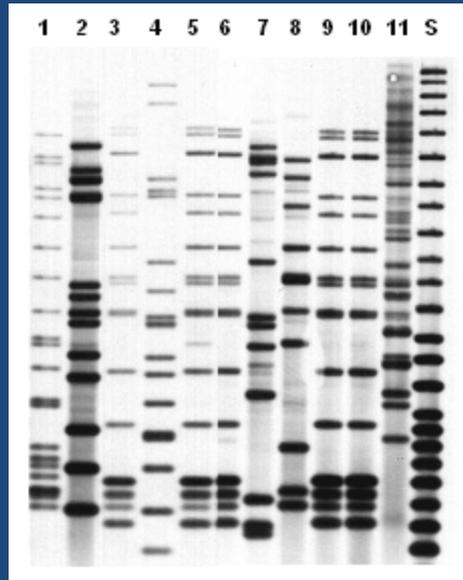


TB Genotyping



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What is TB Genotyping?

- Laboratory-based approach to analyze the genetic material (DNA) of *Mycobacterium Tuberculosis*
- Specific sections of the *M. Tuberculosis* genome form distinct genetic patterns that distinguish different strains

Applications of TB Genotyping

- Discover unsuspected transmission relationships between TB patients
- Establish criteria for outbreak case definitions & identify additional cases in an outbreak
- Determine completeness of contact investigations
- Detect laboratory cross-contaminations
- Distinguish recent infection from activation of an old infection

Source: Tuberculosis Genotyping, CDC, 2008

Tb Genotyping Process

- Specimen is collected from patient (sputum, aspirate, etc.)
- Specimen grows *M. Tuberculosis* and isolate is obtained
- Isolate is submitted to ISDH lab then sent to CDC Lab for genotyping
- Genotyping results are uploaded to the TB Genotyping Information Management System (TB-GIMS)
- Results are reviewed & processed by the TB Epi and sent to LHD if needed

Genotype Results

- Receive individual, de-identified results through TB-GIMS
- Process results to verify patient identity, link to RVCT & surveillance data, and identify cases that have clustered
- Run reports for clustered cases and distribute to LHD as appropriate

Spoligotype

- “Spacer oligonucleotide typing”
- Based on presence or absence of spacer sequences in a 36 base-pair direct-repeat region of the *M. Tuberculosis* genome
- 43 identical spacers show as dark band, converted to series of 1s and 0s
- 43-digit binary code is converted to 15 digit octal code

VNTR-MIRU

- Based on the number of copies of tandem repeats at specific loci of the *M. Tuberculosis* Genome
- 1st 12 loci become MIRU
- 2nd 12 loci become MIRU2
 - Began in 2009
- When more than 9 repeats, letters are used
 - Ex. 11 repeats is shown by a “b”

MIRU Examples

	MIRU locus name											
	02	04	10	16	20	23	24	26	27	31	39	40
No. of Repeats	2	3	2	2	3	4	2	5	3	3	2	2

MIRU designation: 232234253322

	MIRU locus name											
	02	04	10	16	20	23	24	26	27	31	39	40
No. of Repeats	1	4	3	2	2	4	0	4	3	5	4	11

MIRU designation: 14322404354b

PCR & GenType

- Results of Spoligotype and MIRU are assigned a PCRType
 - Ex. PCR00002
- PCRType is combined with MIRU2 to make a GENType
 - Ex. G00010
- PCRType & GENType are consistent between every state and represent unique combinations

Definition for Tuberculosis Genotyping in the United States

Spoligotype:
0000000000003771

Initial 12-locus MIRU-VNTR¹:
223325173533

Sequentially assigned for each unique spoligotype and initial 12-locus MIRU-VNTR combination

PCRType:
PCR00002

+

Additional 12-locus MIRU-VNTR (MIRU2):
444534423428²

Sequentially assigned for each unique spoligotype and 24-locus MIRU-VNTR combination

GENType:
G00010

¹ Mycobacterial interspersed repetitive unit–variable number tandem repeat

² The complete set of 24 loci is referred to as 24-locus MIRU-VNTR and is used for GENType designation for genotype in the U.S.

Genotype Clusters

- When two or more patients match by genotyping methods
 - Either PCRType and/or GENType
- Given unique cluster number by state
 - IN_0002 (PCRType only)
 - IN_0002_001(GENType)
- Patients in the same cluster are assumed to have the same strain
 - May not always identify recent transmission

Should we Investigate?

