

# Evaluating and enhancing pharmacy reporting for tuberculosis surveillance, Arizona, 2011

August 2<sup>nd</sup>, 2012

*Arizona Department of Health Services  
2012 Arizona Infectious Disease Training and Exercise,  
Arizona State University – Tempe, Arizona*

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Arizona Department of Health Services (ADHS)  
Office of Infectious Disease Services  
Tuberculosis Control Program



*Health and Wellness for all Arizonans*



# Infectious Disease Reporting in AZ



Clinical Suspicion or Diagnoses



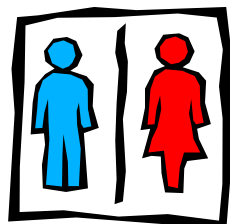
Local Health Departments  
Counties and Tribes



Laboratory Testing



Self-reporting Facilities or Individuals



**TUBERCULOSIS**  
**Pharmacy**



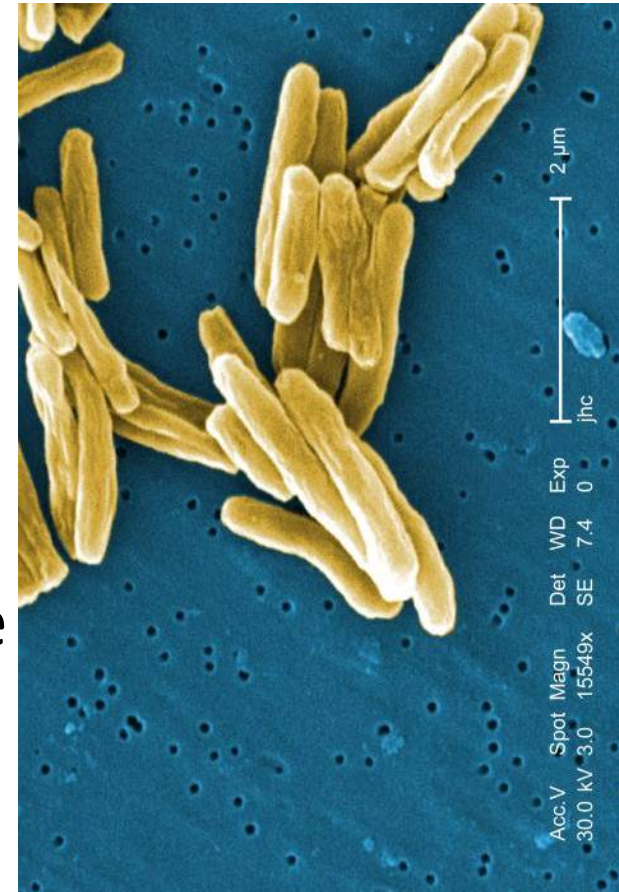
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# Tuberculosis (TB)

- Infection with *Mycobacterium tuberculosis* bacteria
  - typically pulmonary (lungs)
- Highly transmittable
  - aerosolized droplet nuclei from respiratory secretions
- 2<sup>nd</sup> leading cause of infectious disease mortality, worldwide<sup>1</sup>



CDC: <http://phil.cdc.gov/phil/details.asp>

# Tuberculosis Classifications

## Pulmonary TB

Common;  
respiratory infection;  
highly infectious

## Extra Pulmonary TB (EPTB)

Bacilli disseminated  
to other body areas;  
less infectious

**Active TB Disease**

**- Reportable**

*also:*

**Latent tuberculosis infection**

**LTBI**

non-communicable/dormant infection with *M. tuberculosis*

# 2011 Tuberculosis Rates

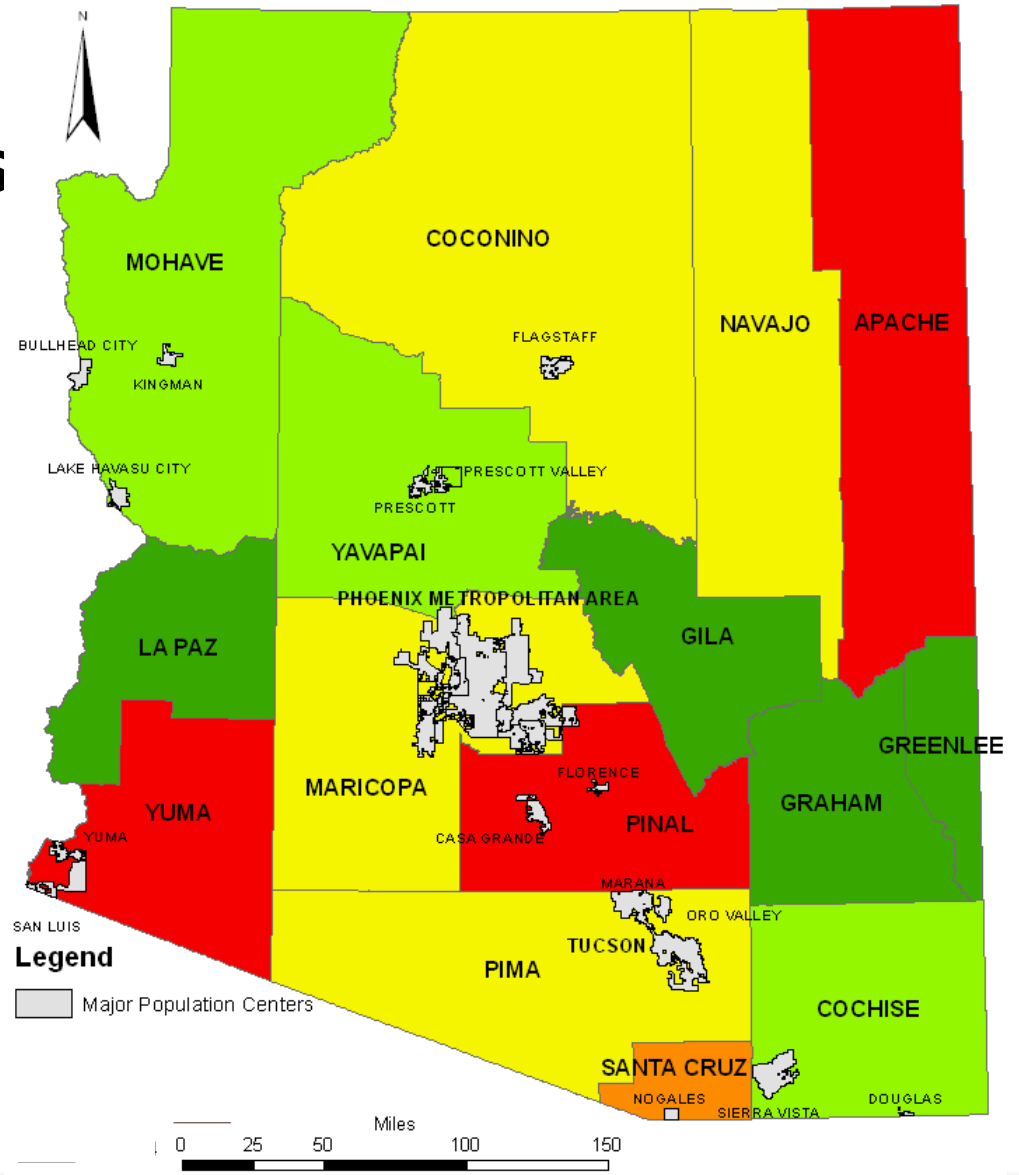
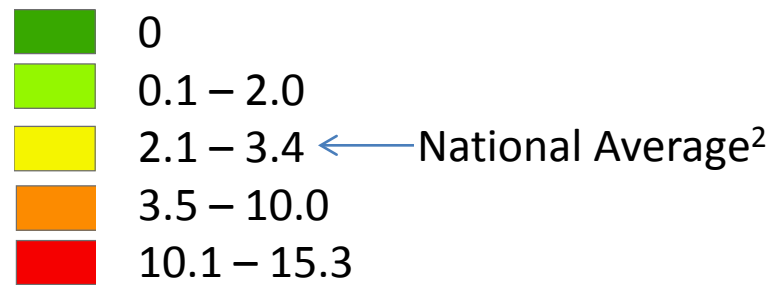
255 Cases in 2011

**AZ:** 4.0 cases per 100,000

**US:** 3.4 cases per 100,000

High Morbidity State

2011 County TB Rates per 100,000



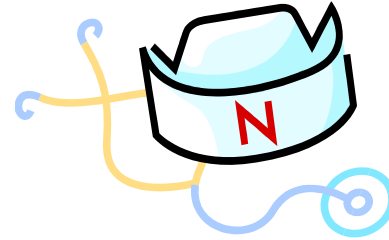
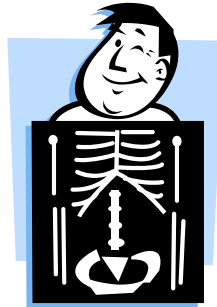
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# Why Pharmacy Reporting for TB?

- Remember:



- Important to catch all cases - transmission
- Coordinate care with local health jurisdictions
- High relapse rate from incomplete therapy<sup>3</sup>

Easy to identify TB prescription medications ...

