Everything in Sequence: Listeriosis Outbreak Investigations in the Era of WGS

Brendan Jackson, MD, MPH

LCDR US Public Health Service

Division of Foodborne, Waterborne, and Environmental Diseases

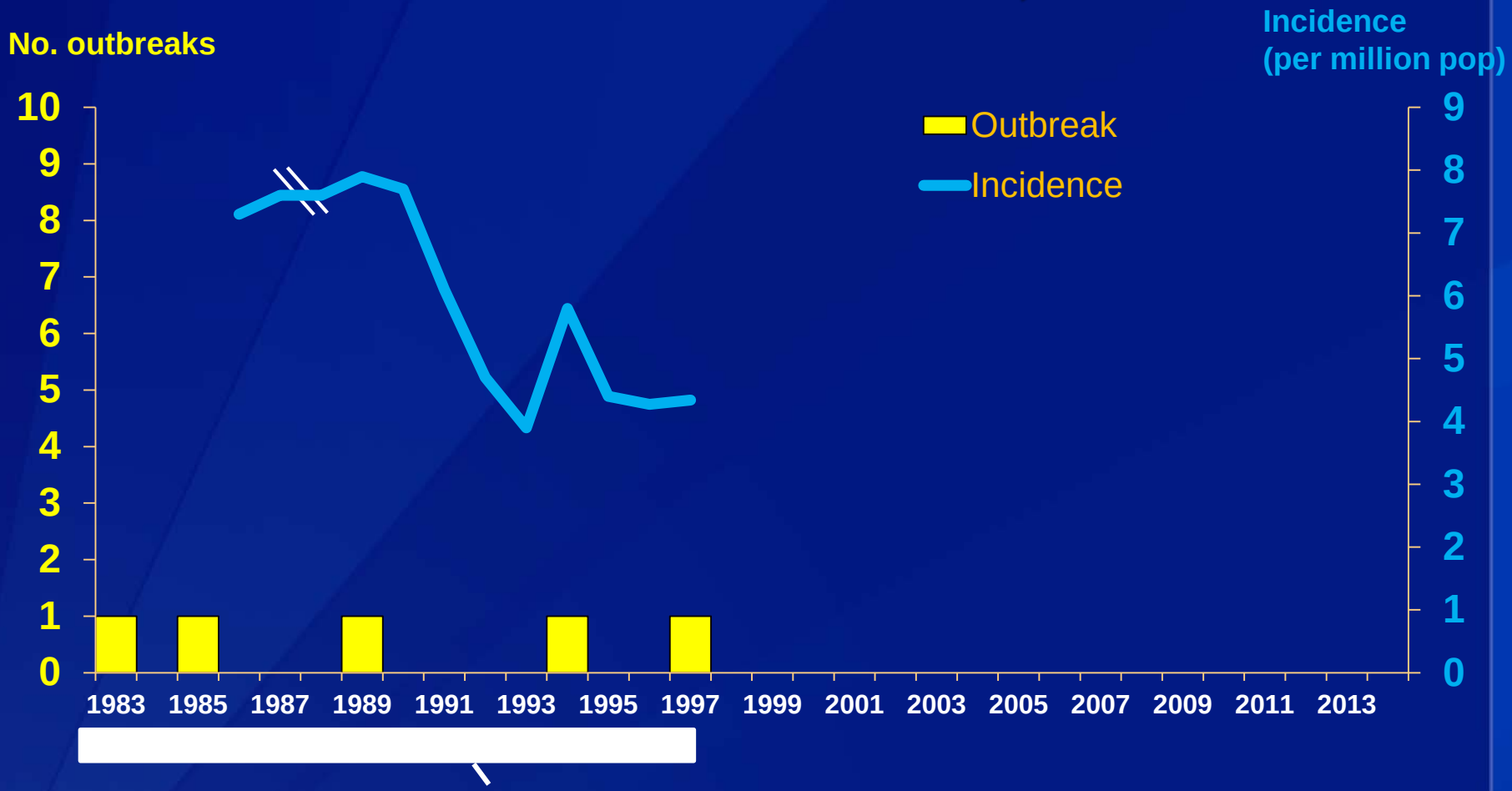
Centers for Disease Control and Prevention

Disclaimers

- *The findings and conclusions in this presentation are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.*

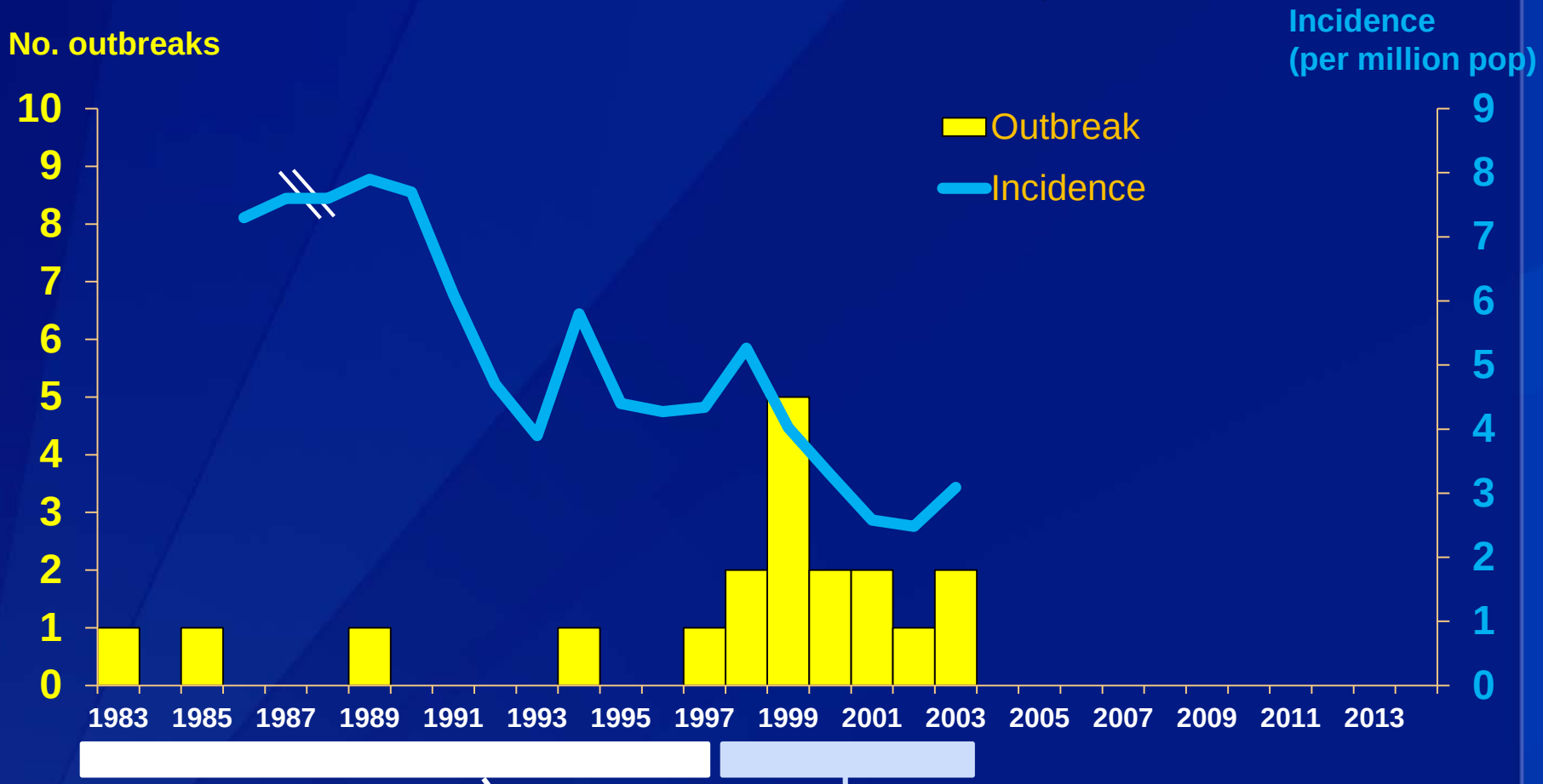
- *No financial conflicts of interest to report.*

