LUNGENLIGA SCHWEIZ
LIGUE PULMONAIRE SUISSE
LEGA POLMONARE SVIZZERA
LIA PULMUNARA SVIZRA

Herzlich Willkommen zum 31. hybriden Tuberkulose-Symposium

Bienvenue au 31e Symposium Tuberculose hybride

LUNGENLIGA SCHWEIZ
LIGUE PULMONAIRE SUISSE
LEGA POLMONARE SVIZZERA
LIA PULMUNARA SVIZRA

Mit Unterstützung von

Avec le soutien de

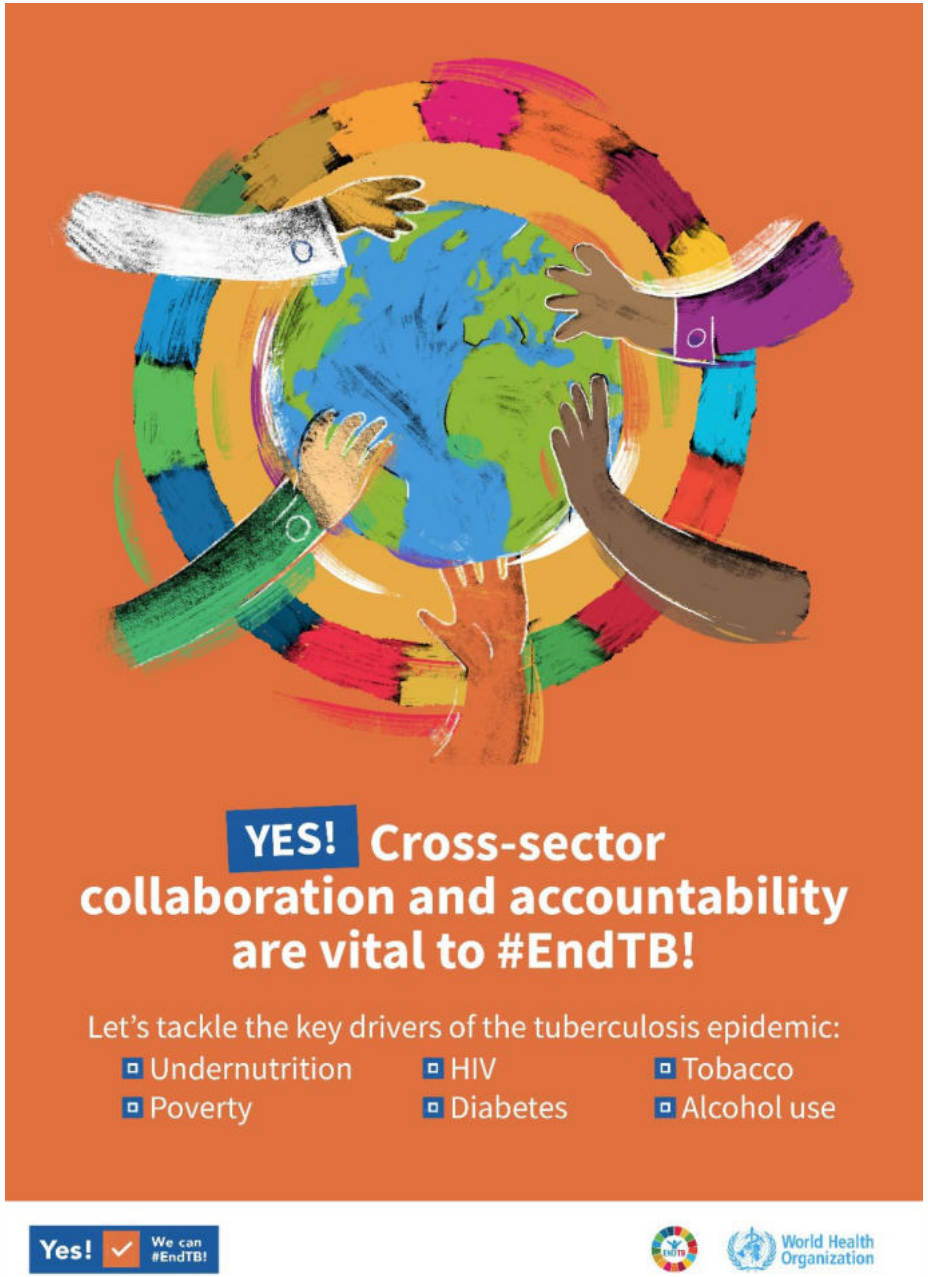
QIAGEN

DiaSorin

Herzlich willkommen zur 31. Ausgabe des Tuberkulose-Symposiums

Dr. Jörg Spieldenner
Direktor Lungenliga Schweiz

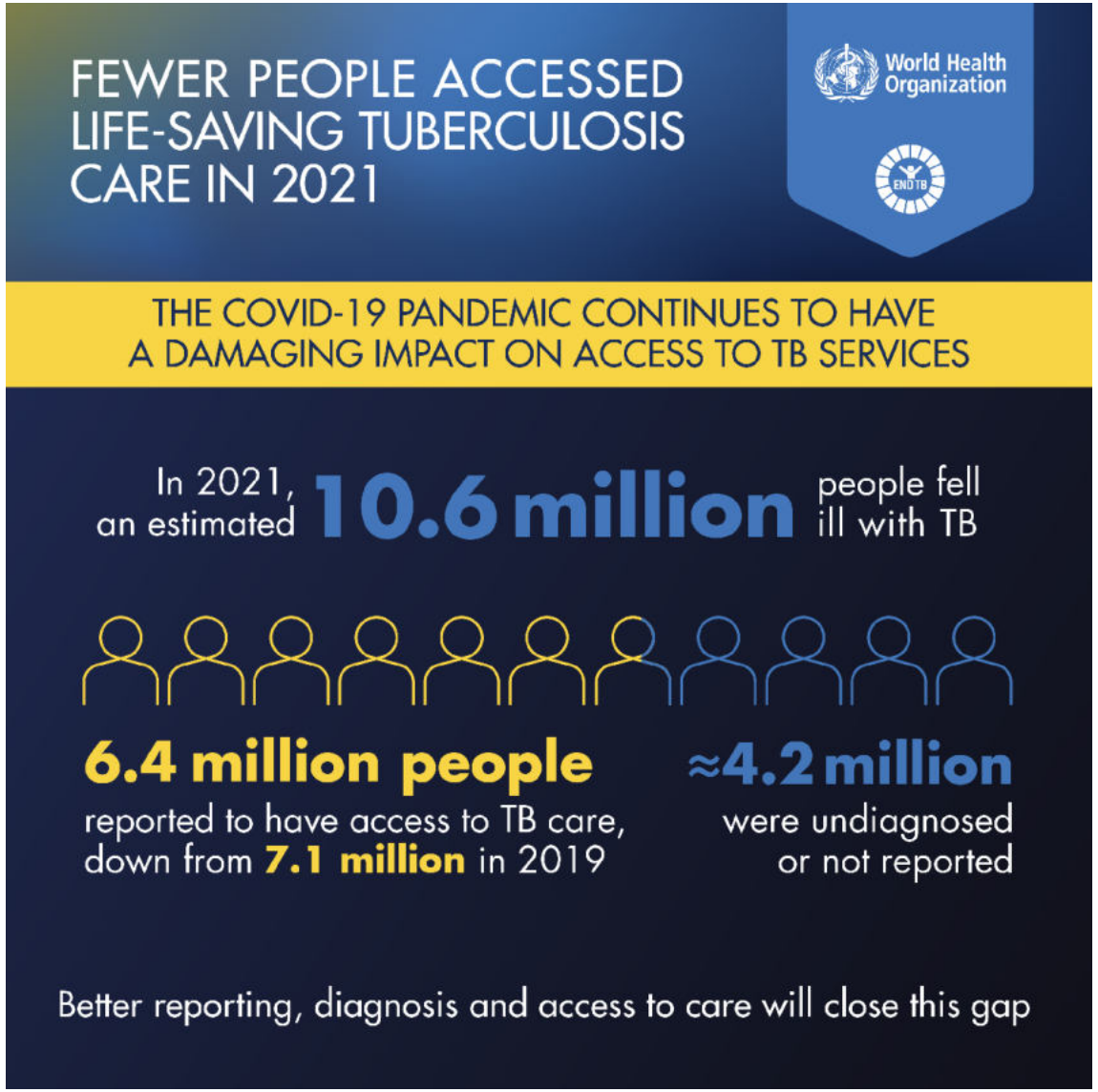
LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE



- Die Lungenliga Schweiz hat sich erneut beworben für den Betrieb des Kompetenzzentrums Tuberkulose 2023-2027

- Gemeinsam mit allen Akteuren in der Schweiz und international möchten wir TB-Betroffene und Ihre Angehörigen bestmöglich unterstützen

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE



- **Detecting TB**: nur entdeckte Fälle können auch behandelt werden und haben Zugang zur Gesundheitsversorgung

- Unterschiedliche Herausforderungen international und in der Schweiz => **Kollaboration ist zentral**

DANKSAGUNG

Eventforum Bern

Sponsoren DiaSorin und Qiagen

IMK

Team der Lungenliga Schweiz

DolmetscherInnen

Scientific Committee

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Case Management

David Augier
Ligue pulmonaire fribourgeoise

Diese Präsentation ist aus datenschutzrechtlichen Gründen nicht verfügbar.

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Enquête d’entrourage tuberculose dans un contexte HIV complexe

Veronica Maglio
Ligue pulmonaire vaudoise

Diese Präsentation ist aus datenschutzrechtlichen Gründen nicht verfügbar.

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Verdachtsfall taucht unter

Renate Stumpf-Wüthrich
Lungenliga St. Gallen - Appenzell

Diese Präsentation ist aus datenschutzrechtlichen Gründen nicht verfügbar.

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Eidgenössisches Departement des Innern EDI
Bundesamt für Gesundheit BAG
Abteilung Übertragbare Krankheiten

Internationale Umgebungsuntersuchung

31. Tuberkulose-Symposium 1. Juni 2023

Philipp Ludin, Wissenschaftlicher Mitarbeiter

Fiktive Beispiele aus dem Alltag

- «Wir haben einen Patienten mit einer Lungentuberkulose aus Brasilien, welcher kürzlich mit dem Flugzeug in die Schweiz gereist ist. Müssen wir die Airline kontaktieren oder wer macht dies? Das BAG?»

- «Eine Patientin mit einer Lungentuberkulose ist mit dem Bus in den Balkan gereist. Wir haben leider nur das Datum der Reise mit Start und Zielort. Leider keine weiteren Angaben vorhanden.»

- «Eine Familie aus Polen hatte beim Besuch in der Schweiz Kontakt zu einer Patientin mit einer Lungentuberkulose. Hier der Name, Vorname und Wohnort der Familienmitglieder.»

Internationale Umgebungsuntersuchung

Gesetzliche Grundlage

International Health Regulations (IHR)

- Umgebungsuntersuchungen in Transportmittel (z.B. Flugzeug, Bus, Zug)
- Austausch von Informationen von Indexpatienten und Kontaktpersonen zwischen betroffenen Ländern

UU in internationalen Transportmitteln

- In der Regel ist das Zielland zuständig, ob eine UU in einem internationalen Transportmittel durchgeführt wird
- Passagierlisten werden i.d.R. durch die nationalen Behörden eingefordert
- Exponierte Personen werden dem Wohnland gemeldet. Das Wohnland (bzw. lokale Behörde) entscheidet über allfällige Massnahmen.
- Wenig Evidenz von TB-Übertragungen in der Literatur vorhanden[1,2,3]

[1] Risk assessment guidelines for infectious diseases transmitted on aircraft (RAGIDA)- tuberculosis, European Center for Disease Prevention and Control (ECDC) (2014)
[2] Kotila et al., Systematic review on tuberculosis transmission on aircraft and update of the European Centre for Disease Prevention and Control risk assessment guidelines for tuberculosis transmitted on aircraft (RAGIDA-TB), Eurosurveillance (2016)
[3] Glasauer et al., International tuberculosis contact-tracing notifications in Germany: analysis of national data from 2010 to 2018 and implications for efficiency, BMC Infectious Diseases (2020)

UU in Flugzeugen

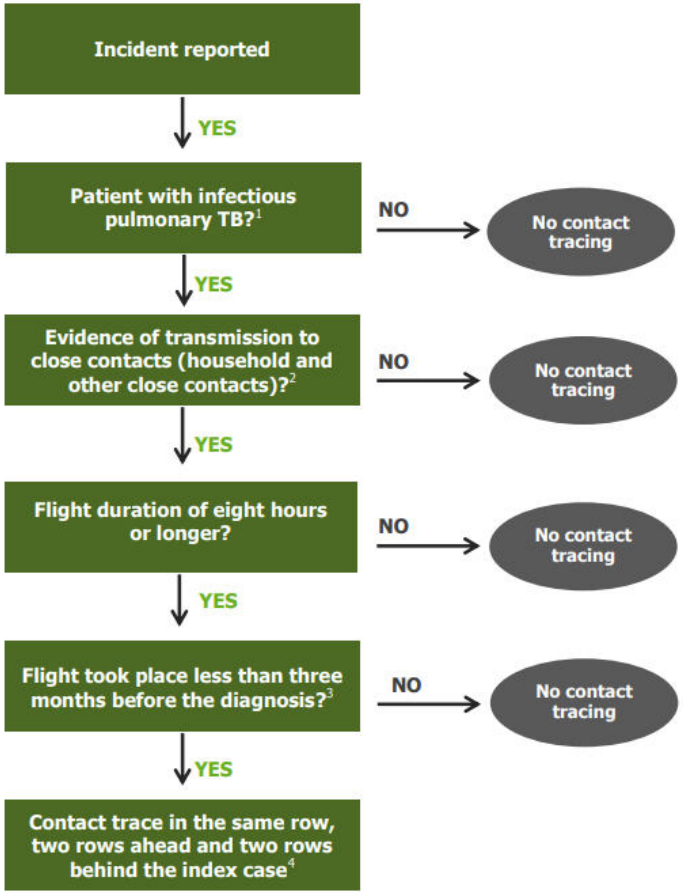
- TB-Übertragungsrisiko wird als sehr gering eingeschätzt -> HEPA Filter
- Geschätztes Risiko: 0.1-1.3% (> 8h Flugdauer, in unmittelbarer Nähe am höchsten)
- Keine aktive TB-Erkrankung nach Exposition in Flugzeug bekannt
- Aufwand für UU sehr gross (diverse Behörden und Akteure involviert)

-> Risk Assessment guidelines for infectious diseases transmitted on aircraft (**RAGIDA**)