# Pharmacy Reporting

- TB has specialized multi-drug therapy
- 6 months to 9 months for susceptible TB
- AZ Administrative Code = Legal Requirement

## Initial prescription for two or more of the listed drugs:

- Rifampin (any)
- Pyrazinamide
- Streptomycin
- Isoniazid
- Ethambutol

## Report to Public Health



# Also Caught by Pharmacy Reports...

- **Nontuberculous *Mycobacterium* (NTM) infections**
  - Often treatment includes reportable anti-TB drugs
  - *M. avium* among immunocompromised
- **TB suspected, empirically treated – later ruled-out**
  - *Nocardia* infection
  - Valley Fever – common in AZ
- **LTBI – same drugs but often fewer**



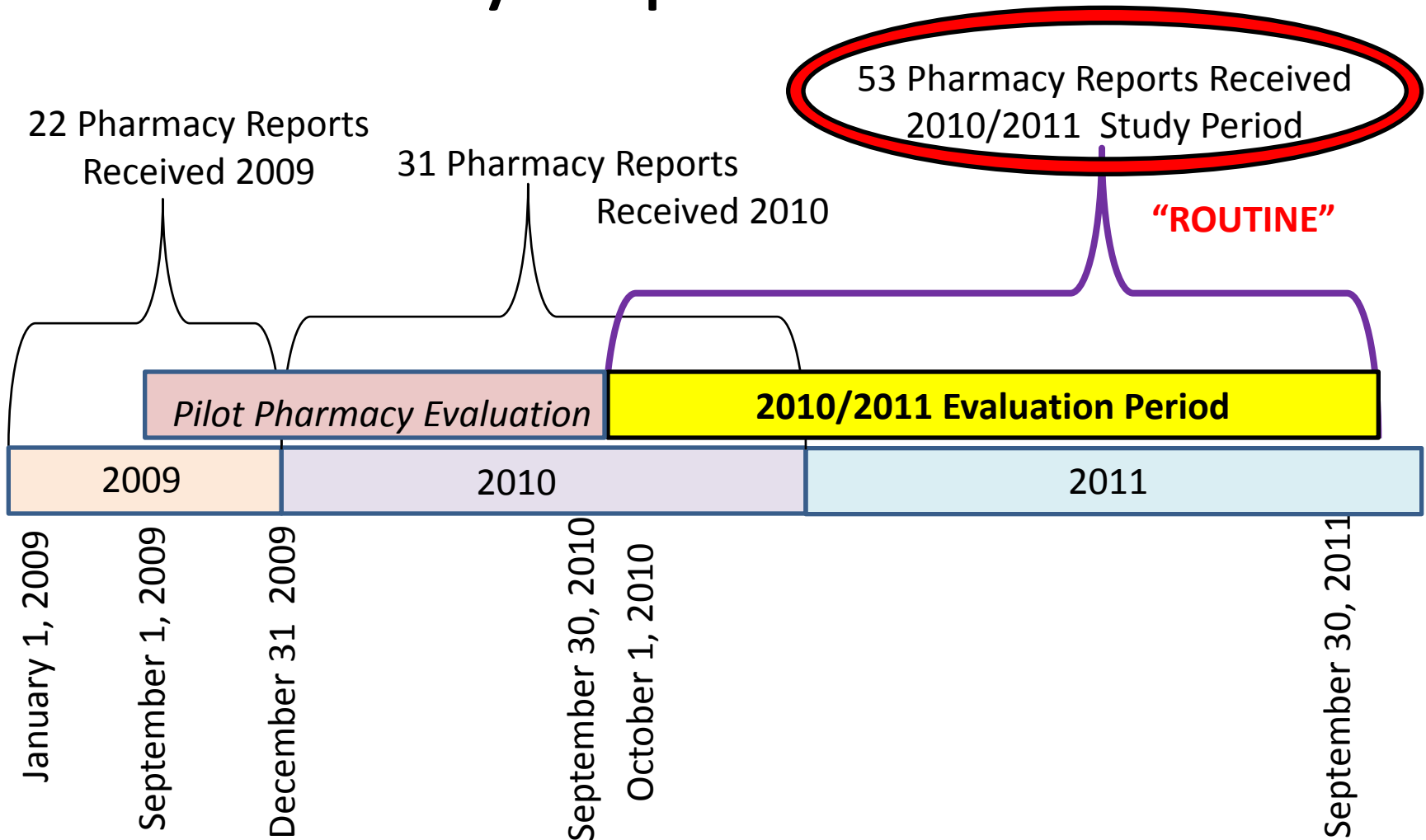
Coccidioidomycosis Chest Radiograph



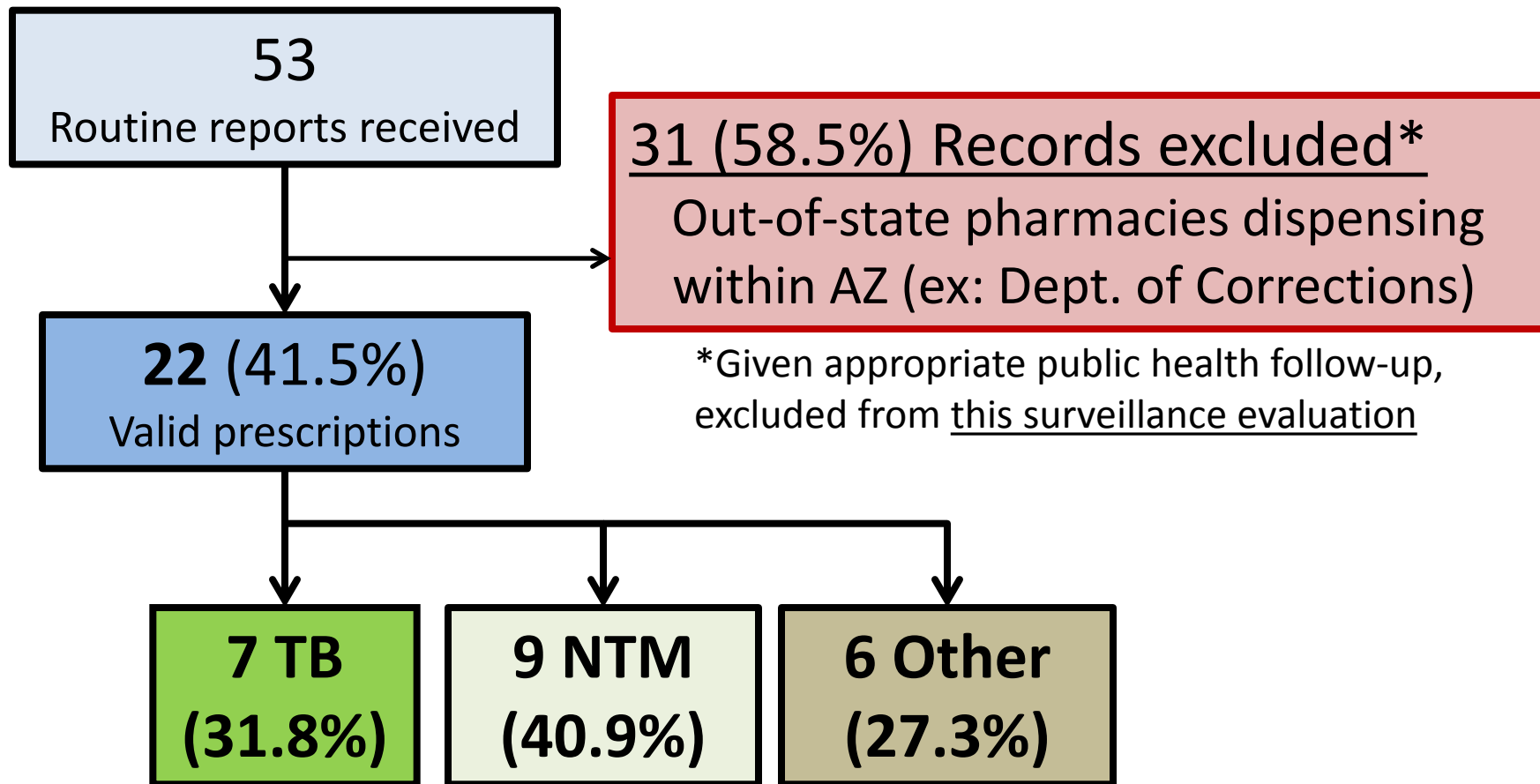
# Evaluation Goals

- 1) Is Arizona pharmacy reporting complete?
- 2) Are there unreported cases of TB?
- 3) Are reporting requirements accurate to identify TB?