Listeria Outbreaks and Incidence, 1983-2014



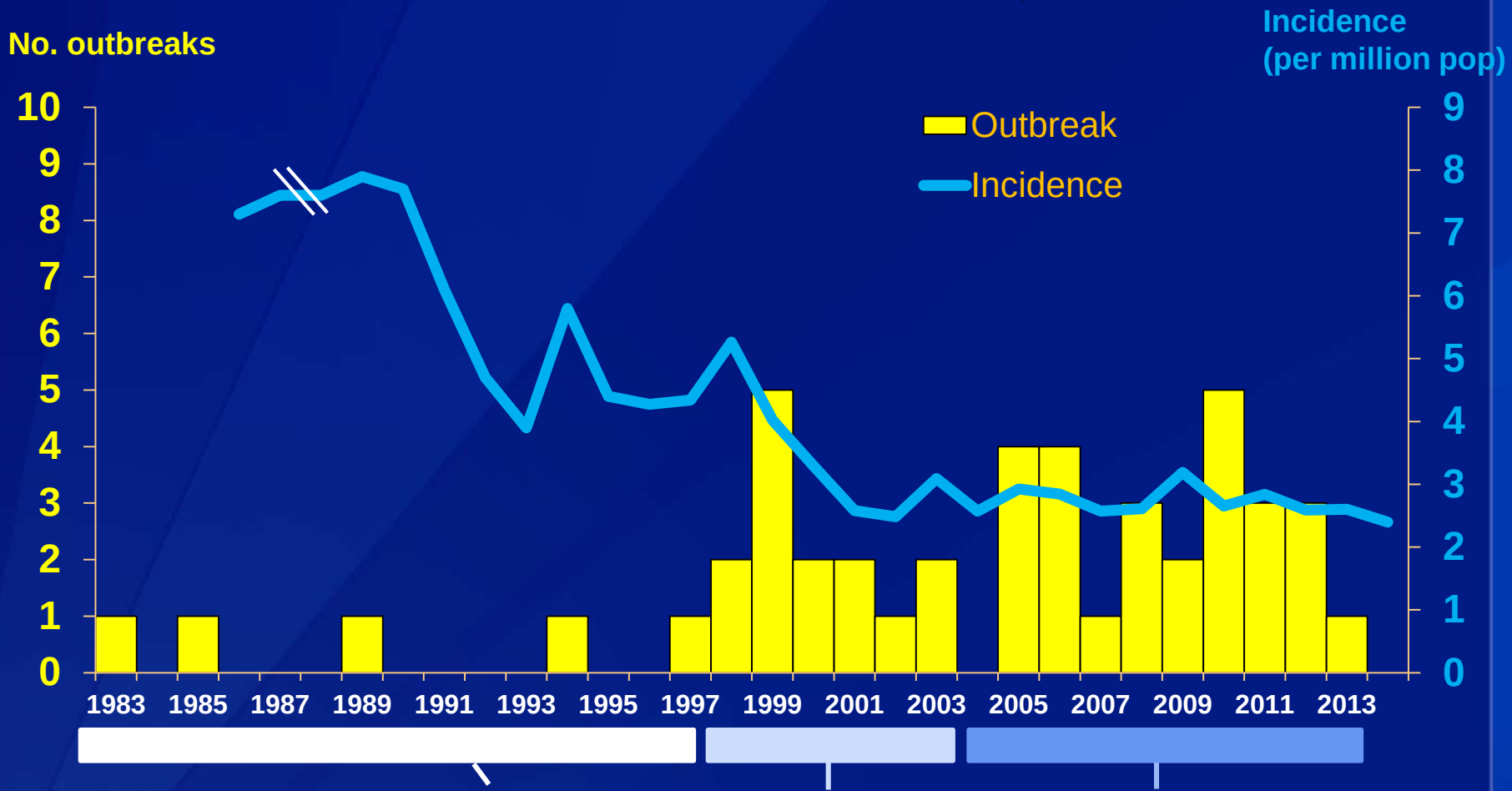
Era	Pre-PulseNet
Outbreaks per year	0.3
Median cases per outbreak	69

Listeria Outbreaks and Incidence, 1983-2014



Era	Pre-PulseNet	Early PulseNet
Outbreaks per year	0.3	2.3
Median cases per outbreak	69	11

