COMPUTER AIDED DETECTION OF PULMONARY TUBERCULOSIS ON DIGITAL CHEST RADIOGRAPHS: A SYSTEMATIC REVIEW

TRIPTI PANDE
ADVANCED TB DIAGNOSTICS COURSE
MC GILL SUMMER INSTITUTE OF INFECTIOUS DISEASES AND GLOBAL HEALTH
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OUTLINE

- Chest radiography vs Computer aided-detection
- Study objectives
- Methods
- Results
- Analysis
- Final remarks
- Future work
## Chest Radiography

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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</thead>
<tbody>
<tr>
<td>Highly sensitive</td>
<td>High cost equipment</td>
</tr>
<tr>
<td>Moderately specific</td>
<td>Inter-professional variability</td>
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<tr>
<td>Useful screening tool</td>
<td>Intra-professional variability</td>
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</tbody>
</table>
COMPUTER AIDED DETECTION

- Definition:
  - Automated system which quantified various image characteristics of chest radiographs

- Functions of CAD:
  - Using DXR and software programs to detect radiographic abnormalities compatible with pulmonary TB
  - Can eliminate problems of delays in interpretation and poor inter-reader variability
PRIMARY AND SECONDARY OBJECTIVES

- **Primary objective:** assess the accuracy for detection of microbiologically confirmed pulmonary TB
- **Secondary objective:** comparing CAD diagnosis to that of clinical officers diagnosing pulmonary TB via chest radiographs
### INCLUSION AND EXCLUSION CRITERIA

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
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<tbody>
<tr>
<td>• Estimating diagnostic accuracy of CAD software</td>
<td>• CAD used for diagnostic modalities other than CXR</td>
</tr>
<tr>
<td>• Detecting pulmonary tuberculosis (PTB)</td>
<td>• Did not use microbiological reference standard</td>
</tr>
<tr>
<td>• Comparing to a microbiologic reference standard</td>
<td>• Studies involving children</td>
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</table>
SEARCH STRATEGY

Search limitations:
- No language restriction
- January 1st, 2010 - December 31st, 2015

Search terms:
- Validated by medical librarian
- Broad search terms used
RESULTS

Potentially relevant citations identified from electronic databases:
N = 455

Duplicates excluded:
N = 103

Unique, potentially relevant citations:
N = 352

Excluded based on review of titles and abstracts:
N = 347
- Diagnosing other infectious diseases or extrapulmonary TB via automated techniques n=51
- Using CAD to diagnose TB without a microbiologic reference: n=24
- Did not evaluate CAD, or evaluated CAD but not with CXR: n=9

Studies included in the systematic review:
N= 5

Pande, Cohen et al. 2016 (accepted)
DATA EXTRACTION

- Year of publication, geographic location
- Study design (retrospective, prospective)
- Inclusion/exclusion criteria
- Method of generating digital radiographs
- Name, version and method for scoring CAD
- Microbiologic reference
- Diagnostic accuracy; sensitivity, specificity, AUC
- Studies comparing to humans: number of human readers and their experience
- Quality assurance: QUADAS 2
## General Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Study design</th>
<th>Microbiologic reference standard</th>
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<tbody>
<tr>
<td>Maduska et al.</td>
<td>Zambia</td>
<td>Retrospective</td>
<td>Smear or culture</td>
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<tr>
<td>Muyoyeta et al.</td>
<td>Zambia</td>
<td>Prospective</td>
<td>Xpert MTB/RIF</td>
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<tr>
<td>Breuninger et al.</td>
<td>Tanzania</td>
<td>Retrospective</td>
<td>Positive culture result</td>
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<tr>
<td>Hogeweg et al.</td>
<td>England South Africa</td>
<td>Retrospective</td>
<td>Smear or culture</td>
</tr>
<tr>
<td>Philipsen et al.</td>
<td>South Africa</td>
<td>Prospective</td>
<td>Culture and clinical criteria</td>
</tr>
<tr>
<td>Year of study</td>
<td>CAD software, version</td>
<td>Country</td>
<td>Reference standard</td>
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</tr>
<tr>
<td>2011</td>
<td>CAD4TB, 1.08</td>
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<td>Smear &amp; Culture</td>
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<tr>
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<td>Culture &amp; Clinical</td>
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Pande, Cohen et al. 2016 (accepted)
ANALYSIS - CAD VS HUMAN INTERPRETATION

Older version (v. 1.07) performed similar to clinical officers

Newer version (v. 3.08) performed similar to expert radiologists

- CAD set to achieve same specificity as non-expert clinician → CAD achieved same sensitivity as other non-experts
- Threshold set to achieve same sensitivity as human readers → CAD achieved lower specificity than radiologist BUT greater than clinical officer
## Analysis - QUADAS-2

<table>
<thead>
<tr>
<th>STUDY AUTHORS</th>
<th>RISK OF BIAS</th>
<th></th>
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<th>APPLICABILITY CONCERNS</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Patient selection</td>
<td>Index test</td>
<td>Reference standard</td>
<td>Flow and timing</td>
<td>Patient selection</td>
<td>Index test</td>
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<tr>
<td>Maduskar et al.</td>
<td>U</td>
<td>L</td>
<td>L</td>
<td>U</td>
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<td>Breuninger et al.</td>
<td>H</td>
<td>L</td>
<td>H</td>
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*Legend: L = low, H= high, U= unclear*

Pande, Cohen et al. 2016 (accepted)
**FINAL REMARKS**

- Important point to remember: evidence base to support the use of CAD is quite limited ($n=5$)

- High sensitivity threshold $\rightarrow$ substantial fall in specificity (vice versa)

- CAD software achieving high sensitivity and specificity would be a major leap for this technology

- Our systematic review mainly highlights:
  - Uncertainty in the nascent evidence base
  - Help guide the direction for future evaluative studies for CAD4TB
  - Accepted for publication in IJ TLD (May 2016)
FUTURE WORK

- **Study design:**
  - Minimize risk of bias using prospective designs
  - Pre-specified threshold scores
  - Microbiologically defined case definitions

- **Generalizability:**
  - Diverse settings and populations
WHO-CAD REVIEW

- Including unpublished studies to increase the study database
- Revised data extraction form
- Performing a meta-analysis as well
ACKNOWLEDGMENTS

- Co-researcher:
  - Chad Cohen

- McGill University:
  - Dr. Faiz Ahmad Khan
  - Dr. Madhukar Pai
  - Naz Torabi (medical librarian)

- FIND:
  - Dr. Claudia Denkinger
THANK YOU!

QUESTIONS?