# Pharmacy Reports & Timeline

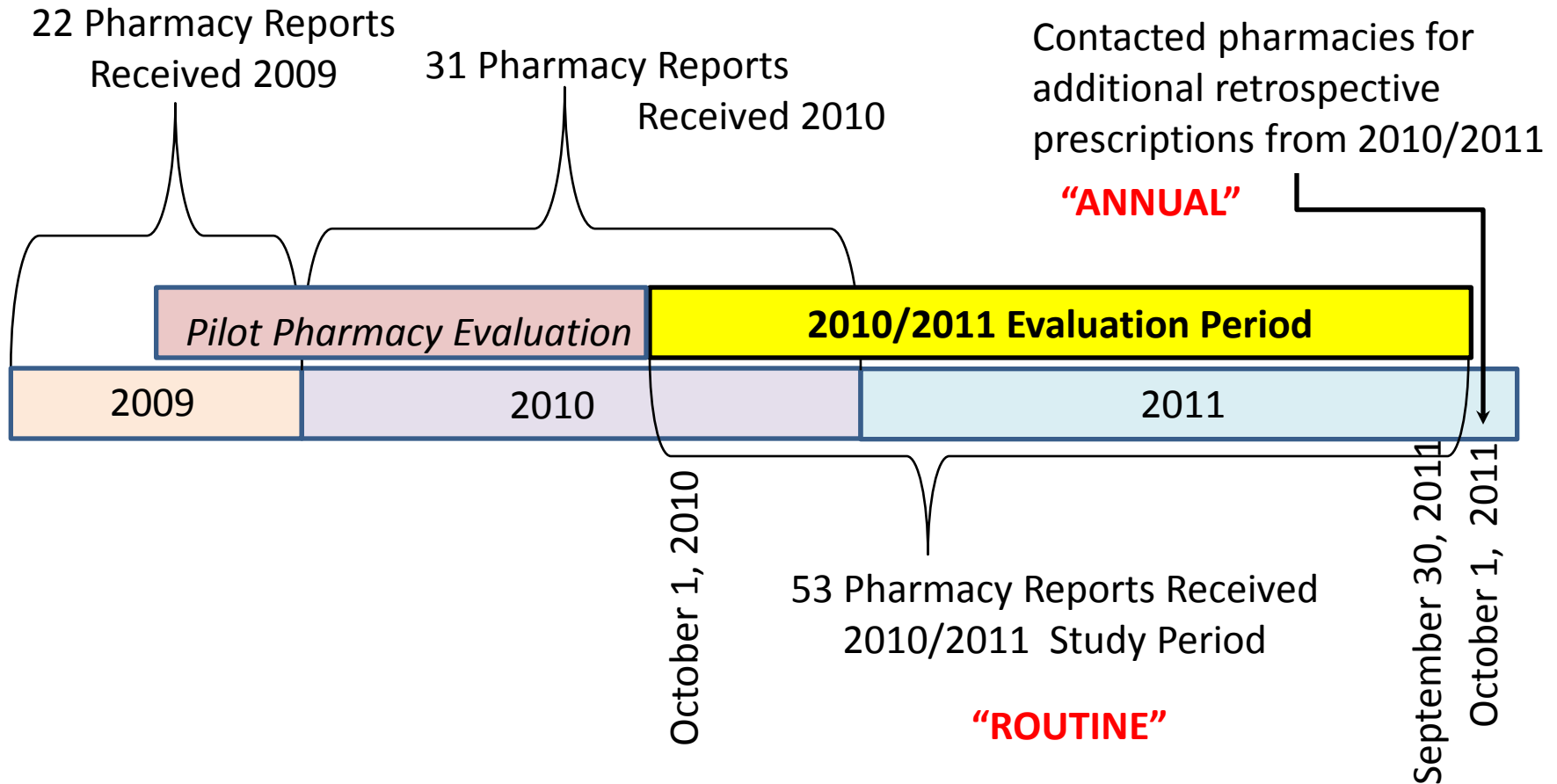


# “Routine” Pharmacy Reporting



# Pharmacy Reports & Timeline

## HOW MANY REPORTS SHOULD WE EXPECT?



# 2011 Pharmacy Evaluation



**Total Pharmacies (N = 1257)**

Arizona Board of Pharmacy (September 15<sup>th</sup>, 2011)

## *Inclusion criteria*

Licensed commercial or hospital pharmacies registered in AZ (Independent, Chain, Hospital, etc.)

## *Exclusion criteria*

Public health jurisdiction pharmacies (Counties)

Non-Arizona pharmacies licensed to distribute in AZ

# “Annual” Report Template

Template for annual report response by mail or email

Pharmacy Information				
Name of Pharmacy		Store Number	Phone Number	
Address	City	Zip Code	County	
Pharmacy Primary Contact	Phone Number	Email		
Prescription records maintained by (circle one):		Paper	Electronically	Both
Electronic alerts when multi-drug anti-tuberculosis prescriptions are filed:		Yes	No	Other:



No Multi-drug prescriptions for anti-tuberculosis medications filled from 10/1/2010 to 9/30/2011

- **Patient: demographics, contact information, medications**
- **Prescribing physician: contact information**

# Evaluation Plan

## ROUTINE

ALL reports received during study period

Pharmacy Exclusions

Prescription Exclusions

Valid prescriptions

Not reported in Annual

Analysis

Patient Outcomes

Routine records confirmed in Annual Reports

## ANNUAL

Reports received through retrospective data request

Prescription Exclusions

Valid prescriptions

Database Matching

Matched Records

Unmatched Records

Physician Follow-up

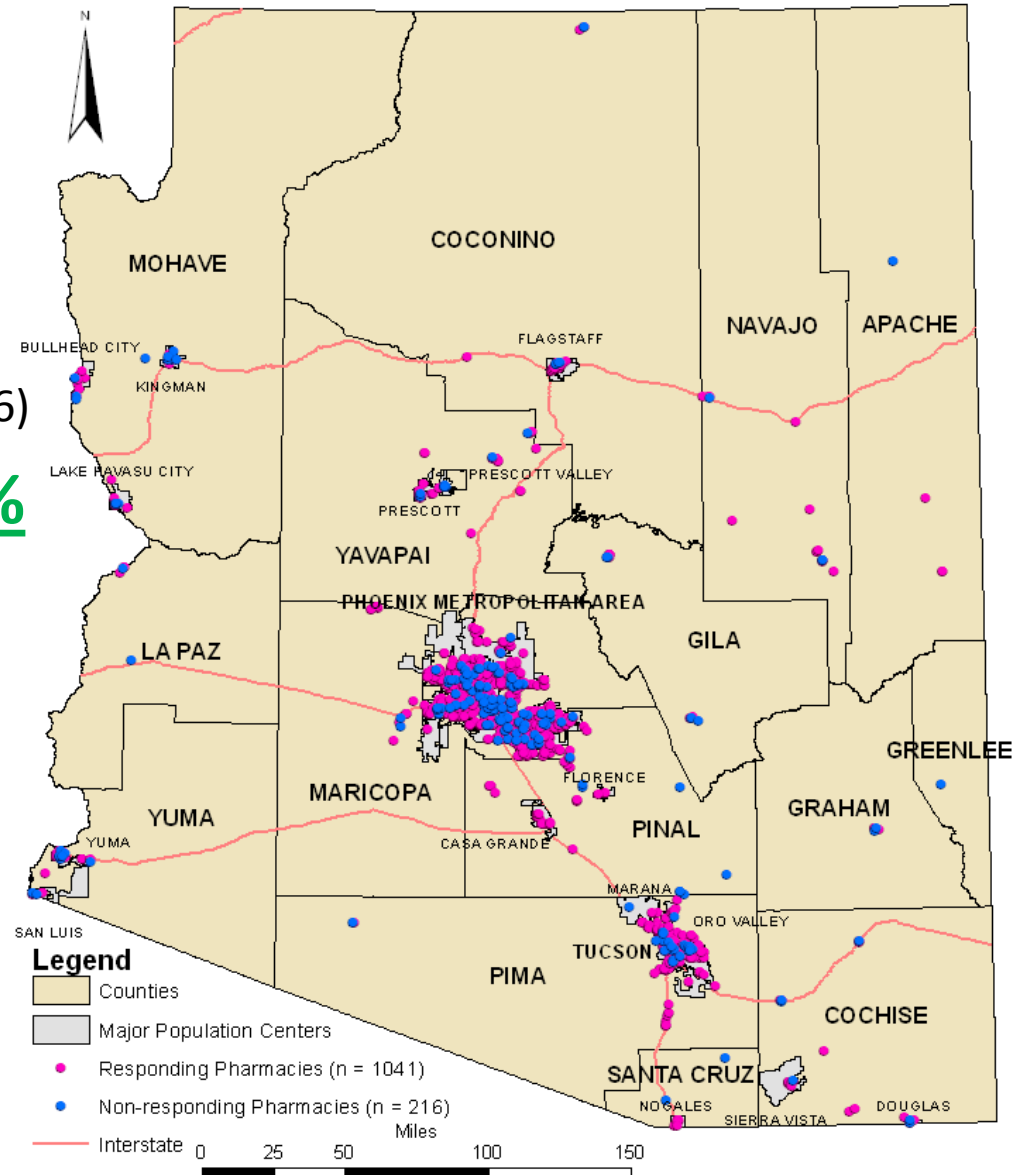
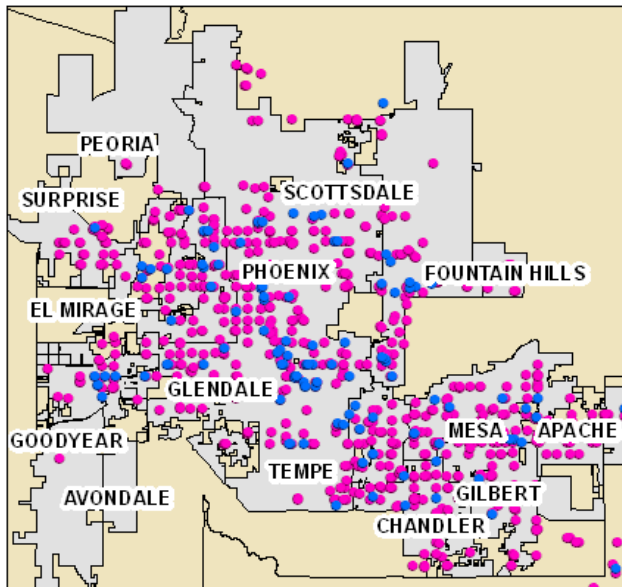
Efficacy of Routine Reporting

# Annual Pharmacy Responses

● Responding Pharmacies (n = 1041)  
● Non-responding Pharmacies (n = 216)

