World Health Organization

END TB

Chest radiography in tuberculosis detection: Summary of current WHO recommendations and guidance on programmatic approaches

GLOBAL TB PROGRAMME

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Background

- For a long time, chest radiography (CXR) for TB detection was placed in the end of diagnostic algorithms because:
  - ➢ Focus was on highly infectious TB (chronic productive cough, smear positive) – "CXR not needed"
  - ➢ Resource constraints (equipment, radiologists, quality assurance)
  - ➢ Large intra- and inter-reader disagreement – low reliability
  - ➢ Low specificity - high risk for over-diagnosis, especially if bacteriological testing is neglected
- However, CXR has always been an important screening and diagnostic tool in clinical settings and prominent part of public health strategies in low-burden countries

But things have changed

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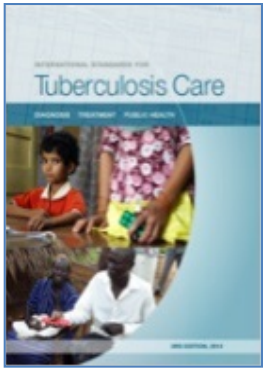
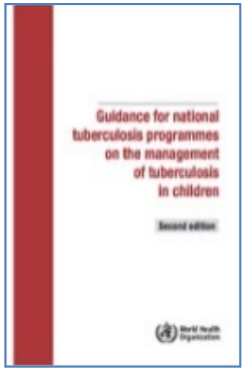
Chest radiography for tuberculosis screening is back on the agenda

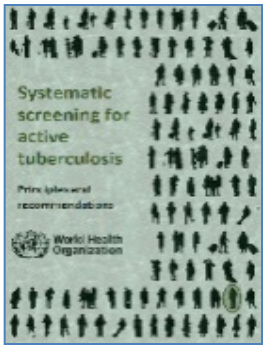
- Higher ambition level for early and complete TB detection, of all forms
- Systematic screening in high risk groups is on the agenda for high burden countries too – rapid and sensitive screening tool needed
- Prevalence surveys: CXR much higher sensitivity than symptom screening
- Rapid, highly sensitive molecular test improves possibility to rule out TB in persons with CXR abnormalities – less risk of false positive clinical diagnosis
- Scale-up of latent TB management – need to rule out active TB
- General imaging services including X-ray availability has increased
- Advances in digital technology: better quality, lower running costs, better storage, opportunities for telemedicine, computer aided reading (CAD4TB)

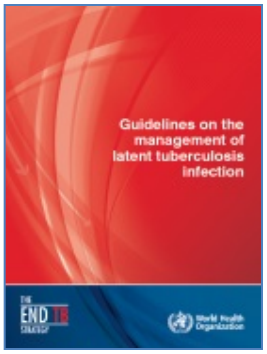


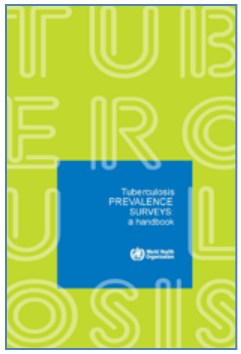
CXR in recent guidelines



- The International Standards of Tuberculosis Care (ISTC)
- Guideline on systematic screening for active tuberculosis
- Guidelines on management of latent tuberculosis infection
- Guideline on childhood tuberculosis
- Implementation manual on Xpert MTB/RIF
- Guidelines on tuberculosis prevalence surveys

