNet– Active pathogen genomics surveillance for enteric diseases



WGS data from pathogens are transmitted to centralized database at CDC in Atlanta, Georgia



PulseNet Monitors for clusters of illnesses with the same molecular “fingerprint”



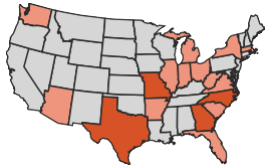
Then tells epidemiologists about potential outbreaks to investigate

Opportunities for investment in public health surveillance – Improving Public Health Reporting

Ill Person

Healthcare Provider

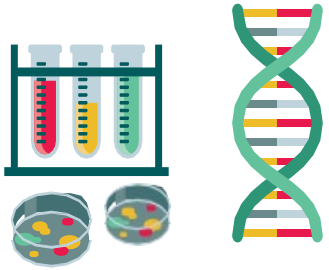
Clinical Lab

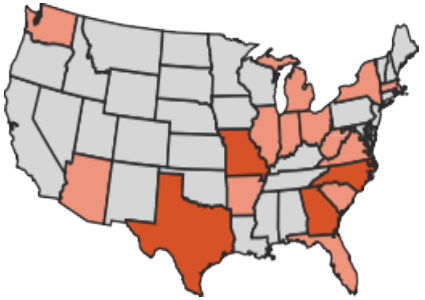


State Reporting Rules

- **1 in 6 Americans get a foodborne illness each year (~55 million cases); WGS data from approximately 60,000 isolates get submitted to PulseNet each year**
- **Not all clinical and diagnostics laboratories comply in a timely manner to forward samples to public health**
- **Not all pathogens that cause foodborne illness are required by states to forward a sample to a public health laboratory**

Opportunities for investment in public health surveillance – Capacity Building

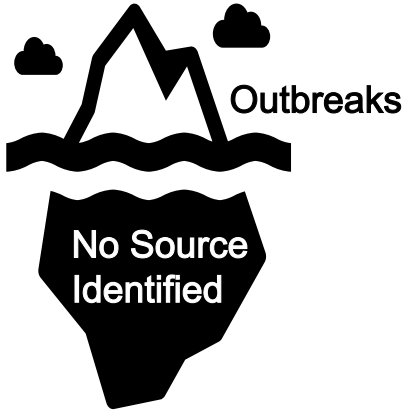




- **Diverse pathogens cause foodborne illness including bacteria, viruses, and parasites – expertise is split across different groups at CDC and Public Health Laboratories and there is not a unified diarrheal sample processing approach**
- **The pathogen genomics surveillance system is not fully funded to sequence all isolates submitted to public health laboratories – can limit or delay ability to detect outbreaks**
- **Some Public Health Departments do not have resources to interview all cases with foodborne illness, interviews are conducted weeks after initial food exposure, limiting ability to identify potential sources**

Opportunities for investment in public health surveillance – building capacity beyond outbreaks

- **Most illnesses reported through PulseNet are not linked to a source**
  - ~10% of isolates are part of an outbreak investigation and only some of those are linked to a vehicle
- **Driving down incidence of foodborne pathogens requires better understanding of the 90% of illnesses not identified as being part of outbreaks**
- **Reoccurring, emerging, and persisting strains account for some of the other 90%**
- **These strains may require different control measures than those used for outbreaks**



CDC REP strains

Culture Independent Diagnostic Testing (CIDTs) for Enteric Diseases and Impact on PulseNet

Symptoms

A person with diarrheal illness seeks medical care and is tested for bacterial infection.

Testing & Diagnostics

REPORT	
Salmonella	✓
E. coli	–
Norovirus	–
Giardia	–

Culture Independent Diagnostic Testing (CIDT)

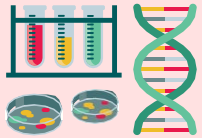
CIDTs can identify the cause of the illness in *hours* without having to isolate the bacteria.

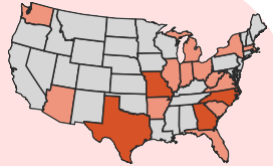
CIDTs **don't produce isolated bacteria needed to detect outbreaks** using WGS

Some clinics send samples to PHLs to isolate bacteria.

Many clinics DO NOT send samples to PHLs to isolate bacteria.

Outbreak Detection





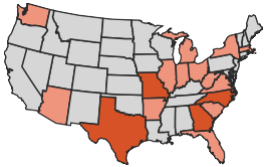
Isolates **not available to detect outbreaks** with WGS.