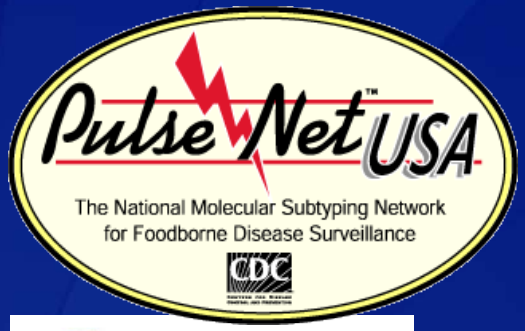
Listeria Outbreaks and Incidence, 1983-2014

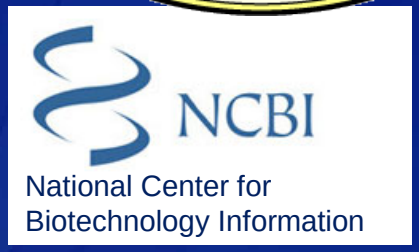


Era	Pre-PulseNet	Early PulseNet	*Listeria* Initiative
Outbreaks per year	0.3	2.3	2.6
Median cases per outbreak	69	11	5.5

Listeria WGS Pilot Project

- Started September 2013
- Goal: Sequence all *Listeria monocytogenes* isolates
- Near real-time (<1 week for patient isolates)

