Digital imaging innovations

for *early* TB case detection

NDWG Annual Meeting 2012
UNION World Conference Kuala Lumpur

Prepared by CheckTB!
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November 13th, 2012

Contents

- Introduction
- Urgent need
- Digital innovations
- Active case finding
- Next steps

Introduction

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- ✓ **Private** consultancy organisation based in The Netherlands, Partner of Stop TB Partnership since 2008
- ✓ **Mission** enable access to Universal TB care by facilitating innovative case finding
- ✓ **Activities**
  - ✓ connecting stakeholders and innovators, designing & facilitating (mostly Dutch Government ORIO supported) project financing;
  - ✓ preparing grant applications for research such as CAD4TB

Stop TB Partnership

Introduction

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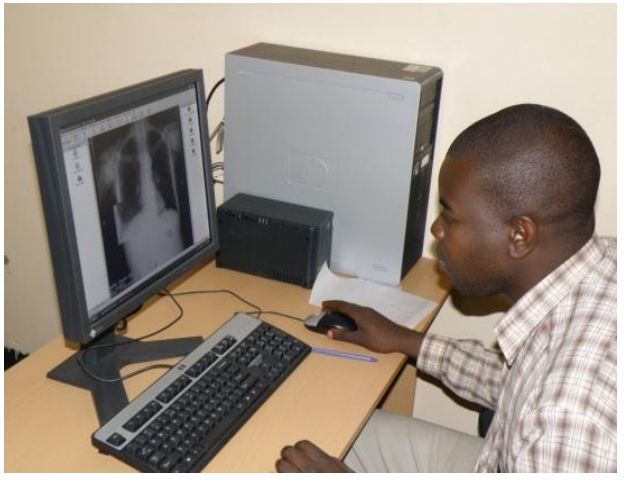
"Accelerating TB case detection in Ghana"

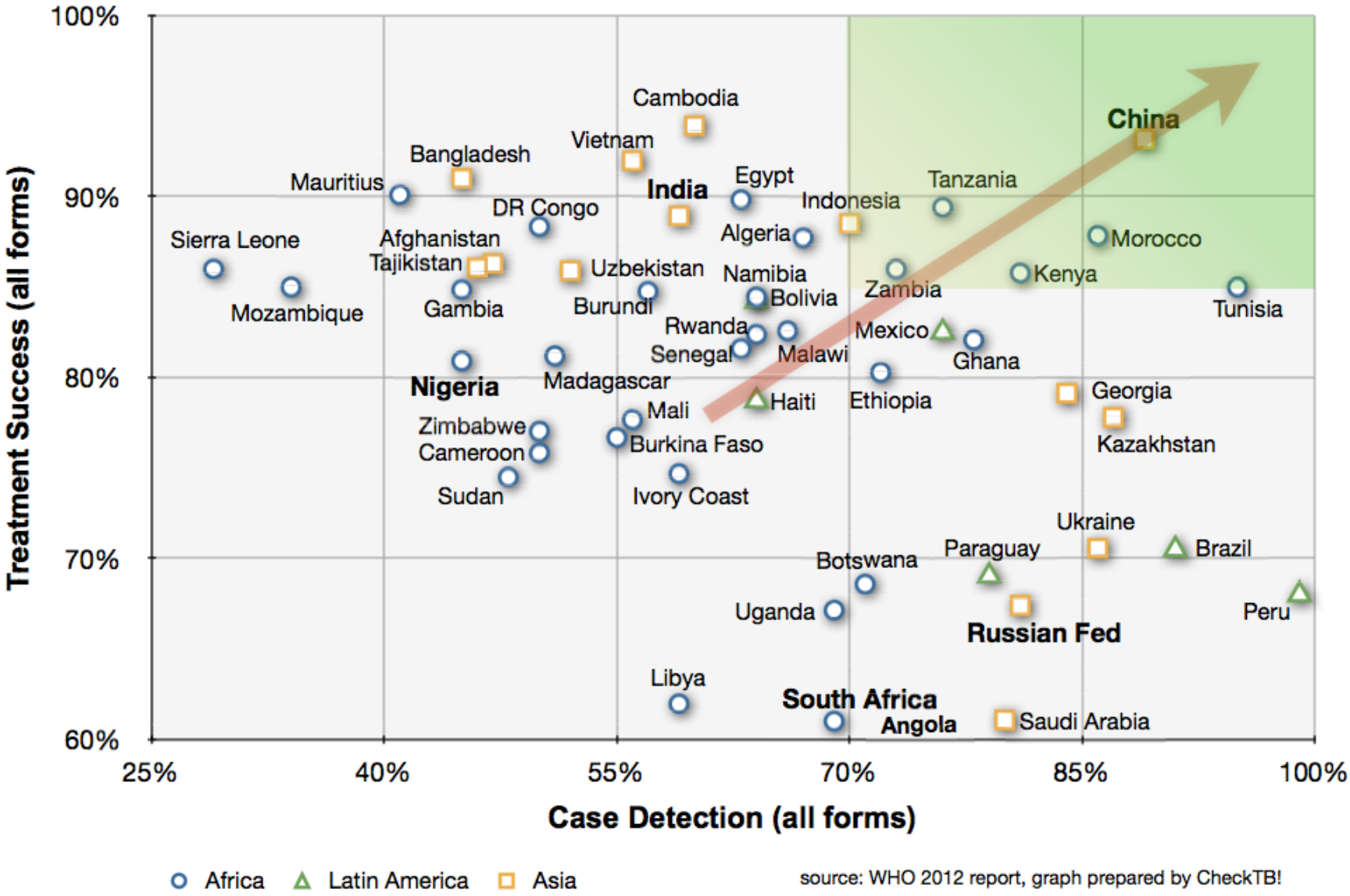
19 mln. Euro investment:

1. Digital X-ray network
2. FM, Xpert MTB/RIF
3. Capacity building
4. Advocacy
5. Operational Research



Urgent need

Further strengthen case detection



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Urgent need

Find more cases earlier

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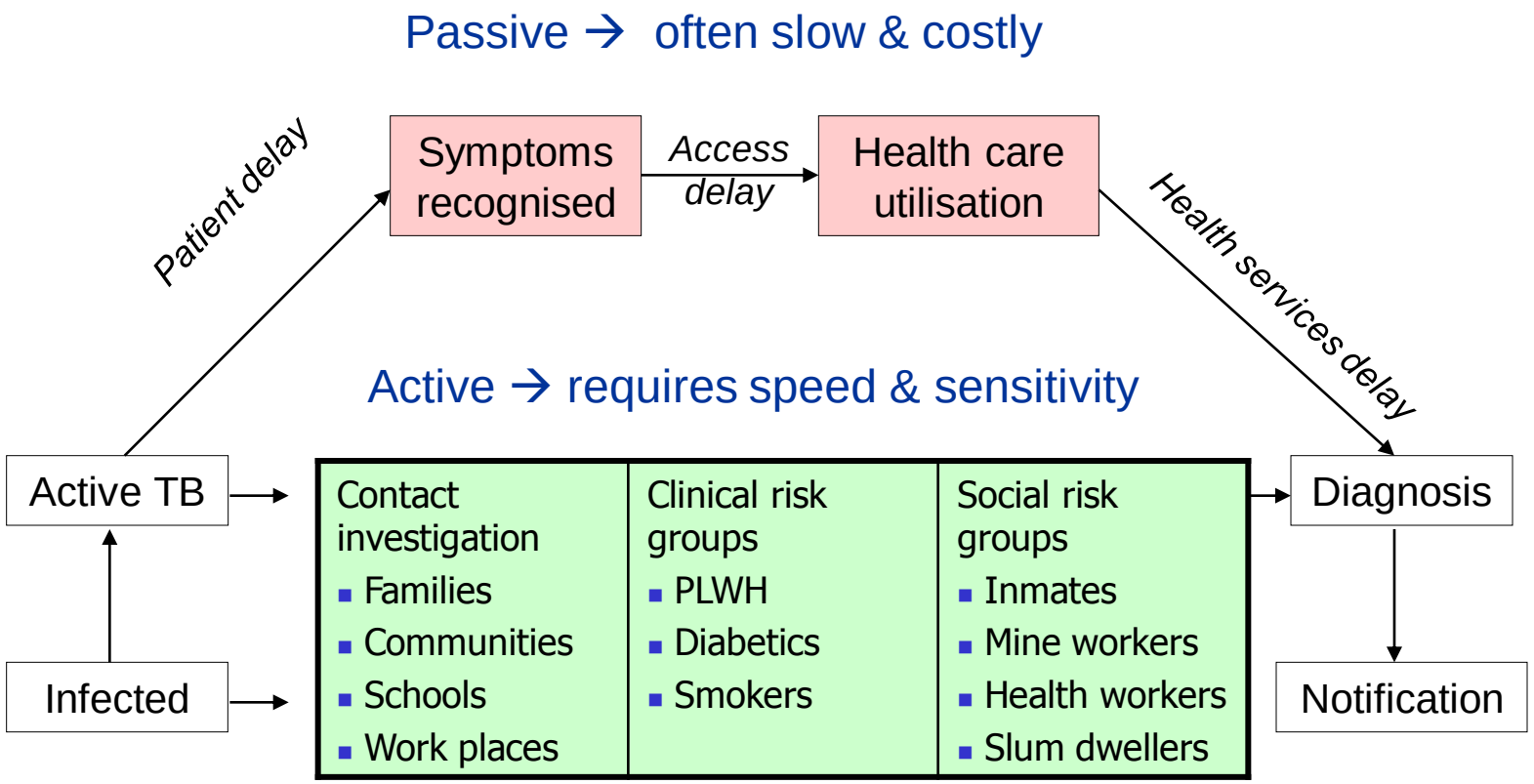

Recent prevalence surveys indicate that screening only on symptoms can miss 50% of the cases, what to do?

WHO DEWG October 2009

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Urgent need

Current diagnostics

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- Culture:
  - Reference standard, but slow, relies on good quality sputum, requires well equipped labs, scarce in high TB burden countries
- Smear microscopy:
  - cheap, low sensitivity (especially in HIV+ subjects) high specificity, relies on good quality sputum and staff motivation
- Xpert MTB/RIF:
  - sensitive and specific, costly when used for all subjects, relies on good quality sputum and constant power supply
- Chest radiography:
  - sensitive at reduced specificity, requires films, chemicals and expertise for accurate reading, too high cost for screening →
  - **Can digital innovations eliminate these CXR drawbacks?**

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Digital innovations

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Strenghts & weaknesses TB diagnostics

Diagnostic:	sensitivity	specificity	speed	low cost per test
Culture				
Smear Microscopy				
X-ray analogue				
Xpert MTB/RIF				
X-ray Direct Digital				

high medium low

Indicative scores on modalities' diagnostic accuracy, productivity and cost effectiveness can differ per population and/or per case finding strategy

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Digital innovations

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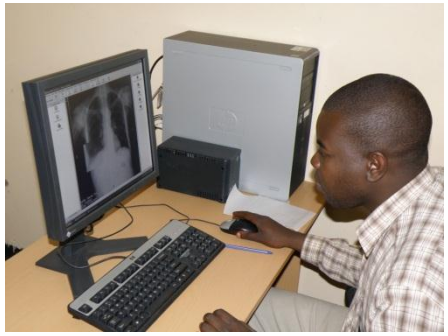
Chest X-ray: from hassle to opportunity

- Analogue
  - poor image readability of sometimes 50% of images*
  - high cost > € 3 per image due to films, chemicals & logistics
  - insufficient expert staff to interpret images on site
  - delay between X-ray exposure and image availability
  - Archiving & retrieval cumber-some, costly & inaccurate

- Direct digital
  - 98+% readability of quality images achieved
  - low cost € 0.30 – € 1.10 per image; no film nor chemicals
  - Computer Aided Detection and tele-diagnosis possible
  - immediately available; s/w tools to diagnose
  - easy storage and instant access to archived images



