Whole Genome Sequencing at the Minnesota Department of Health

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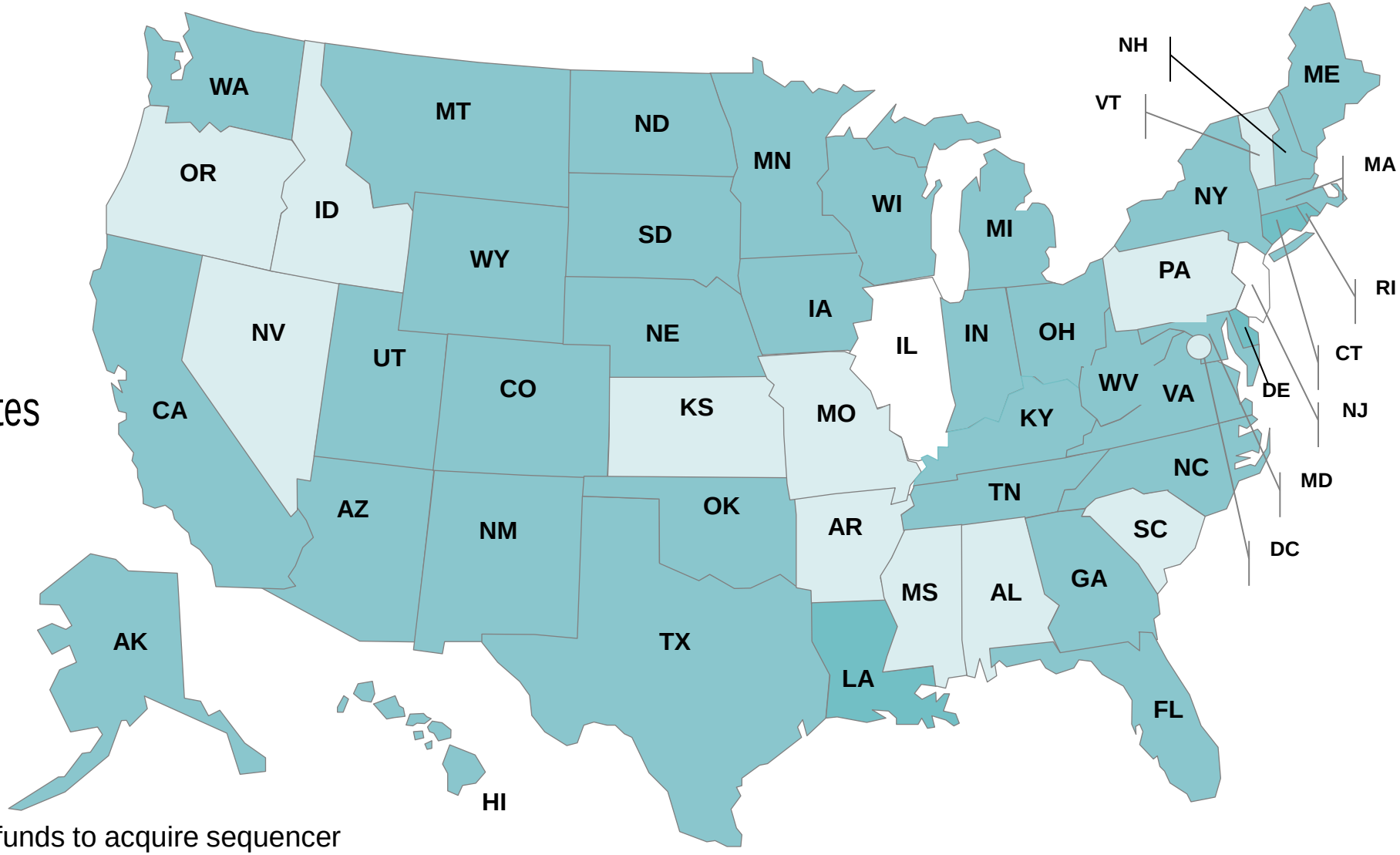
Introduction

- Status on whole genome sequencing (WGS) at public health labs (PHLs)
- Role of WGS at PHLs
- WGS communication at PHLs
- WGS evaluation at PHLs
- Examples of the utility of WGS at PHLs