**82.8%**

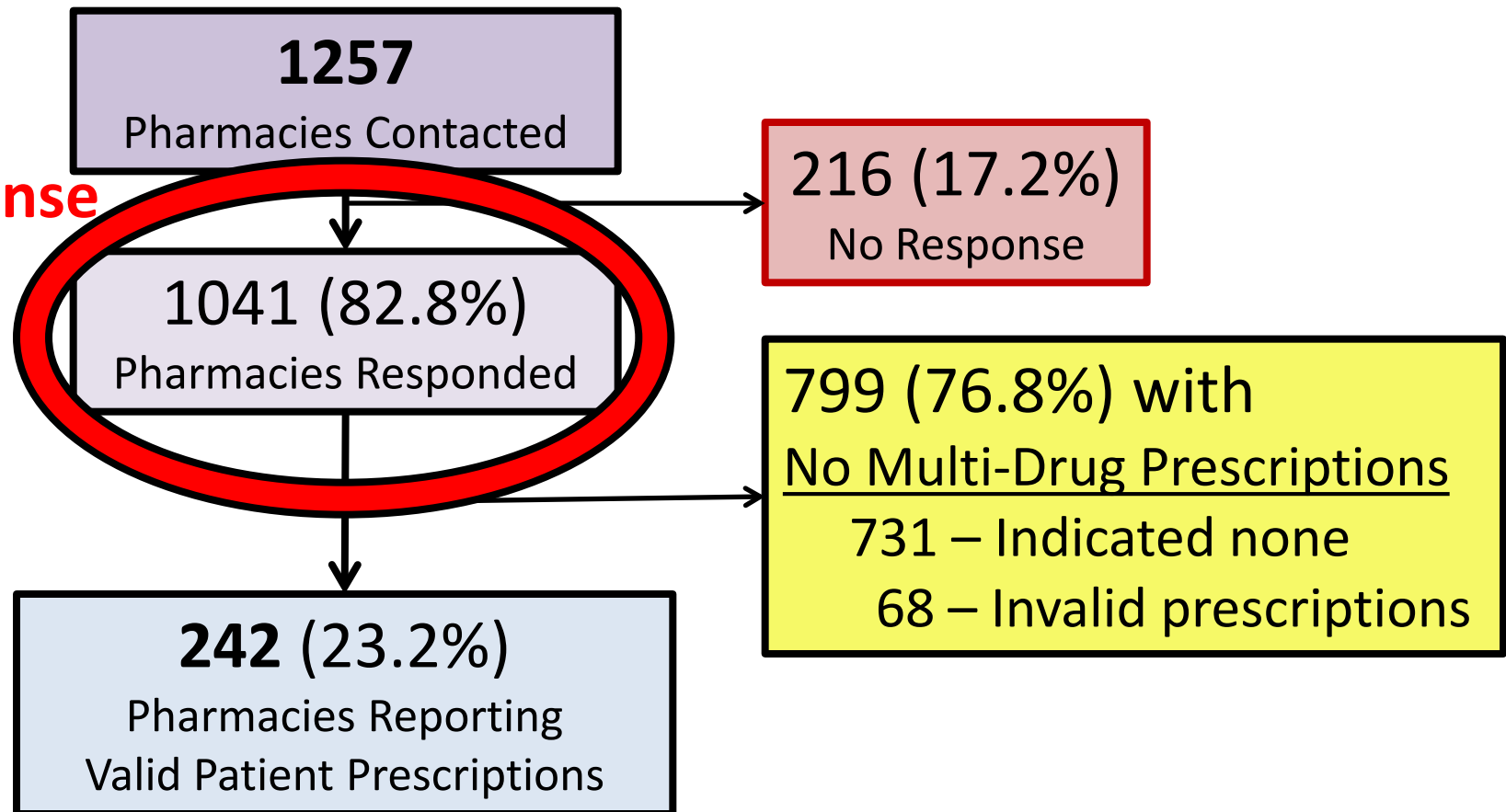
Phoenix Area





# Annual Pharmacy Response Results

**Response  
Rate**



# Annual Patient Prescription Records

310 Pharmacies reporting any prescriptions

**516**  
Total prescription records

146 (28.3%) Records excluded  
20 – All prescriptions out of range  
34 – Monotherapy  
92 – Multiple drugs, different dates

**370 (72.1%)**  
Valid prescriptions \*

\* Individuals can be repeated as reported prescriptions from separate pharmacies.

# Received Reports: Results

## ROUTINE

53  
Reports received

## ANNUAL

516  
Reports received

31 excluded

**Routine Reporting  
Received 4.3%  
95.7% Incomplete**

146 excluded

22  
Valid prescriptions

370  
Valid prescriptions

6 (27.3%)  
Not reported in Annual

16 (72.7%)  
Records confirmed in Annual Reports

**Database  
Matching**

# Record Matching: Databases

## Electronic Report of Verified Case of Tuberculosis (eRVCT)

- Report date (date case was alerted to public health, State or County)

## ADHS TB Control's "in-house" case management (Suspect)

- Report date (date lab is received by ADHS)

## ADHS "Stop TB AZ Registry" for LTBI and Contacts (STAR)

- Service origin date (for cases), date client identified by case (for contacts) or presented for services (targeted testing)

## ASPHL Laboratory Information Management System (LIMS)

- Test completed date

# Record Matching: Results

## Probabilistic Matching Identified

199 / 370 records

53.8%

## Deterministic Matching Identified

183 / 370 records

49.5%

	ERVCT	SUSPECT	STAR	LIMS
Total	58	161	23	117

	ERVCT	SUSPECT	STAR	LIMS
Total	52	157	17	99

Total Matches Identified

206 / 370 records

55.7%

	ERVCT	SUSPECT	STAR	LIMS
Unique	0	70	3	19
Total	60	181	23	118

Matched Records

# Evaluation Outcome Definitions

**TB**

Active Tuberculosis Disease: pulmonary TB  
extra-pulmonary TB  
*(as confirmed by laboratory culture or medical diagnoses)*

**LTBI**

Latent Tuberculosis Infection: non-infectious

**NTM**

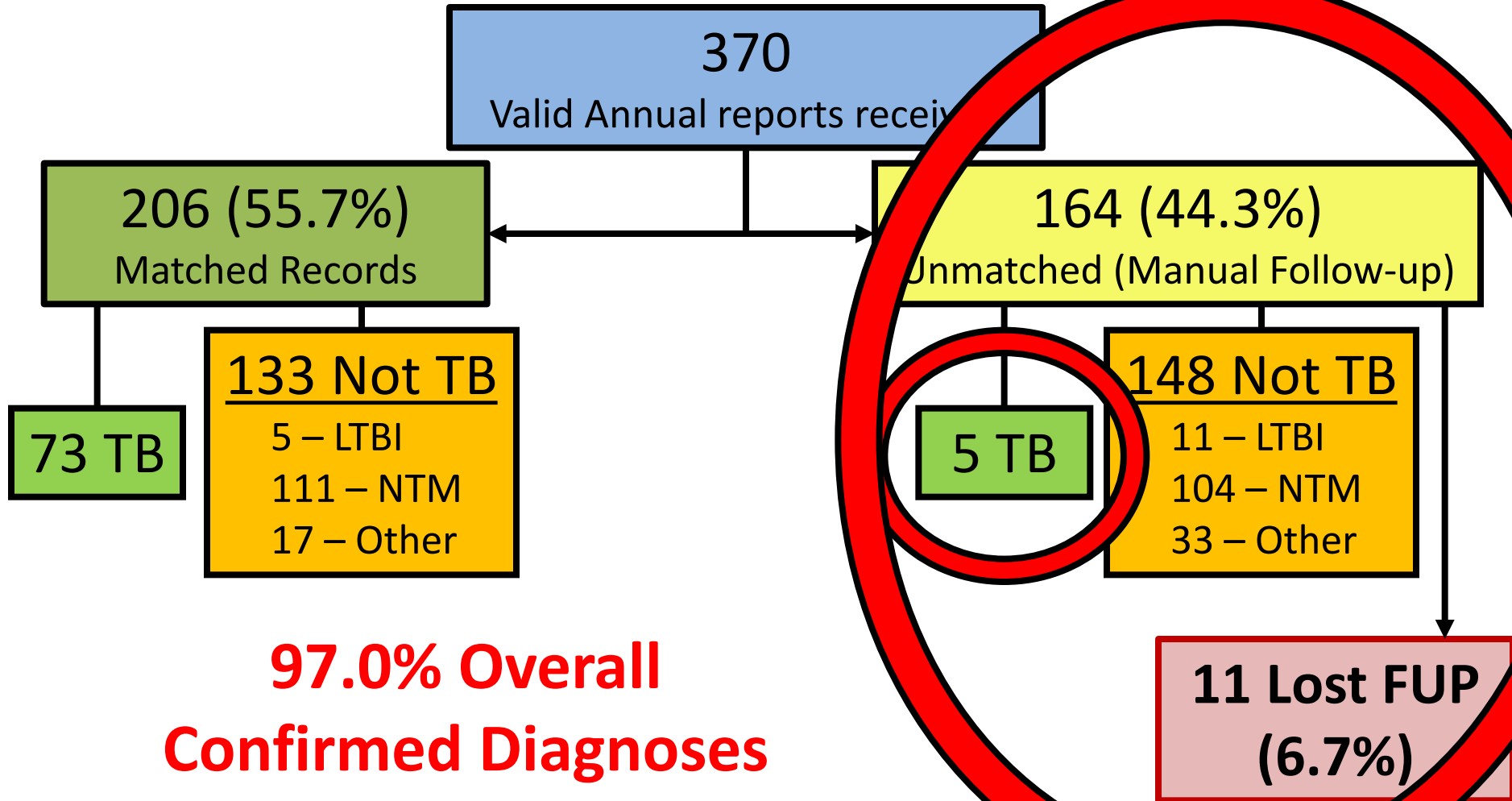
Non-tuberculous *Mycobacterium* infection