*) QA of Chest Radiography, Dr I. Onozaki, UNION World Conference 2008

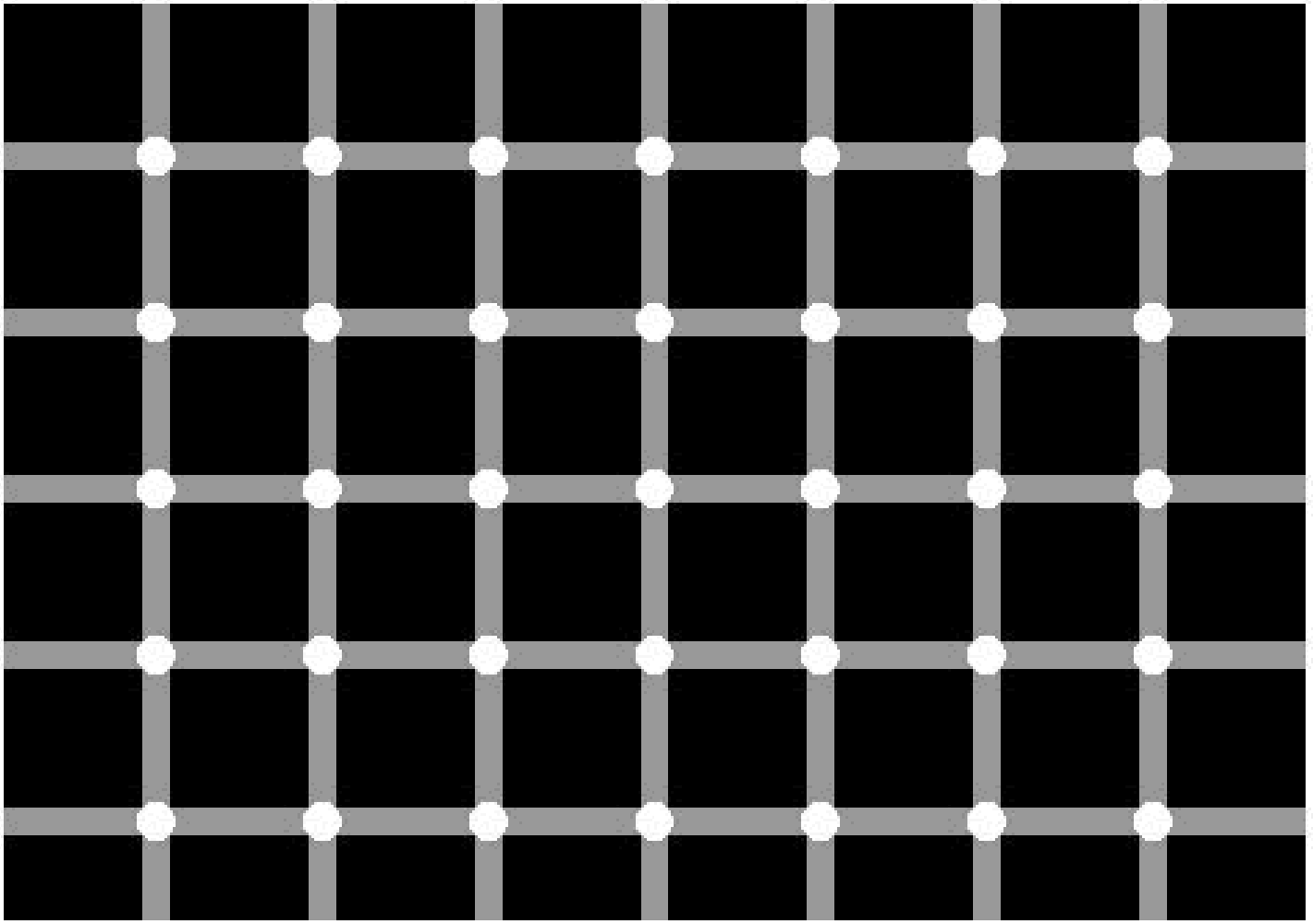
Computer Aided Detection

Why

Lesions in CXR are missed by human readers:

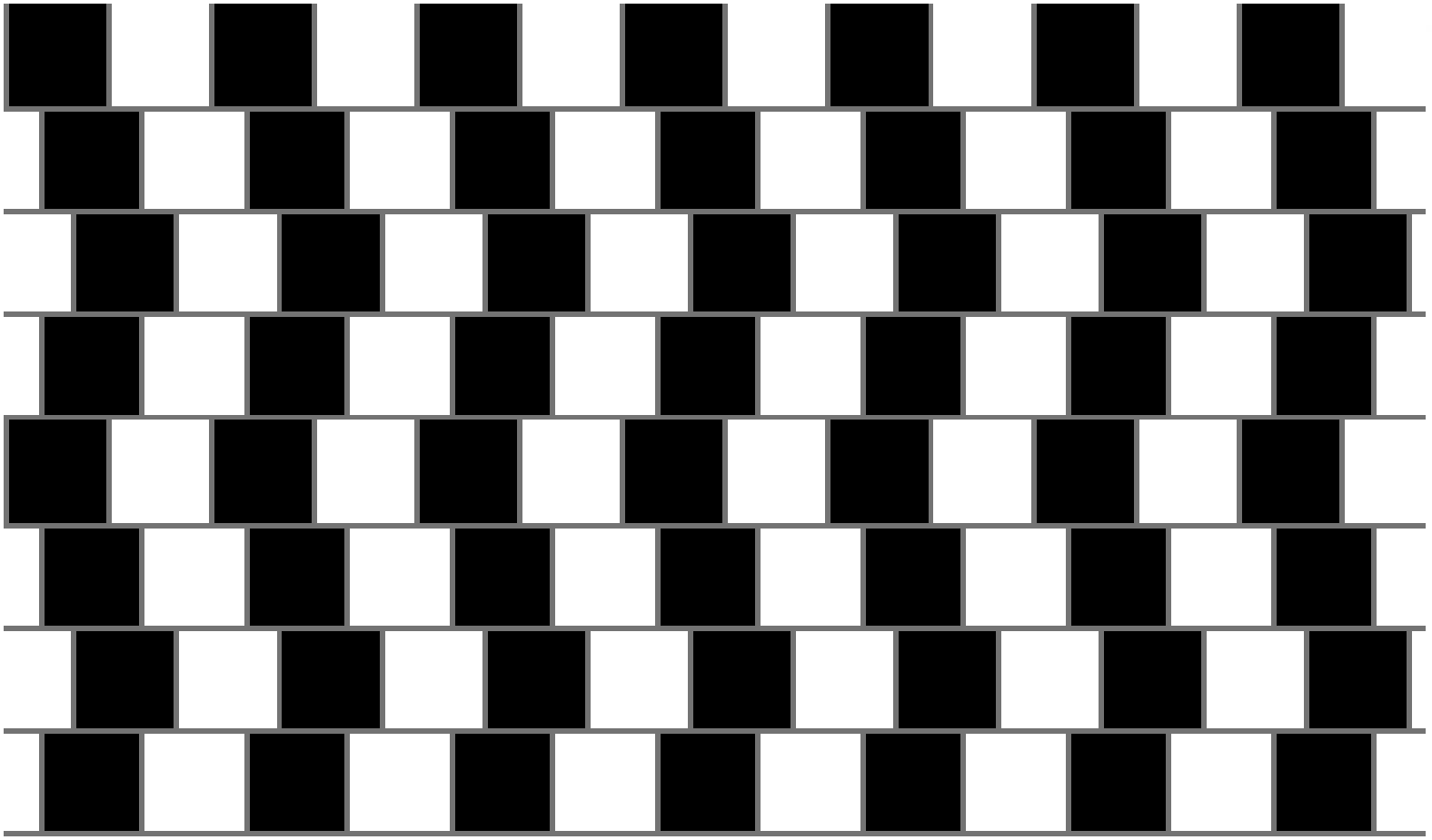
1. 90% of initially missed lesions were visible in retrospect
2. less than 50% of lesions < 1 cm are seen*
3. human readers do make errors in recognition, interpretation and perception……

*) Manning DJ et al, Br J Rad 2004; Muhm JR et al Radiology 1983



Count the black dots…

Do they keep moving?



All the gray lines above are perfectly parallel…

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Digital innovations

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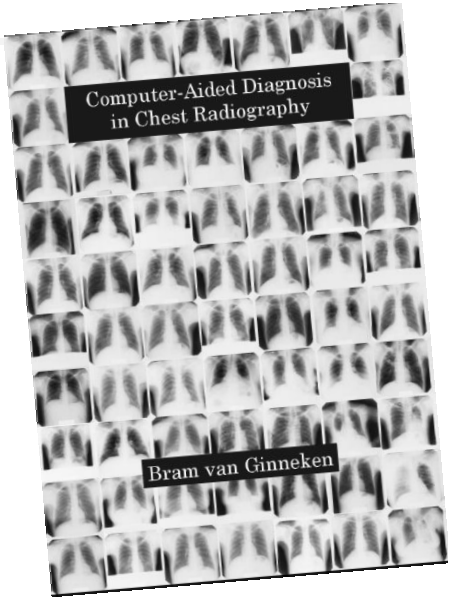
Computer Aided Detection for TB