RAGIDA

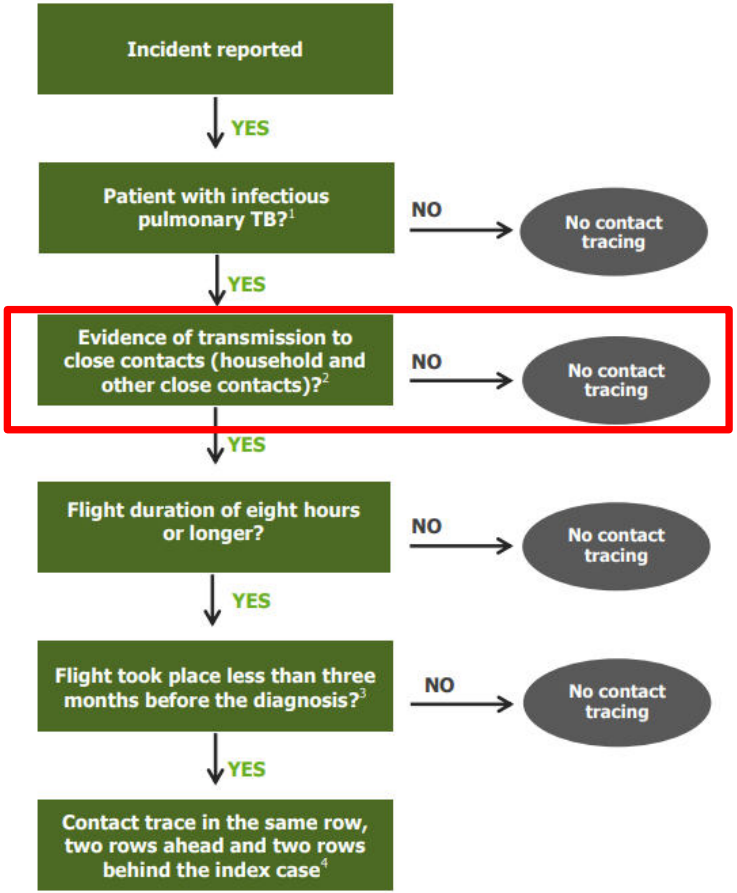
- Risk Assessment guidelines for infectious diseases transmitted on aircraft (u. a. TB)
- Publiziert von European Centre For Disease Prevention and Control
- Basieren auf den WHO Richtlinien
- RAGIDA-TB erstmals 2009 publiziert, Update 2014
- Berücksichtigung von Evidenz, Expertenmeinungen sowie Priorisierung der verfügbaren Ressourcen

Figure 1. **Risk assessment algorithm, TB**



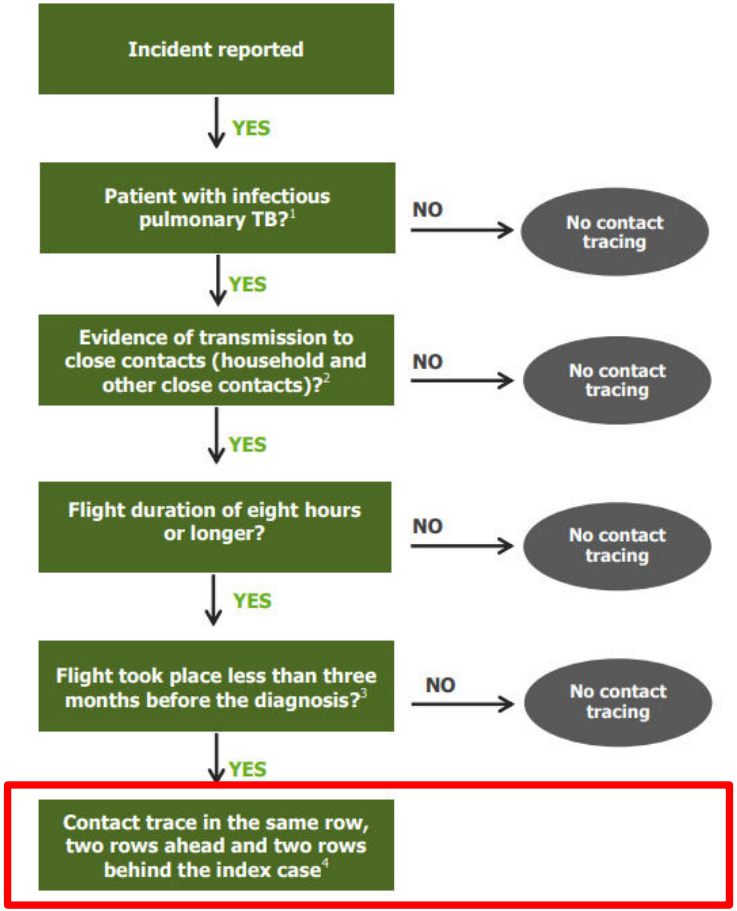
RAGIDA-TB ECDC (2014)

Figure 1. **Risk assessment algorithm, TB**



RAGIDA-TB ECDC (2014)

Figure 1. **Risk assessment algorithm, TB**



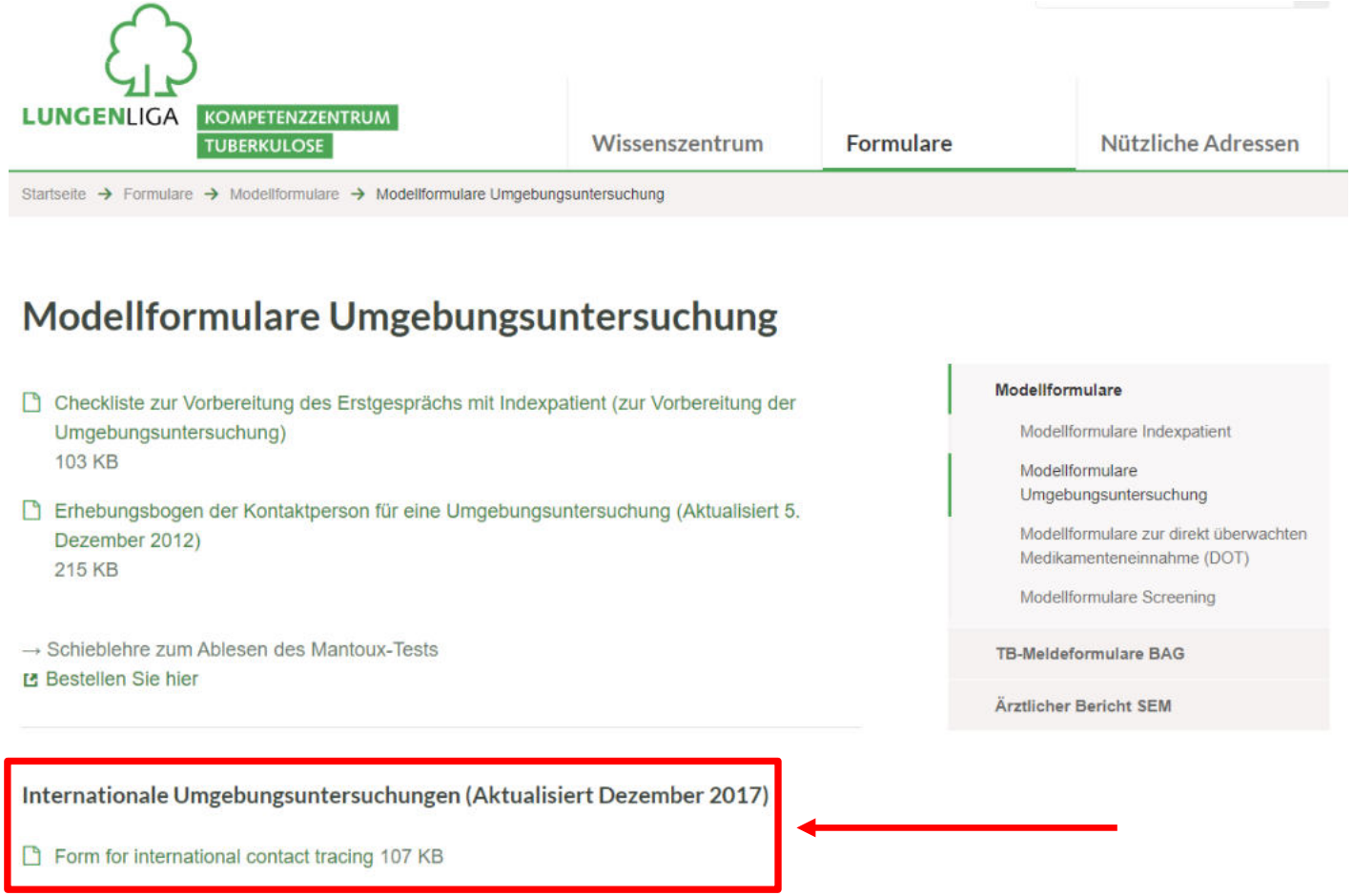
RAGIDA-TB ECDC (2014)

UU in Flugzeugen: Herausforderungen

- Nicht alle Länder befolgen die RAGIDA Richtlinien
- Kein internationales Standard-Formular
- Unvollständige Daten (z.B. klinische Daten zum Indexpatient, Angaben zum Flug, Kontaktdaten von Passagieren)
- Aufwand sehr gross

UU in anderen Transportmittel (z. B. Bus, Zug)

- Keine internationalen Richtlinien vorhanden
- Nur wenig Literatur vorhanden
- Passagierdaten nicht vorhanden oder nur sehr unvollständig
- Geschätztes Risiko grösser als in Flugzeugen (in der Regel keine HEPA-Filter)


LUNGENLIGA
KOMPETENZZENTRUM
TUBERKULOSE
Wissenszentrum
Formulare
Nützliche Adressen
Startseite → Formulare → Modellformulare → Modellformulare Umgebungsuntersuchung
Modellformulare Umgebungsuntersuchung
Checkliste zur Vorbereitung des Erstgesprächs mit Indexpatient (zur Vorbereitung der Umgebungsuntersuchung)
103 KB
Erhebungsbogen der Kontaktperson für eine Umgebungsuntersuchung (Aktualisiert 5. Dezember 2012)
215 KB
→ Schieblehre zum Ablesen des Mantoux-Tests
Bestellen Sie hier
Modellformulare
Modellformulare Indexpatient
Modellformulare Umgebungsuntersuchung
Modellformulare zur direkt überwachten Medikamenteneinnahme (DOT)
Modellformulare Screening
TB-Meldeformulare BAG
Ärztlicher Bericht SEM
Internationale Umgebungsuntersuchungen (Aktualisiert Dezember 2017)
Form for international contact tracing 107 KB

Tuberkulose in der Schweiz

Nathalie Gasser
Leiterin Kompetenzzentrum Tuberkulose
Lungenliga Schweiz

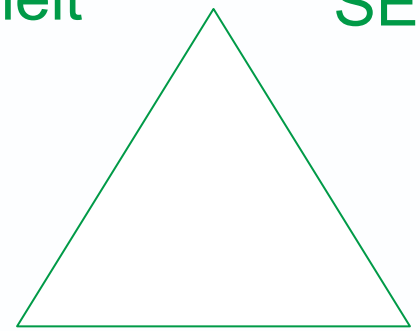
LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Schweizer Strukturen

- **Tuberkulose ist in der Schweiz eine meldepflichtige Erkrankung**
- Verschiedene Akteure spielen eine Rolle in der Prävention und Bekämpfung der Tuberkulose in der Schweiz
- Das Epidemiengesetz gibt die rechtliche Grundlage vor zur Bekämpfung der Tuberkulose

BAG = Bundesamt für Gesundheit

SEM = Staatssekretariat für Migration

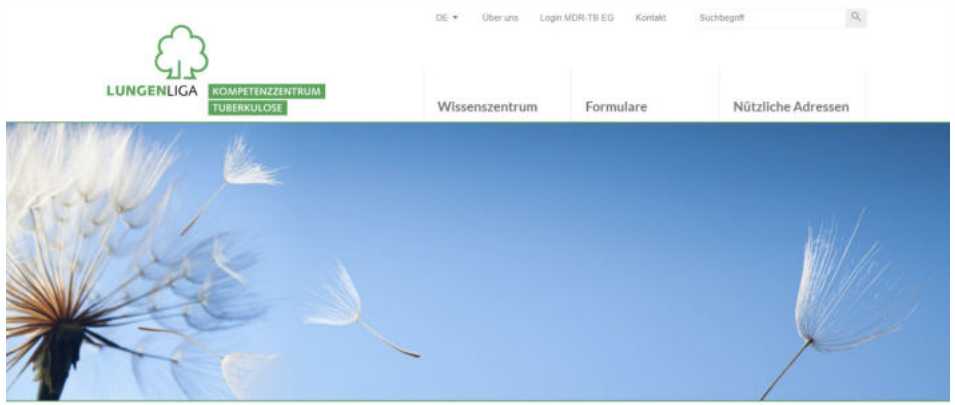


KOMPZ TB = Kompetenzzentrum TB

Kompetenzzentrum Tuberkulose

Das **Kompetenzzentrum Tuberkulose** (KOMPZ TB) unterstützt und berät Fachpersonen in ihrer täglichen Arbeit mit TB-Fällen und Kontaktpersonen

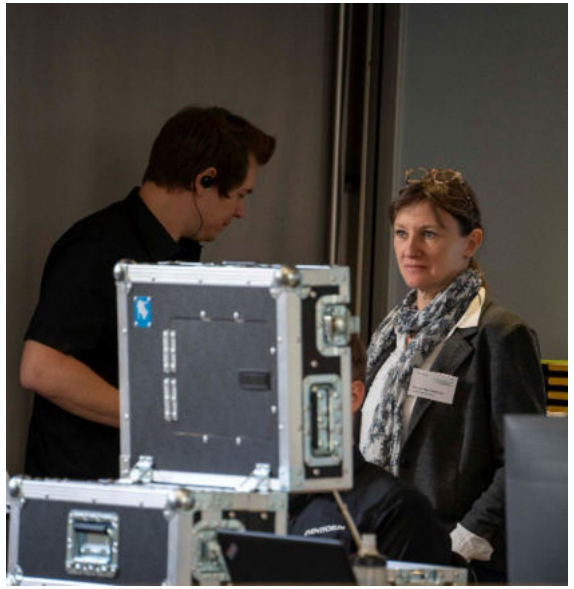
- Online-Kompetenzzentrum tbinfo.ch
- TB-Handbuch zum Management der Tuberkulose in der Schweiz
- Betrieb von TB-Hotline und des MDR-TB Forum
- Sicherung der Medikamentenversorgung und Publikation von Versorgungsengpässen (mit Bundesamt für wirtschaftliche Landesversorgung BWL)
- Jährliche Weiterbildungsveranstaltungen: Basiskurse, Fachtagungen und TB-Symposium



LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Herzlichen Dank für deinen grossartigen Einsatz und alles Gute für deinen weiteren Lebensweg liebe

Monika



LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Herzlich willkommen

Sara Magadzio-Ullmann

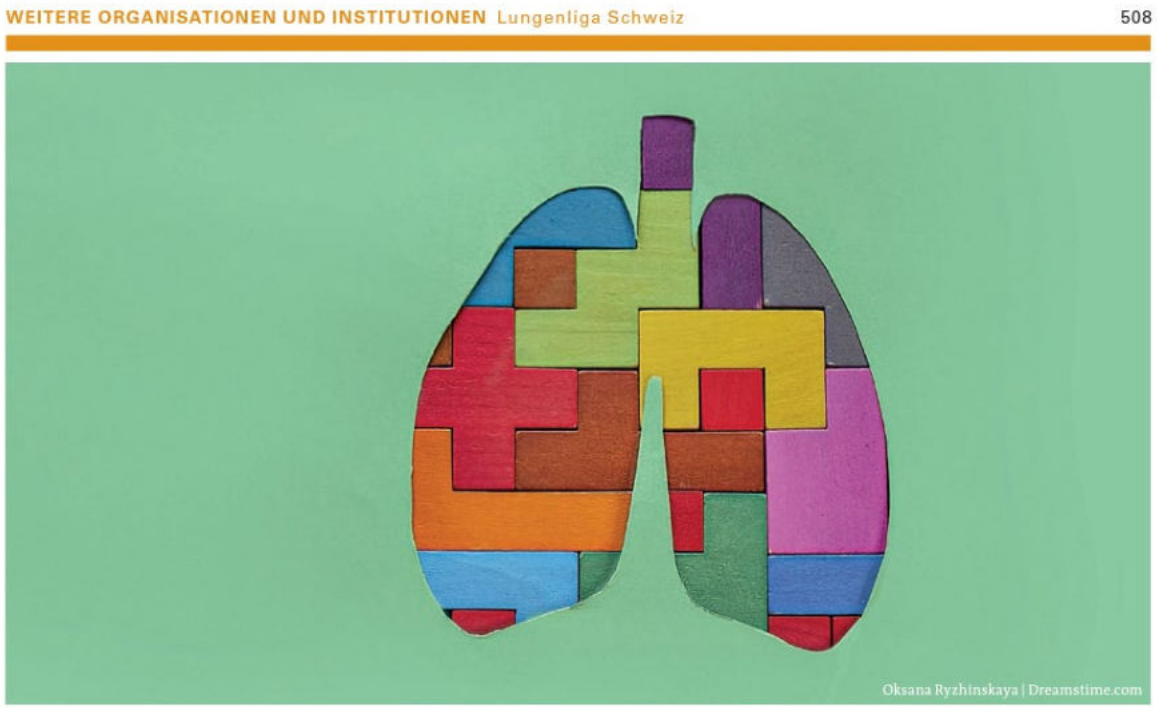
20% im Bereich Tuberkulose tätig

- Administration Kompetenzzentrum TB
- TB-Hotline
- Relaunch der Webseite tbinfo.ch im Juni 2023 + Regelbetrieb
- MDR-TB Forum