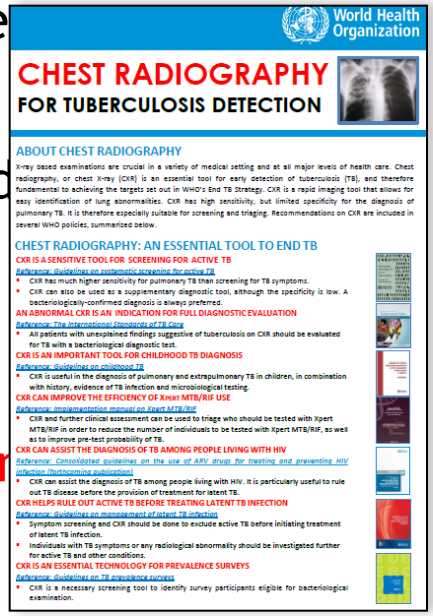






What the guidelines say about CXR

- Important triaging tool for pulmonary conditions including TB
- Useful to decide who should be tested with Gene Xpert MTB/RIF
- Most sensitive TB screening tool and therefore recommended as the first screening test in prevalence surveys
- Optimal first screening tool for screening in high risk groups.
- Recommended tool to rule out TB before initiating LTBI treatment (in well-resourced countries with TB incidence <100/100 000)
- Useful diagnostic tool for non-bacteriologically confirmed for example in PLHIV and children.
- But, still problem with specificity and reliability
- And recommendations have not been consolidated into or document



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CHEST RADIOGRAPHY
FOR TUBERCULOSIS DETECTION

ABOUT CHEST RADIOGRAPHY

X-ray based examinations are crucial in a variety of medical setting and at all major levels of health care. Chest radiography, or chest X-ray (CXR) is an essential tool for early detection of tuberculosis (TB), and therefore fundamental to achieving the targets set out in WHO's End TB Strategy. CXR is a rapid imaging tool that allows for easy identification of lung abnormalities. CXR has high sensitivity, but limited specificity for the diagnosis of pulmonary TB. It is therefore especially suitable for screening and triaging. Recommendations on CXR are included in several WHO policies, summarized below.

CHEST RADIOGRAPHY: AN ESSENTIAL TOOL TO END TB

CXR IS A SENSITIVE TOOL FOR SCREENING FOR ACTIVE TB

Reference: Guidelines on systematic screening for active TB

- CXR has much higher sensitivity for pulmonary TB than screening for TB symptoms.
- CXR can also be used as a supplementary diagnostic tool, although the specificity is low. A bacteriologically-confirmed diagnosis is always preferred.

AN ABNORMAL CXR IS AN INDICATION FOR FULL DIAGNOSTIC EVALUATION

Reference: The International Standards of TB Care

- All patients with unexplained findings suggestive of tuberculosis on CXR should be evaluated for TB with a bacteriological diagnostic test.

CXR IS AN IMPORTANT TOOL FOR CHILDHOOD TB DIAGNOSIS

Reference: Guidelines on childhood TB

- CXR is useful in the diagnosis of pulmonary and extrapulmonary TB in children, in combination with history, evidence of TB infection and microbiological testing.

CXR CAN IMPROVE THE EFFICIENCY OF XPERT MTB/RIF USE

Reference: Implementation manual on Xpert MTB/Rif

- CXR and further clinical assessment can be used to triage who should be tested with Xpert MTB/RIF in order to reduce the number of individuals to be tested with Xpert MTB/RIF, as well as to improve pre-test probability of TB.

CXR CAN ASSIST THE DIAGNOSIS OF TB AMONG PEOPLE LIVING WITH HIV

Reference: Consolidated guidelines on the use of ARV drugs for treating and preventing HIV infection [forthcoming publication]

- CXR can assist the diagnosis of TB among people living with HIV. It is particularly useful to rule out TB disease before the provision of treatment for latent TB.

CXR HELPS RULE OUT ACTIVE TB BEFORE TREATING LATENT TB INFECTION

Reference: Guidelines on management of latent TB infection

- Symptom screening and CXR should be done to exclude active TB before initiating treatment of latent TB infection.
- Individuals with TB symptoms or any radiological abnormality should be investigated further for active TB and other conditions.

CXR IS AN ESSENTIAL TECHNOLOGY FOR PREVALENCE SURVEYS

Reference: Guidelines on TB prevalence surveys

- CXR is a necessary screening tool to identify survey participants eligible for bacteriological examination.