- Using computers for medical image analysis to improve quality and efficiency of screening
- R&D started in 1996, by Bram van Ginneken and Delft Imaging Systems of The Netherlands
- > 2M Euro funding secured 1996 – 2014 with support from Dutch Government
- Based on proven CAD for mammography technology
- Collaborators: Lung Institute Cape Town & Zambart
- R&D ongoing at Diagnostic Image Analysis Group, Radboud University Nijmegen to optimize CAD4TB



Thesis Prof. Bram van Ginneken, 2001

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Digital innovations

CAD4TB objectives & use

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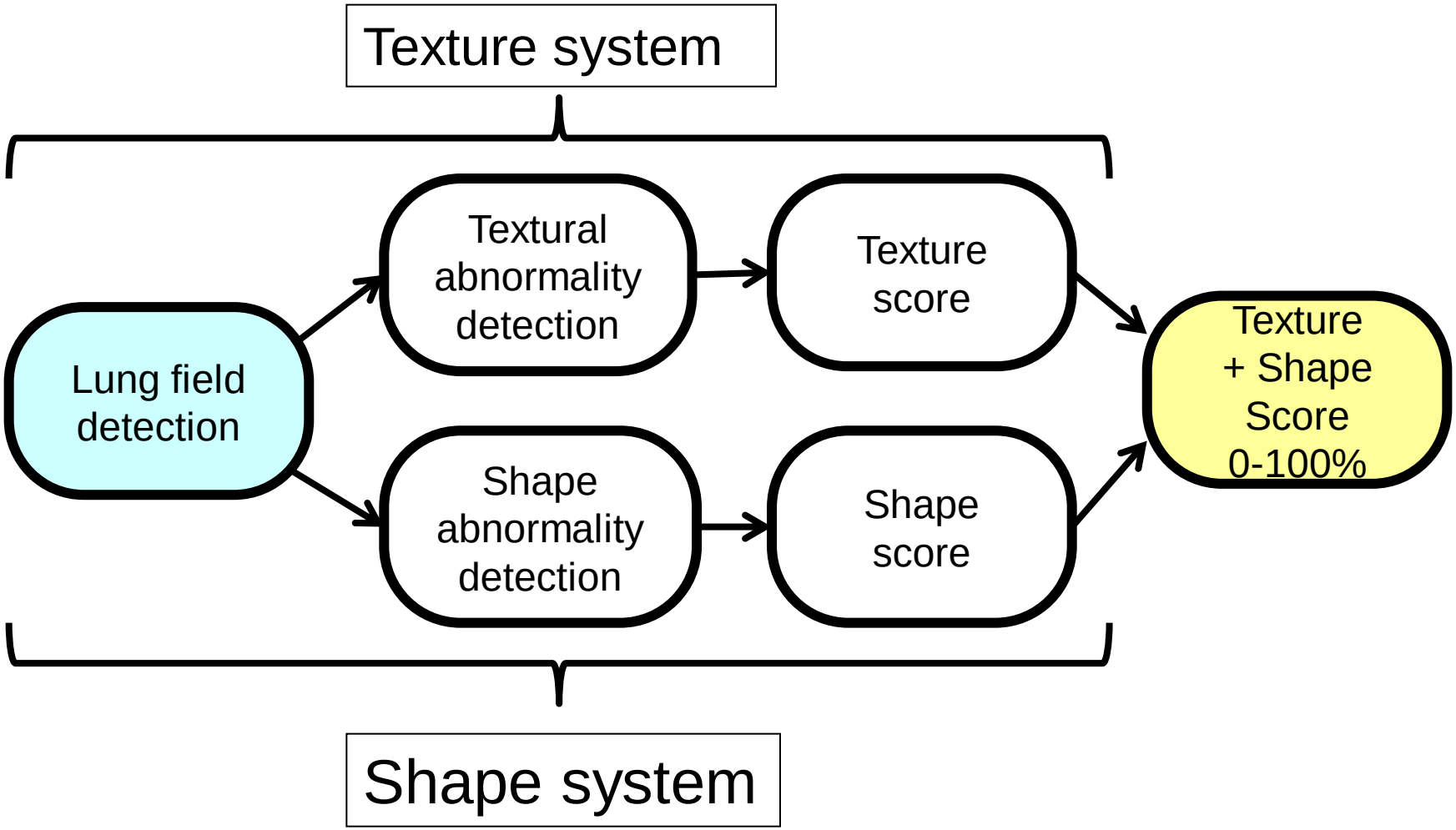
- Research objective: CAD4TB more accurate than best human reader
- First CAD4TB release April 2010; enhanced version September 2012
- Possibilities for use
  - classify normal vs. abnormal images
  - provide a probability (%) of abnormalities consistent with TB
  - marking suspect regions
  - automated abnormality reporting
  - present similar images for reference
- Digital CXR with CAD score can be sent over any mobile phone network for tele-radiology on complex cases in 40 seconds

Digital innovations

Simplified CAD4TB design



Hogeweg L et al, Med Image Comput Comput Assist Interv. 2010

CAD4TB added value

- Provide CAD score & report in 30 seconds at € 0,00 variable cost

- Finds lesions that the human readers missed
- Decreases inter-reader variability

- Supports less experienced readers
- Increases confidence in the presence of lesions

- Potential to detect pre-clinical TB
- Can support monitoring of treatment progress

  - However, human readers can dismiss correct CAD abnormals or can accept false CAD abnormals

