Evaluation of Pyrosequencing for Impact on Tuberculosis Clinical Management and Public Health

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Disclosures

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Pyrosequencing

- Rapid DNA sequencing method
- Identifies mutations associated with resistance to first & second line TB drugs:
  - Isoniazid: *katG, inhA, ahpC*
  - Rifampin: *rpoB*
  - Fluoroquinolones: *gyrA*
  - Injectibles: *rrs*
- Used since March 2012 by Microbial Diseases Lab (MDL)

PSQ Evaluation

Objectives:

- Characterize use of PSQ in California
- Evaluate PSQ performance
- Determine PSQ's effect on clinical decision-making
- Determine if PSQ shortens the time to appropriate therapy (DR and susceptible TB) [PENDING]

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Methods

Specimen inclusion

- Submitted from Aug 1, 2012 to Jul 31, 2013
- Culture isolate or sputum sediment (at least 1+ smear positivity)
- California patients

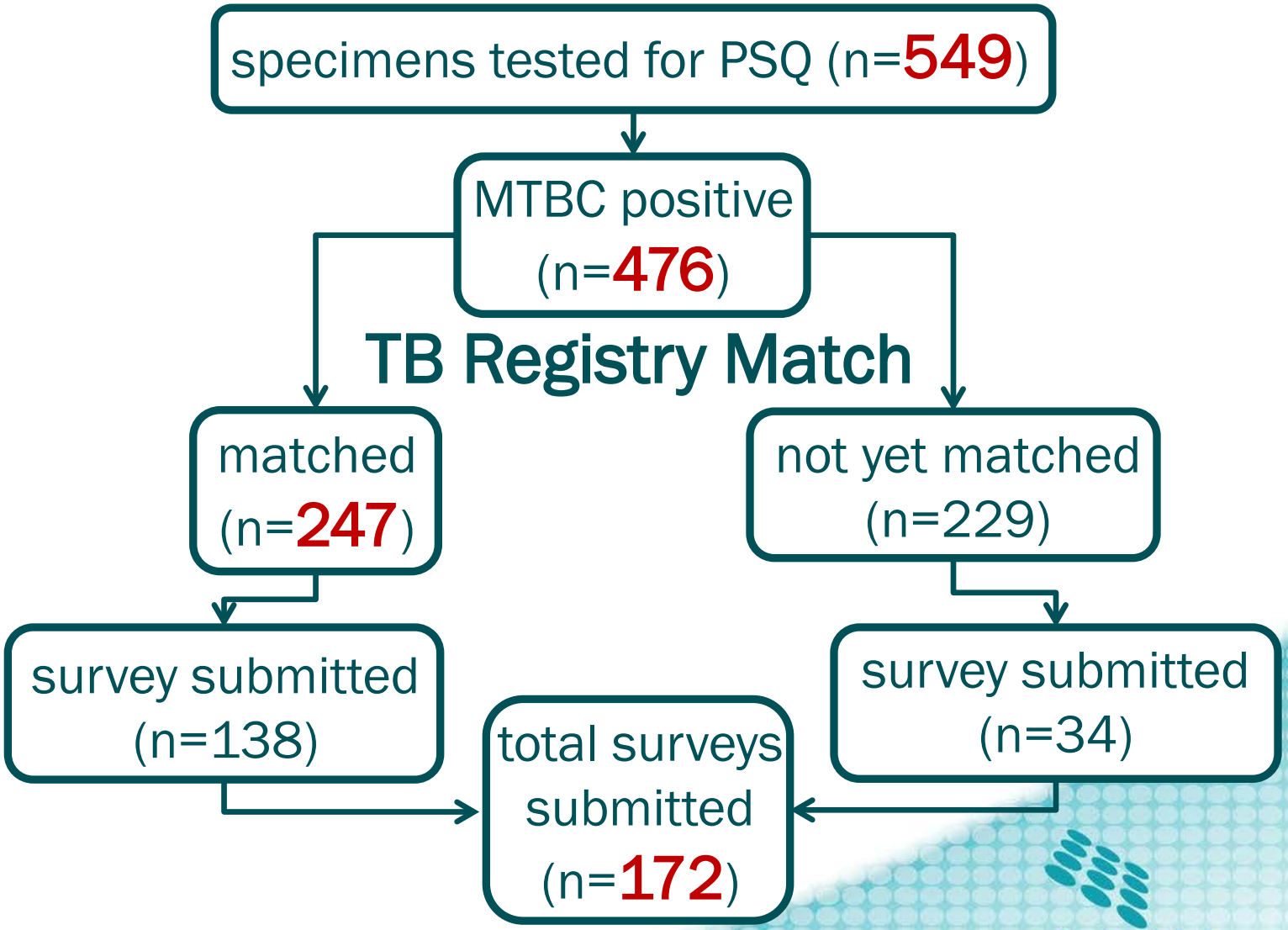
Match to TB Registry

- Deterministic algorithm based on name & date of birth

Survey

- Sent to TB control program/patient's clinician
- Mailing delayed based on specimen type