Thus the summary WHO document: "Chest radiography in tuberculosis detection”

I. Introduction

II. Chest radiography as a triage tool

III. Chest radiography as a diagnostic aid

IV. Chest radiography as a screening tool

V. Technical specification, quality assurance and safety

VI. Strategic planning for use of chest radiography in national tuberculosis programmes

What WHO guidelines don't specify

- Technical specifications, safety, and technical assistance needs specifically for TB, except for prevalence surveys (should be included in generic guidance on radiography)
- Precision on place of CXR in screening and diagnostic algorithms (options only)
- How to use of CXR for clinical diagnosis of pulmonary TB (except the "old smear negative algorithm" and CXR for diagnosis in children).

Document development process

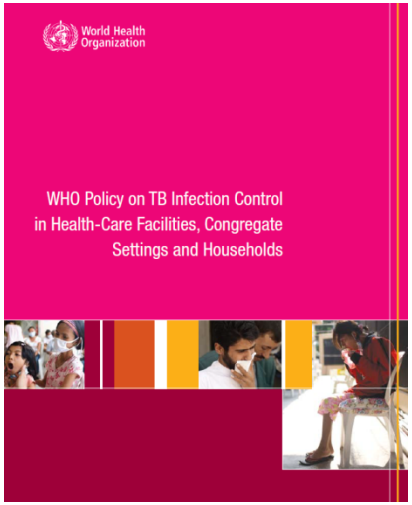
- Advisory group established February 2016
- Review of WHO documents and development of first draft of consolidated guidance on strategic and programmatic use of CXR, April-July 2016
- Presentation to STAG-TB of the plan for developing the document and CAD scoping
- Peer review, August-September 2016 (All invited to the meeting, plus selected others)
- Extended CAD review, March-August 2016
- Meeting 28-29 September 2016 :
  - Finalise guidance on strategic and programmatic use of CXR
  - CAD scoping to decided if a formal guideline process should start
- Revision and finalisation, November 2016

Triage

- Our working definition of triage:

  For the purpose of this document, triaging is defined as <u>the processes of deciding the diagnostic and care pathways for people seeking health care, based on symptoms, signs, risk markers and test results</u>. Triaging involves the assessment of the likelihood of various differential diagnoses as a basis for clinical decision-making. It can follow more or less <u>standardized protocols and algorithms</u> and may be done in multiple steps.

  (Effective triaging that helps identify TB rapidly is important both for optimizing care for the individual and for ensuring good infection control (WHO 2009).)



CXR for triaging for TB

- Proper triage among people seeking care with respiratory symptoms is essential for early and correct TB diagnosis
- Respiratory symptoms are both common and non-specific; even in TB-endemic areas most people seeking care with respiratory symptoms will not have TB

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CXR for triaging for PTB

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✓ Beyond active TB, CXR identifies those with fibrotic lesions, a population at high risk to develop active disease in the future

✓ CXR can help identify other pulmonary conditions that require further evaluation, making it a useful general triage test

CXR Triage to optimize microscopy

- Traditionally, prolonged cough has been the triage criterion for who should undergo bacteriological testing for TB

CXR Triage to optimize microscopy

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- CXR as an additional triage test can reduce the number of patients who undergo bacteriological testing

  – But case detection will still be limited by low sensitivity of cough as the initial triage test

CXR Triage to optimize microscopy (cont.)

- More complete TB detection requires broadening the criteria for who should undergo bacteriological testing, i.e. to all people with any TB-compatible symptom

  - However this can lead to high laboratory workload and more false-positive test results

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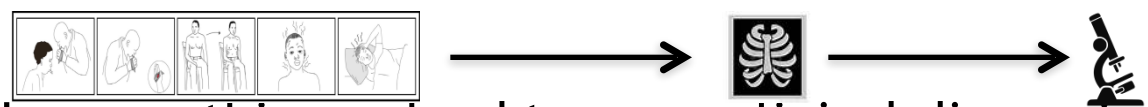
- CXR as an additional triage test to a broader initial test can lead to a high total yield with fewer bacteriological exams overall and fewer false-positive test results



  - However this can lead to more clinical diagnosis of TB, since smear has low negative predictive value

CXR Triage to optimize microscopy (cont.)