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Digital innovations

CAD4TB score illustration

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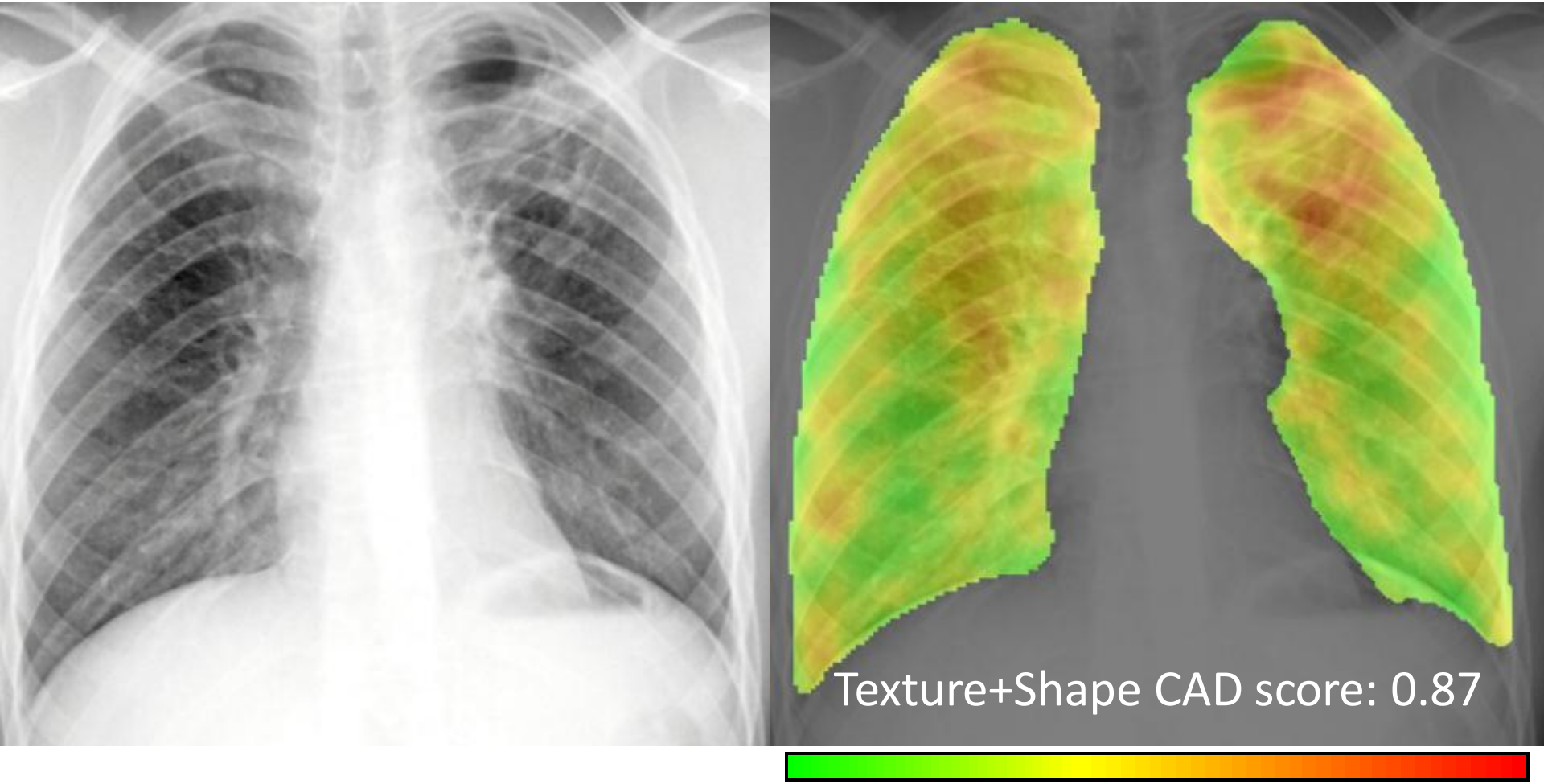

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Digital innovations

CAD4TB results 2011: Find & Treat London

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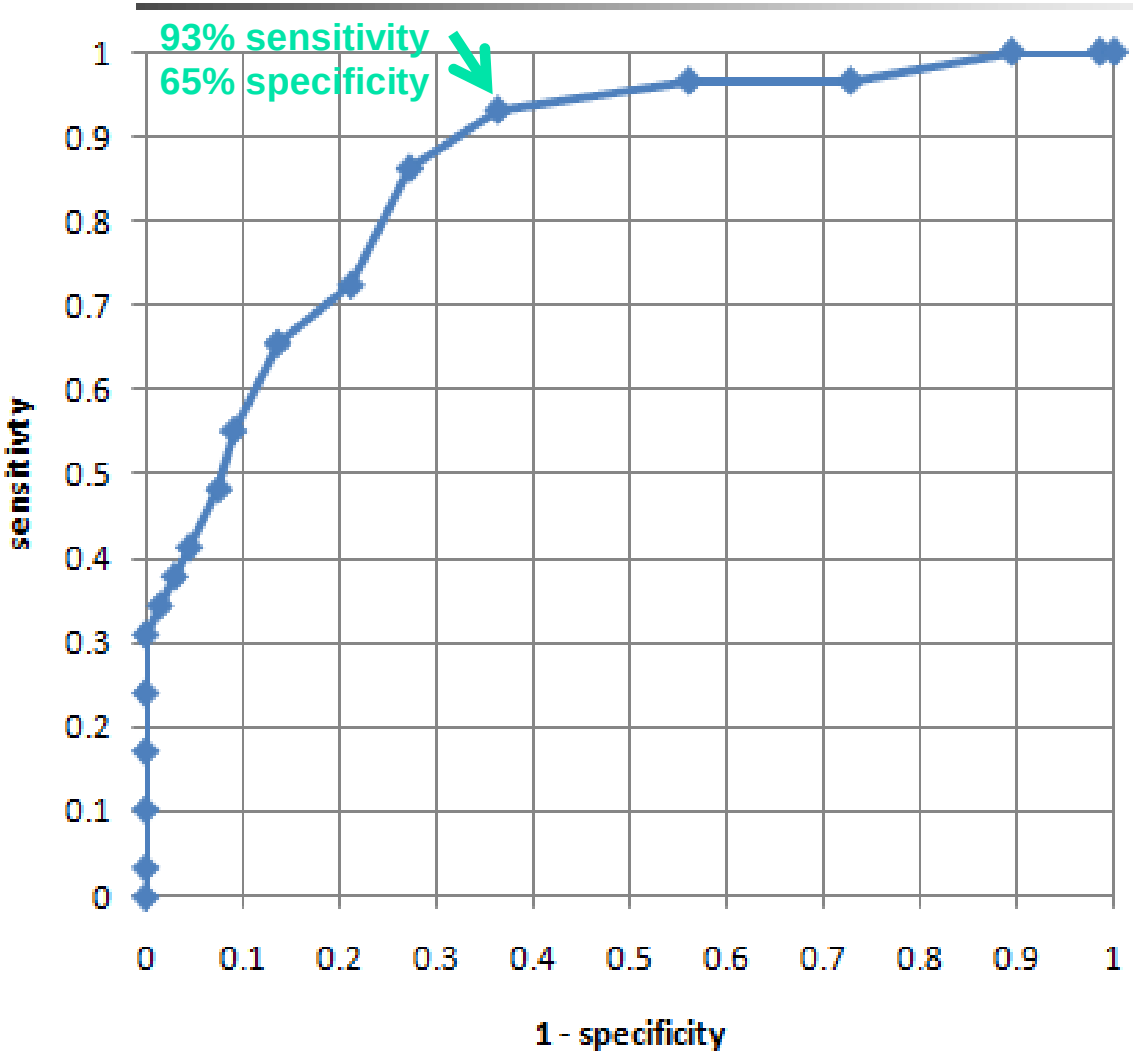
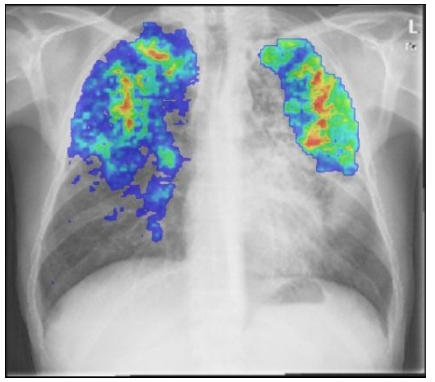


