

# **The Use of Non-clinical Indicators to predict TB Positivity**

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# Disclaimer

- This presentation was supported by the Association of Public Health Laboratories and by the Cooperative Agreement Number U60HM000803 from the Centers for Disease Control and Prevention and/or Assistant Secretary for Preparedness and Response. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Association of Public Health Laboratories, the Centers for Disease Control and Prevention and/or Assistant Secretary for Preparedness and Response.

# Outline

- Background of TB Lab in MA
- Project plan and Objectives
- Laying the foundation (IT enhancements...)
- Data/Results
- Conclusions/Next steps

# Massachusetts TB Lab

- ~20,000 specimens annually
- ~10,000 patients
- ~175-200 positive TB cases annually
- Pre-September 2012 tested ~1% (150-200 specimens) annually by NAAT (GenProbe MTD Direct)
- Summer 2012 awarded funding for Performance evaluation of molecular diagnostic tests for tuberculosis

# Objectives

- To determine if non-clinical indicators are a useful predictor of TB positivity
- To determine if those non-clinical indicators helps MA to reach HP2020 goal

# **HP2020 Guidelines**

**to diagnose 75% of TB cases within 2 days**

- In MA, 25% of all TB cases are non-pulmonary not eligible for NAAT**
- We need to identify 100% of all pulmonary TB within 2 days to meet this goal.**

# Baseline

|                                     | 2009 | 2010  | 2011  | 2012<br>1/1-<br>6/30 | 2013 to<br>(June30) |
|-------------------------------------|------|-------|-------|----------------------|---------------------|
| % tested with<br>NAAT               | 0.7  | 0.85  | 0.84  | 1.8                  |                     |
| # NAAT<br>Positive                  | 47   | 44    | 47    | 19                   |                     |
| # NAAT<br>positive<br>within 2 days | 15%  | 45.5% | 63.8% | 52.6%                |                     |

# Proposal

- 7/1/12 thru 6/30/13
- Test the first respiratory specimen from each patient from designated “High Risk Providers”
  - Determined as high risk by the percentage of TB positive patients
    - Local Boards of Health
    - TB Clinics
    - Departments of Correction
    - State funded hospital
- Collaborate with TB Control to identify and test high suspect cases
- Continue to test all first smear positive respiratory specimens and smear negative physician requests
- Compare the metrics before and after



# Project Plan Outline

1. Discontinue MTD Direct /Validate and implement GeneXpert
  1. Robust validation plan; willing to share
2. Train staff to run GeneXpert
  1. Technically easy, trained lab supervisor and 2 staff
3. Update LIMS
4. Notify providers
5. Design a system to identify and run all appropriate specimens
6. Create data management system

# Project Plan Outline

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# IT Enhancements

- Update LIMS to reflect change from MTD to more generic “NAAT”
- Added language to reflect Rifampin result
  - *Comment: NAAT results will be followed by confirmatory testing with conventional culture and DST methods. This TB NAAT method has not been approved by FDA for clinical diagnostic purposes. However, this laboratory has established assay performance by in-house validation in accordance with CLIA standards.*

# Provider Notification

- Memo to all providers
  - discontinuation of MTD Direct; implementation of Cepheid GeneXpert MTD/Rif
- Second a memo went to high risk providers
  - routine NAAT from first respiratory specimen regardless of smear result
  - Will maintain conventional culture and susceptibility testing
  - No additional cost to provider

# Project Plan Outline

1. Discontinue MTD Direct /Implement GeneXpert
2. Train staff to run GeneXpert
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5. Develop and implement data management system

# Data Management in the lab

- Manual specimen management
- Track which specimens needed NAAT and why
- Lab created spreadsheet
  - First positive smear
  - Smear negative physician request
  - High suspect case from MA TB Control
  - High risk provider
- Lab staff was trained to automatically send any specimen that fit the above categories to “GeneXpert rack”
  - Special GeneXpert rack and accession number added to lab spreadsheet