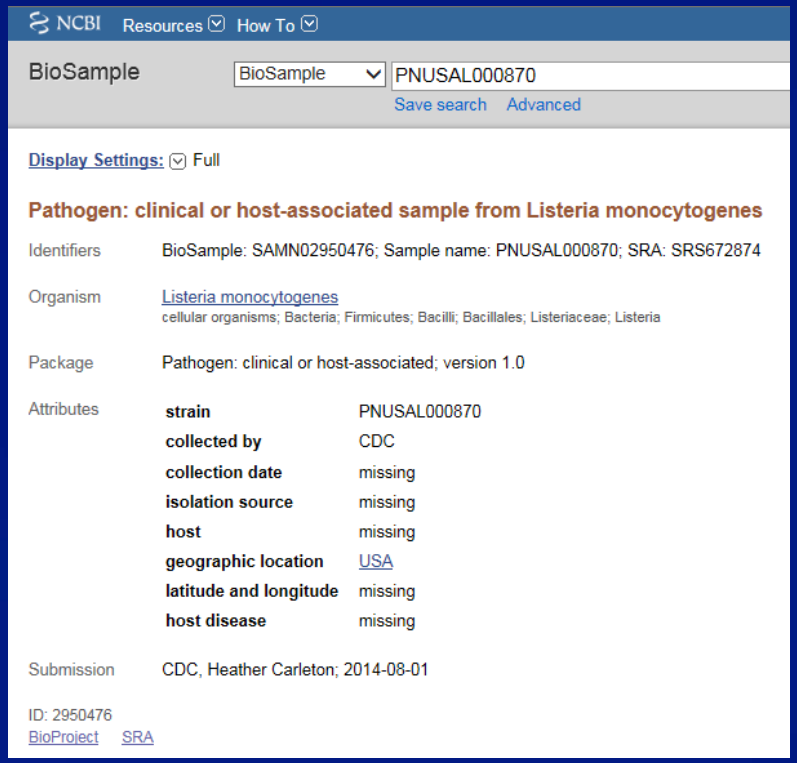




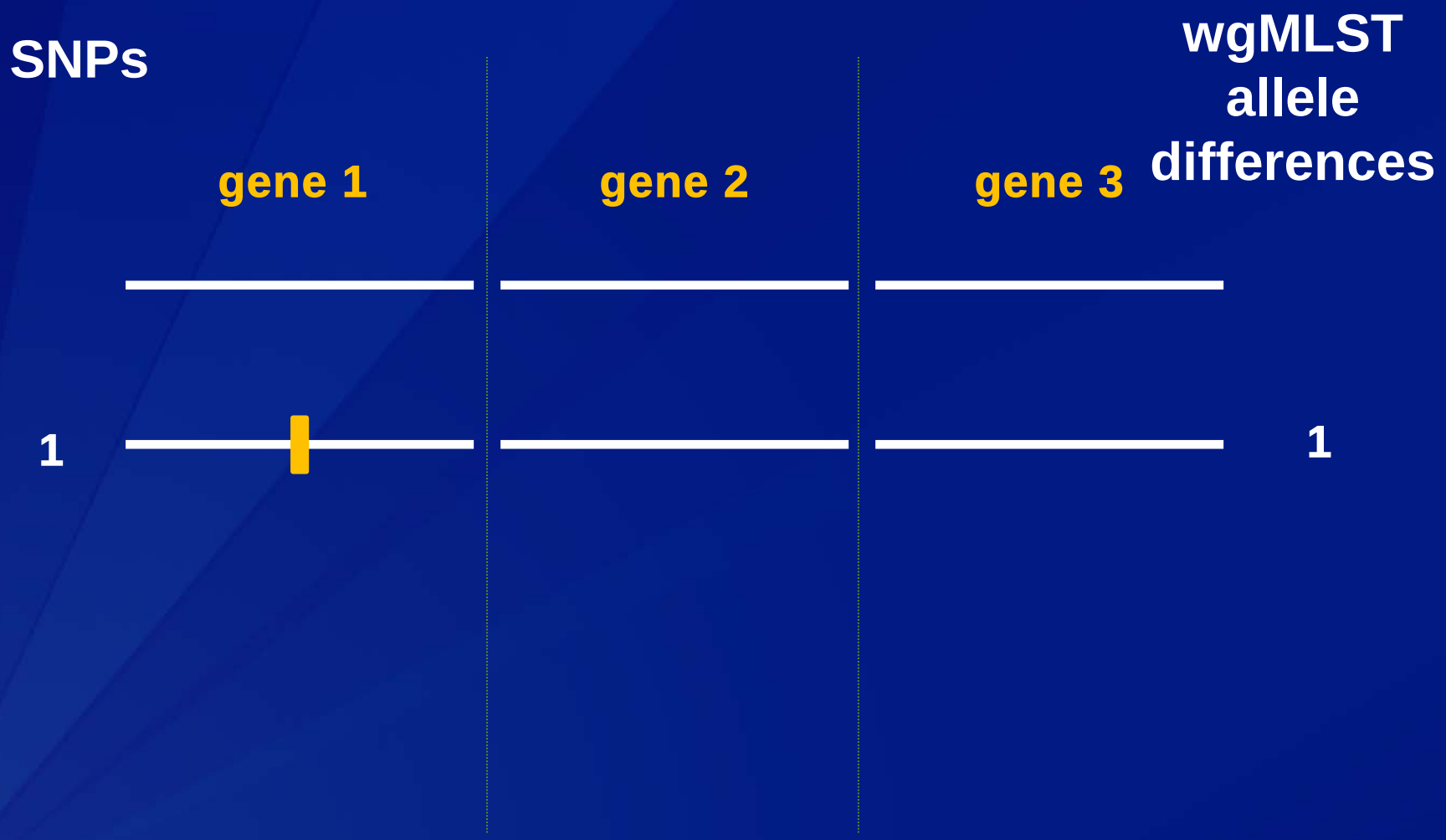
Public Health Agency of Canada

Listeria WGS Analysis Methods

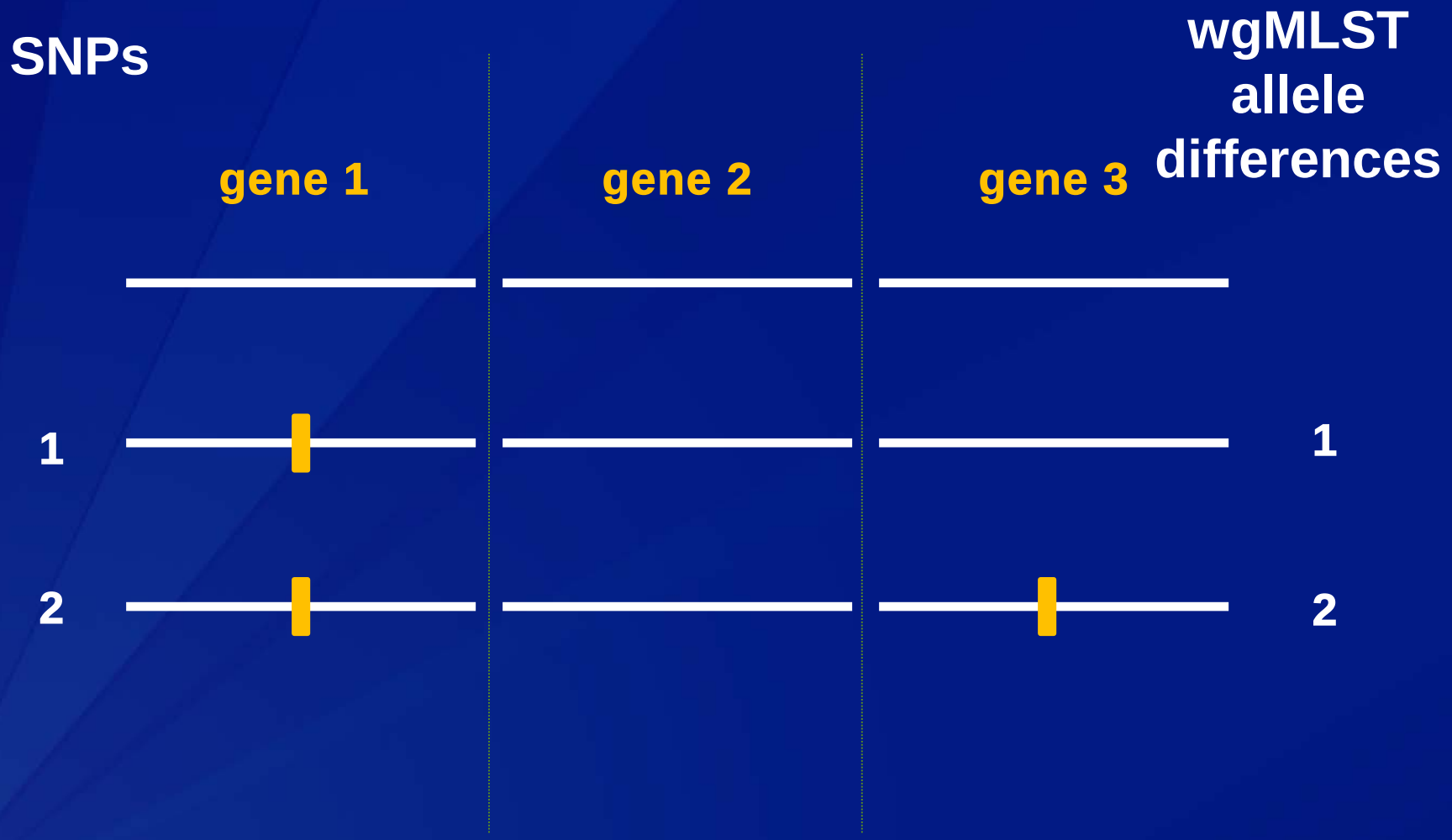
- Kmer
- High-quality single nucleotide polymorphism (hqSNP)
- Whole-genome multilocus sequence typing (wgMLST)