**Other**

Patients treated for TB, then TB ruled-out

**N  
O  
T  
T  
B**

# Patient Outcomes: Diagnoses



# Previously Unreported TB Cases

Report Date	Age/ Sex	Tests Performed (result)	Site of Infection	Risk Factors	Therapy (Start) [Complete]	Case Management	Annual Prescription (date)
05/14/11*	63/F	TST (+) Node Smear (+) Node Culture (-)	Extra-pulmonary TB (EPTB) Lymphatic	Diabetes mellitus, Immunosuppression (non-HIV/AIDS)	(5/24/11) [1/1/2012]	Totally self-administered	RIF, INH, ETH (5/24/11)
11/24/11	41/M	TST (-) Brain Smear (+) Brain Culture (+)	EPTB Brain	Homelessness, Non-injection drug use, Alcohol	(2/5/10) [3/16/2012]	Tx extended-improper case management DOT 110 weeks	INH, PZA, ETH (3/13/11)
12/30/11	56/F	TST (+) Node Smear (+) Node Culture (+)	EPTB Lymphatic	Foreign born > 10 years in US	(6/16/11) [3/01/2012]	Totally self-administered	RIF, INH, ETH (3/2/11)
12/31/11	37/F	IGRA (-) Node Smear (+) Node Culture (-)	EPTB Lymphatic	Foreign born > 10 years in US	(3/10/11) [12/30/11]	Totally self-administered	RIF, INH, PZA, ETH (2/24/11)

**All treated... not managed by Public Health** Extra Pulmonary Tuberculosis

\* Positive smear reported to local health department. Patient not followed-up due to negative culture result.

† Colorado case appropriately reported RVCT in 2010

TB, tuberculosis; NIDU, non-injection drug use; EPTB, extra-pulmonary tuberculosis; HIV/AIDS, human immunodeficiency virus/acquired immune deficiency syndrome; RIF, rifampin; INH, isoniazid; PZA, pyrazinamide; ETH, ethambutol



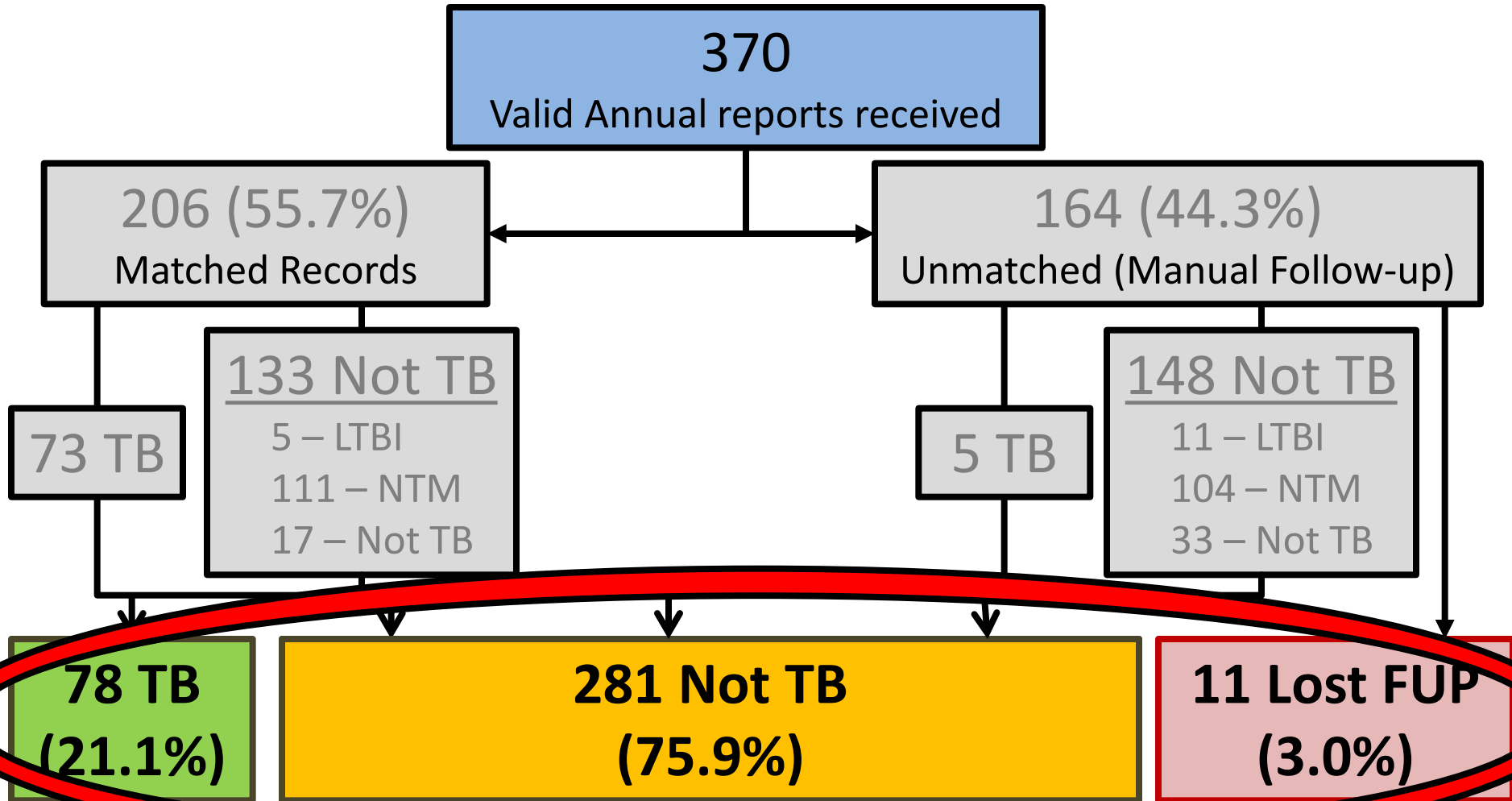
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# Patient Outcomes: Diagnoses



# Analysis: Medication Quantity

- Arizona requires reporting for 2 or more TB drugs
- Compare active TB versus “Not TB” to identify differences in prescription quantities

**TB - 78**

**2 Drugs**  
21 (26.9%)

**3+ Drugs**  
57 (73.1%)

**Not TB - 281**

**2 Drugs**  
216 (76.9%)

**3+ Drugs**  
65 (23.1%)

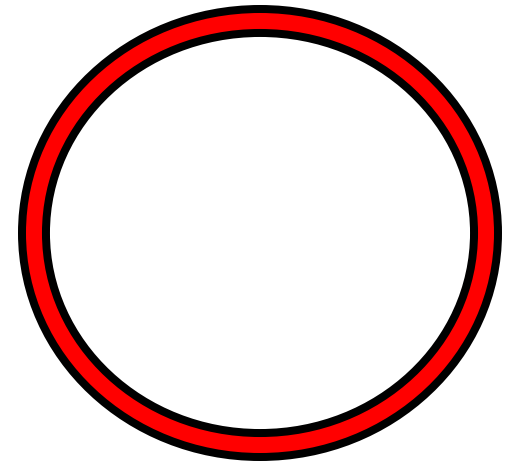
	TB	Not TB	
3+ Drug	57	65	122
2 Drug	21	216	237
	78	281	359

**Fisher's  
exact  
p < 0.001**

TB is significantly associated with 3+ drug prescriptions

# Positive Predictive Value

Routine reporting:



# PPV Significance Testing

Annual Reporting:

PPV  $\geq$  3 Drug = 46.7 (37.9-55.6)

PPV  $\geq$  2 Drug = 21.7 (17.5-26.0)

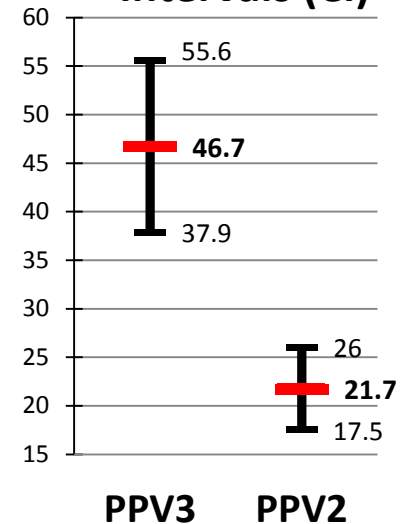
Relative PPV (PPV<sub>3</sub>/PPV<sub>2</sub>) = 2.150

95% CI: 2.134 – 2.167

*Interpretation*<sup>4</sup>:

The lower bound of the 95% CI is well above 1, and therefore PPV<sub>3</sub> is significantly greater than PPV<sub>2</sub>

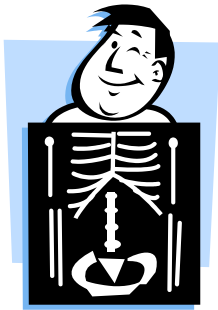
Annual PPV and  
95% Confidence  
Intervals (CI)



# “Unfound” TB Cases using PPV<sub>3</sub>

20 AZ TB cases with pharmacy reports for 2 drugs

Physician Reported



55%

AZ Public Health Lab



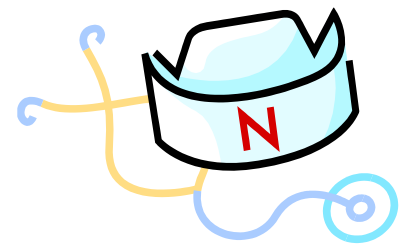
75%

Commercial Labs



60%

Local Health Jurisdiction

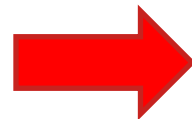


45%

At least 3 reports: 45%

At least 2 reports: 40%

Single other report: 15%



ZERO “unfound” TB case would have gone unreported to public health.