PSQ Analysis Populations



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PSQ use in California

- 255/549 (46%) of specimens were submitted by 3 counties: Los Angeles, San Diego, Alameda
- More than half of all California counties submitted ≥1 specimen
- PSQ was requested for 26% of all smear or culture positive TB cases reported from Aug 2012-Jul 2013

PSQ Specimen Type

	No. (%)		
Total specimens	549		
Sediment		313	(57)
Culture		228	(42)
not stated		8	(1)

Specimens submitted Aug 1, 2012–Jul 31, 2013

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PSQ Results

	No. (%)			
Total specimens submitted	549			
Specimens positive for MTB		476	(87)	
Pan-sensitive*			349	(73)
INH-mono resistant			54	(11)
Rif-mono resistant			8	(2)
Multidrug-resistant			19	(4)
Pre-XDR			9	(2)
XDR			1	(<1)
Other resistance pattern			36	(8)

*No mutations detected

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PSQ results (n=247)

	Phenotypic results		Sensitivity		Specificity	
PSQ result	# resistant	# susceptible	% (95% CI)		%	(95% CI)
Isoniazid						
mutation	39	0	86.7	(73.2-94.9)	100	(98.0-100)
no mutation	6	180				
Rifampin						
mutation	13	0	92.9	(66.1-98.8)	100	(98.2-100)
no mutation	1	208				
Fluoroquinolones						
mutation	3	0	100	(30.5-100)	100	(81.3-100)
no mutation	0	18				

Source: PSQ & TB Registry: initial & final susceptibility results PSQ/TB Registry match: Aug 1, 2012-Jul 9, 2013; CI: confidence interval

*Inconclusive results excluded

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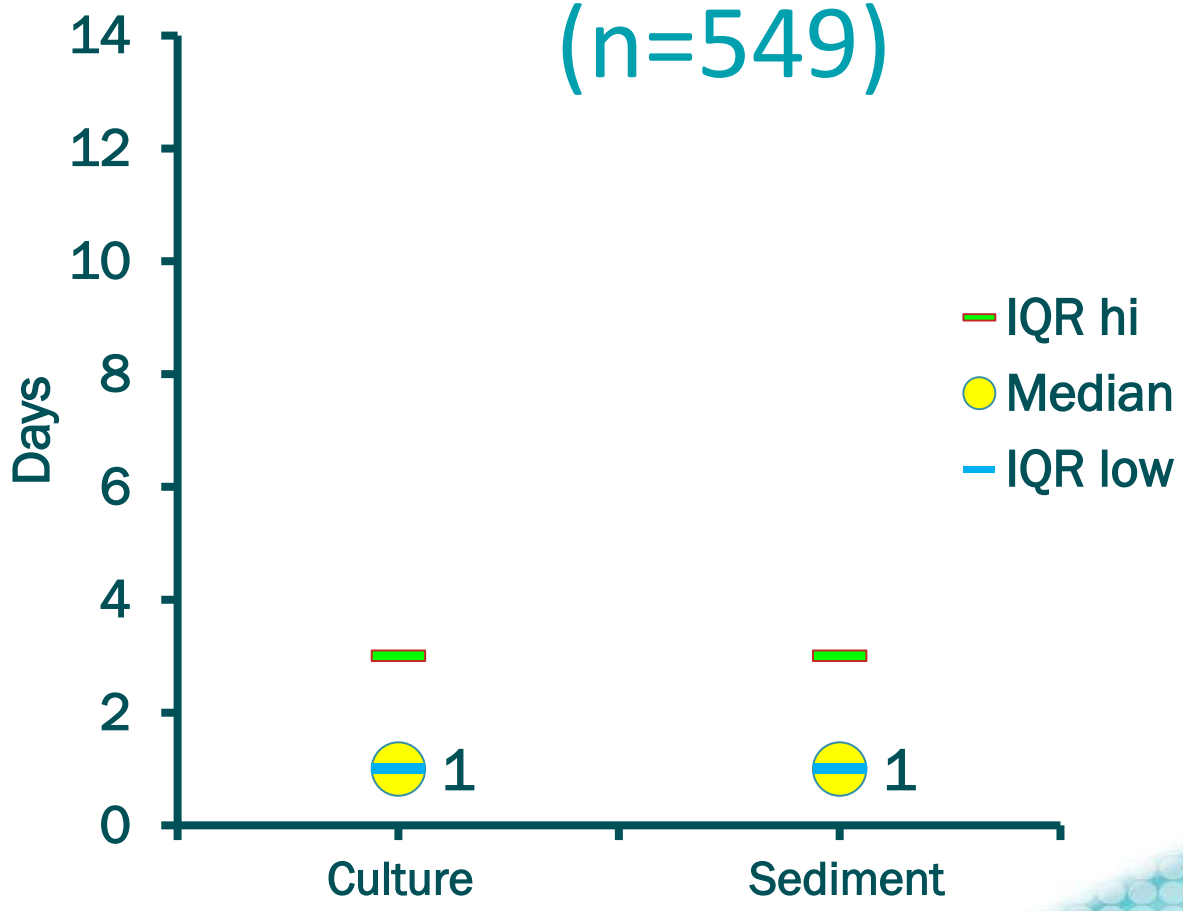
Time from MDL Specimen Receipt to PSQ Result (n=549)