Aktivitäten des Kompetenzzentrums TB 2022/2023

Mai

Publikation SAEZ: Nutzung des tb-screens



Tuberkuloserisiko bei Flüchtlingen aus der Ukraine

Jean-Pierre Zellweger[a], Nathalie Gasser[b]

[a] Dr. med., Kompetenzzentrum Tuberkulose, Lungenliga Schweiz, Bern; [b] Projektleiterin, Lungenliga Schweiz, Bern

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Rückblick 2022/2023

Mai

Publikation SAEZ: Nutzung des tb-screens

Juni

EACCTB Course Helsinki

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Rückblick 2022/2023

Mai
Publikation SAEZ: Nutzung des tb-screens

Juni
EACCTB Course Helsinki

September
Infostand SSI/SSHH Kongress Interlaken

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Rückblick 2022/2023

Mai
Publikation SAEZ: Nutzung des tb-screens

Juni
EACCTB Course Helsinki

September
Infostand SSI/SSHH Kongress Interlaken

Januar
Publikation TB Bericht 2021

Rückblick 2022/2023

Mai
Publikation SAEZ: Nutzung des tb-screens

Juni
EACCTB Course Helsinki

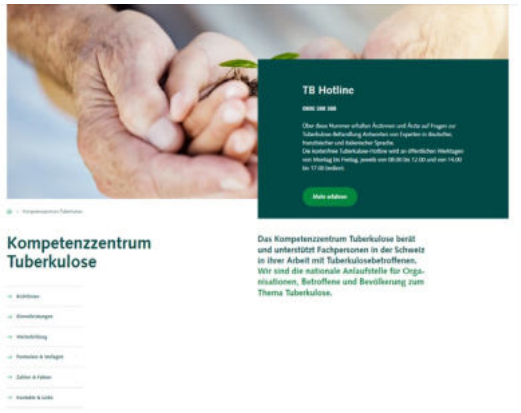
September
Infostand SSI/SSHH Kongress Interlaken

Januar
Publikation TB Bericht 2021

März
Abgabe TB-Offerte

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

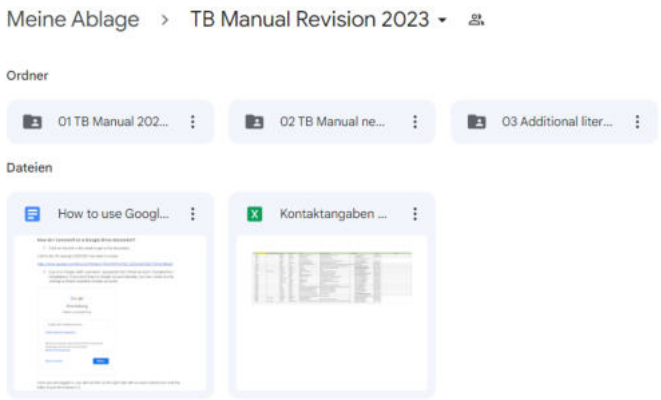
Ausblick 2023



Juni
Relaunch Webseite

Juni
Oral presentation Studie Nora Fritschi Jahreskongress Pädiatrie schweiz

Juni
Publikation TB-Handbuch 2023

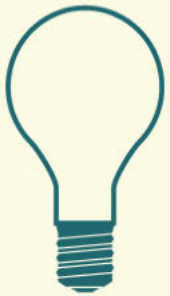


LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Jährlicher Tuberkulosebericht

- Teil des Mandatsvertrags zwischen BAG und LLS ist die Publikation eines jährlichen Berichtes zu den kantonalen Aktivitäten im Bereich Tuberkulose
- Der Bericht dient als **Steuerungsinstrument** für die Kantone, als Überblick für Fachpersonen und als Datengrundlage für weitere Projekte im Bereich Tuberkulose
- Der Bericht wird **dreisprachig** (DE, FR und EN) auf tbinfo.ch veröffentlicht

KEY FACTS TUBERKULOSE SCHWEIZ 2021

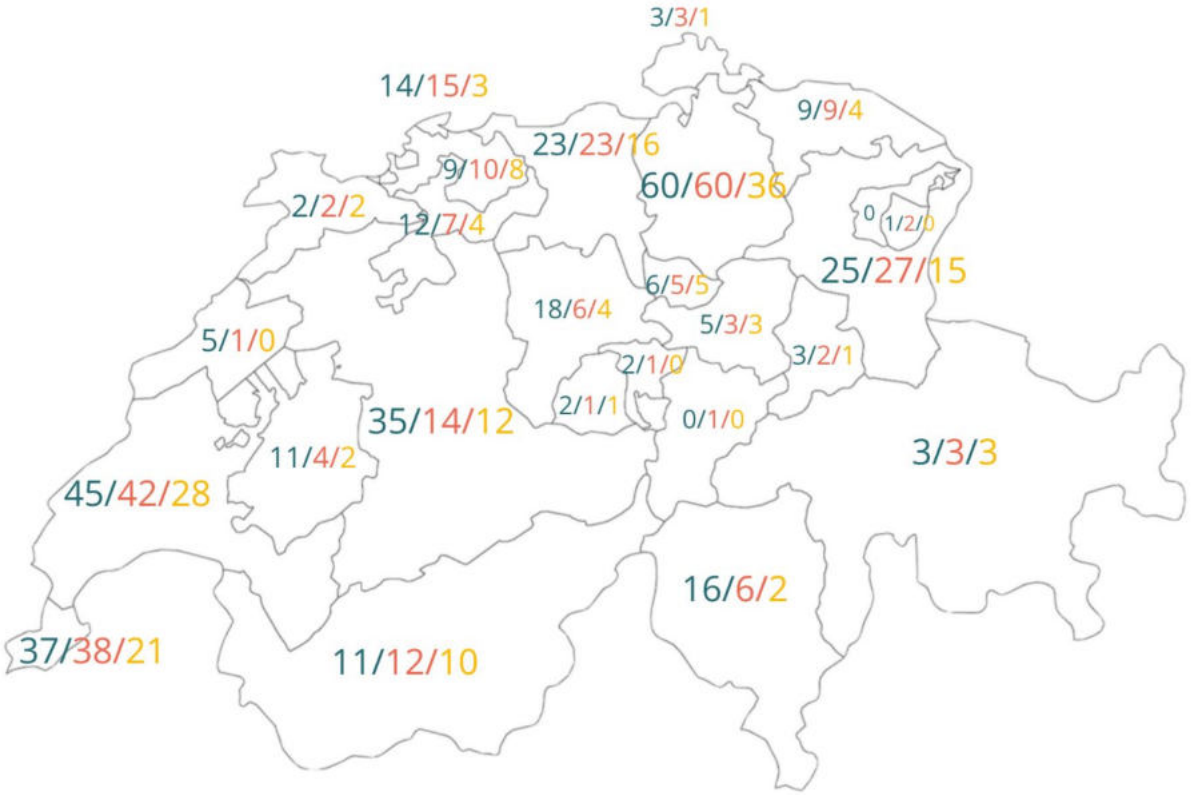


357 GEMELDETE FÄLLE

2021 wurden dem BAG 357 TB-Fälle gemeldet. Dies sind 4% weniger als im Vorjahr.

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Verteilung TB-Fälle 2021

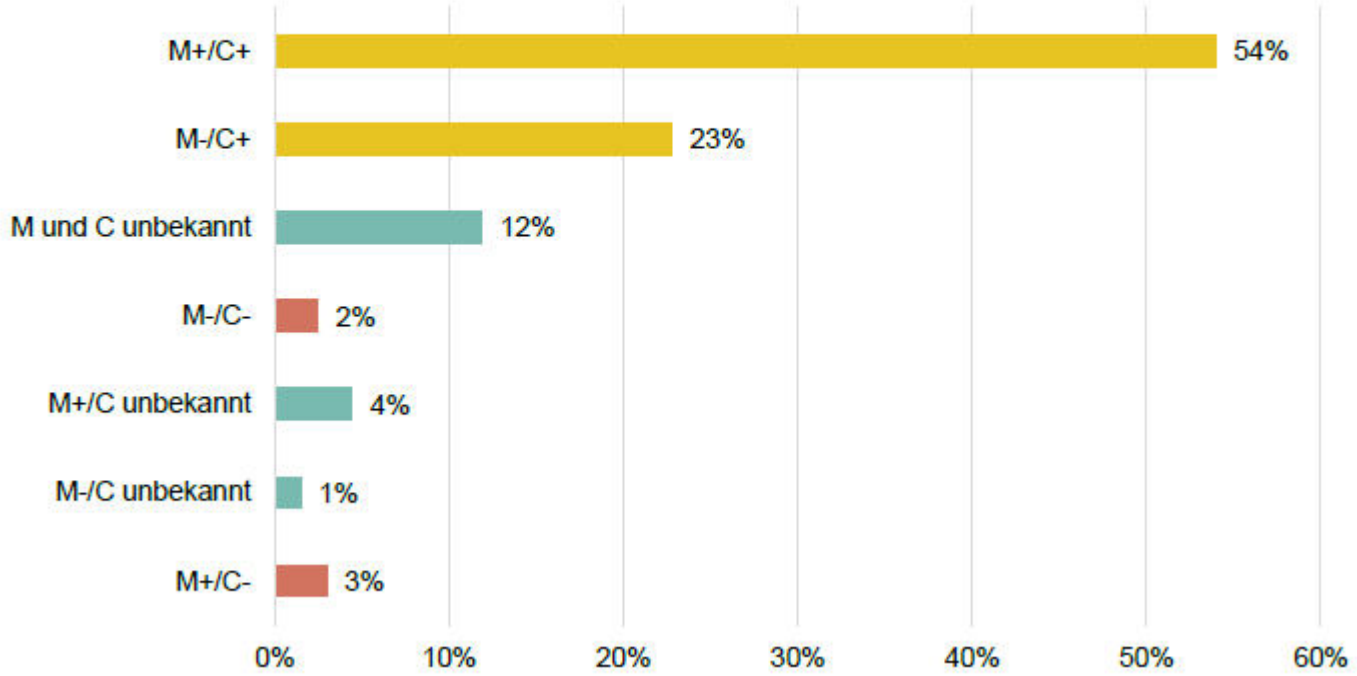


CHARAKTERISTIKA TB-FÄLLE

65% aller TB-Fälle sind pulmonal,
27% rein extrapulmonal.

Die Mehrheit der
Indexpatient*innen ist zwischen
20 und 50 Jahre alt.

Abb. 15: Bakteriologischer Status der pulmonalen TB-Fälle im Jahr 2021 (n=202)

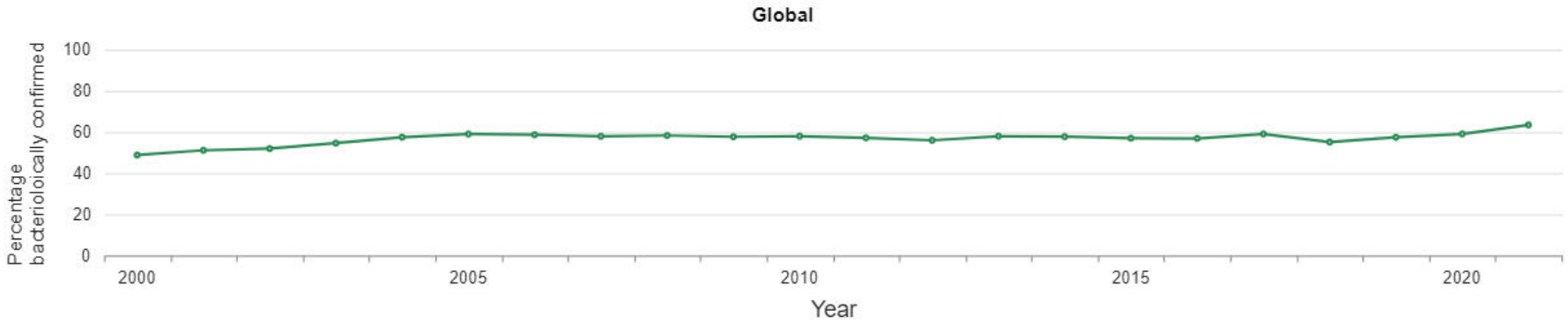


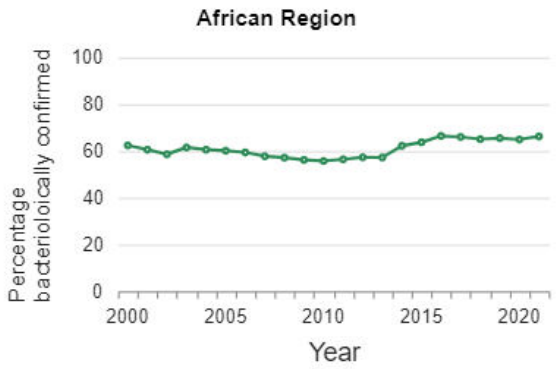
Indonesia C+ cases 56%

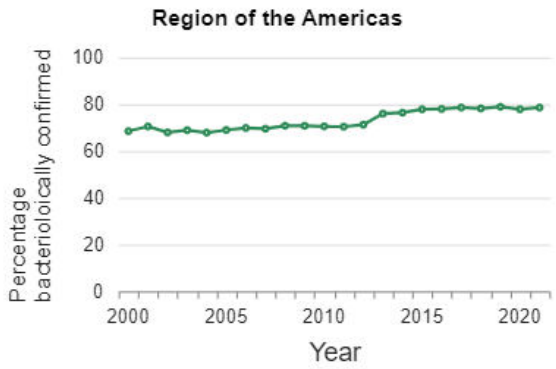
WHO C+ cases 63%

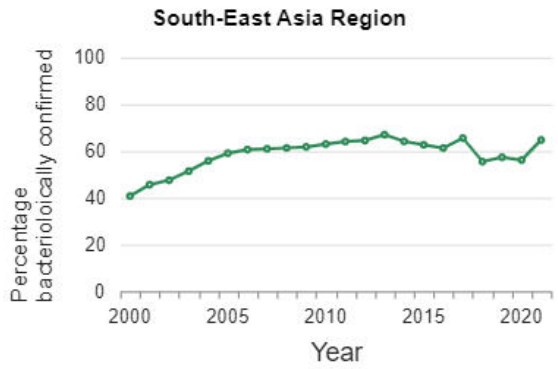
Swiss C+ cases 77%

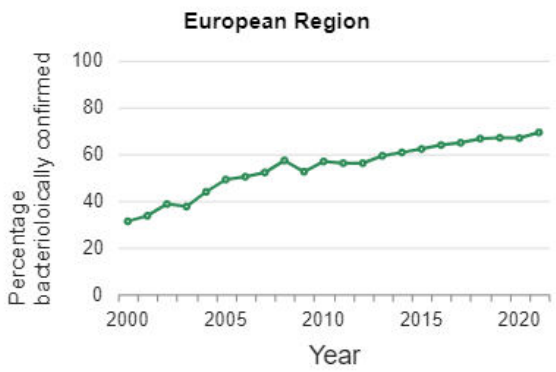
LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