- In hyper-endemic settings, CXR can be used as the initial triage test for all (regardless of symptoms), though it can increase resource demands considerably

- Equivalent to "systematic TB screening in health facilities"
  - However CXR before smear microscopy is still problematic and may lead to clinical diagnosis

CXR Triage to optimize Xpert MTB/RIF

- Replacing smear microscopy with a more sensitive bacteriological test such as Xpert MTB/RIF after cough triaging will increase the yield of bacteriologically confirmed TB, but is considerably more expensive

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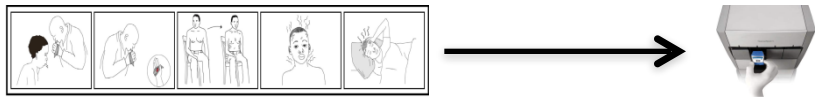
- Adding CXR as a second triage after cough will reduce the number of people to undergo Xpert testing, thereby reducing costs, without significantly reducing the number of TB cases detected

- CXR triage also increases the pre-test probability of TB among those tested with Xpert, reducing the number of false-positive test results
  - However, this approach will still be limited by low sensitivity of cough

CXR Triage to optimize Xpert MTB/RIF (cont.)

- In order for Xpert MTB/RIF to significantly increase case detection it needs to be used with a more sensitive initial triage test, such as all people with any TB-compatible symptom



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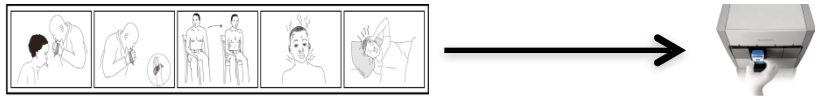


  - However, this approach is expensive and requires large Xpert throughput
- CXR as a second triage test after symptom triaging reduces the number of people to undergo Xpert testing without significantly reducing the number of TB cases detected, thereby reducing laboratory burden and costs

- As before, CXR triaging also increases the pre-test probability of TB among those tested with Xpert, reducing the number of false-positive test results

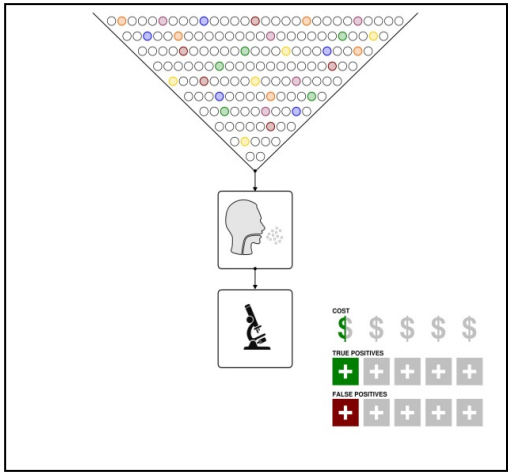
CXR Triage to optimize Xpert MTB/RIF (cont.)

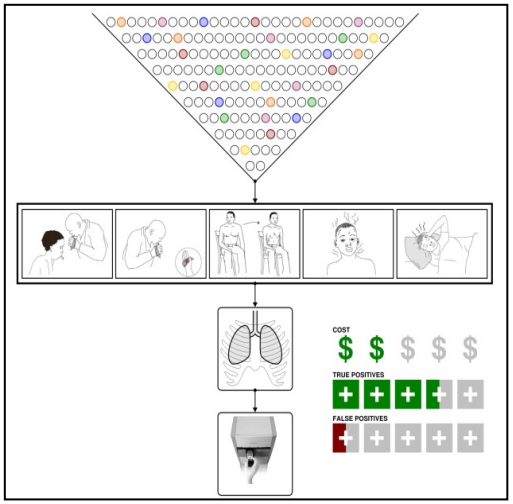
- The most sensitive triage algorithm is CXR followed by Xpert MTB/RIF

  - However this algorithm is expensive and results in more false-positive test results than triaging with symptoms and CXR