PulseNet Sequencing Capacity – September 2017

43 labs in 37 states certified

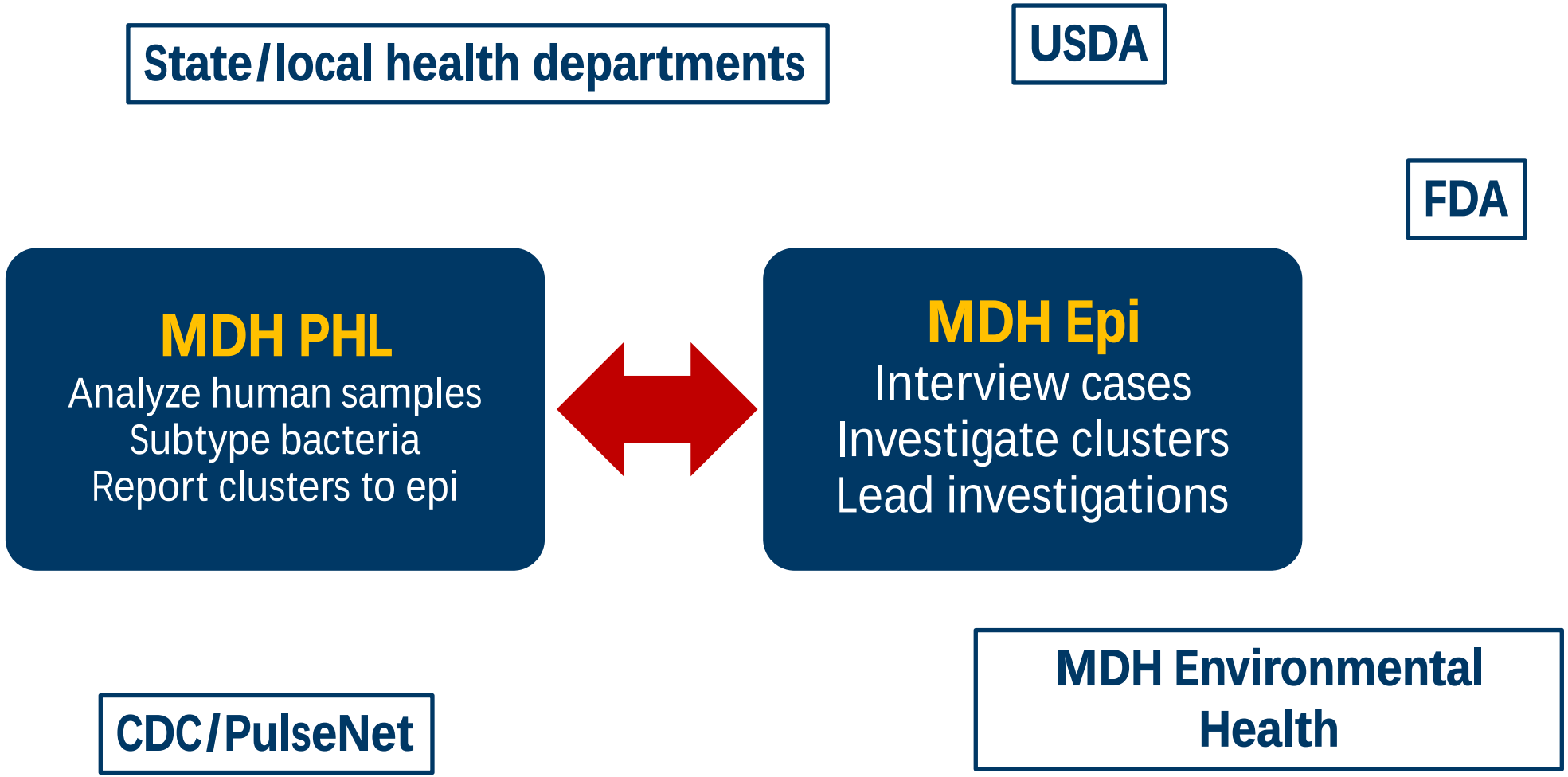


Awarded ELC funds to acquire sequencer
Has sequencer but not certified
PulseNet certified

Challenges of WGS at Public Health Laboratories (PHL)

- Continuing existing methods during transition
- IT issues (storage, software, permissions)
- Training-wet lab
- Training-bioinformatics (sequence analysis)
- Bioinformatics resources
- Ordering reagents

Foodborne Disease Surveillance in Minnesota (traditional)



Interviewing Cases: Minnesota Basic Philosophy

- Interview all cases ASAP
- Collect details on specific exposures
  - Dates
  - Restaurant, grocery store names
  - Brand names
  - Open-ended food histories
- Follow-up interesting hypotheses aggressively
  - Re-interview cases with specific questions, conduct tracebacks, food testing, etc.

Daily Report

Automatic printout of any serotype/PFGE info added into LIMS

- Previous days
- Moving time frame
- Historical perspective
- National clusters

MDH Daily Report

Enteric Isolates Reported on 15-Mar-2003

SPEC	LNAME	FNAME	CITY	AGE	AGENT	SUBTYPE	DATE
01774	Larsen	William	Bloomington	37	Campylobacter jejuni	Fla9	11-mar-03
01770	Simon	Pauline	Minneapolis	72	Campylobacter jejuni	Fla72	10-mar-03
01778	Hilgren	Sven	Rosemount	6	Escherichia coli	MN31	10-mar-03
01773	Hilgren	Cody	Rosemount	5	Escherichia coli	MN31	12-mar-03
01765	Bergstrom	Theresa	Rosemount	31	Escherichia coli	MN31	11-mar-03
01768	Roberts	Maryln	Bemidgi	76	Escherichia coli	MN1	11-mar-03
01777	Desowitz	Robert	St. Cloud	47	Salmonella saintpaul		14-mar-03
01776	Beers	Trevor	Minneapolis	3	Salmonella typhimurium	TM43	10-mar-03
01769	Sampson	Elsa	St. Paul	53	Salmonella typhimurium	TM2B	11-mar-03
01774	Brady	Harold	Bloomington	16	Shigella flexneri 3a		13-mar-03
01767	Crandon	Louise	Chisago	24	Shigella sonnei	SS1	10-mar-03
01764	Petrovich	Helen	Edina	67	Shigella sonnei	SS44	09-mar-03