CIDTs may diagnose foodborne illness more quickly, but they don't produce isolates needed to detect outbreaks.

Opportunities for investment in public health surveillance – Improving Public Health Reporting

CIDT

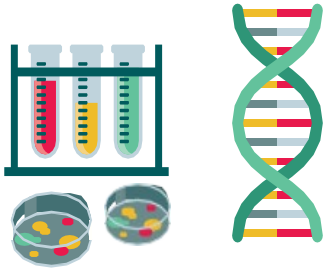
Clinical Lab

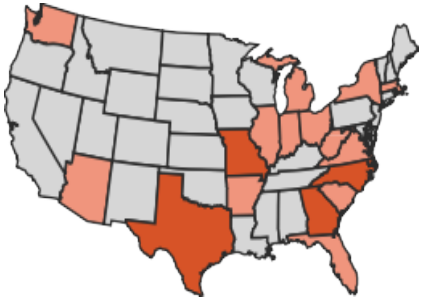


State Reporting Rules

- **Use of CIDT continues to increasing annually (FoodNet 2024)**
- **CIDT do not produce an isolate for WGS, some CIDTs render sample incompatible with culture**
- **Diagnostic and clinical laboratories do not know to or are not required to perform reflex culture for enteric bacteria or forward positive sample to public health**
- **Not all pathogens that cause foodborne illness are required by states to forward a sample to a public health laboratory**

Opportunities for investment in public health surveillance – Capacity Building

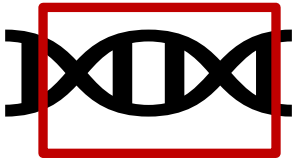




- **Generating strain level subtyping information from a metagenomics sample is challenging in stool (signal is low)**
- **Most metagenomics approaches do not link serotype or antimicrobial resistance information to the pathogen; pathogen and commensal bacteria difficult to distinguish in stool**
- **Public health infrastructure does not have the capacity to support sequencing and bioinformatics for shotgun metagenomics for food safety**

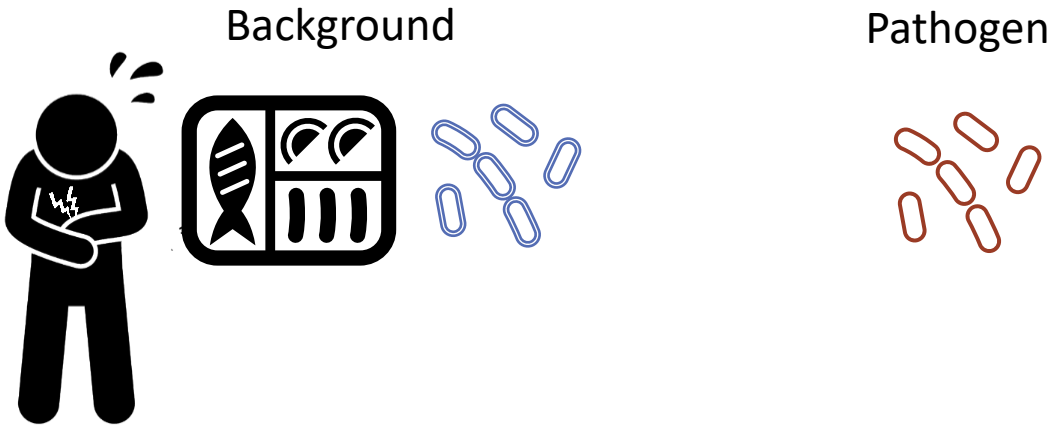
Opportunities for investment in public health surveillance – targeted metagenomics approaches

- Requires prior knowledge of pathogen – CIDT test result
- Amplicon-based approaches can target thousands of informative regions in stool DNA (Highly Multiplexed Amplicon Sequencing)
- Method output is compatible with isolate WGS data
- Generates a pathogen DNA fingerprint for outbreak detection
- Assays can be designed beyond enteric bacteria to focus on multiple pathogen types (virus, parasite) or genes (antimicrobial resistance)
- Assay design can support disambiguation of pathogens from gut commensals
- To deploy this method investments are needed to continue to build assays and capacity in public health



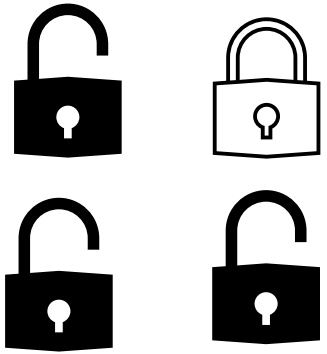
To learn more about HMAS

Opportunities for investment in public health surveillance – Shotgun metagenomics