Relationship Between SNPs and wgMLST Alleles

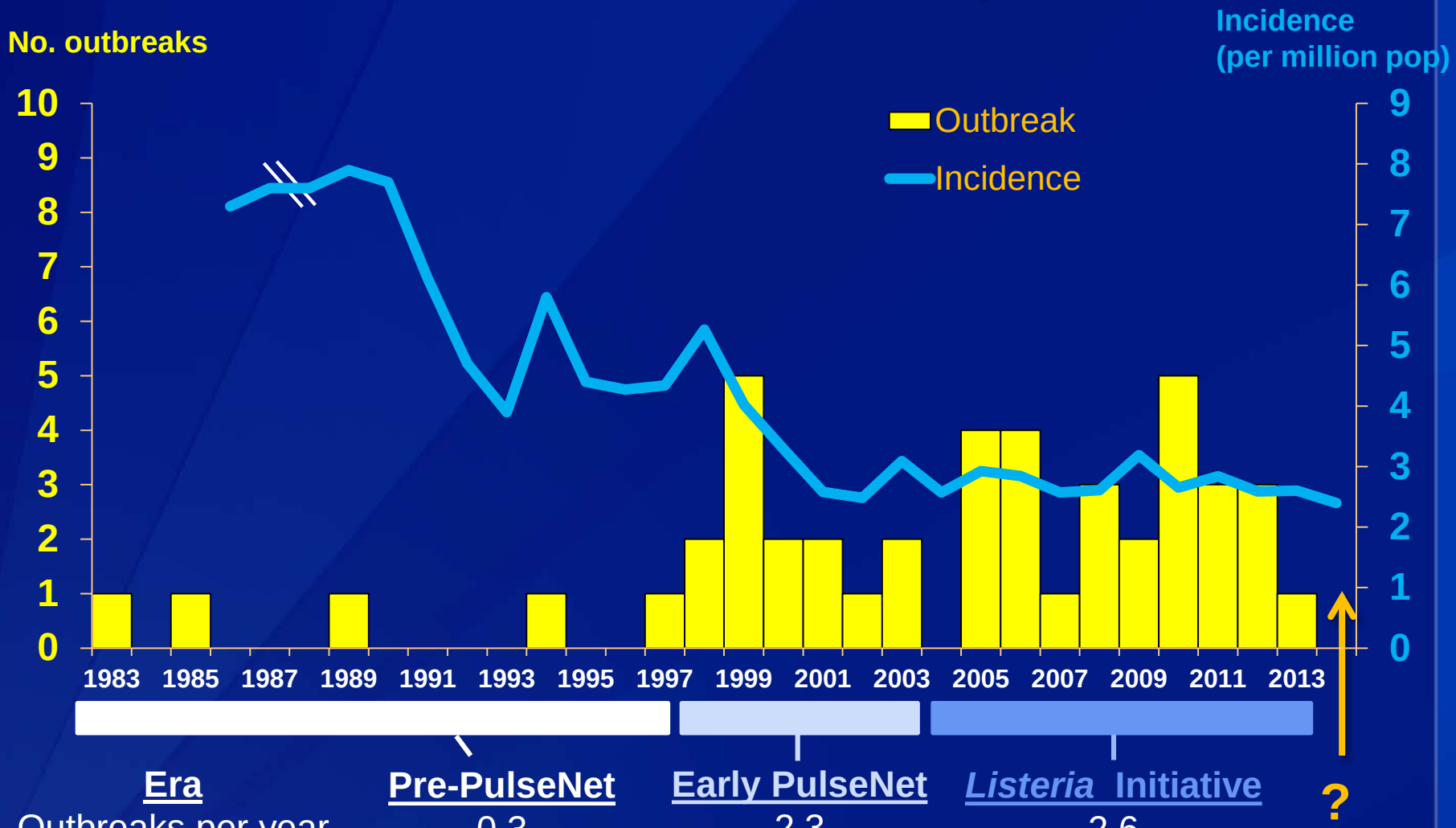


Relationship Between SNPs and wgMLST Alleles



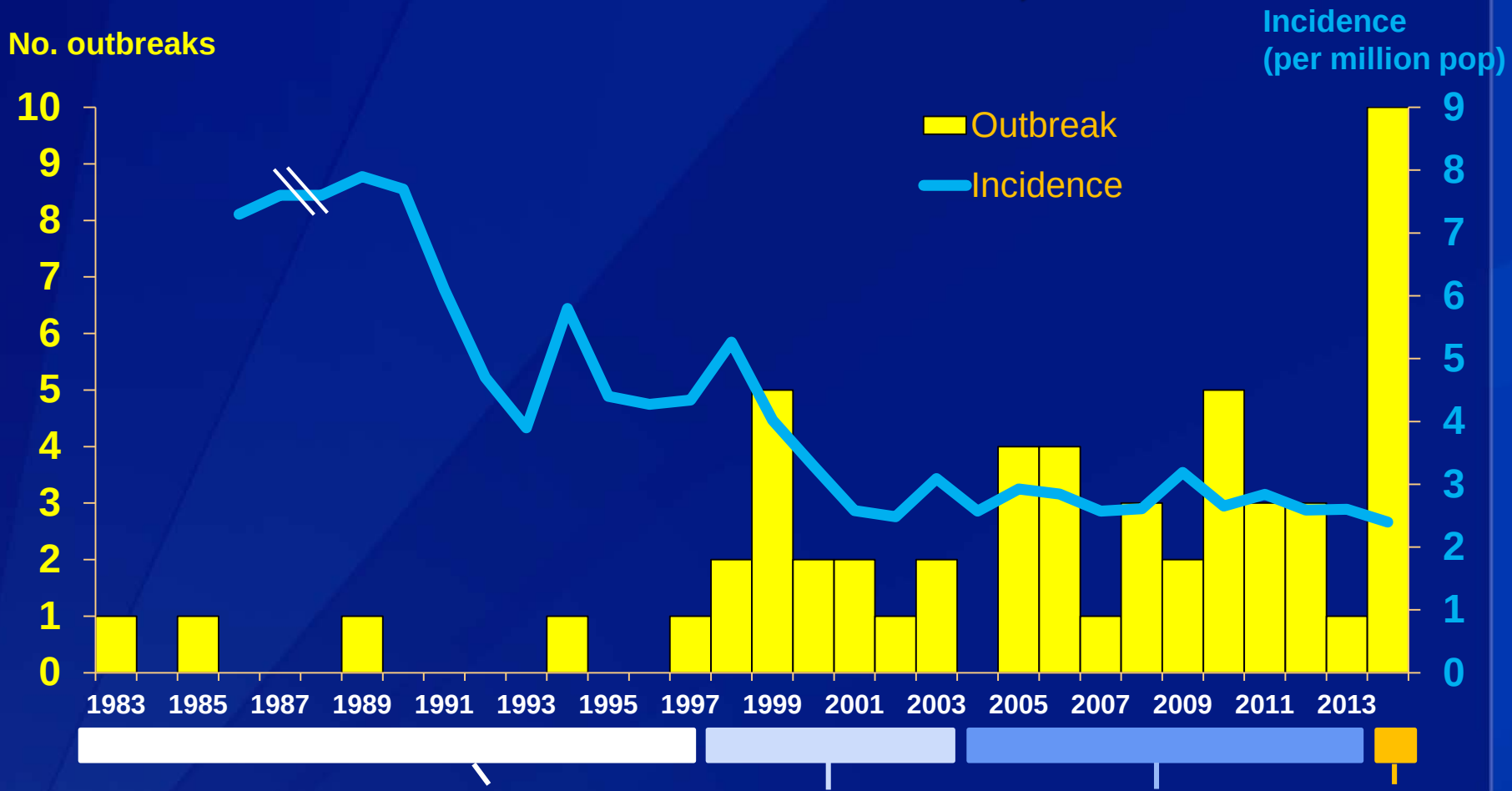
Relationship Between SNPs and wgMLST Alleles