Comparison of yield of triage algorithms

Triage algorithms	TP	FP	FN	TN	Cost per case	NNS
1. Cough -> SSM	107	100	393	99400	143	935
2. Cough -> CXR -> SSM	105	25	395	99475	320	953
3. Any symptom -> SSM	235	637	265	98863	296	426
4. Any symptom -> CXR -> SSM	230	159	270	99341	795	435
5. CXR -> SSM	299	498	201	99002	1842	335
6. Cough -> Xpert	161	50	339	99450	575	622
7. Cough -> CXR -> Xpert	158	12	342	99488	347	633
8. Any symptom -> Xpert	354	318	146	99182	1562	283
9. Any symptom -> CXR -> Xpert	347	80	153	99420	887	289
10. CXR -> Xpert	451	249	49	99251	2065	222





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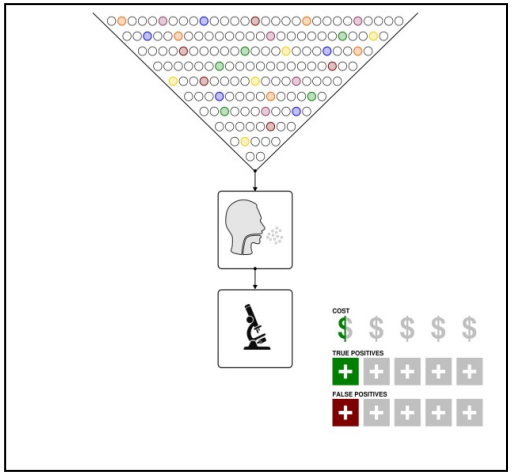

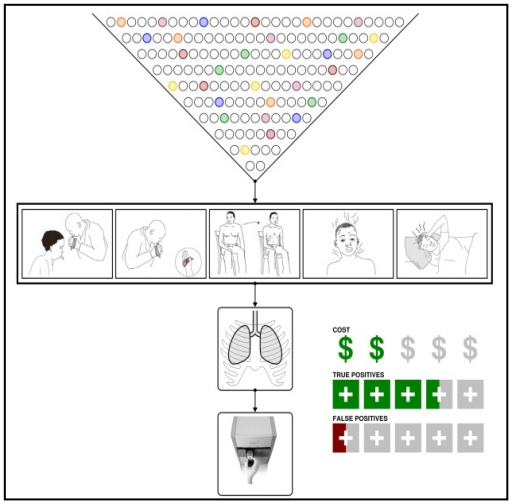

CXR in diagnosis for TB

- CXR alone cannot establish a diagnosis for TB – bacteriological confirmation must always be attempted
- In absence of bacteriological confirmation, sometimes clinical diagnosis is needed
- If patient is not critically ill, a wait-and-see approach can be used
- WHO has no specific guidance on use of CXR in clinical diagnosis
- Proportion of TB patients with non-confirmed TB is a possible indicator for quality control

CXR after a negative bacteriological test

- CXR has previously been recommended to be performed after a negative bacteriological test for diagnosis of non-confirmed TB

  - Rational if diagnosis of infectious TB is the primary priority, or if access to radiography is limited
  - However, can lead to delayed diagnosis and loss to follow up

- Improved access to sensitive and rapid tests such as Xpert MTB/RIF encourages the use of CXR early in triage algorithms

  - Risk of false-positive diagnoses from CXR is minimized (if Xpert results are correctly interpreted and acted upon)
  - Overall case detection is higher
  - Diagnostic delays reduced