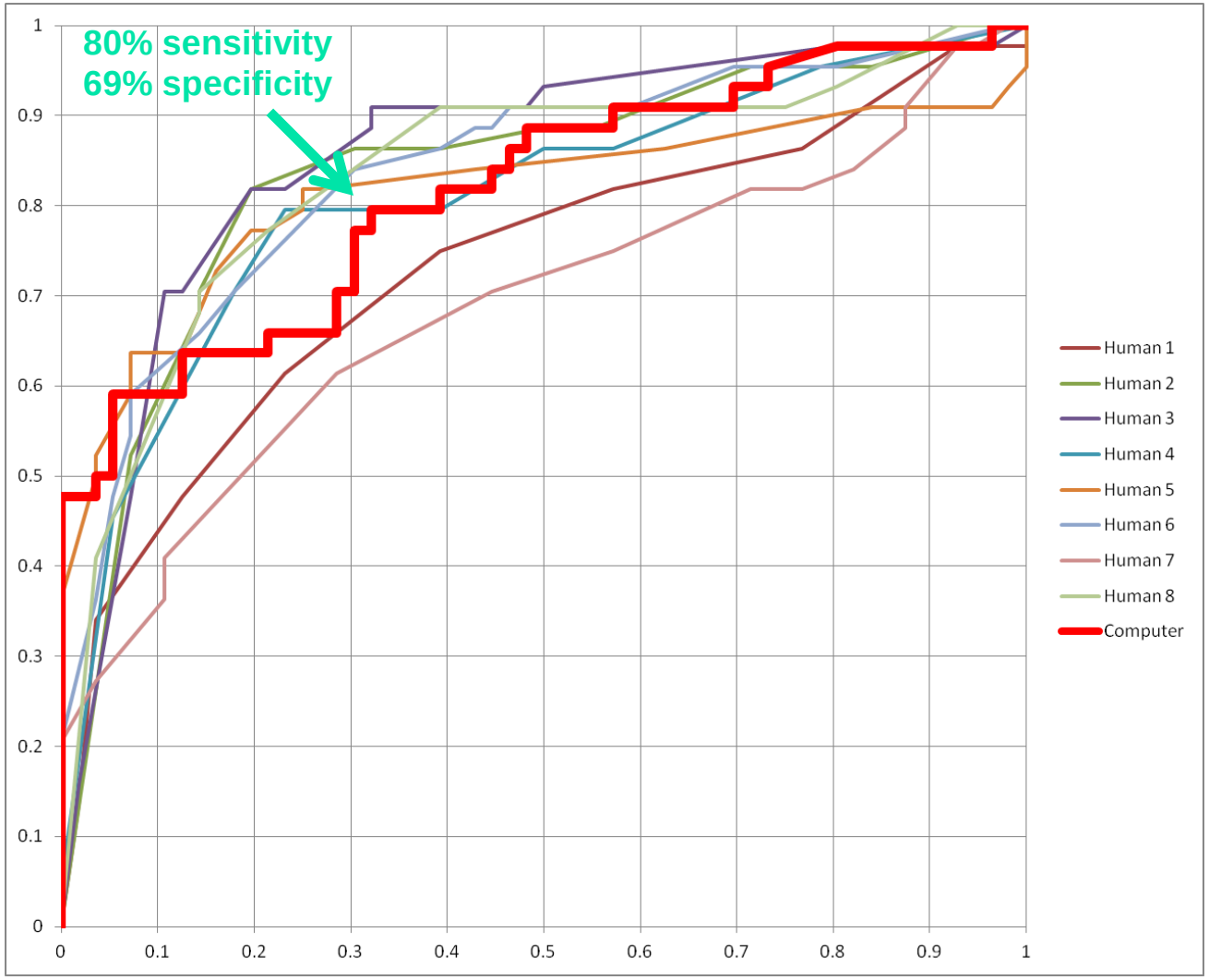


Test set: 95 images from 2009:
-67 consecutive non-TB
-28 TB proven

Hogeweg L et al, Annual Meeting of the Radiological Society of North America, 2011

Digital innovations

CAD4TB results 2012: data from 3 studies



Reference:
Culture Data from South Africa and Zambia (100 cases)

7 human readers with basic training, 1 CRRS certified observer

No significant difference between computer and human readers, except for observer 1 and 7 who are significantly worse than computer

van Ginneken B et al, Annual Meeting of the Radiological Society ofNorth America, 2012

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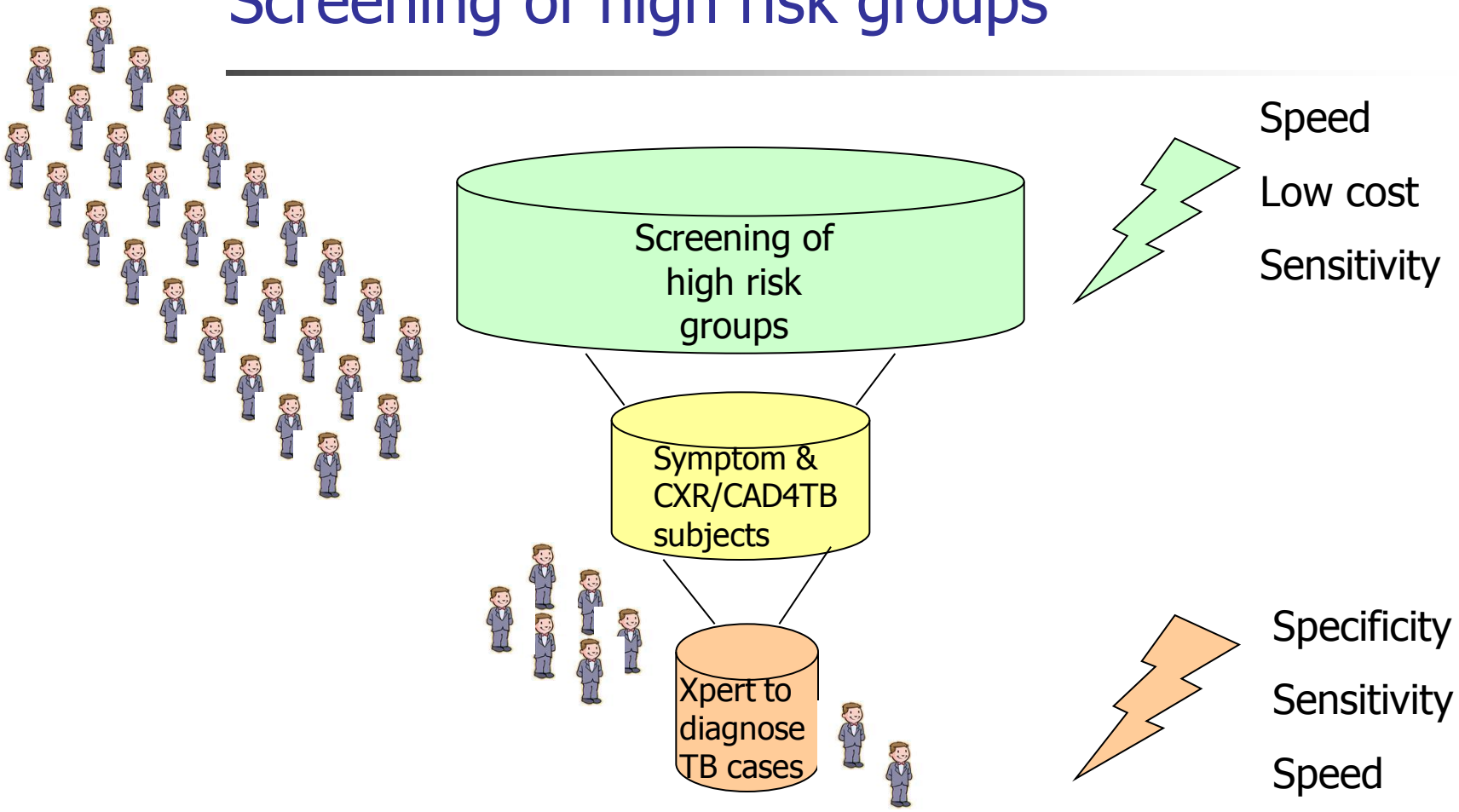
Active case finding

Screening of high risk groups



Can CAD bring higher diagnostic output at same input?