# Conclusions

## Under-reporting of reportable prescriptions

Annual resubmission of all reportable prescriptions

- ✓ *Increase awareness of reporting requirements, adherence and case catchment*

## Unreported TB can be found through pharmacy reporting

Develop educational resources for extra-pulmonary TB reporting

- ✓ *Outreach to physicians and laboratories to ensure TB case catchment*

## Predictive value improved with more specific drug reporting

Reporting for only 3+ anti-TB medication prescriptions

- ✓ *Improve reporting simplicity, accuracy, timeliness and reduce reporting burden*

# Future Directions

- Collaborations with Arizona's 4 largest pharmacy chains (~50% of total facilities) to establish routine electronic record pulls
- Similar Routine/Annual system could be adapted to other diseases with sentinel drugs

# Thank You

## Office of Disease Integration and Services

Carla Chee – *Office Chief*

Ayesha Bashir – *Deputy TB Control Officer (former)*

Julia Skinner – *HIV Capacity Building Epidemiologists*

## ADHS CSTE Mentors

Cara Christ – *Medical Director and Bureau Chief, TB Control Officer*

Shoana Anderson – *Deputy Bureau Chief*

## Office of Infectious Disease Services

Jessica Rigler – *Acting Office Chief OIDS (former)*



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# References

1. World Health Organization. Global tuberculosis control: WHO report 2011. Geneva, Switzerland. Available at: [http://whqlibdoc.who.int/publications/2011/9789241564380\\_eng.pdf](http://whqlibdoc.who.int/publications/2011/9789241564380_eng.pdf). Accessed May 8, 2012.
2. CDC. Trends in tuberculosis – United States, 2011. MMWR 2012; 61(11):181-185.
3. American Thoracic Society, CDC and Infectious Diseases Society of America. Treatment of tuberculosis. MMWR 2003; 52(RR11):1-77.
4. Moskowitz CS, Pepe MS. Comparing the predictive values of diagnostic tests: sample size and analysis for paired study designs. Clin Trials 2006; 3:272: doi 10.1191/1740774506cn147oa. Available at: <http://ctj.sagepub.com/content/3/3/272>. Accessed May 10, 2012.
5. Günther C-C, Bakke Ø, Lydersen S, Langaas M. Comparison of predictive values from two diagnostic tests in large samples. Norwegian University of Science and Technology, Trondheim, Norway. Available at: <http://www.math.ntnu.no/preprint/statistics/2008/S9-2008.pdf>. Accessed May 10, 2012.

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# Introduction

## TB in Arizona

2009: 232 cases  
(3.52 vs 3.8\* per 100,000)

2010: 282 cases  
(4.41 vs 3.6\* per 100,000)

2011: 255 cases  
(4.00 vs 3.4\* per 100,000)

## TB Reporting in Arizona

- Physicians
  - Suspected or confirmed diagnoses of TB
- Laboratorians
  - Positive *M. tuberculosis* cultures
- Pharmacists
  - Rx for anti-TB drugs
- Local Health Jurisdictions

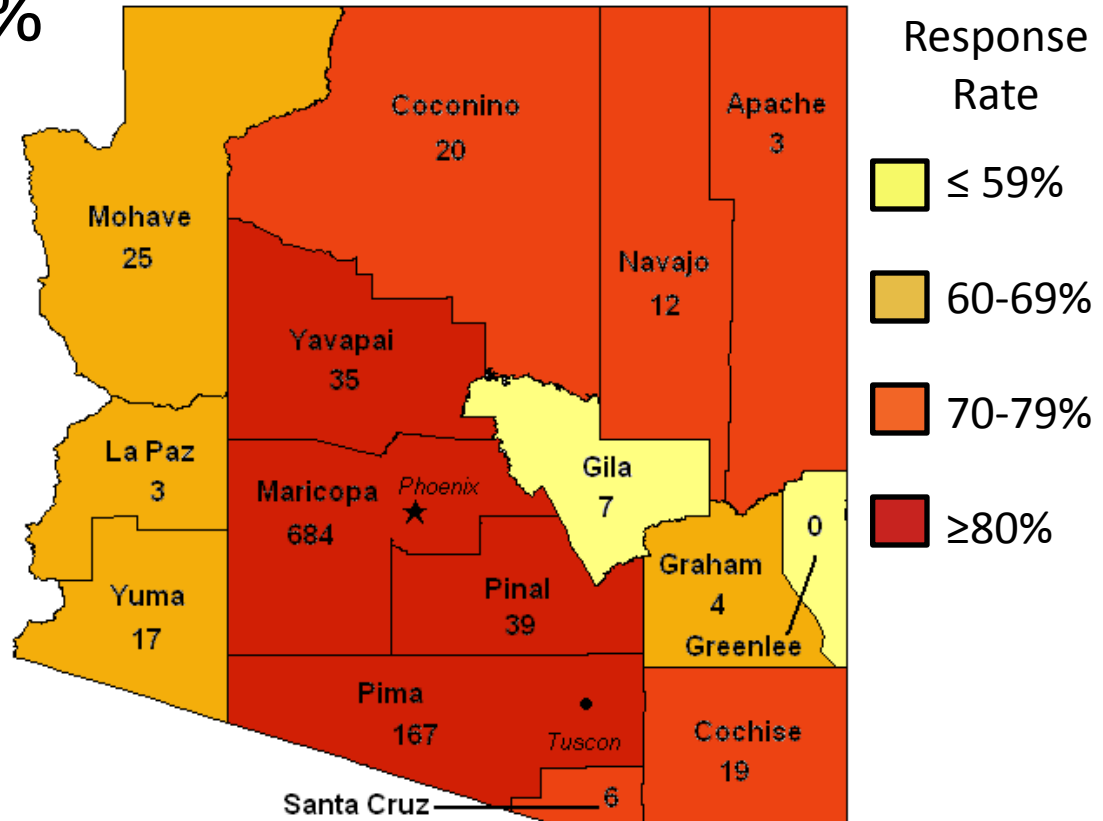
\*US Rates by reported by CDC<sup>2</sup>

# Pharmacy Response

Response Rate: 82.8%

Arizona counties	No. of Pharmacies	No. of Responses (percent)
Apache	4	3 (75.0)
Cochise	25	19 (76.0)
Coconino	26	20 (76.9)
Gila	12	7 (58.3)
Graham	6	4 (66.7)
Greenlee	1	0
La Paz	5	3 (60.0)
Maricopa	805	684 (85.0)
Mohave	40	25 (62.5)
Navajo	16	12 (75.0)
Pima	193	167 (86.5)
Pinal	46	39 (84.8)
Santa Cruz	8	6 (75.0)
Yavapai	43	35 (81.4)
Yuma	27	17 (63.0)
<b>Totals:</b>	<b>1257</b>	<b>1041 (82.8)</b>

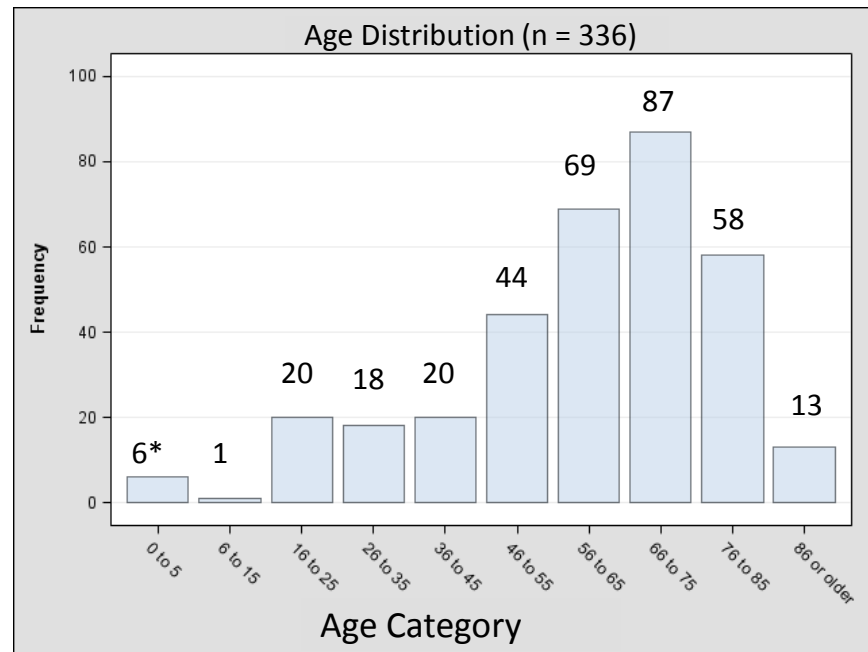
Arizona Counties (number of responses)