# High Suspect Specimens

- Created a file in a shared drive for lab and TB Control
  - TB control adds patient information
- Notifies lab supervisor to watch for specimen
  - Email, phone call, monthly meetings
- Lab Supervisor ensures specimen is run via NAAT when it arrives

# High Risk Provider Query

- IT created a report that pulls all first respiratory specimens on each patient submitted from predetermined high risk provider
  - Boards of health, department of corrections, TB clinics, state funded hospital
- Lab supervisor runs this report daily
- Lab supervisor checks list against the “master spreadsheet” or GeneXpert rack kept in the lab



# Laboratory Information “Master Spreadsheet”

| Accession Number | Processed Date | Date added to the Rack | Reason for NAAT and date NAAT performed            |                                  |  |  |
|------------------|----------------|------------------------|--|----------------------------------|--|--|
|                  |                |                        | First smear positive respiratory specimen received | Smear negative physician request | Suspect case per TB Control daily report | High risk provider group identified by LIMS Report |
|                  | 9/4/2012       | 9/5/2012               |  |                                  |  | 9/5/2012   |

# Data flow to project manager

- Each week:
- Lab supervisor sent a copy of the lab spreadsheet to the project manager
- Data was merged into MA data table
  - Shared quarterly with APHL along with a progress report
  - Manual merge
- Project manager was responsible for compiling and analyzing data “weekly”

# Project Plan Outline

1.  Discontinue MTD Direct /Implement GeneXpert
2.  Train staff to run GeneXpert
3.  Update LIMS
4.  Notify providers
4.  Develop and Implement specimen and data management system
  1. Manual management of data and specimens
  2. Not pretty but it seems to work

# Results

|                   | NAAT Pos<br>Culture Pos | NAAT Pos<br>Culture Neg | NAAT Neg<br>Culture Pos | NAAT Neg<br>Culture Neg |
|-------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Smear<br>Positive | 47                      | 1                       | 0                       | 41                      |
| Smear<br>Negative | 12*                     | 9                       | 5                       | 292**                   |

- 5/12 are newly identified TB cases
- \*\*17 culture results still pending

# Specimens tested by reason code

|                            | Total Number Tested | Number (%) NAAT Positive | Number (%) Culture Positive |
|----------------------------|---------------------|--------------------------|-----------------------------|
| First smear positive       | 63                  | 25 (39.7)                | 25 (39.7)                   |
| Smear negative request     | 107                 | 14 (13.1)                | 11 (10.2)                   |
| Suspect pos per TB Control | 33                  | 5 (15.2)                 | 4 (12.1)                    |
| High risk provider         | 182                 | 10 (5.5)                 | 9 (4.9)                     |
| Combo (more than 1 reason) | 28                  | 13 (46.4)                | 12 (42.9)                   |

\*Combination reasons most frequently first smear positive with suspect or high risk provider

# High Risk Providers

|                           | Total Number Tested | Number (%) NAAT Positive | Number (%) Culture Positive         |
|---------------------------|---------------------|--------------------------|-------------------------------------|
| TB Clinics                | 111                 | 3(2.7)                   | 6(5.4)                              |
| Departments of Correction | 1                   | 0                        | 0                                   |
| Boards of Health          | 23                  | 3(13)                    | 1(4.3)<br>(1 culture still pending) |
| State Hospital            | 71                  | 7(9.9)                   | 7(9.9)                              |

# Numbers of Individual Patients from BOH and DOC 2009-2013

|     | 2009 | 2010 | 2011 | 2012 | 2013<br>(through<br>6/30/13) |
|-----|------|------|------|------|------------------------------|
| BOH | 40   | 94   | 60   | 95   | 27                           |
| DOC | 3    | 0    | 12   | 9    | 0                            |