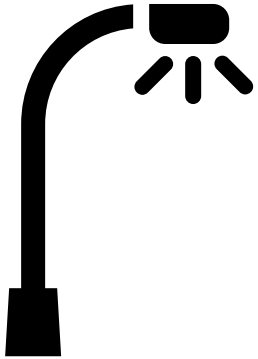


- **Pathogen agnostic approach to identify potential pathogen**
- **Signal to noise issue makes it challenging to get strain level information needed for enteric disease surveillance - stool contains nucleic acids from ill person, food, pathogenic bacteria, and commensal bacteria**
- **Need methods to enrich pathogen DNA to generate a molecular subtype**

Opportunities for investment in public health surveillance – beyond currently reported pathogens



One in four foodborne outbreaks are caused by unknown agents[1]

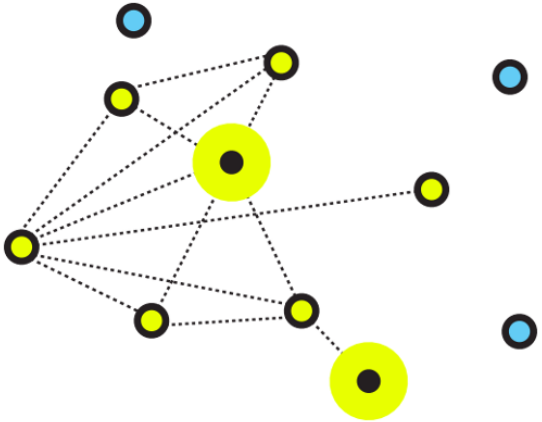


Current methods and tests not designed to identify novel pathogens or detect gaps in existing methods

There are collection recommendations, but nowhere to analyze them

Scallan et al., EID Journal, 2011

Unresolved foodborne outbreaks: Cost to public health



$1000-3000 per case

Estimate of epi and lab resource cost

Alice White, CO Integrated Food Safety COE

Pathogen agnostic approaches can address gaps in existing methods

DISPATCHES

Emergence and Spread of *Chlamydia trachomatis* Variant, Sweden

Björn Herrmann, Anna Törner, Nicola Low, Markus Klint, Anders Nilsson, Inga Velicko, Thomas Söderblom, and Anders Blaxhult

A variant of *Chlamydia trachomatis* that had escaped detection by commonly used systems was discovered in Sweden in 2006. In a nationwide study, we found that it is now prevalent across Sweden, irrespective of the detection system used. Genetic analysis by multilocus sequence typing identified a predominant variant, suggesting recent emergence.

In 2006 a new variant of *Chlamydia trachomatis* (nvCT) tion systems in late 2006 in response to the emergence of nvCT. The statistical methods are described in the online Technical Appendix (available from http://www.cdc.gov/EID/content/14/9/1462-Techapp.pdf). The total number of chlamydia cases detected in Sweden in the first 6 months of 2006 was lower than that in 2005, and the proportion of tests that were positive also fell (Table 1). In 2004, the proportion of positive chlamydia tests was similar whether laboratories used Abbott/Roche or BD test systems. From 2004 to 2005, there was a relative reduction of 3.4% (95% confidence interval [CI] 5.8–1.0) in chlamydia positivity in laboratories using the Abbott or Roche methods ($p = 0.006$) but no change in the proportion of positive samples in laboratories using the BD test system (–0.4%, 95% CI –4.2 to +3.5). During the first 6 months of 2005 and 2006, the positivity rates of samples tested by Abbott or Roche systems fell further; samples tested that used the BD system remained stable. The estimated difference in proportions of chlamydia-positive samples in counties that used Abbott or Roche tests compared with counties that used the BD method was –9.5 % (95% CI –14.1 to –4.7, $p = 0.0005$), after baseline differences and county differences in testing were controlled for