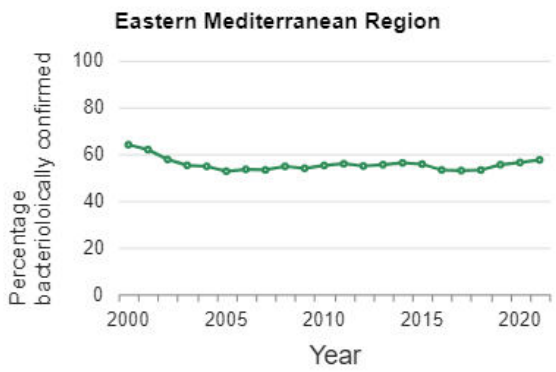


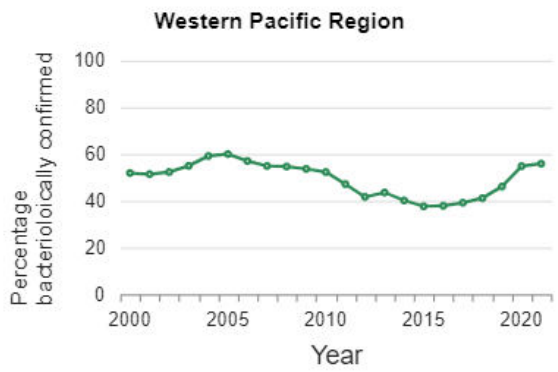






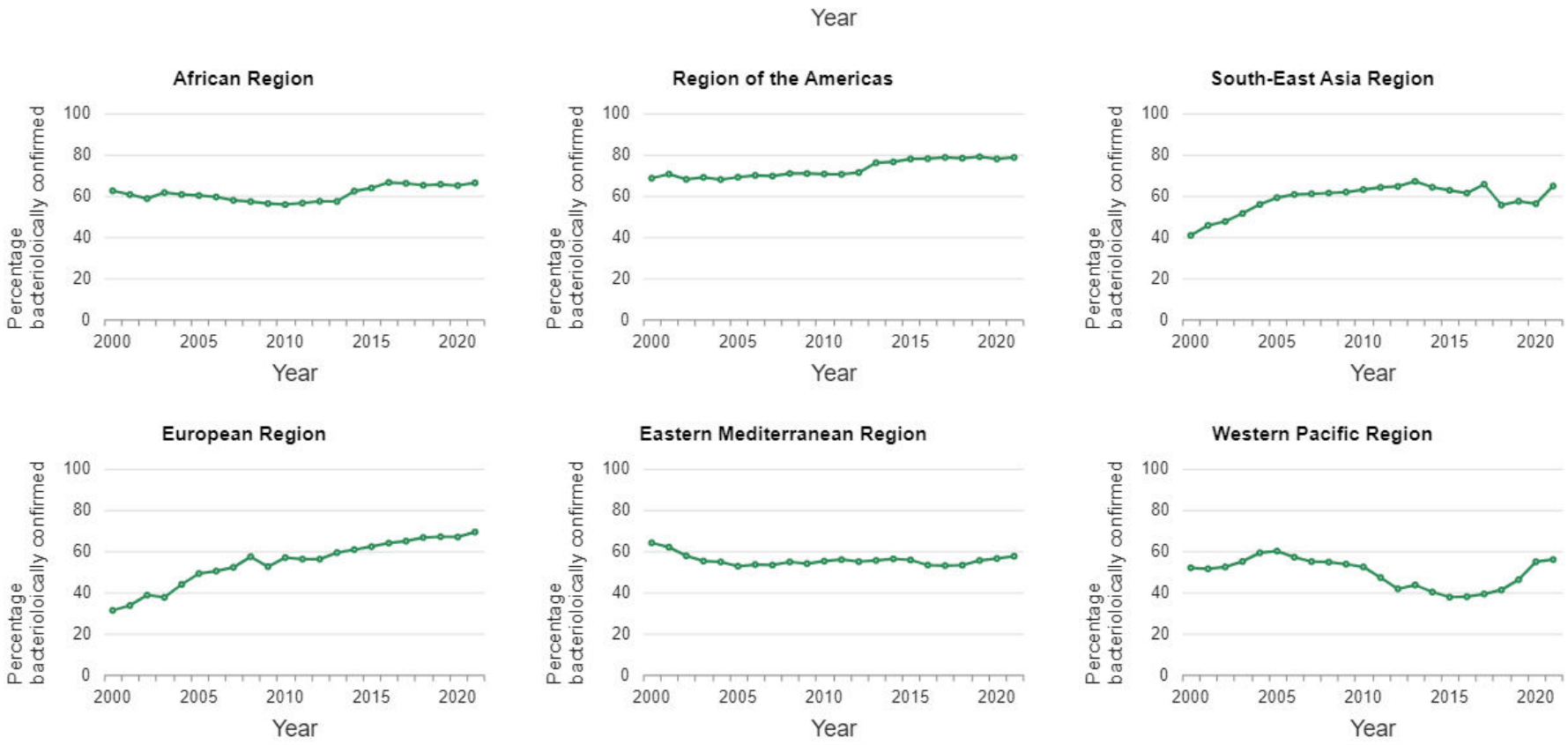






Quelle: WHO Global TB report 2022, Fig. 3.2.1.

People diagnosed with TB using culture, rapid molecular tests recommended by WHO, lateral flow urine lipoarabinomannan (LF-LAM) assays or sputum smear microscopy are defined as “bacteriologically confirmed” cases of TB. The microbiological detection of TB is critical because it allows people to be correctly diagnosed and started on the most effective treatment regimen as early as possible. People diagnosed with TB in the absence of bacteriological confirmation are classified as “clinically diagnosed” cases of TB. Bacteriological confirmation of TB is necessary to test for resistance to first-line and second-line anti-TB drugs; such testing can be done using rapid molecular tests, phenotypic susceptibility testing or genetic sequencing at reference-level laboratories.



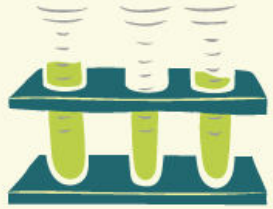
Quelle: WHO Global TB report 2022, Fig. 3.2.1.

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

181

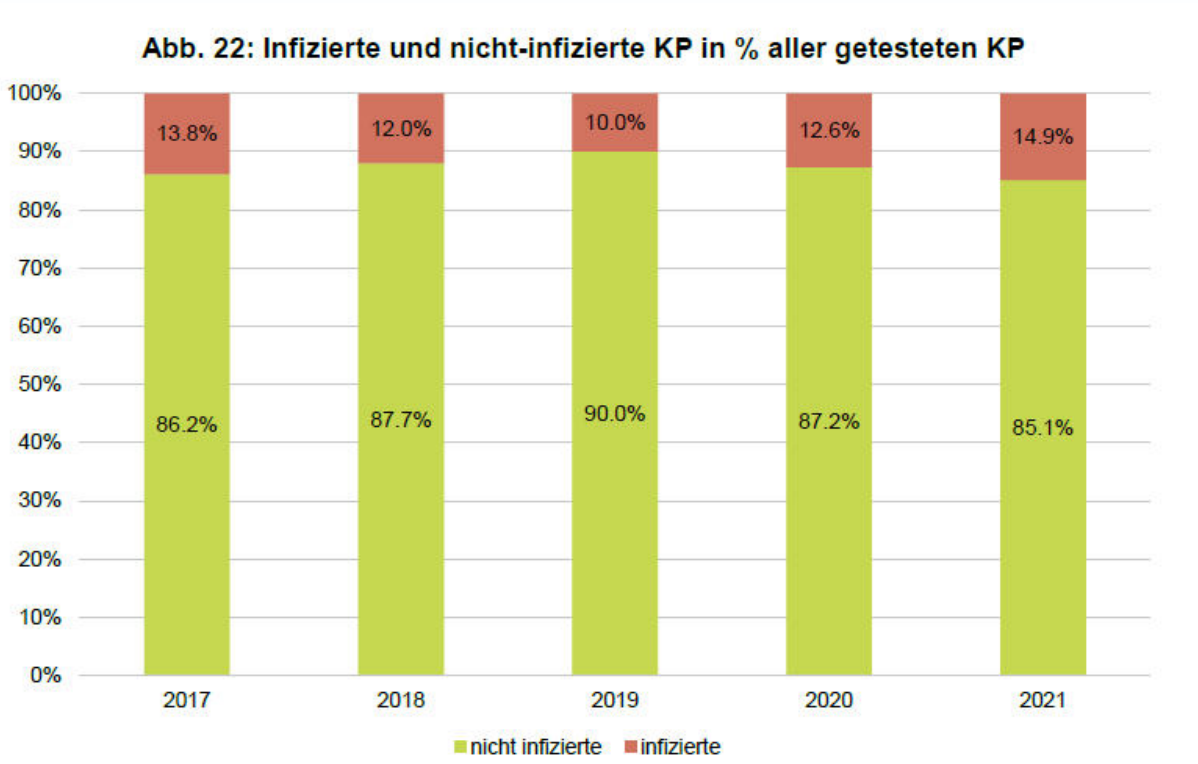
UMGEBUNGSUNTERSUCHUNGEN wurden durchgeführt

Dafür wurden 1023 Kontaktpersonen getestet, 152 davon gelten als infiziert.



Einflussfaktoren auf Positivitätsrate TBI (14.9%)

- Restriktionsgrad der UU
- Wie viele Personen befanden sich im engen Umfeld des IP?
- Wie ansteckend war der IP vor Diagnose?
- Zeit zwischen Ausbruch der TB und Diagnose
- Sensitivität und Spezifität der Tests



LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

PRÄVENTIVE TBI THERAPIEN

73 % aller infizierten Kontaktpersonen begannen eine TBI-THERAPIE, 47% davon schlossen ihre Therapie ERFOLGREICH ab.

Swiss TPT completion rate
47%

Swiss TPT children (<5)
100%

PRÄVENTIVE TBI THERAPIEN

73 % aller infizierten Kontaktpersonen begannen eine TBI-THERAPIE, 47% davon schlossen ihre Therapie ERFOLGREICH ab.

WHO TPT completion rate 86%

Swiss TPT completion rate 47%

WHO TPT children (<5) 35%

Swiss TPT children (<5) 100%

Take Home Message

- Tuberkulose in der Schweiz wird **gut erkannt, behandelt und nachverfolgt**
- Im weltweiten Vergleich schneidet die Schweiz besser ab als viele der erfassten Länder
- Zentral wichtig ist die präventive TBI Therapie vor allem bei exponierten Kleinkindern sowie Personen mit **erhöhtem Risiko** für eine Progression => PERISKOPE Rechner als Hilfsmittel
- Wichtig bleibt es weiterhin, an TB als **Differentialdiagnose** zu denken – gerade bei hohen Migrationsaktivitäten und ähnlichen Symptomen von anderen Erkrankungen (COVID-19, Grippe, RSV, COPD)

Mehr Luft fürs Leben

Vielen Dank für Ihre Aufmerksamkeit!

Ein grosses Dankeschön auch an alle

Kantonalen TB-Fachstellen

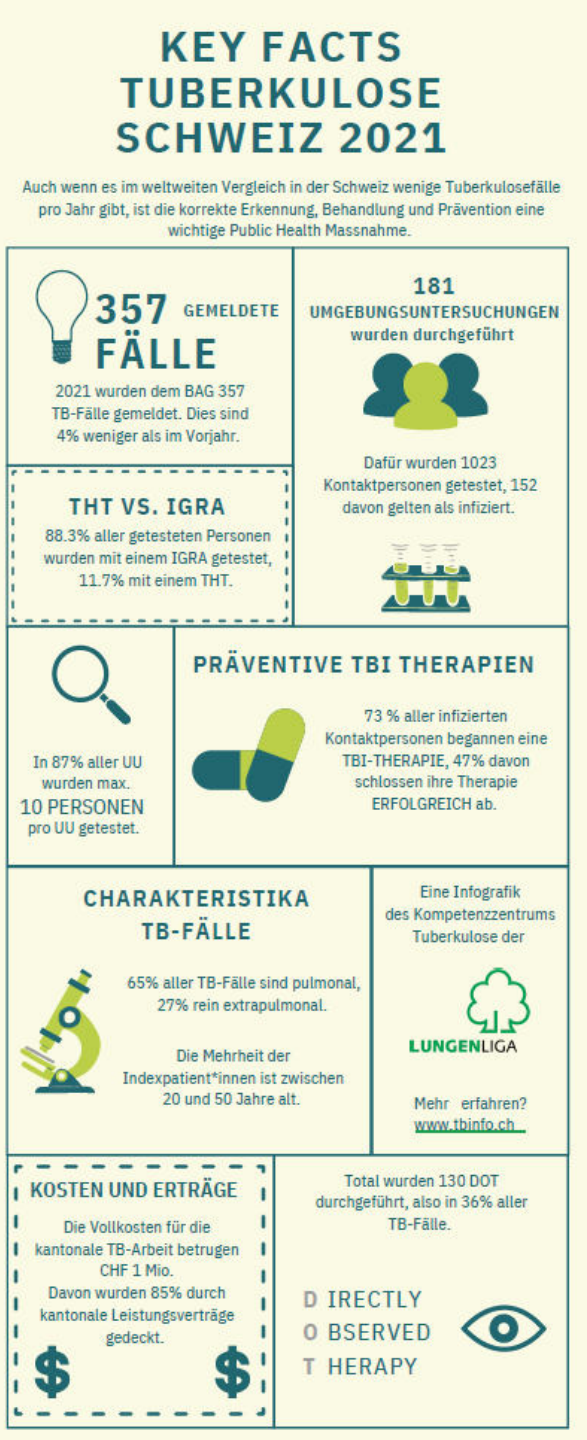
Fachpersonen, die TB-Betroffene und Ihre Angehörigen betreuen

Medizinischen Beraterinnen und Berater des KOMPZ TB

Kolleginnen und Kollegen beim BAG, SEM, BWL und weiteren Partnern

Mitarbeitenden in den Spitälern und Labors

Dem Team des Eventforums und der Lungenliga Schweiz und allen Helferinnen und Helfern heute



Quellenangaben

Bericht Kantonale Tuberkulose-Aktivitäten 2021

WHO Global TB Report 2022

WHO Global TB Report App

RKI Bericht zur Epidemiologie der Tuberkulose in Deutschland für 2020

Materialien des Kompetenzzentrum Tuberkulose

WHO: World TB Day 2023 Visual

Remise du prix SwissTB 2023

Prof L.P.Nicod

President de la Fondation Swiss TB

1.06.2023

SwissTB is a Member of the StopTB Partnership

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Swiss TB Committee

- Prof L.P.Nicod
  Präsident
- Prof. Jean Paul Janssens
  Vizepräsident
- Prof. Jean Pieters
- Prof. Peter Sander
- Prof. Pascal Meylan
- Dr Otto Brändli
- Dr. Irène Garcia
- Dr Gunar Günther
- Dr Onya Opota
- Dr Jessica Mazza Stalder
- Prof. Stewart Cole
- Dr Otto Schoch
- Dr. med. Jean-Pierre Zellweger

Every year since 2002, the Swiss Foundation for Tuberculosis Research awards the CHF 10'000 Swiss TB Award for outstanding work by Swiss researchers.