- Is it a common cluster?
- Are the cases in the same county or area?
- How far apart in time are the cases?
- Do the cases share a common Country of Birth?
- Have we identified Epi-Links in this cluster before?
- How many cases are involved?
- Are the cases “High-Risk?”
 - Congregate settings, HIV+, children, MDR, homelessness

Cluster Investigation

- Receive fax from TB Epi with several documents
 - Cluster Report from ISDH Database
 - Cluster Snapshot from TB GIMS
 - National Distribution Map from TB GIMS
 - Surveillance Summary from TB GIMS

Genotype Report By Cluster Designation #Name?

Name (Last, First)	Country of Birth	Race	Smear	Count date	County	Spoligotype MIRU1	Epi link (y/n)	Comments
Cluster assignment	DOB	Sex	Source	RVCT#		MIRU2 PCR# GENType	Source cas	
[REDACTED] IN_0144_001	India	Asian	Not Done Pleura	2014IN144600100	LaPorte	47777777413071 232224253322 253573352213		Immigrant. No other risk factors. Contact to active case in Cook Co in 1996.
		Male				PCR01847 G02880		
[REDACTED] IN_0144_001	India	Asian/India	Positive Sputum	1/1/2009 2009IN090201003	Allen	47777777413071 254326223633 246363113616	No	unemployed
		Male				PCR01847 G02880		

Cluster Snapshot for G02880

Cluster Definition

GENType: G02880

PCRTYPE: PCR01847

Date Range: 08/01/2005 - 08/30/2015

State/County/Region: INDIANA

Lineage: IndoOceanic (L1)

Date Type: Count Date

State Cluster Name2: IN_0144_001

cases in cluster: 2

Data Completeness

Genotype Coverage: 95.7%

#Patients with PCRTYPE but no MIRU2 result: 0

#Isolates with no linked surveillance record: 0

Genotype report date of most recent isolate without surveillance record:

Cluster Detection

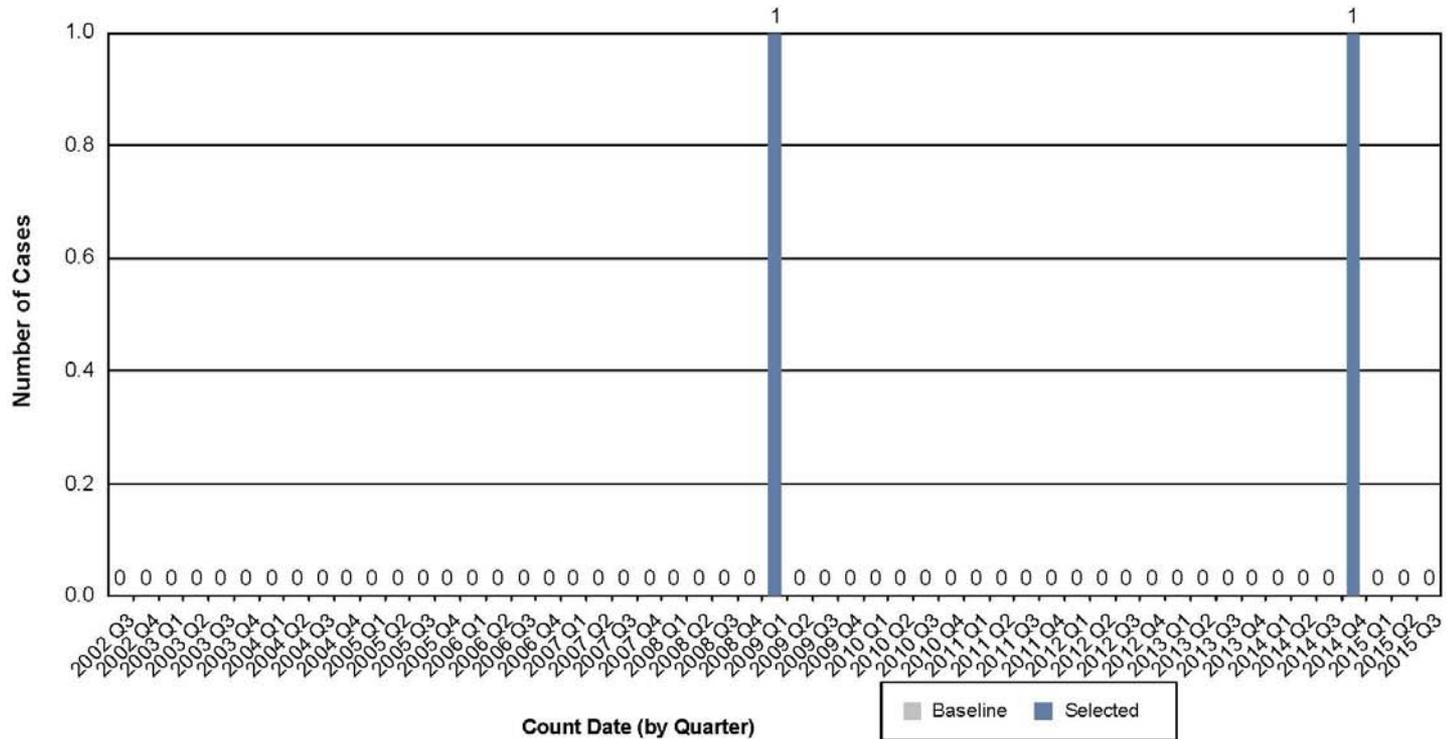
Alert Level: N/A

Recent change in alert level:

Alert level and LLR are only available for single county areas.

Cluster Snapshot for G02880

Time



The Epidemic Curve has been expanded to display the historical occurrence of cases for 3 years prior to dates selected. The first blue column will include all cases in the quarter regardless of whether they are in selected timeframe or are part of baseline period.

Geography

# cases in rest of state: N/A	% of all cases in this state with this genotype: 0.24
Five other counties with most cases: N/A	
# cases in adjacent states: 0	Adjacent states with cases:
# cases in entire rest of U.S.: 12	% of all cases in U.S. with this genotype: 0.02

Cluster Snapshot for G02880

Person

Comparative demographics (selected jurisdiction vs. rest of U.S.) n(%)

Characteristic	INDIANA	Rest of U.S. n (%)
Race/Ethnicity		
Asian	2 (100.0%)	10 (83.3%)
Black	0 (0.0%)	1 (8.3%)
Multiple Race	0 (0.0%)	1 (8.3%)
Gender		
Female	0 (0.0%)	3 (25.0%)
Male	2 (100.0%)	9 (75.0%)
Birth		
Foreign Born	2 (100.0%)	12 (100.0%)

High risk characteristics of transmission or poor outcome n(%)

Characteristic	n (%)
Case with smear positive and cavitary pulmonary disease	0 (0.0%)
Homeless	0 (0.0%)
Corrections	0 (0.0%)
Long Term Care Facility	0 (0.0%)
Any substance abuse	0 (0.0%)
Alcohol abuse	0 (0.0%)
Non-IDU	0 (0.0%)
IDU	0 (0.0%)
MDR	0 (0.0%)
INH resistance only	0 (0.0%)
Child (<5 years)	0 (0.0%)
Child (5-14 years)	0 (0.0%)
HIV	0 (0.0%)
Dead at diagnosis or died while on therapy	0 (0.0%)

Among Foreign Born within INDIANA

Years in U.S	n (%)
<2	1 (50.0%)
2-5	0 (0.0%)
>5	1 (50.0%)