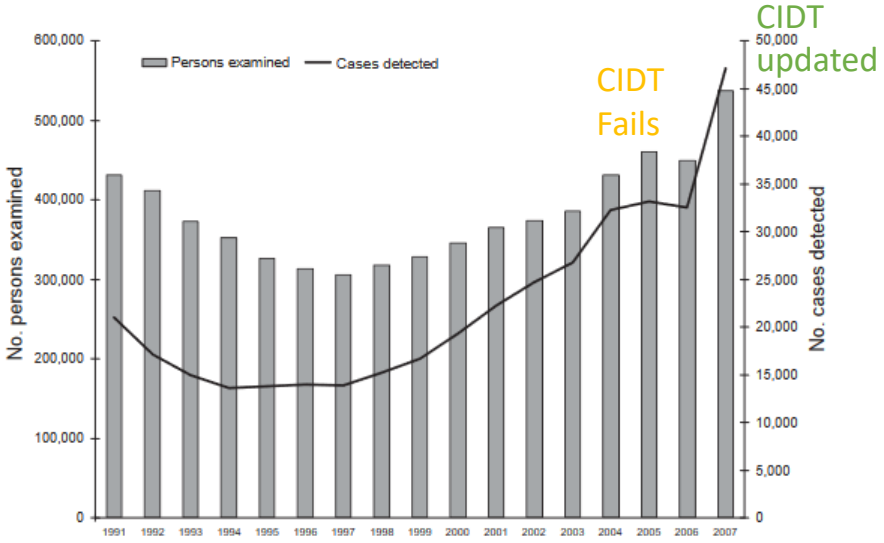
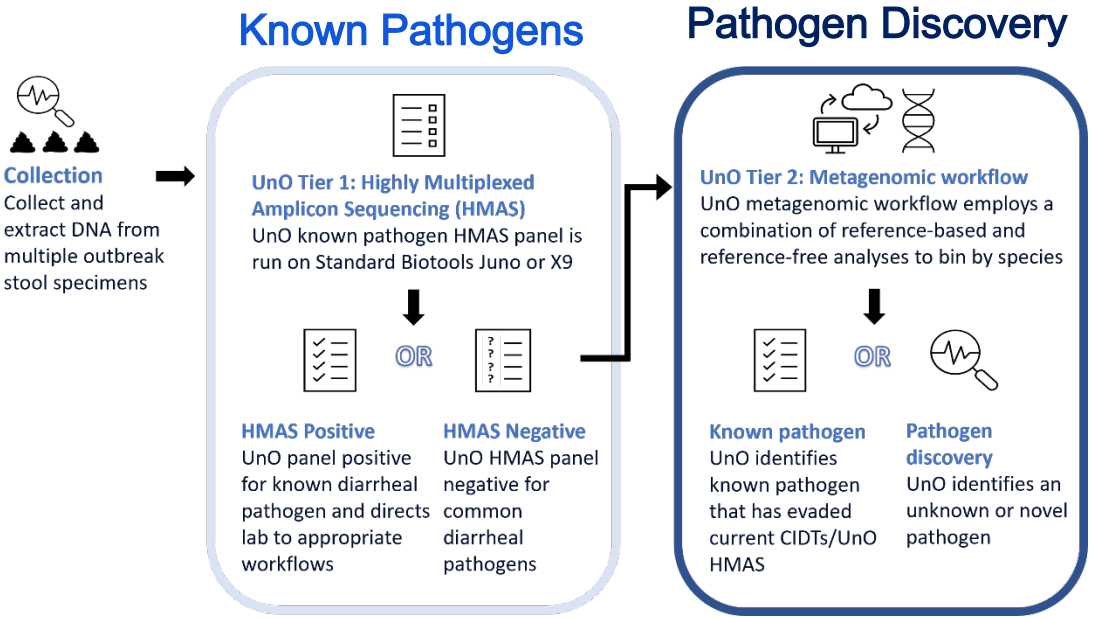


Figure 2. *Chlamydia trachomatis* reports, Sweden, 1991–2007. The number of persons examined and cases detected in 2007, when diagnostic tests for chlamydia had been changed, is in line with the increasing trend from 2004 and before. The figures for 2005 and 2006 reflect the failure to detect cases of the new chlamydia variant in some counties.

- **When pathogens escape existing CIDT molecular targets, additional methods are needed to identify gap**

Opportunities for investment in public health surveillance: Leveraging unknown outbreak (UnO) to identify potential new or underreported enteric pathogens



- Requires investment to develop methods, build capacity in laboratory, epidemiology, and bioinformatics

To learn more reach out to our team

Opportunities for investment in public health surveillance for enteric diseases

- Opportunities to invest and improve public health reporting and public health capacity for isolate and sample-based surveillance as well as case interviews
- Opportunities for investment beyond traditional outbreak detection by understanding more about REP strains and other isolates not part of outbreaks and characterizing potential new pathogens causing foodborne outbreaks
- Opportunities to invest in unified approaches for diarrheal surveillance that include bacteria, viruses, and parasites
- Opportunities to develop new approaches for strain level subtyping of enteric bacteria that can be deployed in public health

More Information:

PulseNet

Foodborne Outbreaks

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