Active case finding

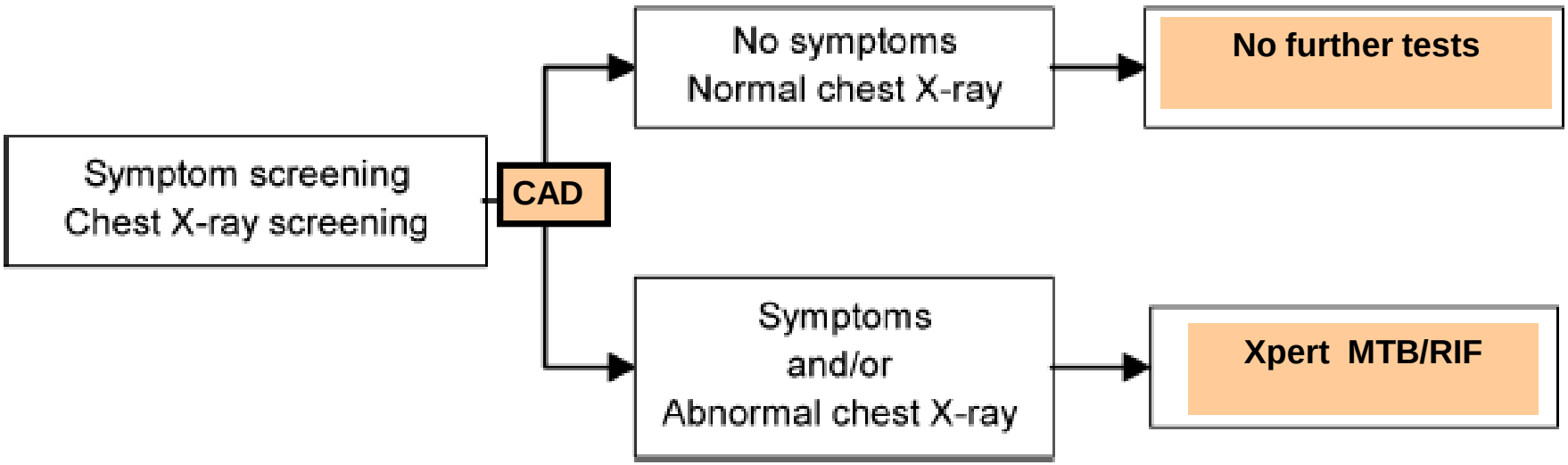
CAD4TB for risk group screening

- Active case finding in risks groups:
  - Large datasets need to be evaluated in short period
  - Human reader often not accurate enough in screening setting
  - Often too slow and costly if done by human readers only

- CAD requirement
  - Accurate standalone CAD with a sensitivity and specificity at least equal to the trained human reader
  - Immediate reading and score at minor variable cost
  - Ability to select threshold CAD score for Xpert eligibility

Active case finding

CAD4TB for risk group screening



TBREACH study ZAMBART, Zambia

- First prospective study of CAD4TB prototype used standalone to select subjects eligible for an Xpert test
- Findings indicate that:
  - CAD is sensitive for predicting TB detection by Xpert
  - CAD sensitivity increases with higher CAD score.
- Full results are being presented at the CDC late breaker session at Union World Conference by Dr. Monde Muyoyeta, ZAMBART.

Economics of screening - simulation

- At **www.checktb.com** under "Economics of screening" cost and yield simulations can be made online for:
  - **Strategy 1:**
    - Screening all risk group members on symptoms & CAD → only identified subjects to be tested on Xpert MTB/RIF
  - **Strategy 2:**
    - All risk group members tested directly on Xpert MTB/RIF

Economics of screening - simulation

- Assumptions summary

X-ray/CAD - Xpert MTB/RIF	
Prevalence in high risk group	5%
Capital investment digital X-ray/CAD	€ 179.000
Capital investment Xpert machine (4 cartridges)	€ 13,462
Cost per Xpert test (including 10% logistics cost)	€ 8,45
Depreciation period in years	8
Average # of screens per day	120
# of working days per year	250
Average # of tests per day per 4 cartridges unit	15
Efficiency rate of Xpert tests	0,90
Number of screens per year	30.000

Active case finding

Economics of screening – supply side

Strategy	CAD+Xpert	CAD+Xpert	Xpert only
Accuracy	**CAD high HIV+**	**CAD low HIV+**	**Xpert**
Sensitivity %	80	93	95
Specificity %	70	65	99
Expected results			
Risk pop. screened	30.000	30.000	30.000
Valid Xpert tests performed	9.750	11.370	30.000
CDR %	76	88,35	95
Cases detected per year	1.140	1.299	1.397
Cost €			
Total cost per year	€ 153.670	€ 169.861	€ 341.817
Cost per case detected	€ 135	€ 131	€ 245
Cases detected at fixed budget of € 170,000	**1.140**	**1.299**	**699**

Strategy "CAD + Xpert" has potential to detect up to 85% more cases per € 100,000 budget compared to "Xpert only"

Economics of screening – demand side

Assumptions CAD + Xpert for "one Stop TB" service

- 120 risk group members screened/day; suspect rate 30%
- Patient delay: → 1 hour transport
- Access delay: → 1 hour waiting time
- Services delay: 84 → 0,5 hours as no further tests
  36 → 4 hours including Xpert test

1. Average subject time to get screened or diagnosed:
   - (2,5 * 84) + (36 * 6 hours)/120 = 3,5 hours
2. Average time to start treatment: 6 hours with 1 visit only

Strategy "CAD + Xpert" has potential to decimate patient cost, time to diagnose as well as economic barriers to access care

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Next steps

Ongoing research CAD4TB

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- To increase CAD specificity
  - Remove artificial objects to reduce false alarms
  - Suppress normal anatomy to improve texture analysis
  - Measure cavities
  - Integrate clinical data (HIV status and CD4 count if available)
  - E-learning for users
- To better determine CAD impact on yield and cost
  - More research needed