Listeria Outbreaks and Incidence, 1983-2014



Era	Pre-PulseNet	Early PulseNet	*Listeria* Initiative
Outbreaks per year	0.3	2.3	2.6
Median cases per outbreak	69	11	5.5

Listeria Outbreaks and Incidence, 1983-2014

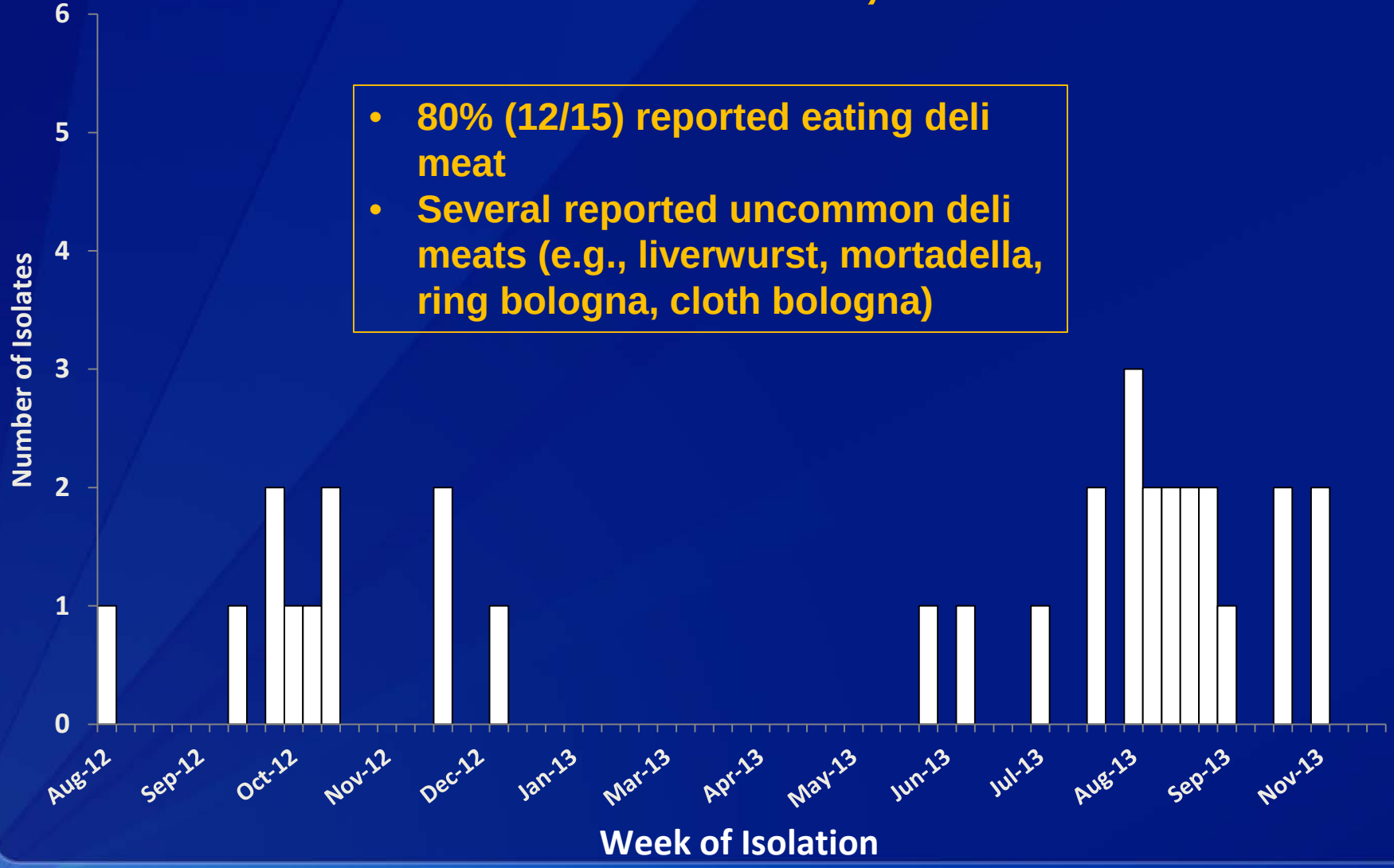


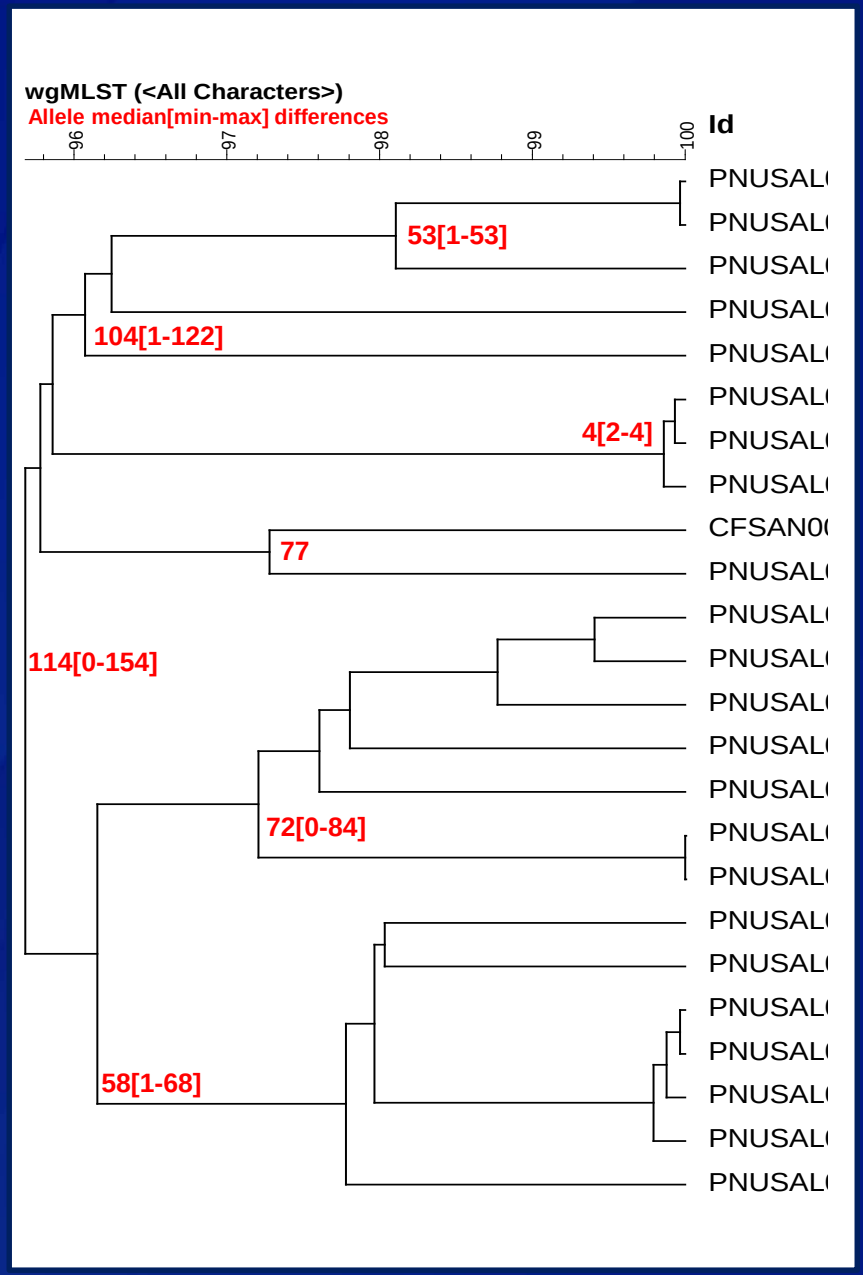
Era	Pre-PulseNet	Early PulseNet	*Listeria* Initiative	WGS
Outbreaks per year	0.3	2.3	2.6	10
Median cases per outbreak	69	11	5.5	3