Names are fictitious

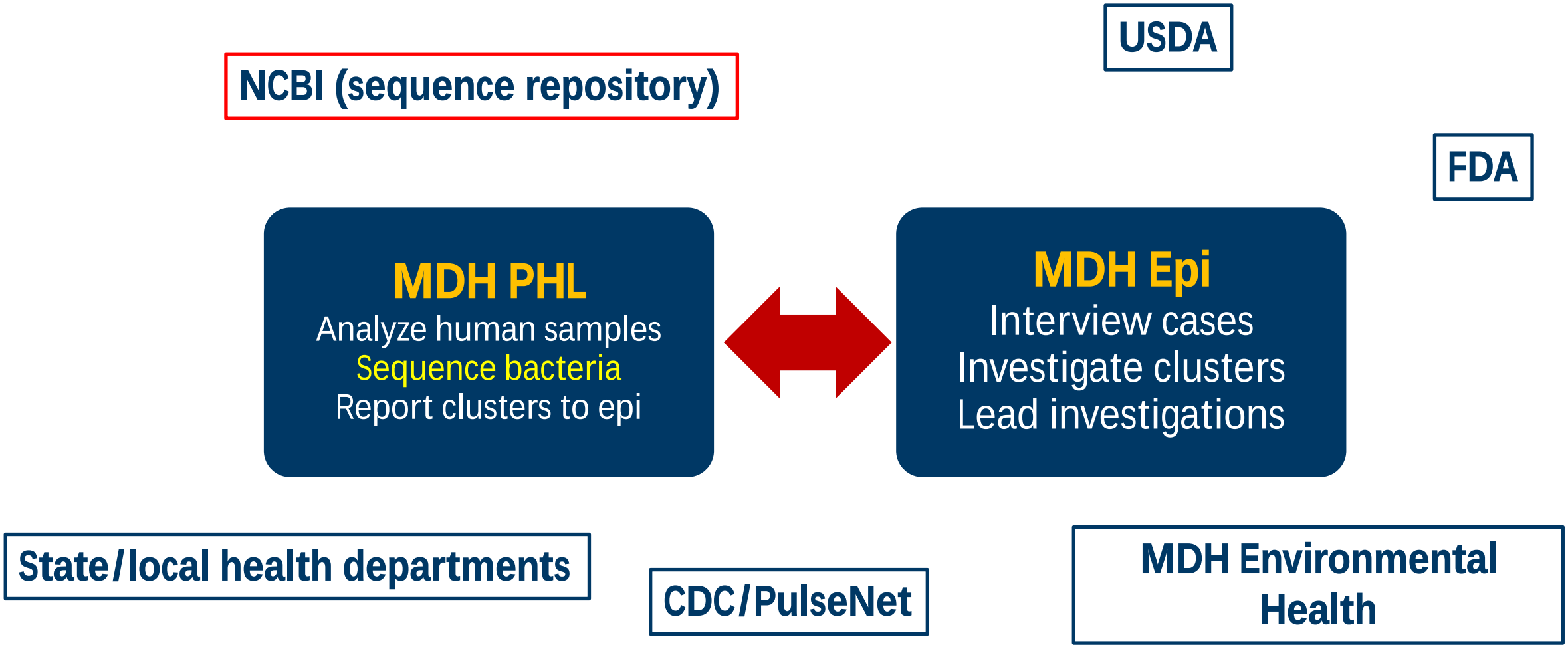
MDH Daily 30 Line Listing

Moving Frame Subtype / Serotype History

SPEC	LNAME	FNAME	CITY	AGE	AGENT	SUBTYPE	DATE
01778	Hilgren	Sven	Rosemount	6	Escherichia coli	MN31	10-mar-03
01773	Hilgren	Cody	Rosemount	5	Escherichia coli	MN31	12-mar-03
01765	Bergstrom	Theresa	Rosemount	31	Escherichia coli	MN31	11-mar-03
01762	Hilgren	Elizabeth	Rosemount	24	Escherichia coli	MN31	10-mar-03
01760	Edlestein	Michael	Invr Grove Hts	7	Escherichia coli	MN31	08-mar-03
01758	Langley	Joel	Rosemount	6	Escherichia coli	MN31	06-mar-03
01743	Sigurson	Marie	Rosemount	8	Escherichia coli	MN31	06-mar-03
01768	Roberts	Maryln	Bemidgi	76	Escherichia coli	MN1	11-mar-03
01777	Desowitz	Robert	St. Cloud	47	Salmonella saintpaul		14-mar-03
01776	Beers	Trevor	Minneapolis	3	Salmonella typhimurium	TM43	10-mar-03
01762	Horlath	Brett	Minneapolis	5	Salmonella typhimurium	TM43	10-mar-03
01747	Peterson	Mary	Minneapolis	9	Salmonella typhimurium	TM43	29-feb-03
01769	Sampson	Elsa	St. Paul	53	Salmonella typhimurium	TM2B	11-mar-03
01771	Yang	Xiong	Duluth	47	Salmonella typhimurium	TM2B	29-feb-03

Names are fictitious

Foodborne Disease Surveillance in Minnesota (WGS-current)