CXR for screening for TB

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- **Low specificity of CXR** for TB screening (46-89%)
  - Means the test will also be abnormal in individuals with other lung abnormalities besides TB that also need to be followed up (e.g. cancer, pneumonia, emphysema) -> benefit to individual being screened
  - Also identifies individuals with inactive TB/fibrotic lesions, who are at high risk of developing active TB in future and require follow-up
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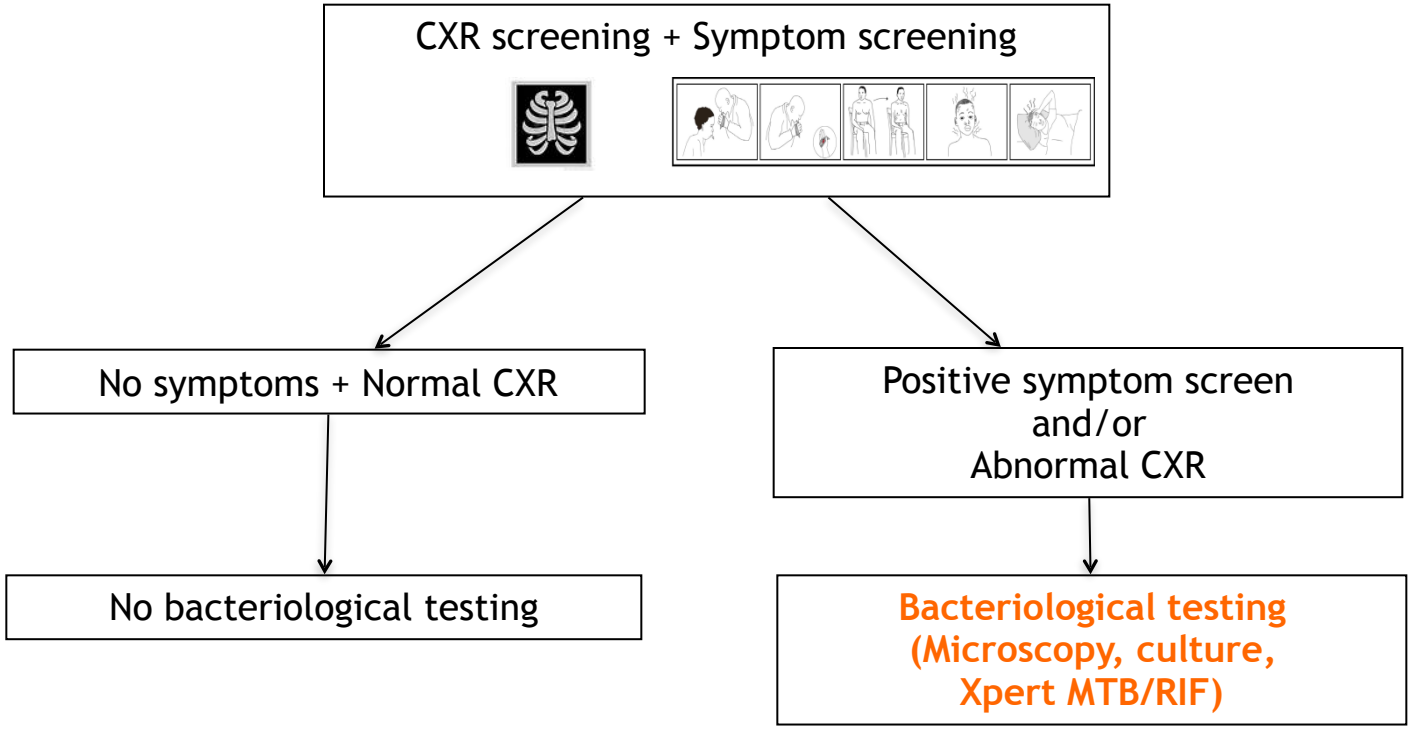
  - However, means it needs to be coupled with a bacteriological test with high sensivitiy and specificty for diagnosis
- While the preferred screening tool based on test accuracy, can be expensive and logistically challenging to use, especially in ACF (outside of health facility)