HOW DID WGS AFFECT INVESTIGATIONS?

PFGE Cluster Possibly Associated with Uncommon Deli Meats, 2012–2013

- 80% (12/15) reported eating deli meat
- Several reported uncommon deli meats (e.g., liverwurst, mortadella, ring bologna, cloth bologna)





wgMLST analysis by Enteric Diseases Laboratory Branch, CDC

wgMLST analysis by Enteric Diseases Laboratory Branch, CDC

Cluster Investigation
December 2013

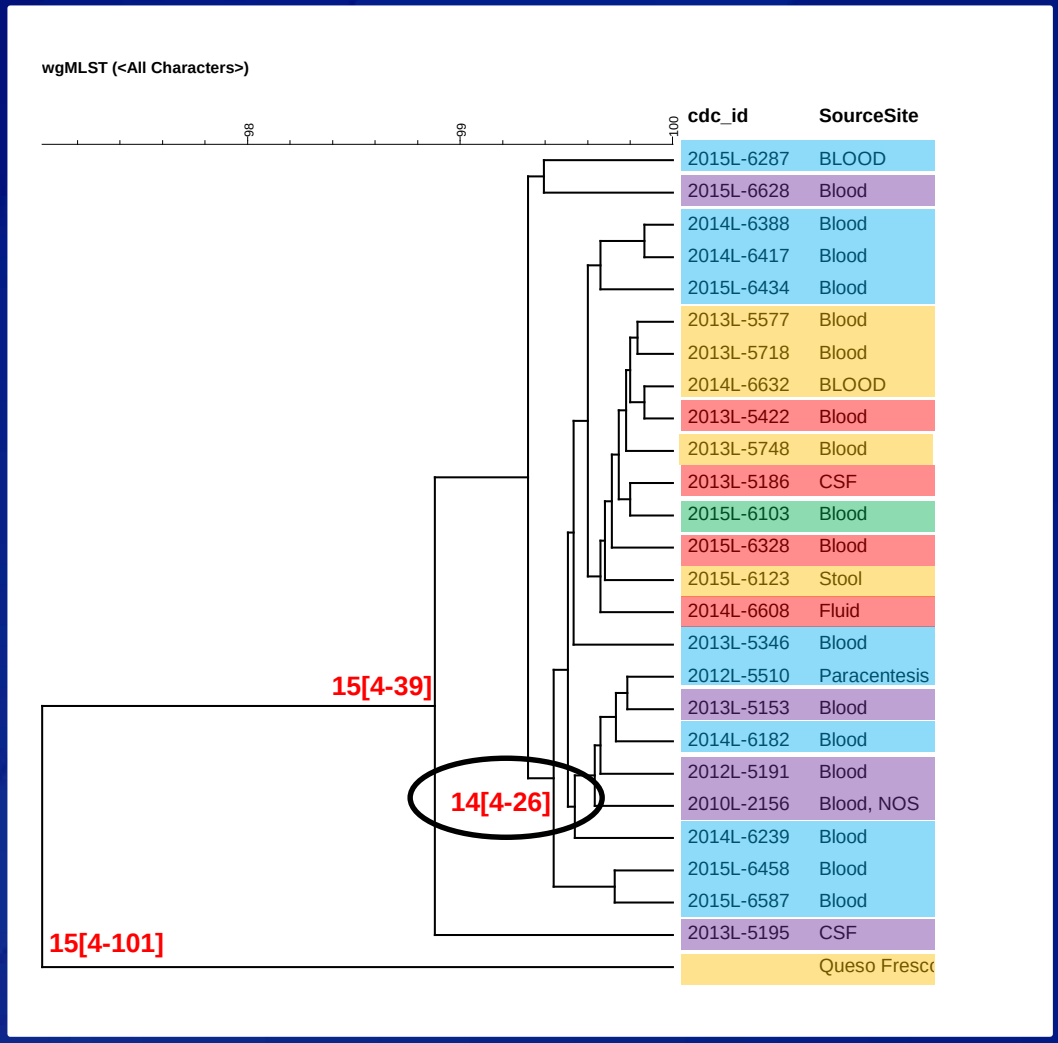
- **PulseNet identifies PFGE cluster of 4 cases with rare pattern**
  - California (2), Illinois (1), Massachusetts (1)
  - Specimen collection dates July–December 2013
- **All 4 patients seemed to be of Middle Eastern descent (Armenia, Syria, and Yemen)**
- **2 patients interviewed with supplemental form**
- **Unable to identify common food**
- **Cluster closed in January 2014**