LAUREATES

2022 Swiss TB Award
Dr Nora Fritschi. -
2021 Swiss TB Aw
Fabian Arnold, Miriam Sarah Weber and Imre Gonda
2020 Swiss TB Award
Nina T. Odermatt f and Tobias Broger
2019 Swiss TB Award
Ms Kathrin Zürcher and Ms Marie Ballif
2018 SwissTB Award
Dr. Andrej Trauner and Dr. Anna Rominski
2017 SwissTB Award's Special Prize
Kathrin Zürcher
2017 SwissTB Award
Dr. Paul Murima and Dr. Michael Zimmerman
2016 SwissTB Award's Special Prize
Christian Schürer
2016 SwissTB Award
Dr. Mireia Coscolla -
2015 SwissTB Award
Dr. med., Dr. nat. med. Jan Rynbiker -
2015 SwissTB Award
PhD Giulia Manina -
2014 SwissTB Award
PhD Sònia Borrell -
2014 SwissTB Award
PhD Olga T. Schubert -
2013 SwissTB Award
Dr. Lukas Fenner -
2013 SwissTB Award
PhD Ruben C. Hartkoorn -
2012 SwissTB Award
Dr. Alexandre Harari -
2011 SwissTB Award
Dr. Neeraj Dhar -
2010 SwissTB Award
Dr. Claudia Sala -
2009 SwissTB Award
Dr. Wilfried Weber -
2008 SwissTB Award
Nicole Scherr and Dr. Srinivas Honnappa -
2007 SwissTB Award
Dr. Corinne Loeuillet -
2006 SwissTB Award
Dr. Claudia Tueller und Dr. Reto Guler -
2005 SwissTB Award
Drs. Liem Nguyen, Anne Walburger, Giorgio Ferrari, Anil Koul -
2004 SwissTB Award
Dr. Andreas Diacon -
2003 SwissTB Award
Prof. Dr. Gaby Pfyffer -
2002 SwissTB Award
Maria Olleros

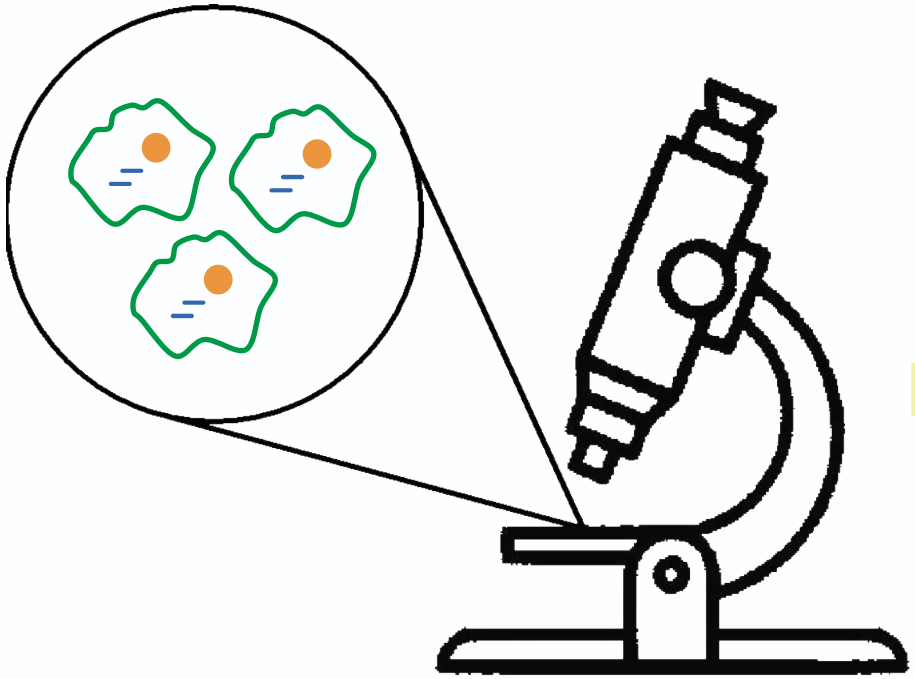
Award 2023: Dr Ophelie Rutschmann

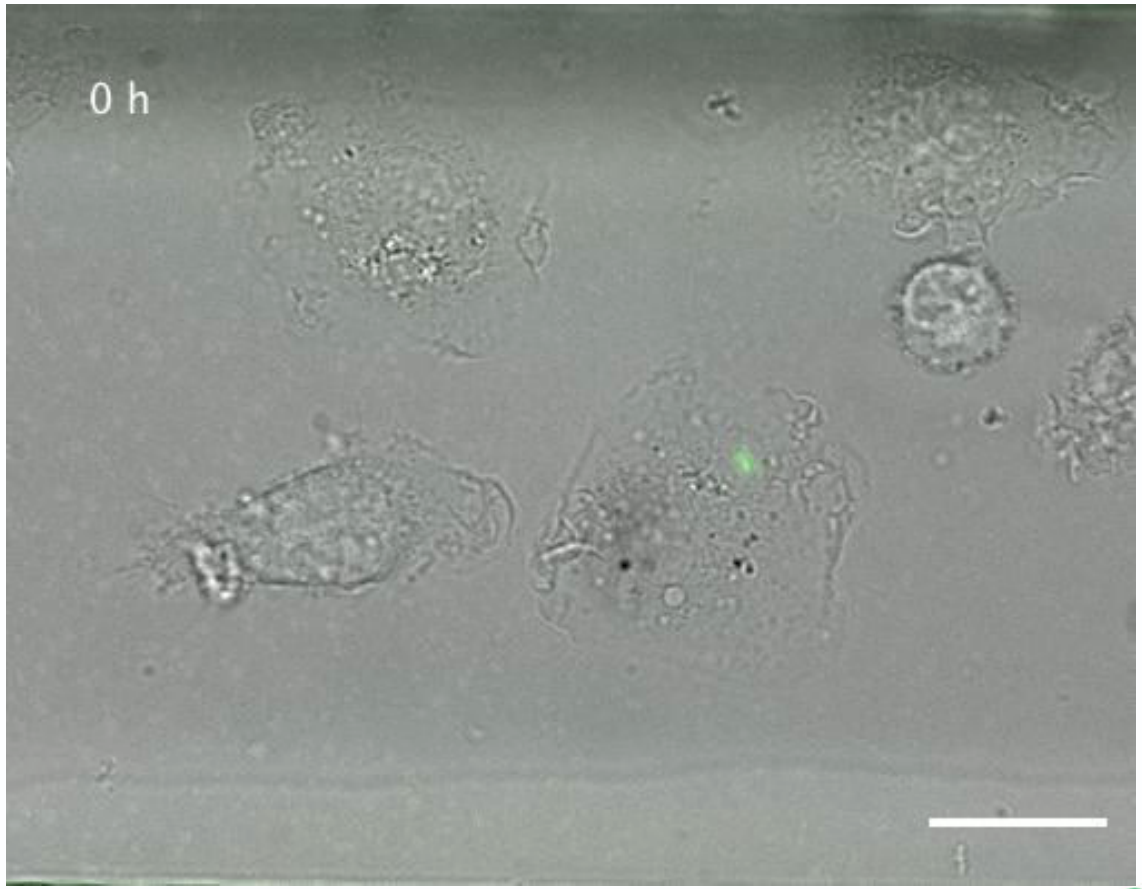
Preexisting Heterogeneity of Inducible Nitric Oxide Synthase Expression Drives Differential Growth of Mycobacterium tuberculosis in Macrophages (mBio 13: e0225122)

By Ophélie Rutschmann, EPFL, Lausanne

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

We use time-lapse microscopy to study single-cell interactions between macrophages and *M.tuberculosis*



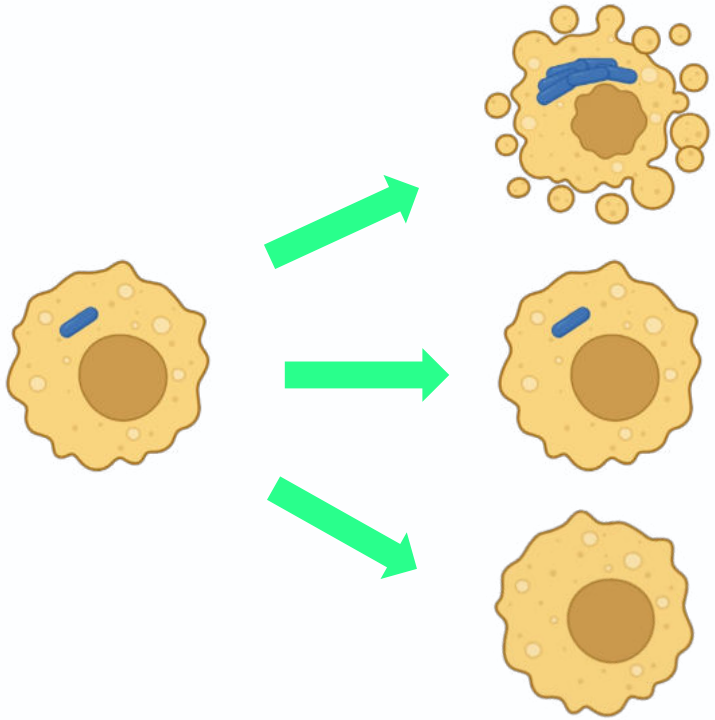


Long-term time-lapse fluorescence microscopy of murine macrophages infected with GFP-expressing *Mtb*

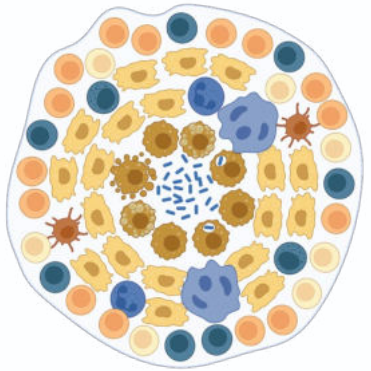
Scale bar: 15 µm

Macrophages are instrumental to the control of *M. tuberculosis*

Alveolar macrophages are the first host cells to contact the bacteria



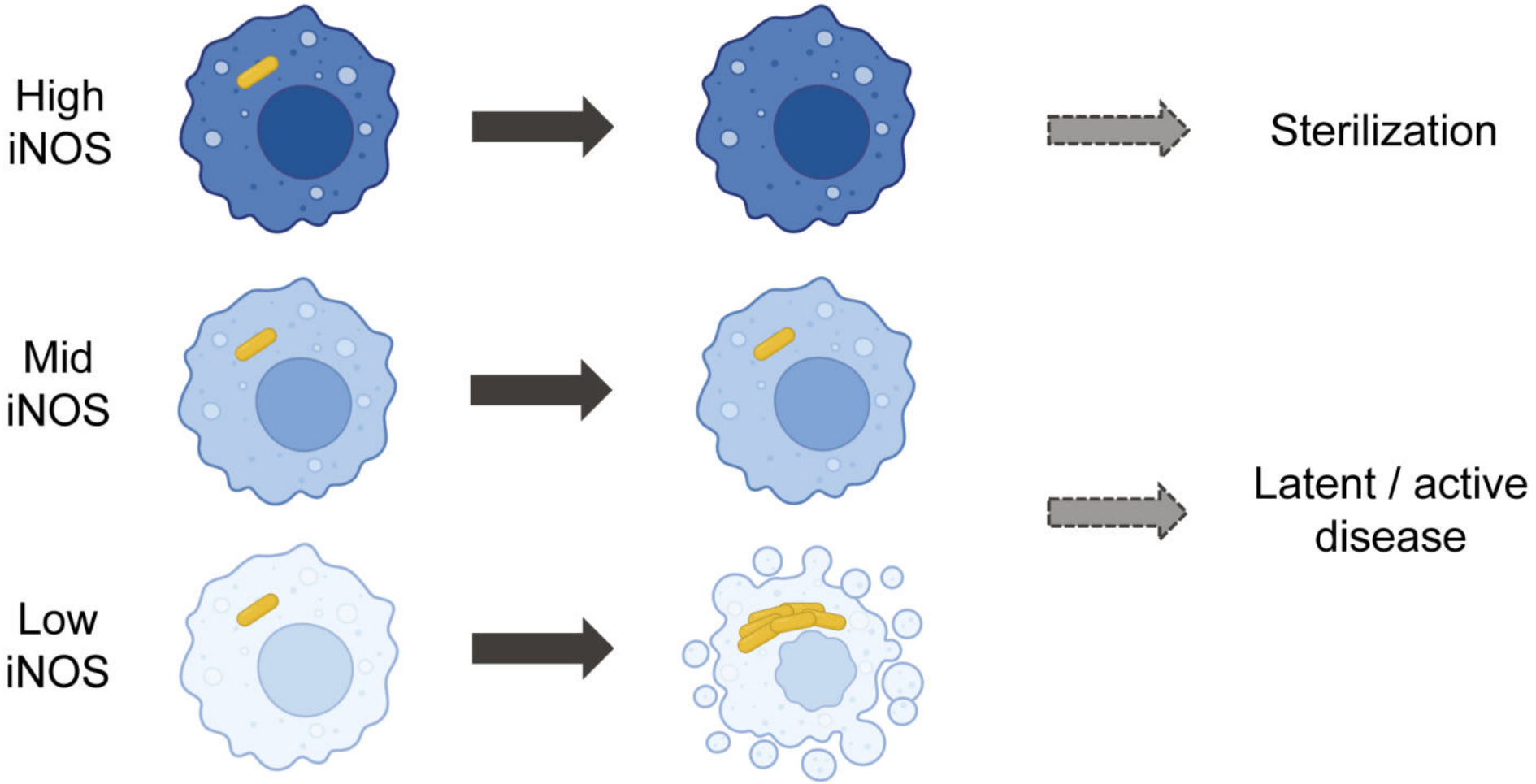
Interstitial macrophages are the main cells forming the granuloma



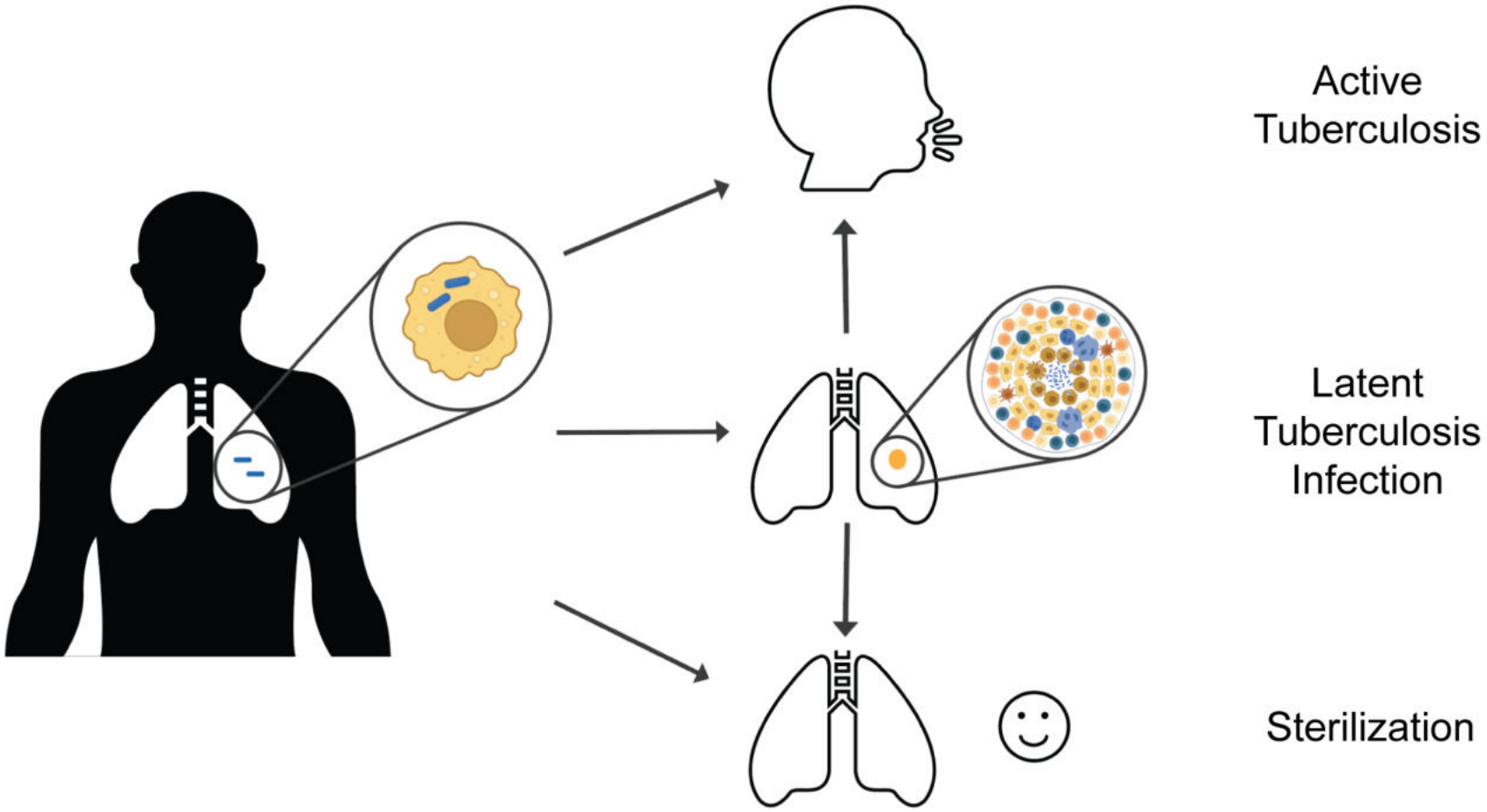
5-10%

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Heterogeneity in iNOS expression by macrophages explains differential control of intracellular *M. tuberculosis*