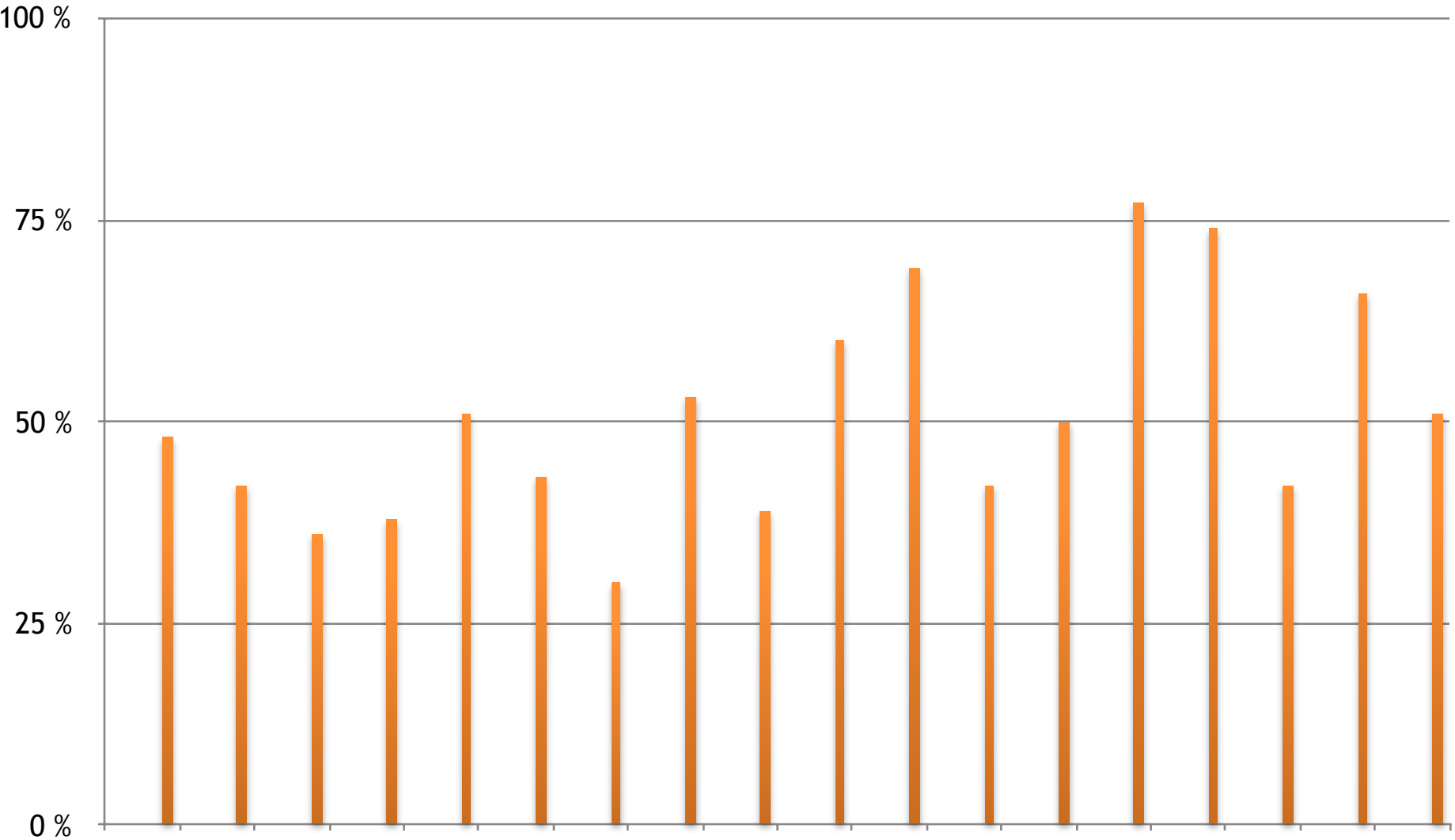
CXR use in prevalence surveys

- Specific context of PTB screening in which individuals sampled from entire population are screened
- Low relative prevalence requires high sensitivity in screening approach

  ➡ CXR in combination with symptom screen to identify individuals to undergo bacteriological exam offers the most sensitive screening tool