				PFGE			WGS					
	MDH Acce	Collection Date	Sequence d Date	y PFGE Patter n	dary PFGE Patt	PFGE Cluste	to closest neig	Closest MN neighbor(s) (SNPS)	Other State Matches (SNPS)	Date in	WGS Investigati on cod	Epi comment
650	E2015017856	12/9/2015	1/11/2016	SE11	B116		4	E15-15718, E15-13909 (6)		1/14/2016	2015036	
639	E2015018531	12/20/2015	1/11/2016	SE48	B231			E15-930 (6)		1/14/2016	2016002	Traveled to Do
059	E2016000204	12/30/2015	1/11/2016	SE43	B18					1/14/2016		
058	E2016000176	12/31/2015	1/11/2016	SE11	B6		5	E15-17571, E15-14301 (5), E15-8119 (5), E15-7968 (5)		1/14/2016	2015039	
064	E2016000287	12/31/2015	1/15/2016	SE11	B6					1/21/2016	2016007	Punta Cana, D
070	E2016000456	12/31/2015	1/15/2016	SE1	B1					1/21/2016		
060	E2016000215	1/1/2016	1/11/2016	SE9	B161		5	E15-6737, E15-5181 (6), E15-4475 (6)		1/14/2016		
065	E2016000376	1/3/2016	1/15/2016	SE164	B41					1/21/2016		
077	E2016000740	1/11/2016	1/25/2016	SE164	B214		1	E15-15239		1/28/2016	2016001	
078	E2016000801	1/13/2016	1/25/2015	SE222	B214		2	E15-17439		1/28/2016		Same patient a
085	E2016001029	1/20/2016	1/29/2016	SE9	B161		0	E16-1099		2/4/2016	2016003	Same patient a
087	E2016001099	1/20/2016	1/29/2016	SE9	B161		0	E16-1029		2/4/2016	2016003	same patient a
088	E2016001120	1/21/2016	1/29/2016	SE19	B116		2	E15-6737, E15-4512 (3), E15-4475 (3)		2/4/2016	2016008	Playa del Carm
086	E2016001071	1/22/2016	1/29/2016	SE11	B116					2/4/2016		
089	E2016001421	1/24/2016	1/29/2016	SE48	B231		2	E15-18531		2/4/2016	2016002	Traveled to Do
101	E2016001531	1/25/2016	2/12/2016	SE11	B6		2	E16-1746, E16-1533		2/22/2016	2016004	Dominican Rep
096	E2016001474	1/26/2016	2/5/2016	SE11	B181		0	MDH-2014-00857		2/9/2016		
097	E2016001477	1/26/2016	2/5/2016	SE9	B161		2	E16-1029 (2), E16-1099 (2)		2/9/2016	2016003	
098	E2016001504	1/26/2016	2/5/2016	SE43	B18		0	E16-204 (0)		2/9/2016		
099	E2016001533	1/27/2016	2/5/2016	SE11	B6					2/9/2016	2016004	Dominican Rep
100	E2016001566	1/29/2016	2/5/2016	SE43	B72		0	E15-12170 (0), E14-14938 (1)		2/9/2016		
114	E2016001746	1/29/2016	2/12/2016	SE11	B6		2	E16-1533, E16-1531		2/22/2016	2016004	Dominican Rep
102	E2016001727	1/30/2016	2/12/2016	SE11	B116					2/22/2016	2016005	
116	E2016001974	2/1/2016	2/12/2016	SE1	B1					2/22/2016		
104	E2016001927	2/4/2016	2/12/2016	SE11	B6		2	E16-287		2/22/2016	**2016007**	LTF
125	E2016002209	2/8/2016	2/19/2016	SE43	B72		3	E15-14909		2/24/2016		
128	I2016002162	2/9/2016	2/19/2016	SE11	B78		1	E16-1746, E16-1531, E16-2268 (2), E16-1533 (3)		2/24/2016	2016004	Dominican Rep
127	E2016002341	2/10/2016	2/22/2016	SE11	B116		2	E15-6737, E15-4475, E15-4250, E15-5181 (4), E15-5672 (4)		2/25/2016	2016008	Playa del Carm
124	E2016002268	2/12/2016	2/19/2016	SE11	B6		1	E16-1531, I16-2162(2), E16-1746 (2), E16-1533 (3)		2/24/2016	2016004	Dominican Rep

Lab ID

PFGE pattern

Number of SNPs

Lab ID for closely related isolates

Cluster ID

Thu 5/11/2017 1:23 PM

MN_MDH_PFGE

SE WGS Clusters- 5.11.17

To

Retention Policy AllMail_90 (90 days) Expires 8/9/2017

Cluster 2017001: 2 new isolates are 1-5 SNPs from others in the cluster. Now 8 isolates total. (Marijke, SE11B6)

E2017005289

E2017004460

Cluster 2017008: 2 new isolates are 1-5 SNPS from others in the cluster. Now 4 isolates total. (SE11B116)

I2017005940-1

E2017003821

Cluster 2017010: 1 new isolate is 0 SNPs from others in the cluster. Now 3 isolates total. (SE11B6)
E2017006068

NEW Cluster 2017013: 2 isolates are 0 SNPs from each other.