Differential single-cell infection outcomes could explain heterogeneity in tuberculosis disease progression



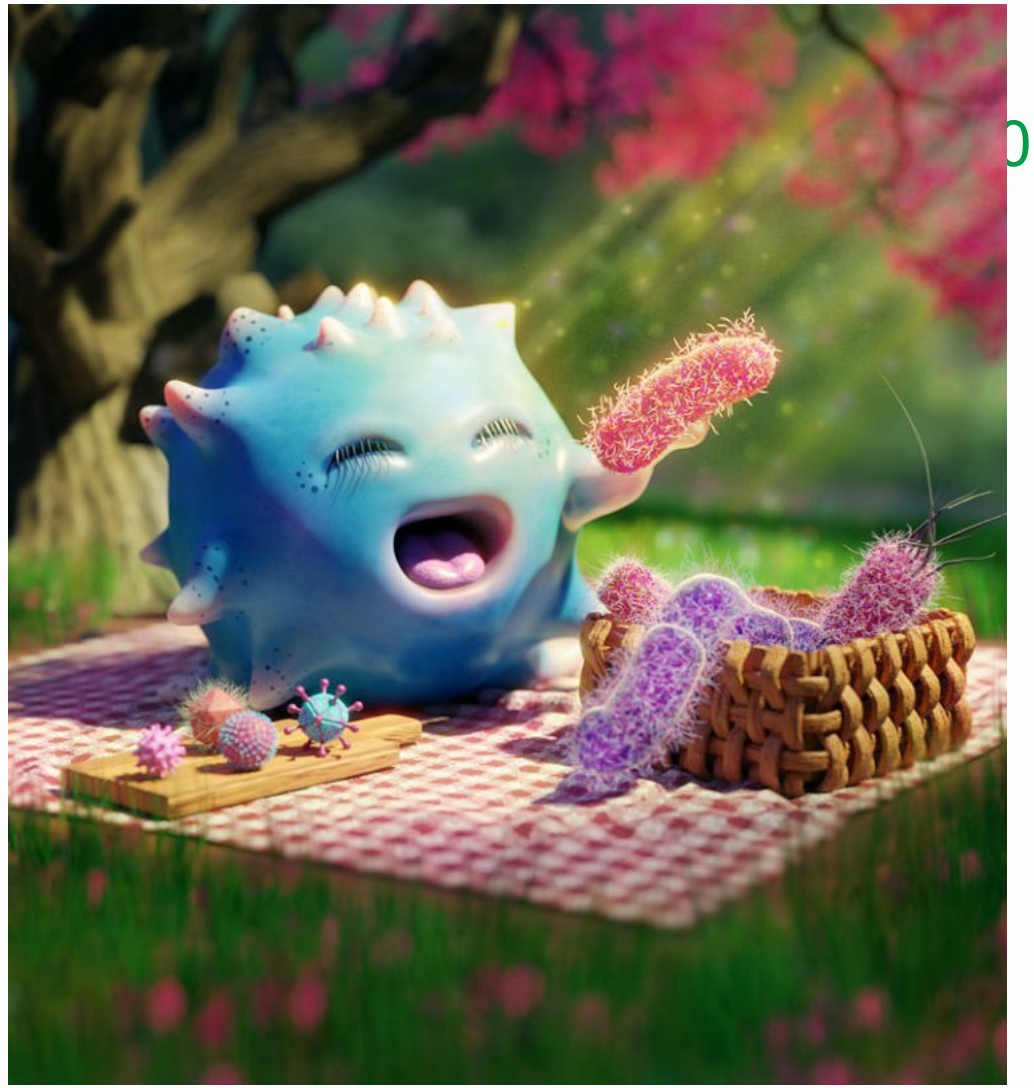
Since a tuberculosis infection can start with a **single bacteria** contacting a **single macrophage**, how well this macrophage controls this initial infection can determine how the disease progresses

Aknowledgements

Laboratory of Microbiology and Microtechnology:

Prof. John McKinney Dr. Chiara Toniolo

And all the members of the McKinney lab!



LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Stellenbosch
UNIVERSITY
IYUNIVESITHI
UNIVERSITEIT

forward together
sonke siya phambili
saam vorentoe

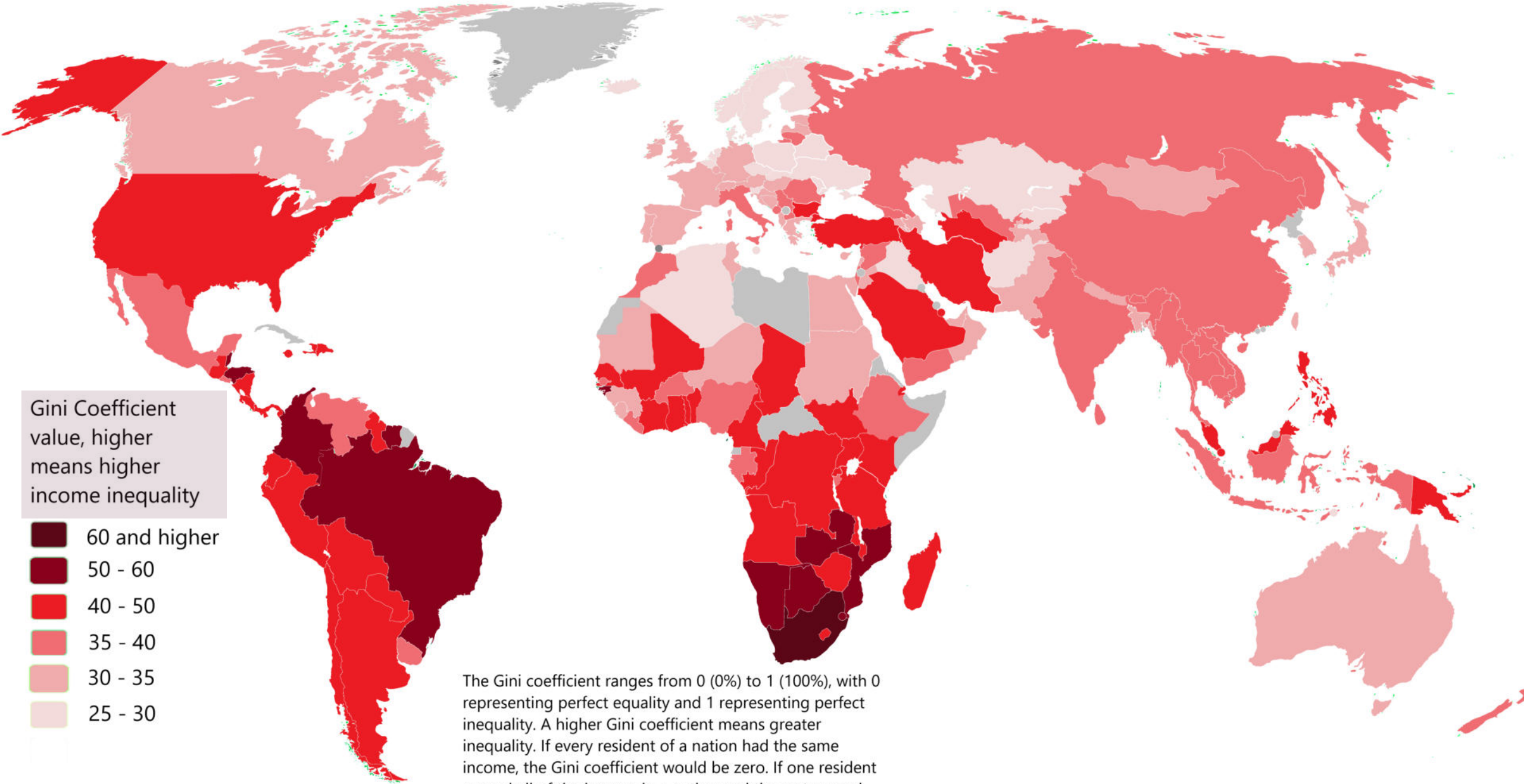
Challenging the status quo: (some) recent research on diagnosing tuberculosis using new technologies

31st Tuberculosis Symposium

1 June 2023

Grant Theron | gtheron@sun.ac.za | CLIME group

Professor, DSI-NRF Centre of Excellence for Biomedical Tuberculosis Research; South African Medical Research Council Centre for Tuberculosis Research; Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa



The Gini coefficient ranges from 0 (0%) to 1 (100%), with 0 representing perfect equality and 1 representing perfect inequality. A higher Gini coefficient means greater inequality. If every resident of a nation had the same income, the Gini coefficient would be zero. If one resident earned all of the income in a nation and the rest earned zero, the Gini coefficient would be 1.

ACKNOWLEDGING A TEAM EFFORT

FIND

(from whom some slides are adapted)

GROUP OVERVIEW

CLIME (CLInical Mycobacteriology and Epidemiology)

- ~50 trainees and staff headquartered at the Medical Campus recruiting **30-50 people a week** from four primary care facilities and two hospitals
- Three focus areas:
    1. **Diagnosis**
        a) **TB**
        b) **Drug Resistance**
    2. Infectiousness and transmission
    3. Microbiome
- *Our mission is to find **simple and translatable solutions** to improve the lives of people suffering from TB **through excellence in research and training***

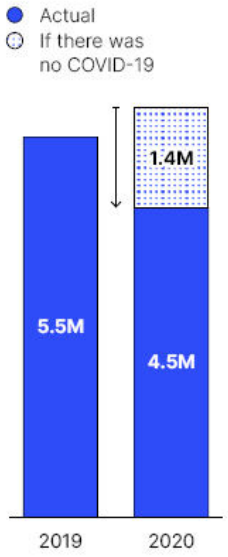
WHY (RE)-FOCUS ON DIAGNOSTICS?

COVID-19 undid a decade's progress in our fight against TB

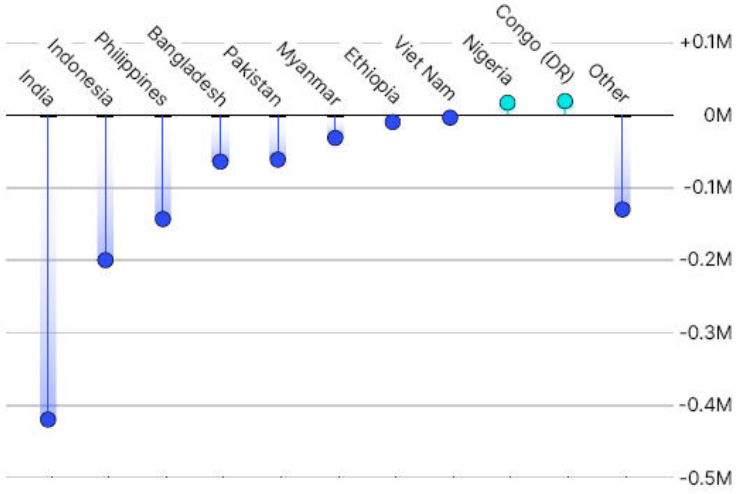
People treated for TB

Change, 2019-2020

By **portfolio**

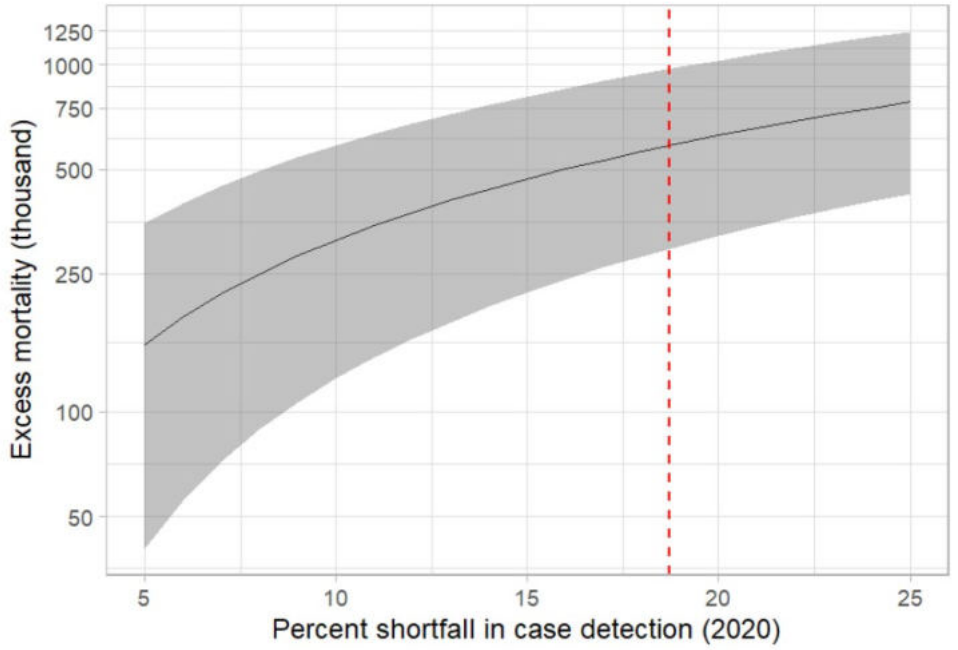


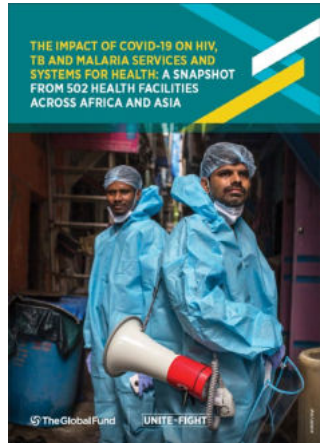
By **country** (10 countries with largest share of results in 2019)



The 'If there was no COVID-19' estimates are based on grant targets adjusted by grant performance prior to COVID-19. The country graphs include countries with comparable results in both years, therefore, the total results in 2019 and 2020 might be slightly lower than the total number of services seen in the other parts of this report and in the online platform.

Estimated excess TB mortality globally





WHY (RE)-FOCUS ON DIAGNOSTICS?