All MTB pos PSQ Specimens: Aug 2012–Jul 31, 2013

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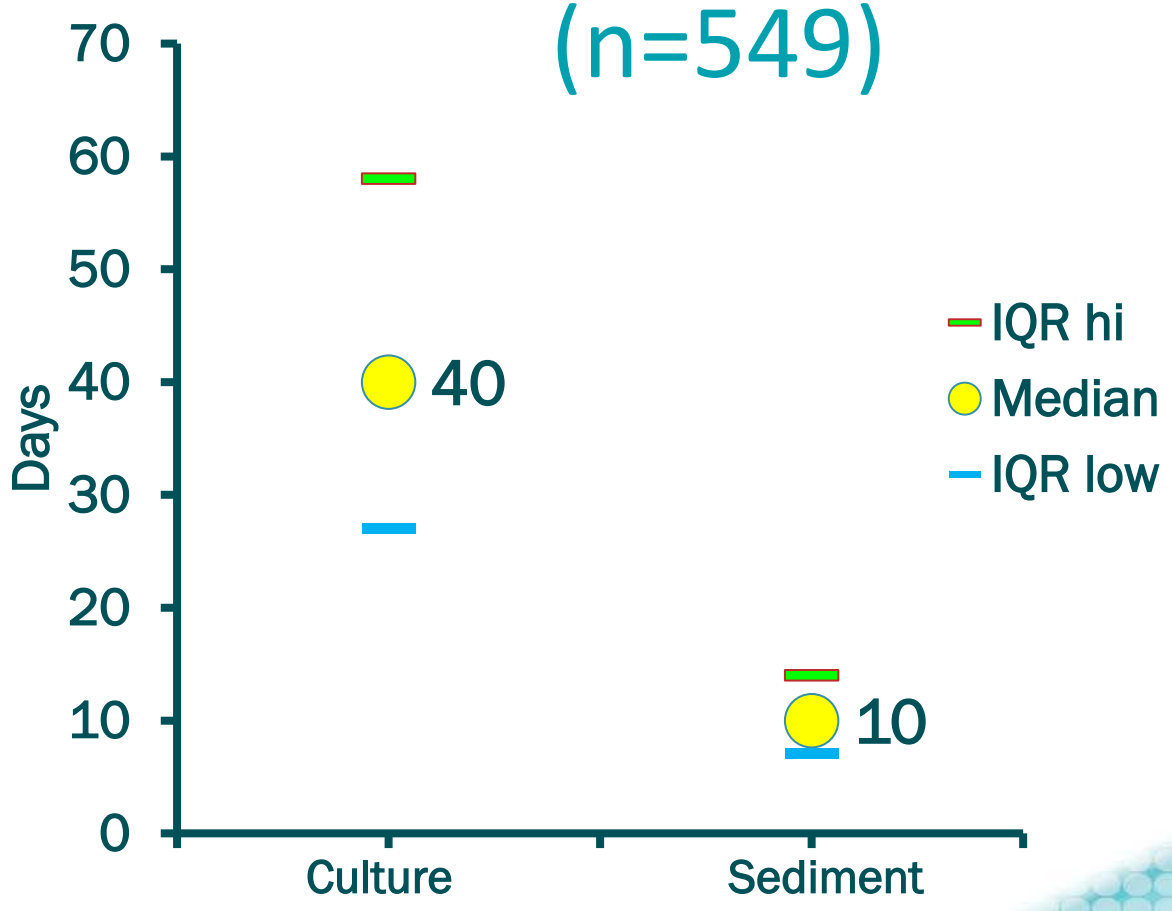
Time from Specimen Collection to PSQ Result (n=549)



All MTB pos PSQ Specimens: Aug 2012–Jul 31, 2013

Reason PSQ Ordered

Reason (n=172)	No. (%)	
Increased MDR risks	108	(63)
Increased MDR stakes	48	(28)
Laboratory	28	(16)
Mixed/contaminated culture	6	(21)
Confirmation of phenotypic results	13	(46)
Follow-up on GeneXpert results	9	(32)
Other	35	(20)
Unknown	6	(3)