Most common countries cases with this genotype from (Max. 3 listed): INDIA

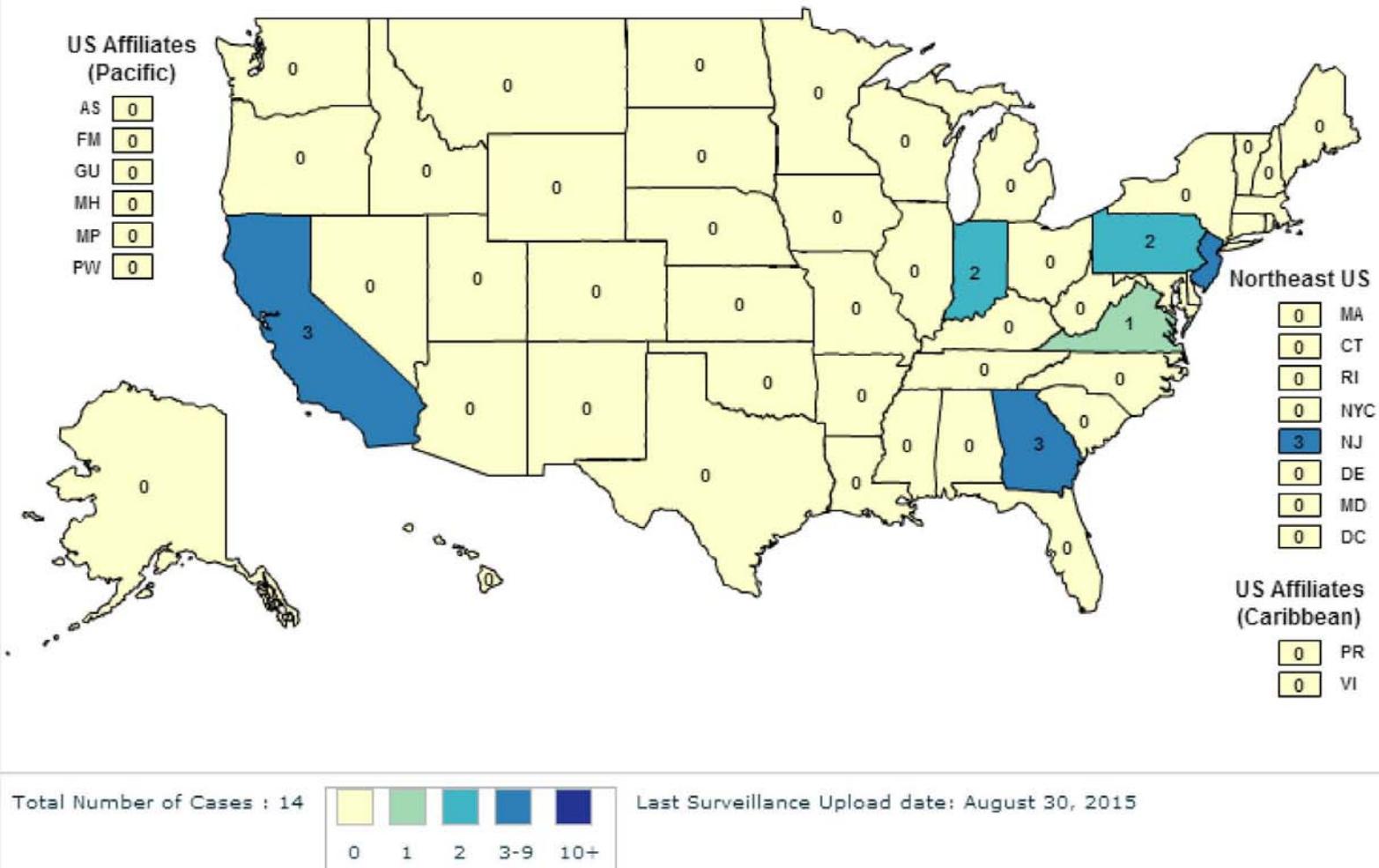
Total number of countries: 1

Cluster Snapshot for G02880

Line List

StateCaseNo	Cnt.Date	County	Age3	RaceHisp	CountryLN	YrsInUS2	Smear	Cavity	DrugRes	HIV	SubAbus	Corr	Homeless	ReasEval
2014IN144600100	12/01/2014	LAPORTE	65+	ASIAN	INDIA	29	NOT	N	None	NEG	N	N	N	ABXRAY
2009IN090201003	01/01/2009	ALLEN	45-64	ASIAN	INDIA	0	NEG	N	None	NEG	N	N	N	IMMEXAM

G02880, National, September 01, 2005 - September 04, 2015



Surveillance Summary of G02880

State: INDIANA Family Name: IndoOceanic (L1)
 County: ALL City: NA
 Region: NA PCRType: PCR01847
 Spoligotype: 47777777413071 24-locus MIRU-VNTR: 254326223633 246363113616
 Date Range: 09/01/2005 - 09/04/2015 Date Type: Count Date