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

….but we were already bad at diagnosing TB

- Of annual 10M cases, 4.1M undiagnosed
- 1 in 3 TB patients bacteriologically confirmed
- 1 in 5 TB patients diagnosed with a WHO-recommended molecular test
- 1 in 3 with DR-TB are tested and put on relevant treatment

And existing tools are inadequate

- 50% of TB in people who do not meet symptom thresholds for confirmatory testing
- No good tools that can be done at primary care, where most people present but infrastructure is weak
- Overreliance on sputum

TALK OVERVIEW

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

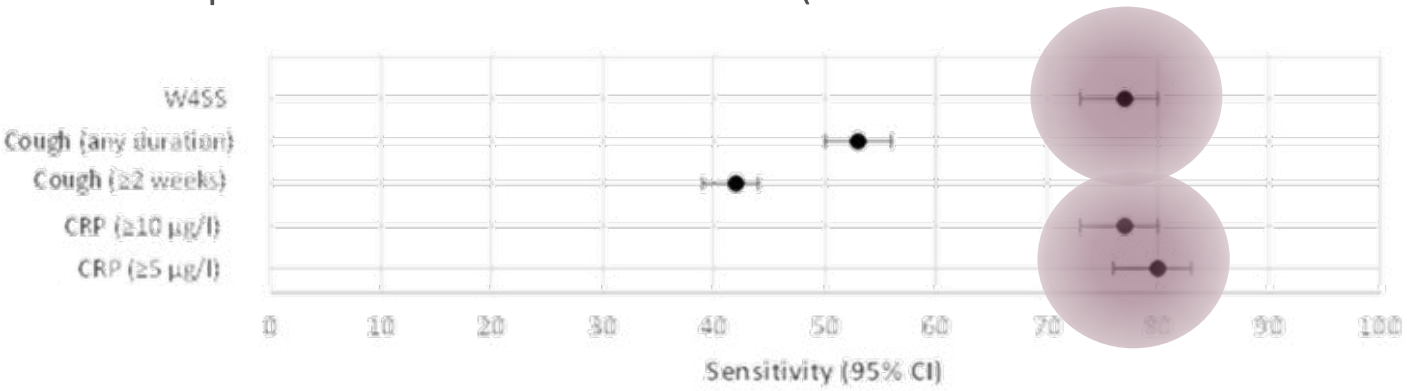
Diagnostics

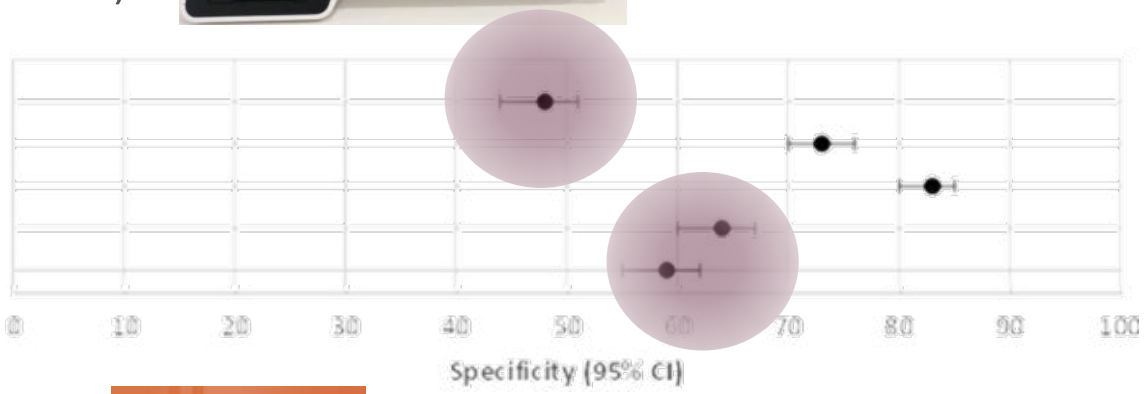
- CRP and RNA for triage of ART-initiators without syndromic preselection
- PREdicting the Future of Incipient Tb (PreFIT) in exposed contacts
- Machine-learning-based cough audio-based testing for TB
- Cough Audio TriaGE for TB (CAGE-TB)
- Something from nothing: Use of Xpert MTB/RIF Ultra on contaminated cultures
- Emergence of bedaquiline resistance in patients with complex treatment histories
- Tongue and breath tests
- AI-based dCXR
- Diagnostic yield

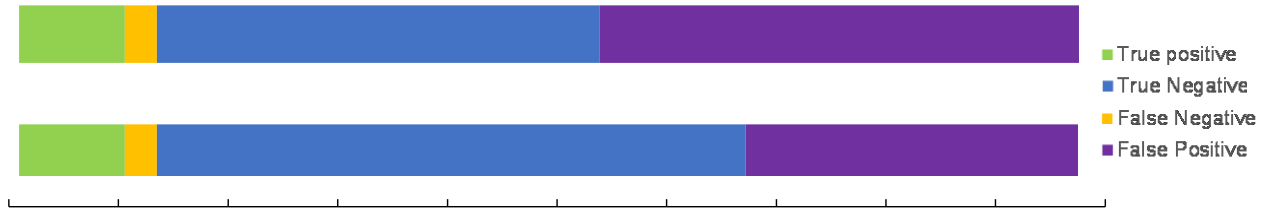
ALTERNATIVES TO SYMPTOMS

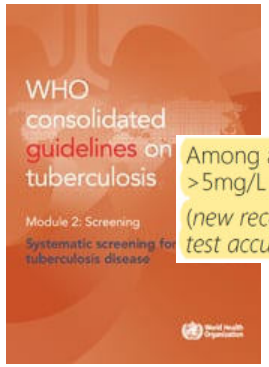
POC C-reactive protein is superior to symptoms as a triage

- ART-initiators tested for TB irrespective of symptoms
- Sputum induction done (double culture ref. standard)







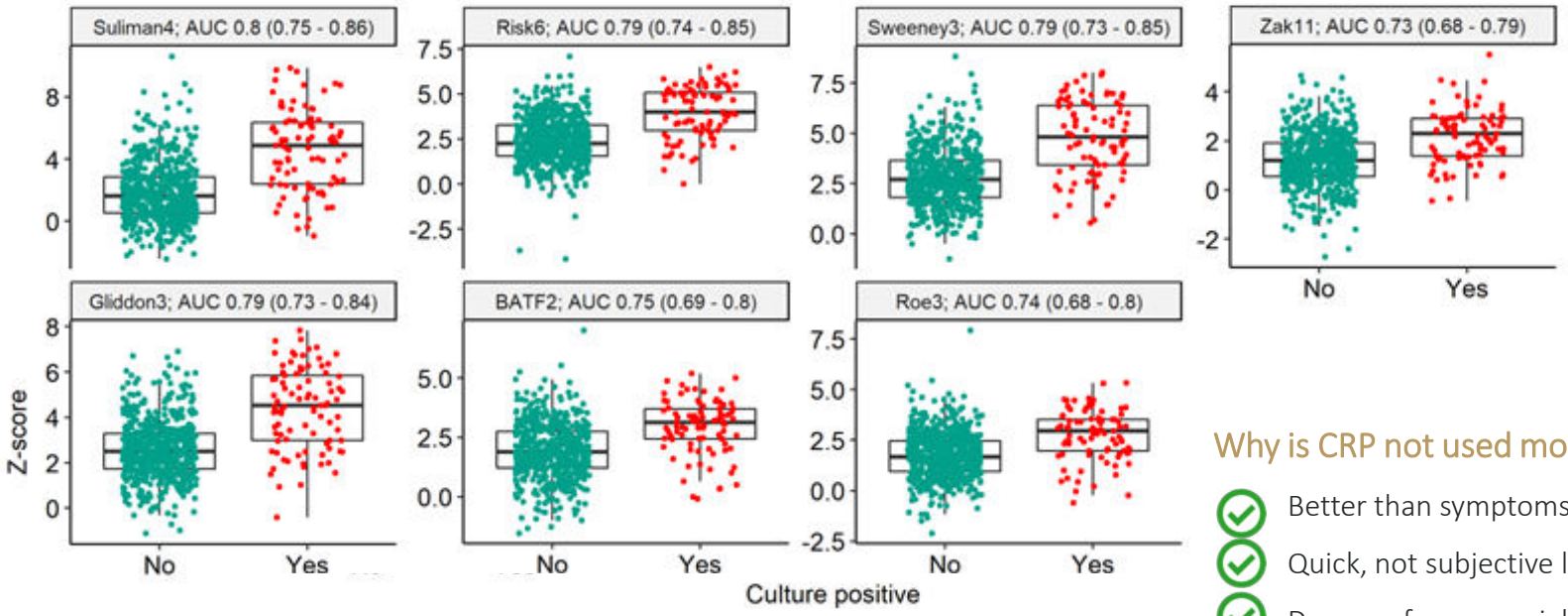


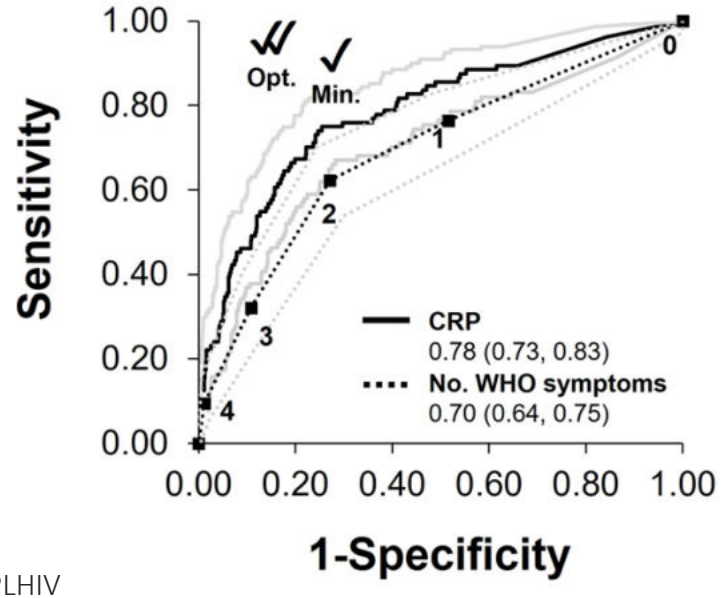
Among adults and adolescents living with HIV, C-reactive protein using a cut-off of >5mg/L may be used to screen for TB disease

(new recommendation: conditional recommendation, low certainty of evidence for test accuracy).

NOVEL TRIAGE TOOLS

Host RNA signatures do not outperform CRP





Why is CRP not used more?

- Better than symptoms in PLHIV
- Quick, not subjective like symptoms
- Dozens of commercial devices, many handheld and can be done at POC
- WHO endorsement
- No other biomarkers likely to beat it in short term. New biomarkers must always be evaluated vs. existing tools
- High burden countries failing to implement CRP <u>one year</u> after WHO guidance issued

ONE POSSIBLE USE CASE FOR HOST RNA SIGNATURES?

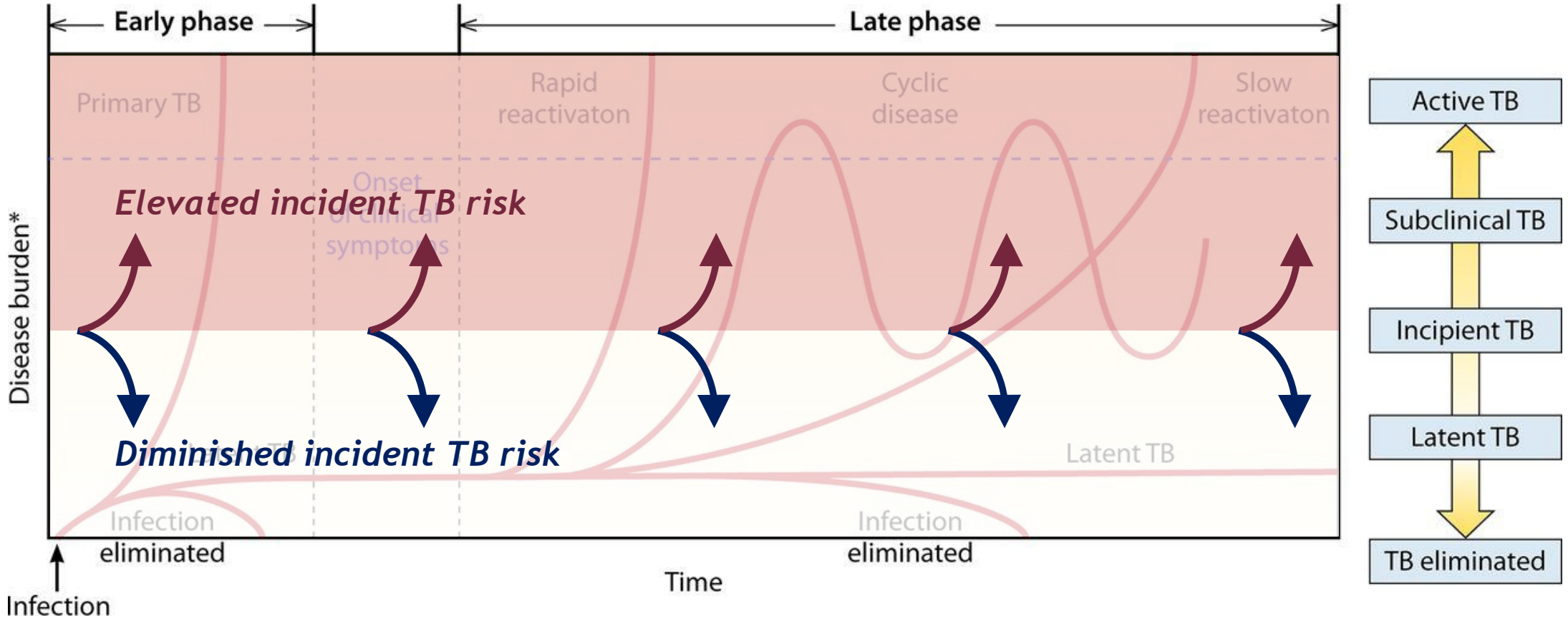
Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