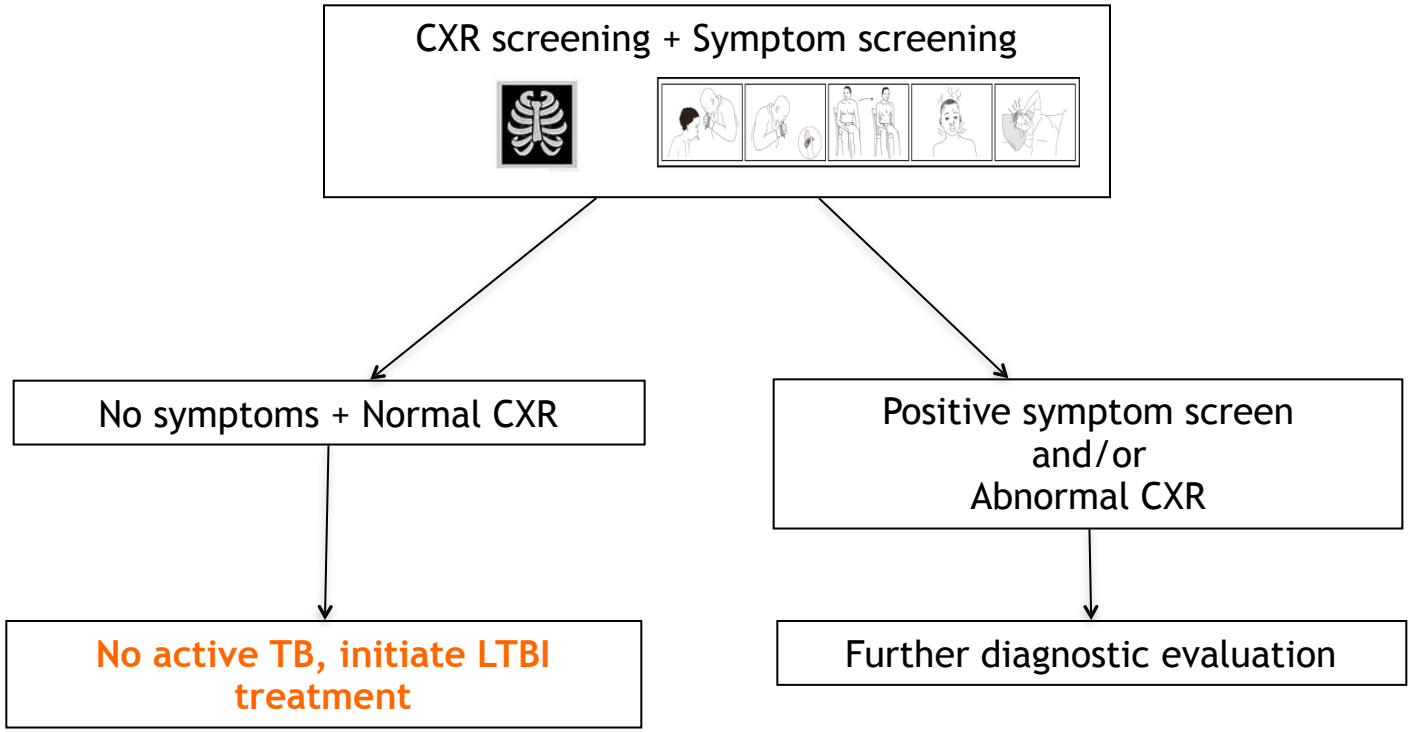
Large % of TB symptom-negative, CXR-positive in recent prevalence surveys



CXR to rule out TB for LTBI treatment

- LTBI guidelines state that CXR should be used in combination with symptom screening to rule out active TB before initiating treatment for LTBI

  ➡ The combination of any abnormality in CXR + any TB suggestive symptoms offers the highest sensitivity and negative predictive value to rule out TB



Next steps for CXR guidance from WHO

- CXR guidance summary document and factsheet will be published in next few weeks (November 2016), with newsflash
- WHO is further assessing the need for additional guidelines on CXR
- Would be integrated with guidelines on laboratory tests in order to provide advice on the entire diagnostic pathway