

# Gold Standards for Microscopy Studies: Pros and Cons

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# Options for Gold Standards

- Culture-based gold standards
- Microscopy-based gold standards
  - Composite microscopy results (“Any test positive”)
  - Blinded re-checking by expert reader
- ? Automated NAAT (GeneXpert)

# Culture-based reference standards

- Pros
  - Independent gold standard
  - Highly specific
  - Higher sensitivity than any other TB test
- Cons
  - Imperfect sensitivity
  - High infrastructure requirements
  - Unsatisfactory results if QA inadequate
    - Over decontamination → false negatives
    - Contamination → false positives

**Culture is best reference standard but is not always feasible**

# “Any Test Positive”

		Method Y	
		Positive	Negative
Method X	Positive	25	5
	Negative	30	40

## “Sensitivity”

- Method X:  $30/60 = 0.50$
- Method Y:  $55/60 = 0.92$

- Pros
  - Simple to do
- Cons
  - Assumes all positives are true positives
  - True accuracy of each technique unknown

# “Blinded Re-checking”

		Experienced Reader				Experienced Reader	
		Positive	Negative			Positive	Negative
Method X	Positive	25	5	Method Y	Positive	30	20
	Negative	10	60		Negative	5	45

	“Sensitivity”	“Specificity”
Method X	$25/35 = 0.71$	$60/65 = 0.92$
Method Y	$55/60 = 0.86$	$45/65 = 0.69$

- Pros
  - Relatively simple/inexpensive
  - Accounts for potential false positives
- Cons
  - Requires an experienced reader
  - Requires slide storage, transport and re-staining
  - True accuracy of each technique unknown

# Automated NAAT

- Pros
  - Identifies virtually all smear-positive cases
  - Highly specific
  - Minimal infrastructure requirements
  - Less concern with specimen transport than for culture
- Cons
  - High cost
  - Imperfect sensitivity
  - True accuracy of each technique unknown

# Summary

- Greater concern for false positive microscopy results at peripheral clinics, especially with fluorescence microscopy
- Gold standards other than culture can elucidate differences between microscopy methods
  - Both techniques performed on same patients
  - Both techniques performed by same or similar individual(s)
  - Results interpreted blindly
- Hierarchy of gold standards for comparison studies
  - Culture
  - ? Automated NAAT
  - Blinded re-checking by experienced reader
  - “Any smear-positive”