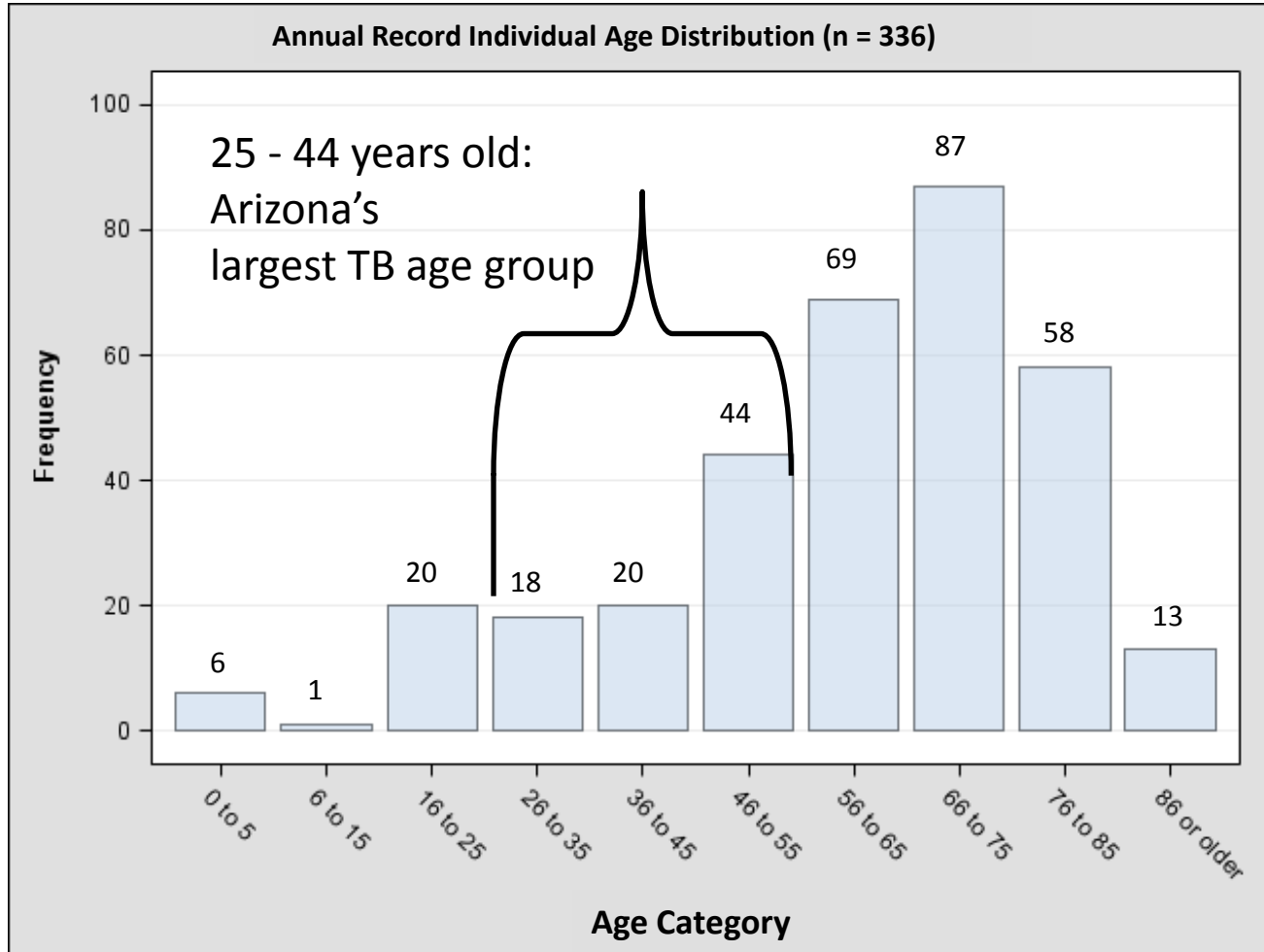
# Annual Records Demographics

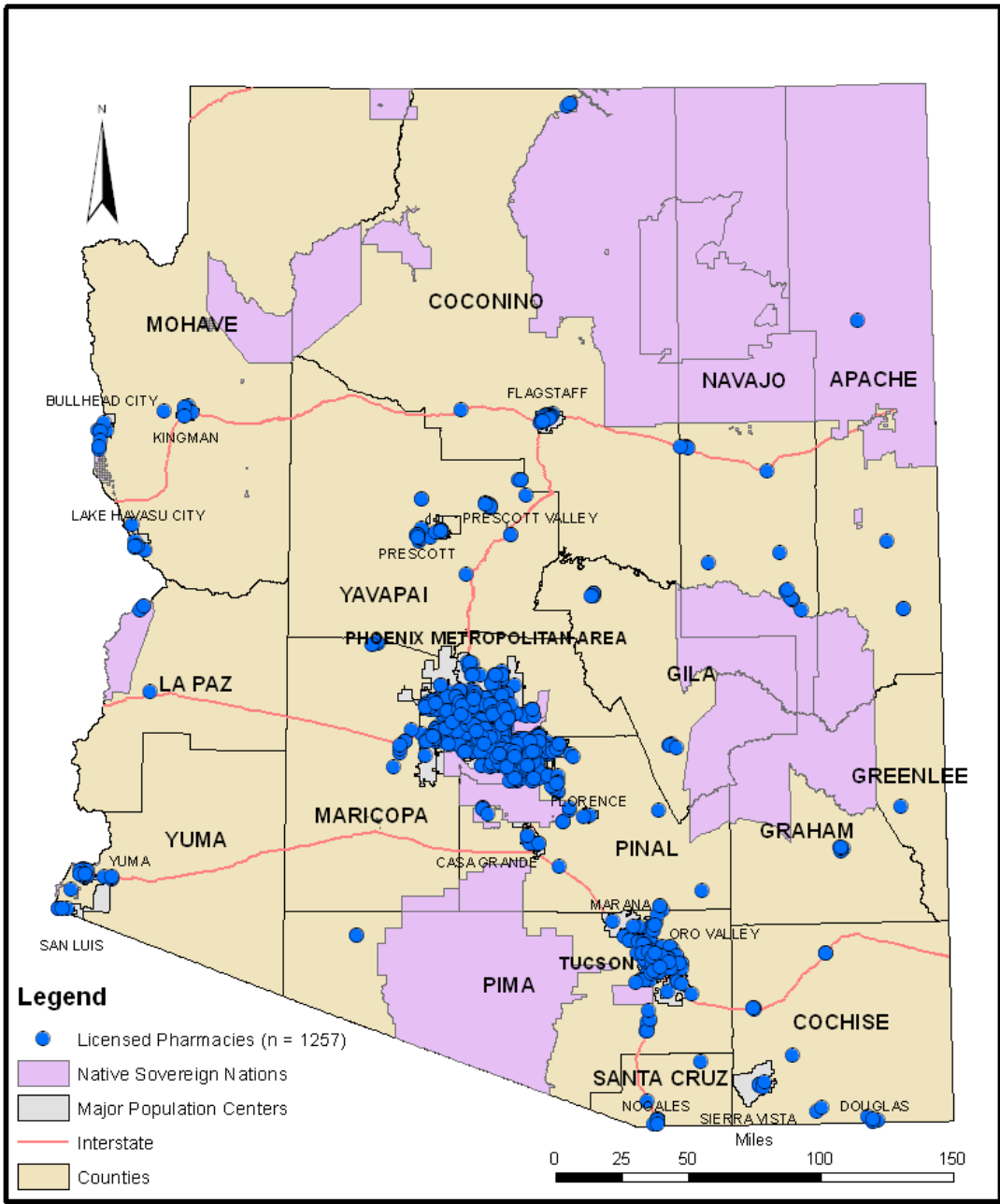
- Individuals (N = 351)
- 92.0% Arizona residents (323/351)
  - 17 States + Mexico (CA, CO, DE, HI, ID, IL, KS, MO, MT, NJ, NM, NV, OR, SD, TX, WA, WI)

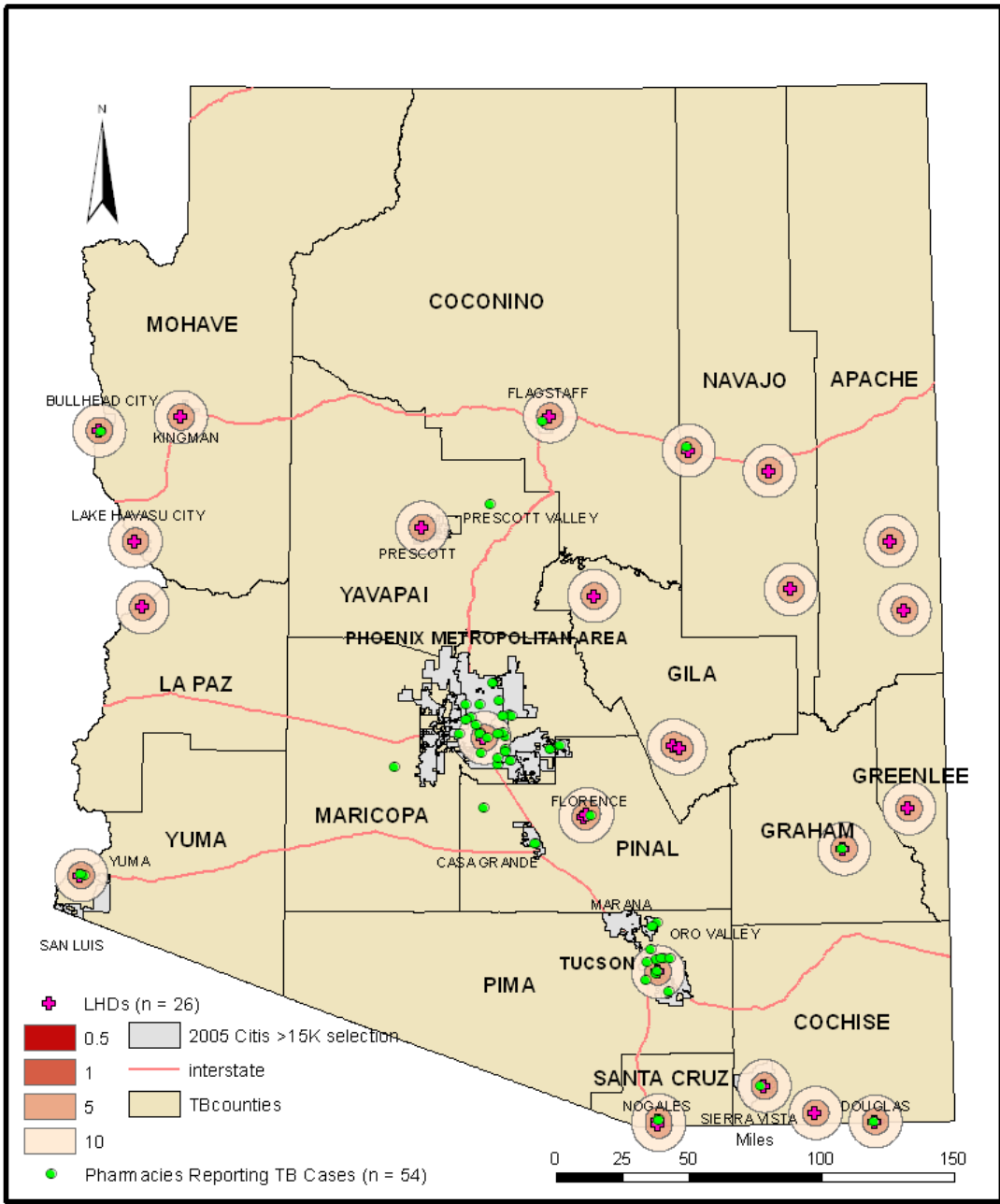
Arizona counties	No. of Patients (percent)
Apache	1 (0.3)
Cochise	8 (2.5)
Coconino	1 (0.3)
Gila	1 (0.3)
Graham	3 (0.9)
Greenlee	0
La Paz	0
Maricopa	206 (63.8)
Mohave	4 (1.2)
Navajo	5 (1.5)
Pima	50 (15.5)
Pinal	23 (7.1)
Santa Cruz	6 (1.9)
Yavapai	11 (3.4)
Yuma	4 (1.2)
<b>Totals:</b>	<b>323</b>