E2017003849 (SE235B78)

E2017005056 (SE181B93)

NEW Cluster 2017014: 2 isolates are 0 SNPs from each other. (SE9B161)

E2017004452

E2017004814

NEW Cluster 2017015: 2 isolates are 0 SNPs from each other. (SE11B6)

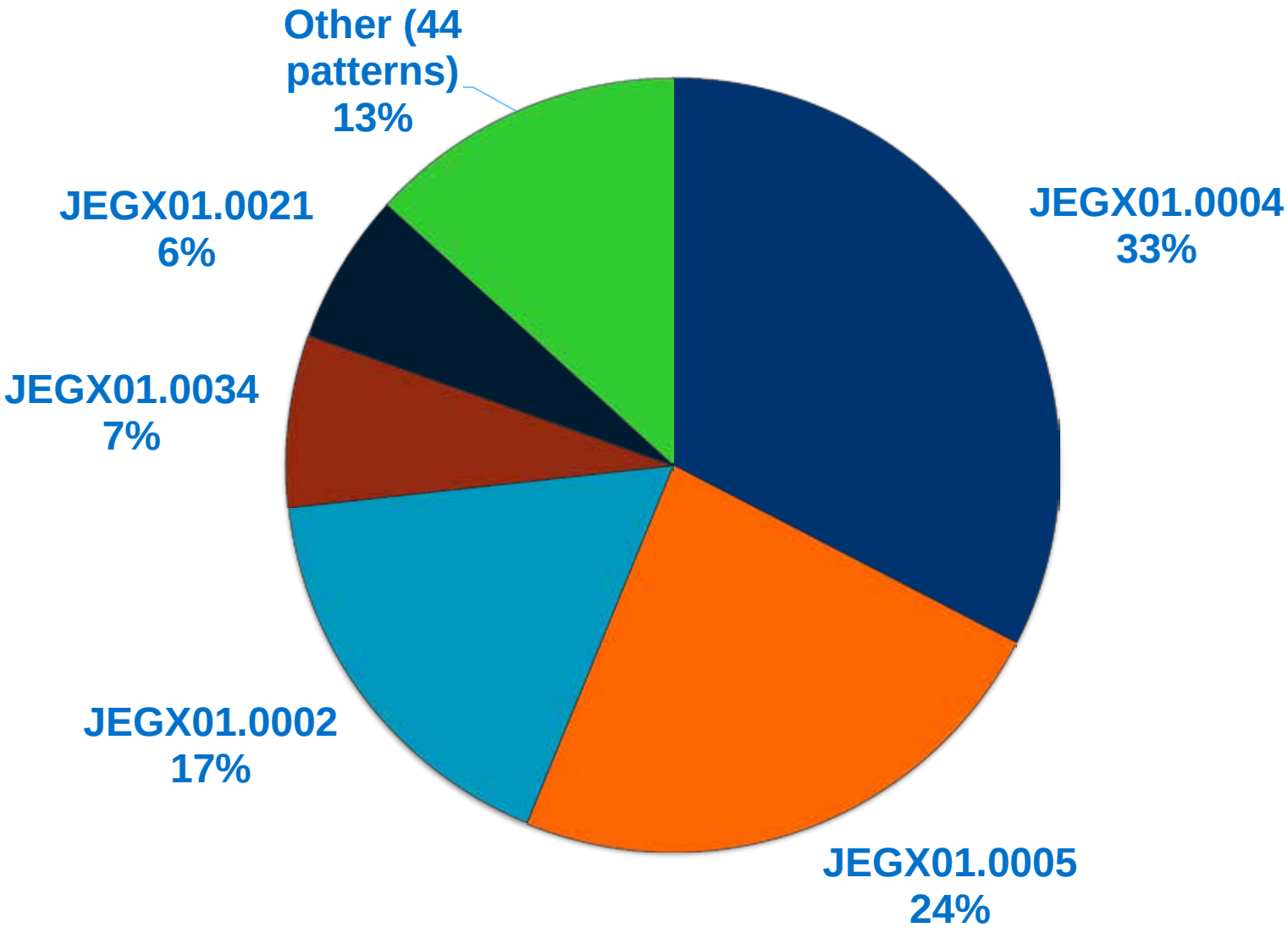
I2017005906-1

E2017006005

Salmonella Enteritidis

- SE is the most common *Salmonella* serotype in Minnesota, and second most common serotype in the U.S.
- Very clonal
  - 4 PFGE types comprise 76% of PulseNet database
- MDH performs PFGE with 2 enzymes

Percent *Salmonella* Enteritidis *Xba*I PFGE Patterns, Minnesota 2014-2015 (n=445)