# Results

|                   | NAAT Pos<br>Culture Pos | NAAT Pos<br>Culture Neg | NAAT Neg<br>Culture Pos | NAAT Neg<br>Culture Neg |
|-------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| Smear<br>Positive | 47                      | 1                       | 0                       | 41                      |
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## TAT among 5 smear negative new cases

| rcvd-smear | smear-naat | rcvd-naat | naat-result | smear-result | rcvd-result | Rcvd-result |
|------------|------------|-----------|-------------|--------------|-------------|-------------|
| 2          | 0          | 2         | 20          | 20           | 22          | 22          |
| 4          | 0          | 4         | 21          | 21           | 25          | 25          |
| 1          | 1          | 2         | 10          | 11           | 12          | 12          |
| 1          | 0          | 1         | 20          | 20           | 21          | 21          |
| 1          | 0          | 1         | 19          | 19           | 20          | 20          |

Did this alter the treatment of the patient?

# How did Rifampin Resistance Correlate?

|                            | Culture Result   | DST   |
|----------------------------|--|---|
| <b>Rif Sensitive X64</b>   | ●55 MTB  | ●54 susceptible, 1 overgrown,   |
| <b>Rif Resistant X2</b>    | 2 MTB  | ●2 Resistant  |
| <b>Rif Undetermined X4</b> | <ul style="list-style-type: none"> <li>●1 MTB</li> <li>●1 MTB (MAC in concurrent culture)</li> <li>●1 MAC (MTB in concurrent culture)</li> <li>●1 Pending</li> </ul> | <ul style="list-style-type: none"> <li>●Susceptible</li> <li>●Susceptible</li> <li>●Not tested; MTB not isolated</li> <li>●pending</li> </ul> |

# Rifampin Results

| NAAT Result                  | Culture Result | DST (Rif only) Result | Comments  |
|------------------------------|----------------|-----------------------|---|
| <b>Positive/undetermined</b> |                |                       |   |
| <b>Positive/undetermined</b> | <b>MTB</b>     | <b>SUSCEPTIBLE</b>    |   |
| <b>Positive/undetermined</b> | <b>MTB</b>     | <b>SUSCEPTIBLE</b>    | <b>PREV POS/<br/>ALSO<br/>MAC<br/>POS</b>                   |
| <b>Positive/undetermined</b> | <b>MAC</b>     |                       | <b>New Pos<br/>Patient;<br/>patient<br/>also has<br/>TB</b> |

| <b>NAAT Result</b>         | <b>Culture Result</b> | <b>DST (Rif only) Result</b>                |
|----------------------------|-----------------------|---|
| <b>Positive/ Resistant</b> | <b>MTB</b>            | <b>RESISTANT (previous known resistant)</b> |
| <b>Positive/ Resistant</b> | <b>MTB</b>            | <b>RESISTANT</b>                            |

# Did we achieve HP2020 Goal?

|                             | 2009 | 2010 | 2011 | 2012 | 2013 to<br>(June30) |
|-----------------------------|------|------|------|------|---------------------|
| % tested with<br>NAAT       | 0.7  | 0.85 | 0.84 | 1.95 | 2.6                 |
| # TB cases<br>within 2 days | 15   | 20   | 30   | 54   | 16                  |
| % NAAT pos<br>within 2 days | 38   | 45.5 | 63.8 | 52.6 | 45.7                |

# Where do we go from here?

- We will continue to work to meet the HP2020 goal
- No significant additional burden to lab
- We will continue to routinely run these 4 groups
  - First positive smear
  - Smear negative physician request
  - High suspect case from MA TB Control
  - High risk provider
- Discontinue the lab spreadsheet=happy lab staff
- Continue to use the shared file for high suspects from TB Control
- Continue to use high risk provider query to catch specimens that may be missed
- Expand to identify other groups with a high likelihood of being positive
  - Ie 25-44 year old?
  - Foreign born or foreign travel?

# Response from partners

- From Submitters
  - Happy with the fast result;
  - learning to request it more
- From lab staff
  - Prefer it to previous tests we used
  - Easy to incorporate it into the work flow
- From TB Control
  - Extra benefit: began to discuss specific cases at monthly meetings between lab and TB Control
  - Lab has been invited to clinical reviews with nurses
    - Hear impact on treatment
    - How NAAT helps case management

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