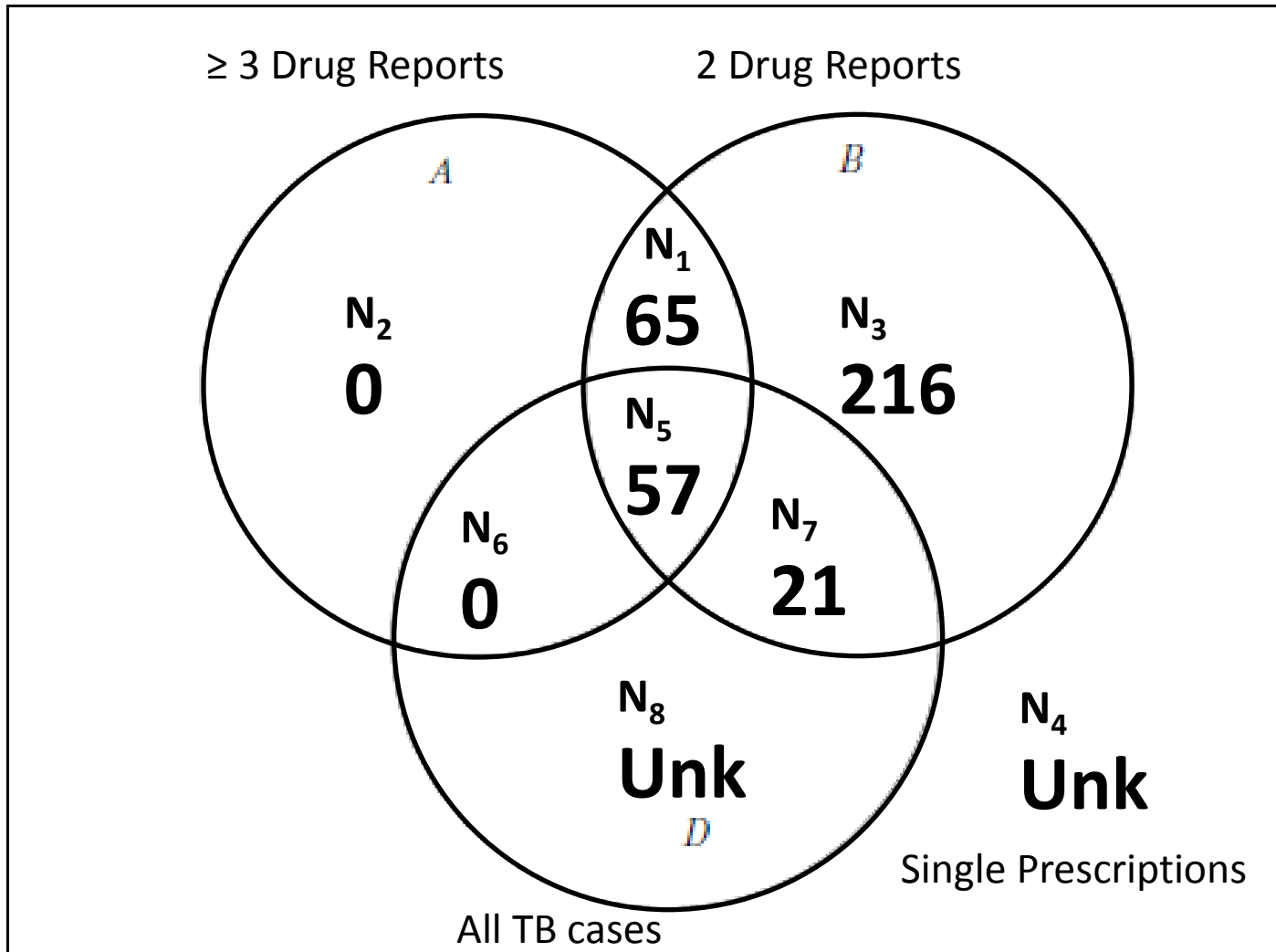


# Age Distribution







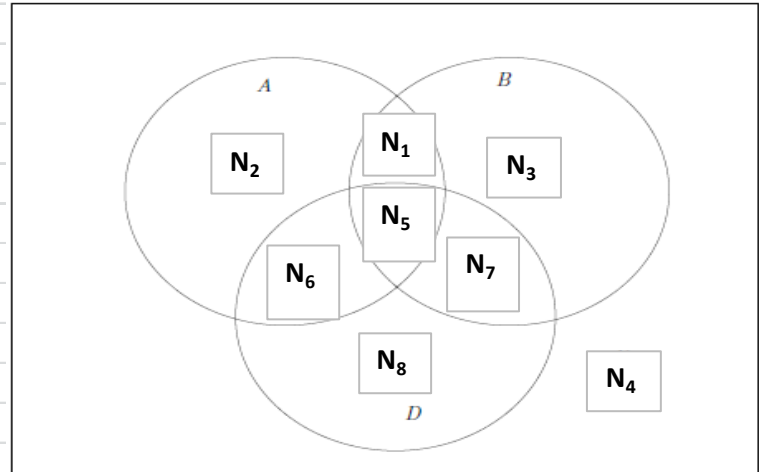


Reference 5



## COMPARISON OF 2 POSITIVE PREDICVITIVE VALUES

Relative Positive Predictive Value	A = ≥ 3 Drug Reports	N <sub>1</sub>	65
	B = ≥ 2 Drug Reports	N <sub>2</sub>	0
	D = TB disease	N <sub>3</sub>	216
PPV A = ≥ 3 Drug PPV		N <sub>4</sub>	-
		N <sub>5</sub>	57
		N <sub>6</sub>	0
PPV B = ≥ 2 Drug PPV		N <sub>7</sub>	21
		N <sub>8</sub>	-
		N	359



relative positive predictive value	2.1503783
rPPV = PPV A / PPV B	
Natural Log rPPV =	0.7656438
variance of rPPV = $\sigma^2P$	0.0057209

$$\frac{1}{(N5 + N7)(N5 + N6)} \times [N6(1 - PPVB) + N5(PPVB - PPV1) + 2(N7 + N3)PPVA \times PPV B + N7(1 - 3PPVA)]$$

0.000224921 x 25.43527 = 0.005721

95% Confidence Intervals of rPPV

$\log rPPV \pm Z_{1-\frac{\alpha}{2}} \frac{\sqrt{\sigma^2P}}{N}$	+	0.773468	exponentiated =	2.167269
	-	0.75782	exponentiated =	2.133619

relative positive predictive value = 2.15 (2.13-2.17)

The lower bound of the 95% confidence interval is well above 1 and therefore PPV A is significantly higher than PPV B

# “Lost” Cases using PPV<sub>3</sub>

## 21 TB cases not reported by annual 3+ drug reporting:

- 11/15 had positive ASPHL specimens submitted
  - ✓ 4 remaining = 3 individuals; All Symptomatic
    - 2/3 EPTB Patho/Cyto Cx (+) Commercial lab
    - 1/3 Sp Smear (-); Cx (-); MD Dx
- 6 Remaining:
  - ✓ 1 Lung Structure; Cyto Smear (+); Commercial lab Cx (+)
  - ✓ 1 Nervous System; Smear/Cx (-); DOC;
  - ✓ 2 Pulm; Related children, Contact Investigation; CXR Ab
  - ✓ 1 Osteo-articular TB reported in 2004, on Tx for life
  - ✓ 1 Colorado TB Case – not in any AZ state DB