	INDIANA		Other US	
	n	%	n	%
Age (years)				
0 - 4	0	0.0	0	0.0
5 - 14	0	0.0	0	0.0
15 - 24	0	0.0	0	0.0
25 - 44	0	0.0	5	41.7
45 - 64	1	50.0	5	41.7
65+	1	50.0	2	16.7
Unknown	0	0.0	0	0.0
Sex				
Male	2	100.0	9	75.0
Female	0	0.0	3	25.0
Birth				
US-Born	0	0.0	0	0.0
Foreign-Born	2	100.0	12	100.0
Unknown	0	0.0	0	0.0
Race/Ethnicity				
Hispanic	0	0.0	0	0.0
American Indian/Alaska Native	0	0.0	0	0.0
Asian	2	100.0	10	83.3
Black	0	0.0	1	8.3
Native Hawaiian/Pacific Islander	0	0.0	0	0.0
White	0	0.0	0	0.0
Multiple Race	0	0.0	1	8.3
Unknown	0	0.0	0	0.0
Homeless in past year				
Yes	0	0.0	1	8.3
Excessive Alcohol Use				
Yes	0	0.0	2	16.7
Drug Use (injecting/non-injecting)				
Yes	0	0.0	0	0.0
Incarcerated at Diagnosis				
Yes	0	0.0	0	0.0
HIV Status				
Positive	0	0.0	1	8.3
Negative	2	100.0	6	50.0
Other/Unknown	0	0.0	5	41.7
TOTAL	2		12	

*Note: 'County: ALL' refers to all the counties in the state.

Surveillance Summary of G02880

State: INDIANA Family Name: IndoOceanic (L1)
 County: ALL City: NA
 Region: NA PCRType: PCR01847
 Spoligotype: 47777777413071 24-locus MIRU-VNTR: 254326223633 246363113616
 Date Range: 09/01/2005 - 09/04/2015 Date Type: Count Date

	INDIANA		Other US	
	n	%	n	%
Drug Susceptibility Results				
Susceptible to initial testing of	2	100.0	10	83.3
first line drugs ¹				
INH resistant only	0	0.0	0	0.0
RIF resistant only	0	0.0	0	0.0
PZA resistant only	0	0.0	2	16.7
MDR ²	0	0.0	0	0.0
XDR ³	0	0.0	0	0.0
Other resistance pattern ⁴	0	0.0	0	0.0
Missing/unknown for first line of drugs ⁵	0	0.0	0	0.0
TOTAL	2		12	

- 1.Includes INH, RIF, and EMB. PZA is included when results are available.
- 2.MDR indicates resistance to at least RIF and INH. May be resistant to other drugs, but not meet criteria for XDR.
- 3.XDR indicates resistance to RIF, INH, any fluoroquinolone and at least one injectable TB drug.
- 4.Any other combination of resistance patterns to the four first line drugs that do not fit into other categories.
- 5.Any patient with unknown/missing for RIF, INH or EMB, with or without PZA results.

*Note: 'County: ALL' refers to all the counties in the state.

Surveillance Summary of G02880

State: INDIANA

County: ALL

Region: NA

Spoligotype: 477777777413071

Date Range: 09/01/2005 - 09/04/2015

Family Name: IndoOceanic (L1)

City: NA

PCRType: PCR01847

24-locus MIRU-VNTR: 254326223633 246363113616

Date Type: Count Date

There are no US born cases born outside the 50 states and DC.

*Note: 'County: ALL' refers to all the counties in the state.

Surveillance Summary of G02880

State: INDIANA

County: ALL

Region: NA

Spoligotype: 477777777413071

Date Range: 09/01/2005 - 09/04/2015

Family Name: IndoOceanic (L1)

City: NA

PCRType: PCR01847

24-locus MIRU-VNTR: 254326223633 246363113616

Date Type: Count Date

Country of Birth for Foreign-Born TB Cases

Country	INDIANA		Other US	
	n	%	n	%
INDIA	2	100.0	11	91.7
KENYA	0	0.0	1	8.3
Total	2	100	12	100

*Note: 'County: ALL' refers to all the counties in the state.

Cluster Investigation, Cont.

- Review case information for possible epi-links
 - Charts
 - Contact Investigations
 - Interview Notes
- Discuss cases with other involved case managers or involved staff to collect all information available
- Determine need to re-interview cases

Cluster Investigation, Cont.

- Re-interview cases to find epi-links
 - Expand on original interviews
 - Cover broader time period
 - Use location/activity prompted questions based off of other case information, if possible
- Report back findings to TB Regional Nurse & TB Epi
 - TB Epi documents findings for future use
- Decide need for further action

Why Investigate Clusters?

- Identification of Outbreak & initiation of outbreak plan
- Identification of missed contacts and need for expanded contact investigation and testing
- Identification of source case or need to search for undetected infectious case

Genotyping in Indiana, 2014

- 97.6% of culture-positive cases were genotyped
- 63.8% were identified as part of a cluster
- 19 new genotype clusters identified
- Three ongoing outbreaks

QUESTIONS?