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Next steps

Suppress ribs for texture analysis

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Conclusions

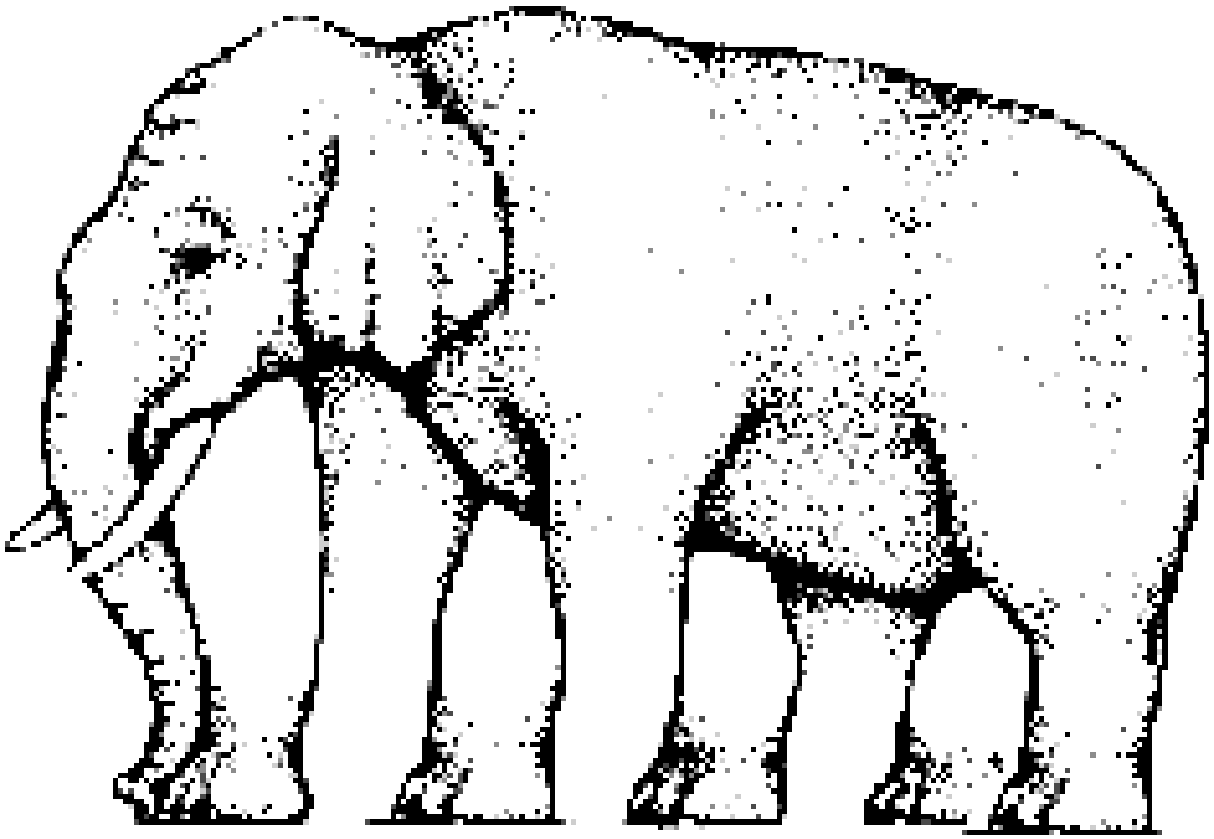
1. "The way forward in *Chest X-ray* is to use quality digital images for
   - immediate & distant reading
   - efficient storing & electronic interpretation with CAD".

2. "Increasing case detection will have to be through good screening (radiology) followed by a sensitive and specific test (Xpert)".

3. First results indicate that ***CAD4TB as triage for Xpert*** has the potential to make case finding ***faster and more cost effective for provider and patient → higher diagnostic output at same input***

Sources:
1. Dr. D. Enarson IUATLD World Conference, Paris October 18th 2008
2. Dr Leopold Blanc WHO in communication to CheckTB! Deceomber 2010

Quiz on human image interpretation!



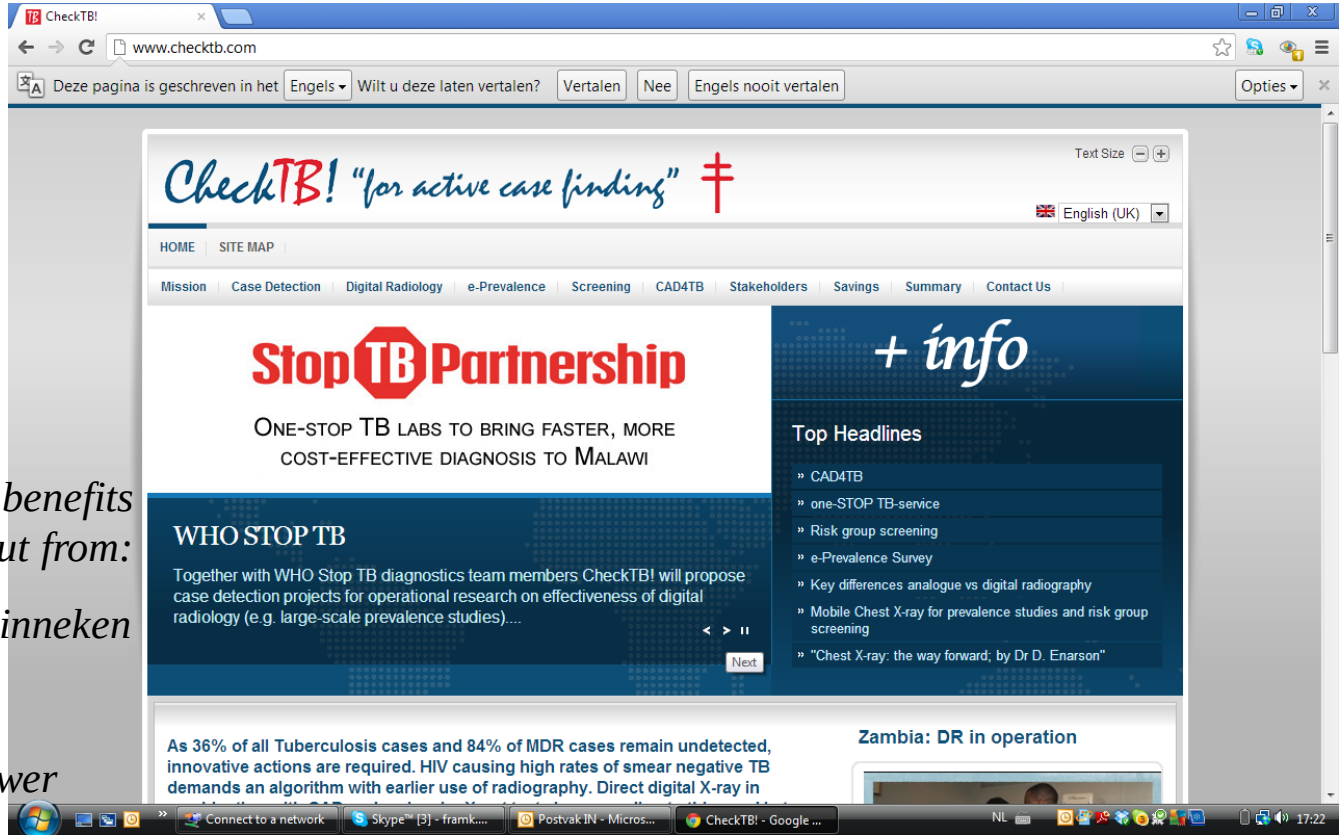
How many legs has this elephant?

We may need a CAD4Elephants…

Thanks for your attention!

for more information

you can visit www.checktb.com



This presentation benefits from valuable input from:

Prof. Bram van Ginneken

Dr Knut Lonnroth

Dr Miranda Brouwer