Cluster Investigation
August 2015

- **PulseNet identifies cluster of 12 cases with different PFGE pattern, also rare**
  - California (7), Massachusetts (2), New York (2), Colorado
  - Specimen collection dates 2013–2015
  - 10 sequenced isolates ≤25 alleles by wgMLST

- **More WGS analysis shows isolates from 2010–2015 with 4 other PFGE patterns are also highly related, including isolates from 2013 cluster**

wgMLST Phylogeny as of Sept. 16



- 5 different PFGE patterns
- All isolates from patients except “unrelated” food isolate at bottom

WGS analysis by Enteric Diseases Laboratory Branch, CDC

Investigation Unfolds

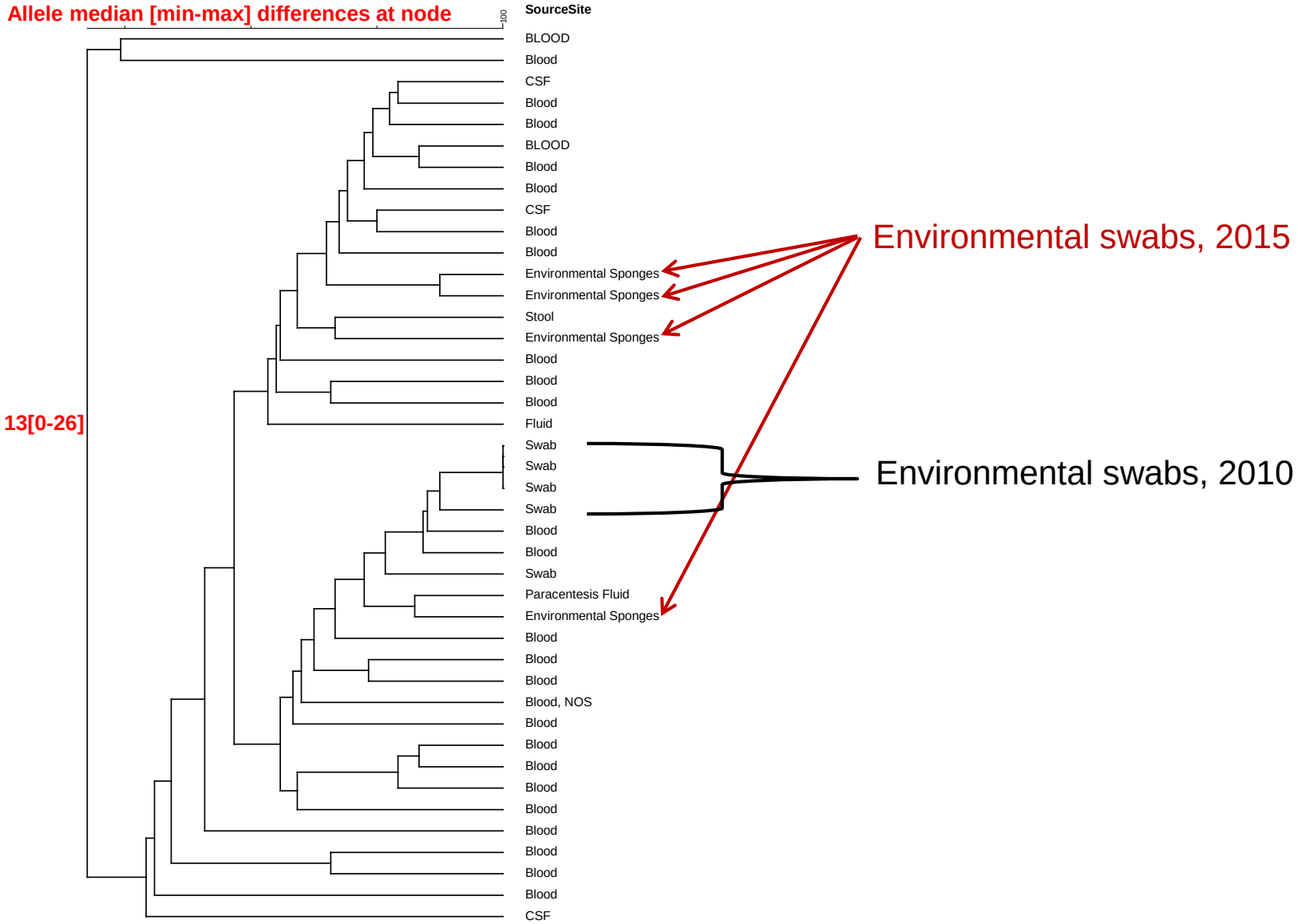
- **With more cases**
  - Middle Eastern connection still present
  - Soft cheese association identified (OR 26, p <0.001), mostly Middle Eastern and Mediterranean style
  - Suspect Company A based on brands reported

- **PulseNet finds matching 5 environmental isolates from Company A cheese production facility in 2010**

One dead, 24 sick from multi-state Listeria outbreak linked to soft cheeses

By Debra Goldschmidt, CNN
Updated 1:39 PM ET, Fri September 18, 2015

wgMLST Phylogeny as of Nov. 13



WGS analysis by Enteric Diseases Laboratory Branch, CDC

Unlikely to Be Implications of WGS

[Person A] drew the "yes" side of the first debate question [at International Association for Food Protection annual meeting], ***"Is shoe leather epidemiology dead in the era of whole-genome sequencing?"***

-Food Safety News. July 27, 2015

"You catch things far earlier" with sequencing, said [Person B]. "It can be two cases. ***If you see a match, Bam! You've got em."***

-Reuters. August 27, 2015

A New Era
Listeria WGS

- Helped detect more clusters and solve more outbreaks
- Focused epidemiological resources
- Identified new food sources of listeriosis
- Epidemiologic data remain essential
- WGS not just for *Listeria* anymore

Acknowledgments

State, Local, and Territorial Health Departments

Advanced Molecular Detection Initiative

Food and Drug Administration

US Department of Agriculture's Food Safety and Inspection Service

National Center for Biotechnology Information

Enteric Diseases Laboratory Branch

Enteric Diseases Epidemiology Branch

Outbreak Response and Prevention Branch

Epidemic Intelligence Service

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333

Telephone: 1-800-CDC-INFO (232-4636)

Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

Public Interest

U.S. Google Search Trends for “Listeria”