>1 reason can be selected

Prevalence of MDR TB by Reason PSQ was ordered

Reason (n=172)	MDR	
	No. (%)	
Increased MDR risks (n=108)	11	(10)
Increased MDR stakes (n=48)	1	(2)
Laboratory (n=28)	5	(18)

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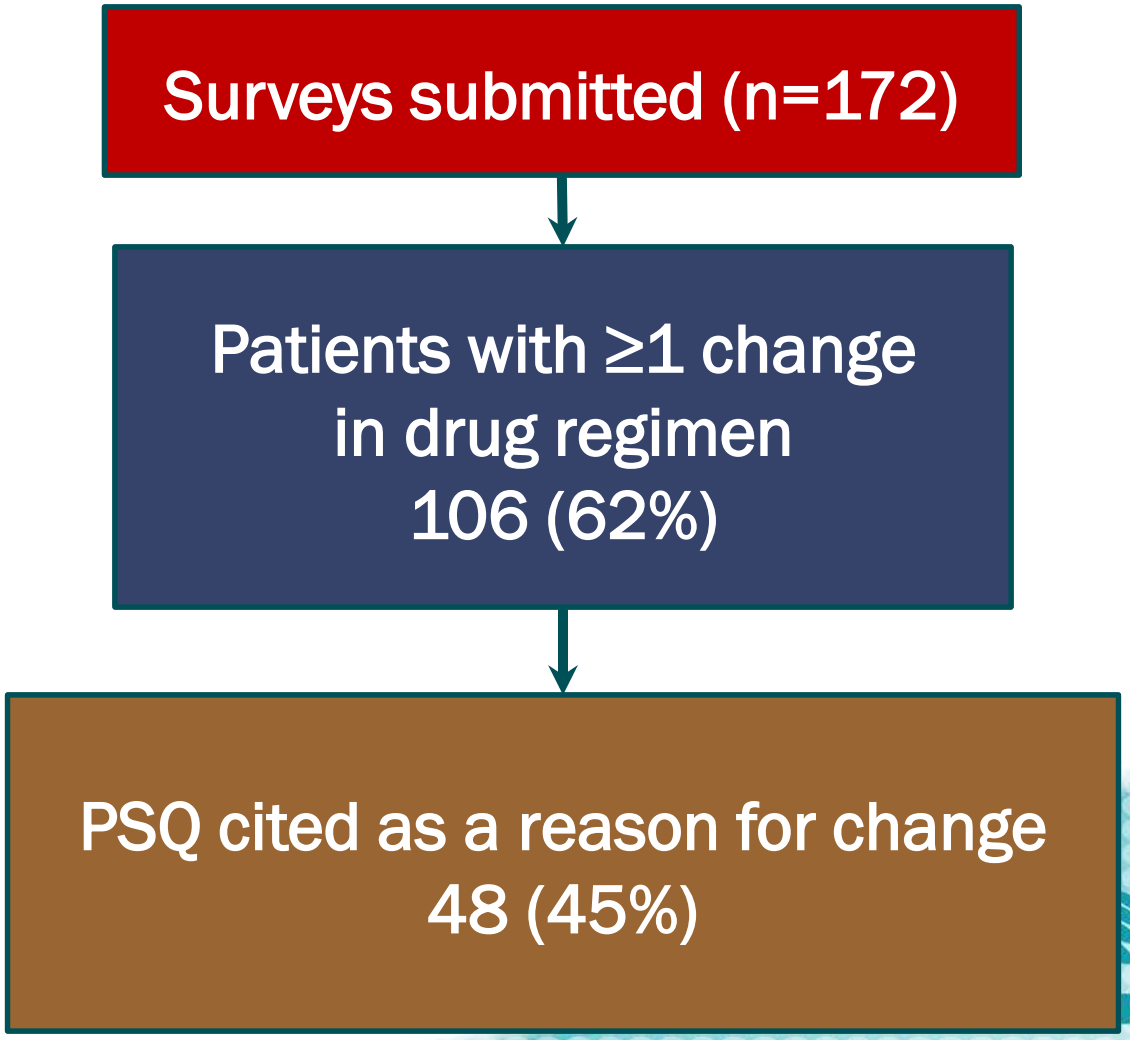
Drug Regimen Changes Among Patients Tested with PSQ



Analyses in Progress

- Determine whether PSQ shortened time to start of MDR TB regimen
- Further analyze the impact of PSQ on the clinical management of patients
- Examine how discrepancies between PSQ and phenotypic DST were resolved

Conclusions

- PSQ is widely used & its turnaround time and test performance are good
- Reducing specimen submission time is needed to maximize the benefit of PSQ
- In a majority of cases, PSQ was requested because patient is thought to be at increased risk for MDR TB
- PSQ affects treatment decisions in almost half of TB cases

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