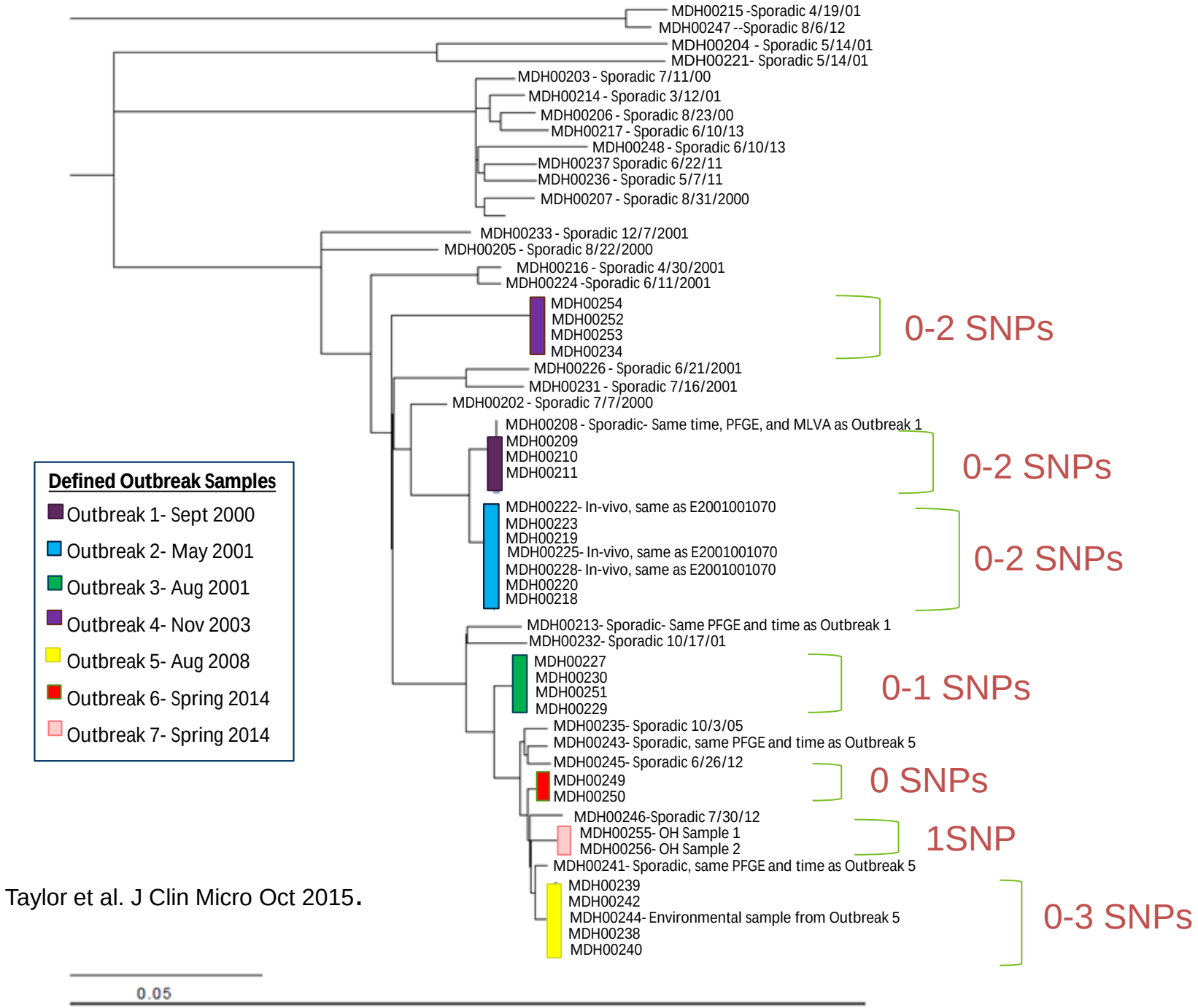


SE Retrospective Study

- Stability
- Typeability
- Discriminatory power
- Epidemiological concordance
  - Epidemiologically linked isolates should have same type
  - None linked isolates should have different types

Retrospective Samples (n=55)

- Well characterized isolates (PFGE and MLVA), exposure information (epi)
- 7 separate outbreaks (n=25)
- 22 sporadic isolates
- *In vivo* (n=4)
- 4 sporadic? isolates (same subtype/time as OB, no known OB exposure)
- Joint lab/epi project
- Partnered with New York DOH for analysis



Taylor et al. J Clin Micro Oct 2015.

Retrospective Study Conclusions

- Stable: few SNPs within person over time
- Typeability: all isolates able to be typed
- Diversity: high diversity for isolates not related
- Epidemiological concordance
  - Few SNP differences within outbreak
  - Sporadic (unrelated) isolates very different compared to outbreak isolates

Prospective Study

Compare ability of WGS and PFGE to identify clusters and outbreaks of SE in real-time

Prospective Study

- April - December, 2014
- All isolates have PFGE and WGS performed in real-time (WGS goal TAT <1 week)
- Each cluster (identified by any method) will be investigated as possible outbreak
- WGS cluster defined as isolates ≤5 SNPs over 2 months
- Foodborne disease epidemiologists interviews all cases with trawling questionnaire

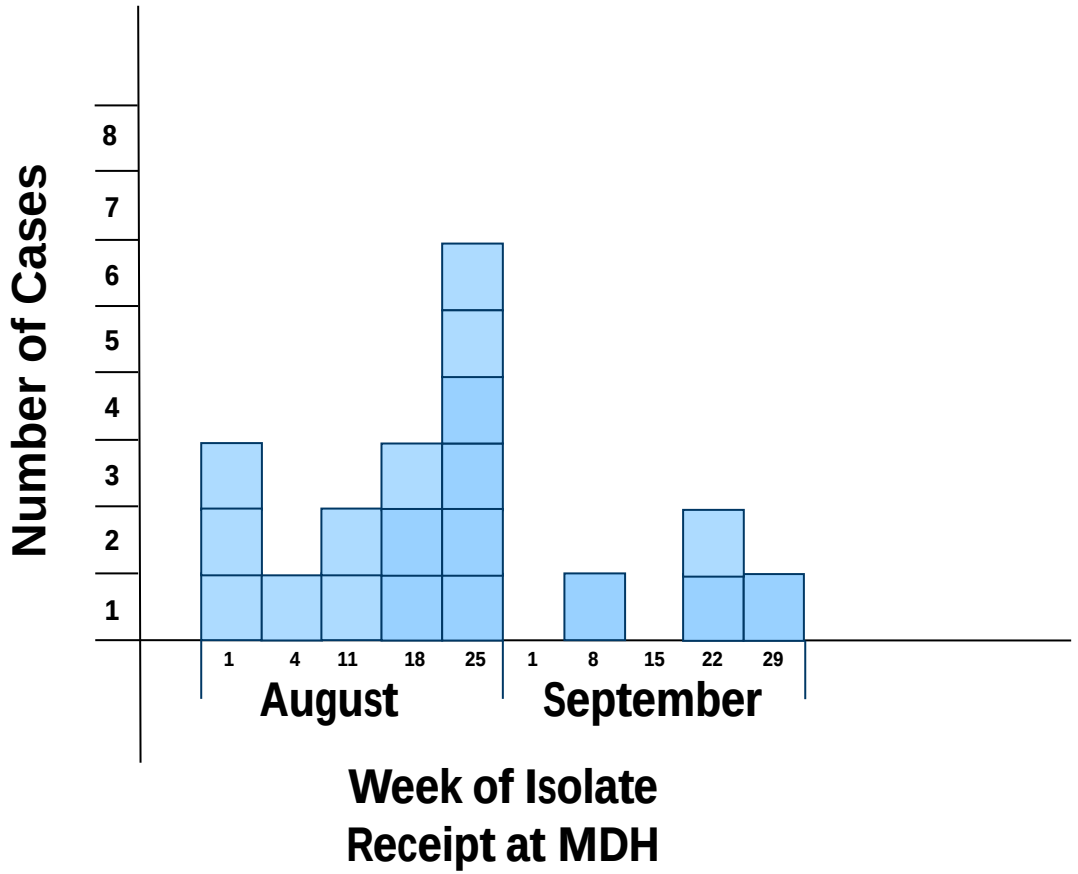
SNP Differences in Sporadic Isolates

MN PFGE pattern	CDC PFGE pattern (JEGX01.)	N	Average SNP differences with PFGE pattern
SE1	4	56	93
SE43	5	41	56
SE11	3	16	82
SE77	21	13	32
SE10	34	13	77

Prospective Results-cluster analysis

	PFGE	WGS
# of clusters	12	25
Mean # in cluster (range)	9 (2-44)	3 (2-8)

All *Salmonella* Enteritidis JEGX01.0004/JEGA26.0002 Isolates Received August-September 2014 (n=19)



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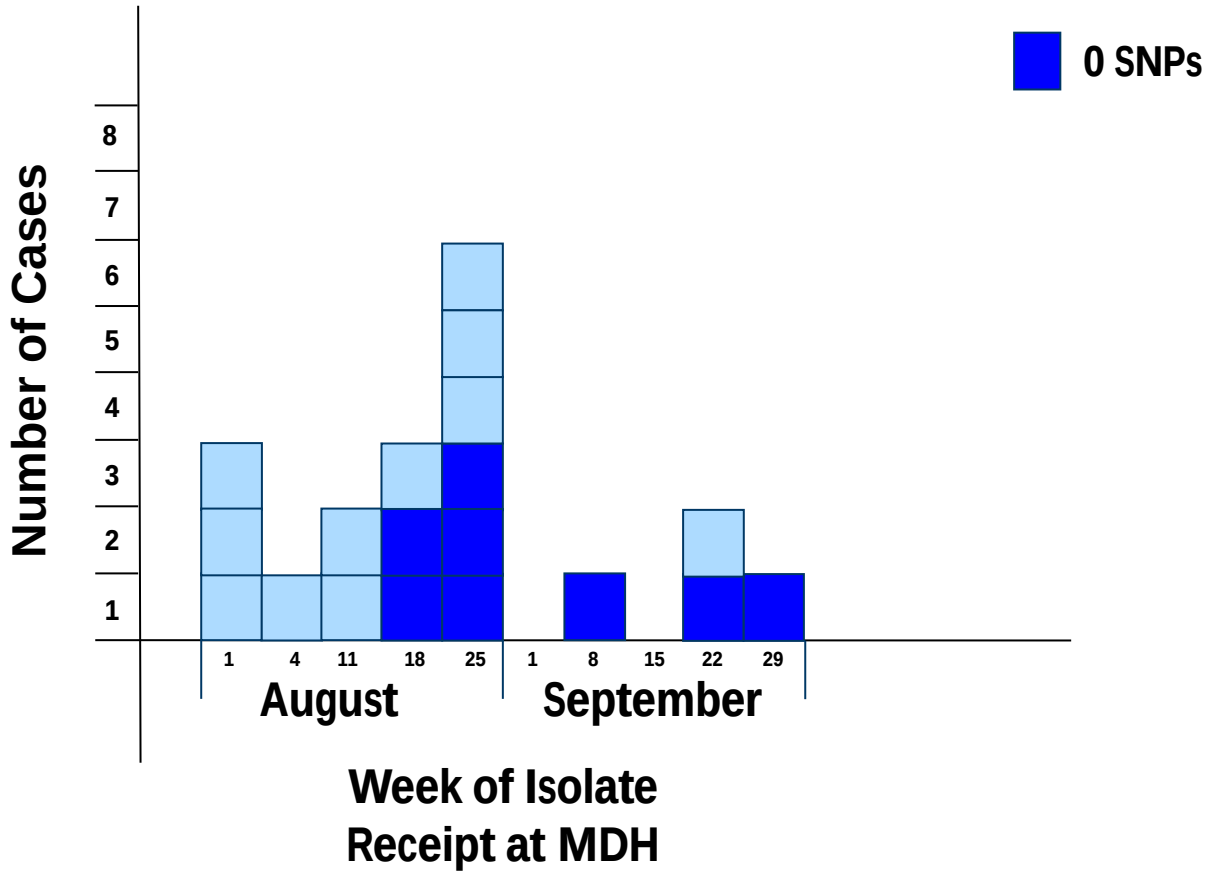

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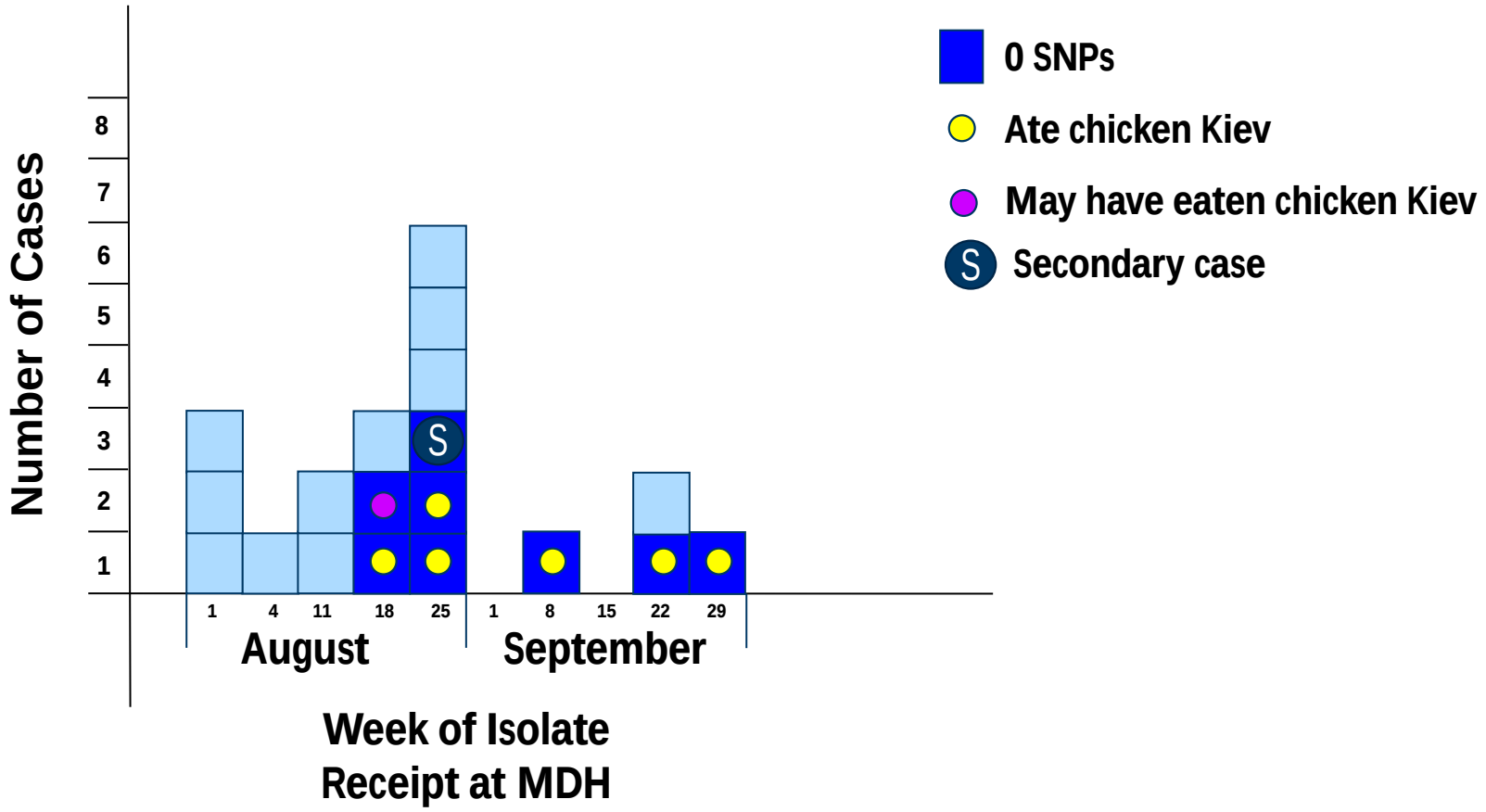

Future of WGS at PHLs

- Use of WGS at PHLs will continue to increase
- WGS will provide more information methodically compared to current methods
  - WGS will begin to replace traditional methods-serotyping, AST, virulence marker detection
- WGS nomenclature will improve data sharing
- Data sharing/communication will become easier

Conclusions

- WGS is being widely adopted by PHLs
- WGS is a tool that can identify clusters/outbreaks better than traditional methods
- There are continued challenges with implementation of WGS at PHLs
- Speed and communication will continue to be vital aspects of outbreak detection

DEPARTMENT OF HEALTH

Thank you!

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