Predicting future TB in contacts of people with TB

PreFIT
Predicting the Future: Incipient TB

EDCTP

Predicting future TB in contacts of people with TB

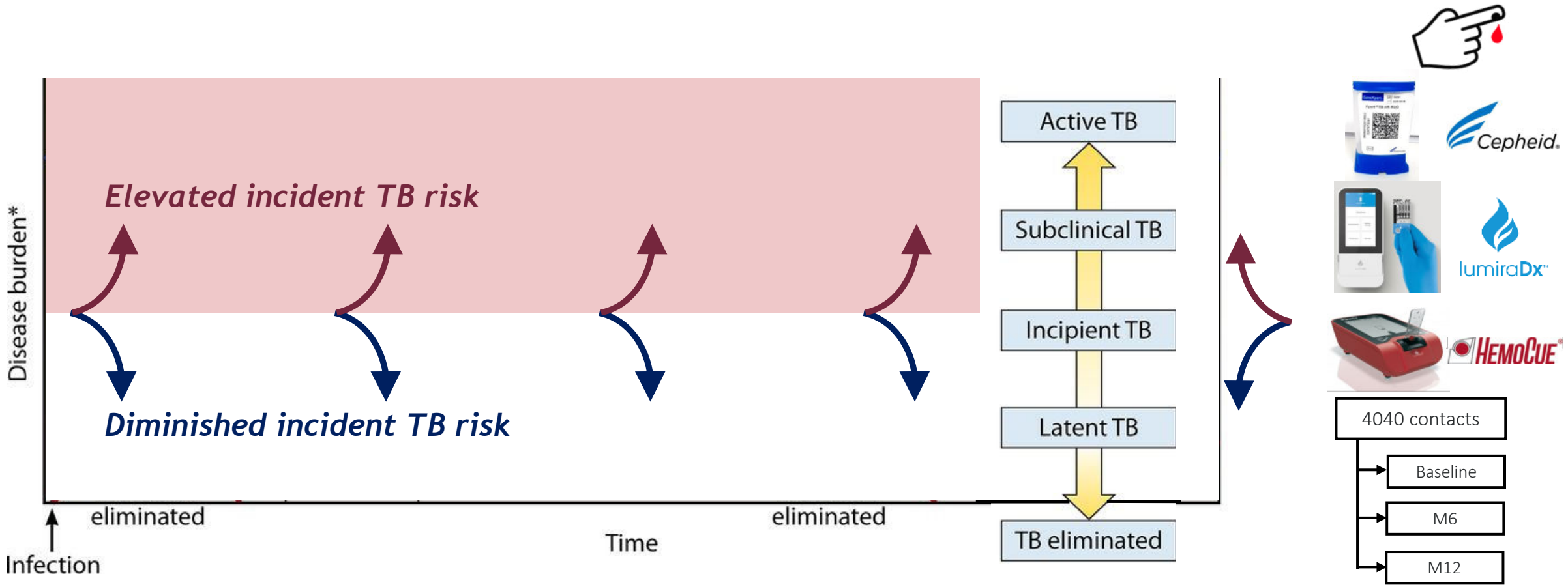


PMC6148193

PreFIT
Predicting the Future: Incipient TB

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

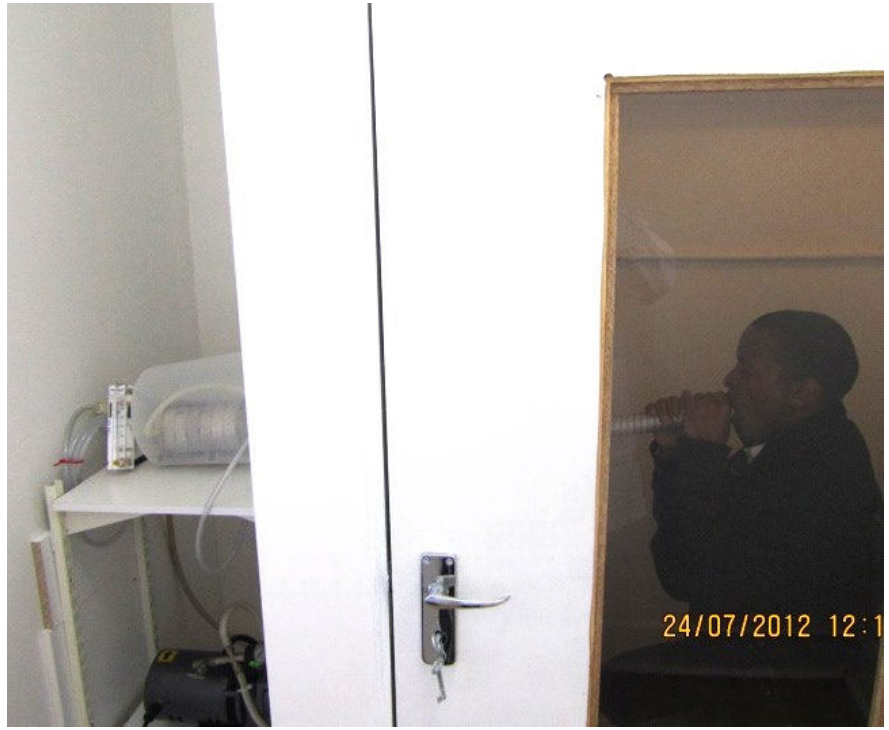
Predicting future TB in contacts of people with TB

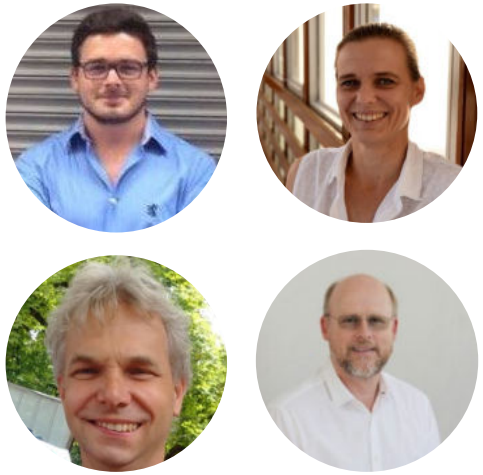


COUGH AUDIO: AN IDEAL BIOMARKER?

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

TB cases have a different sounding cough to healthy people

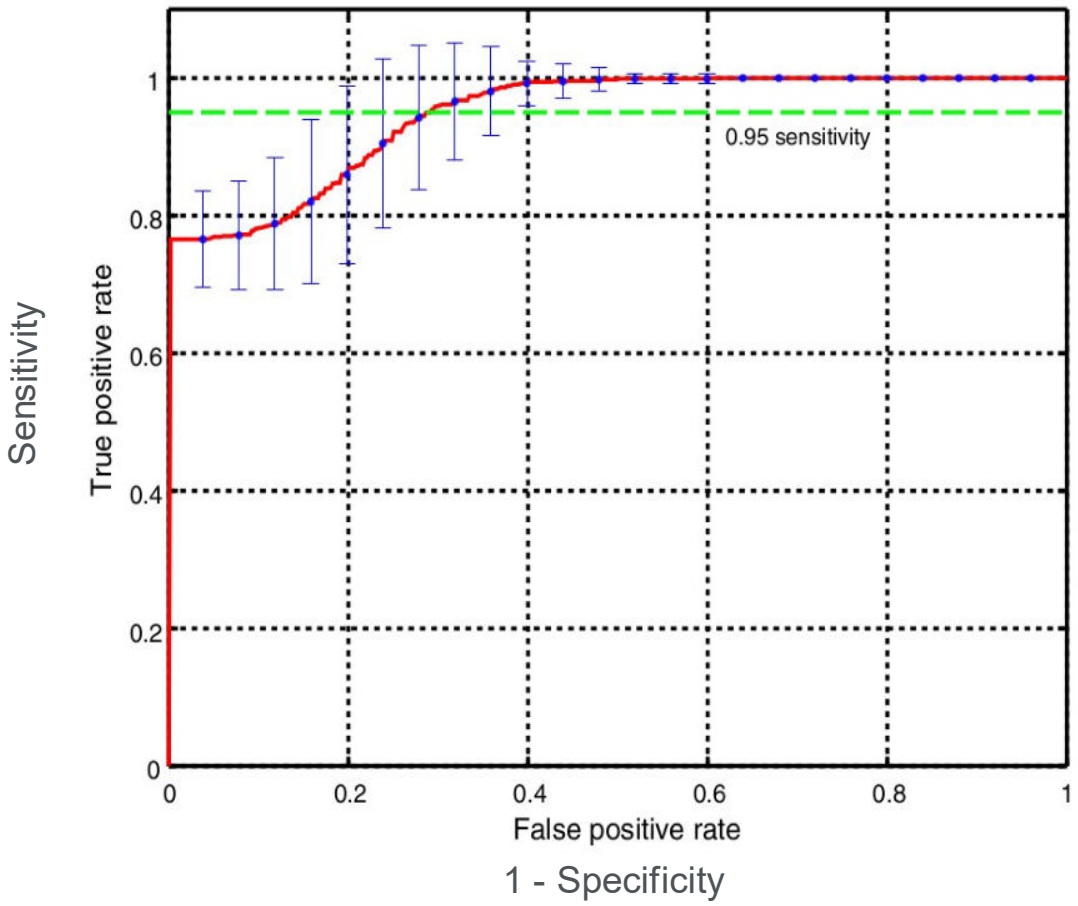


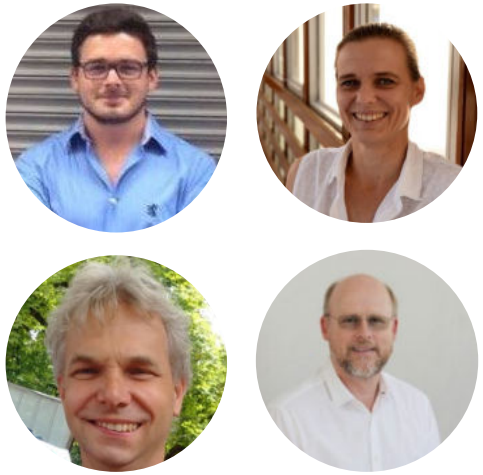


COUGH AUDIO

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

TB cases have a different sounding cough to healthy people





10.1088/1361-6579/aab6d0

COUGH AUDIO

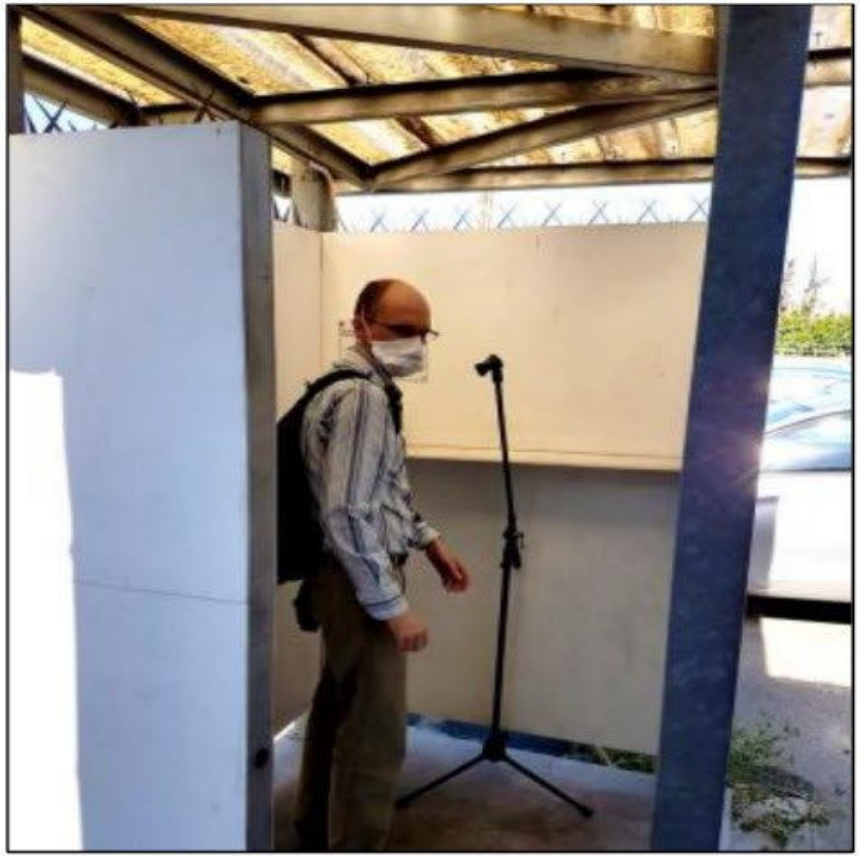
Can cough audio rapidly triage people for confirmatory testing in a real-world setting?

- People with presumptive TB sampled in a clinic (noisy) sputum induction enclosure at primary care using a brief forced cough
- Done by minimally trained community health workers
- Sputum culture reference standard

COUGH AUDIO

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

Can cough audio rapidly triage people for confirmatory testing in a real-world setting?

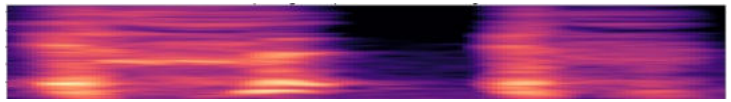


COUGH AUDIO AT THE CLINIC

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

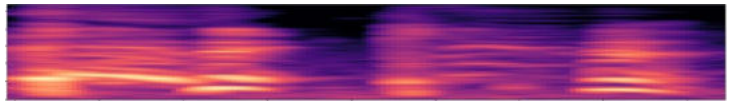
People with TB have a different sounding cough to sick people

Cough audio spectrograms:

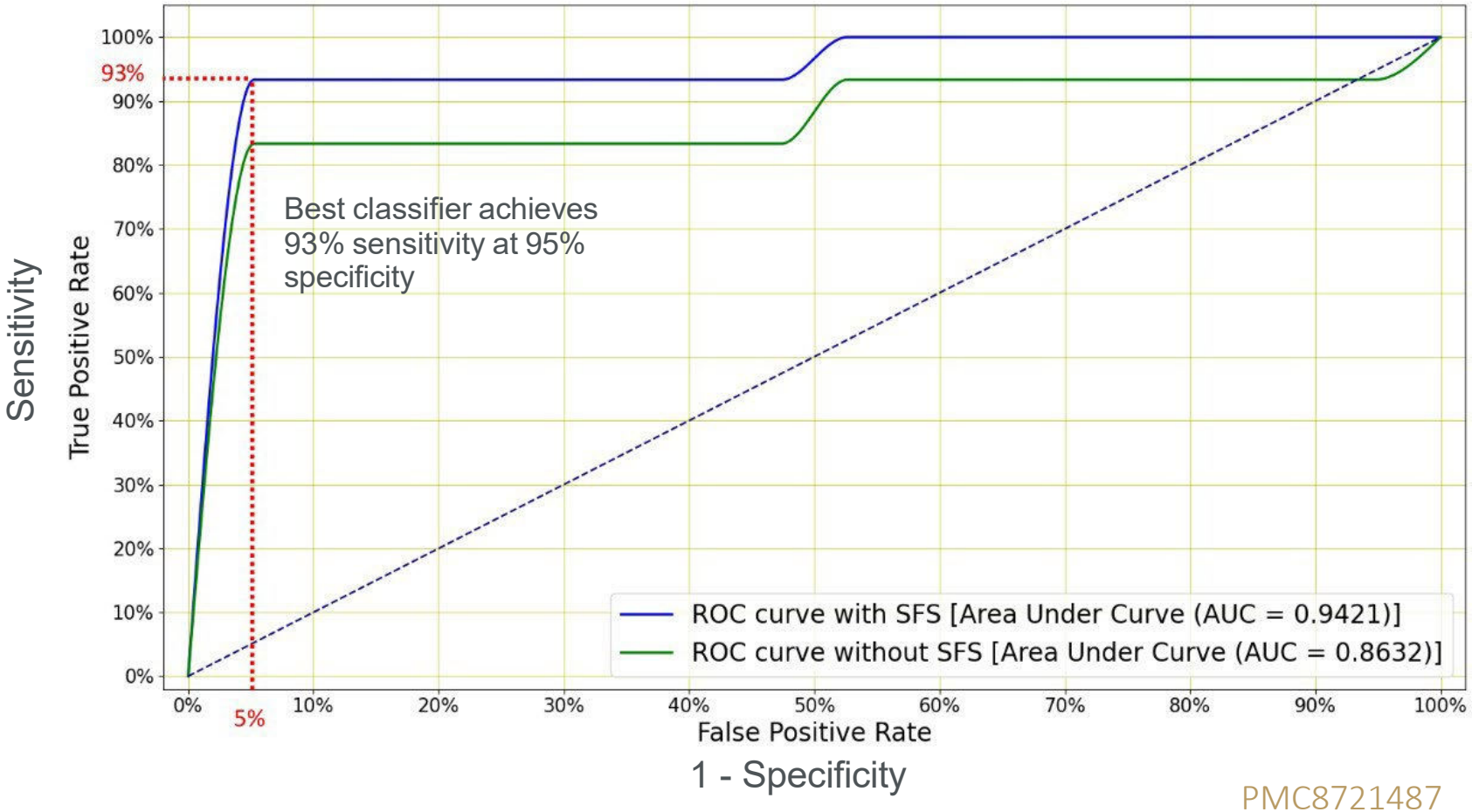


TB

Sick but non-TB



COVID-19



PMC8721487

COUGH AUDIO TRIAGE FOR TB study

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

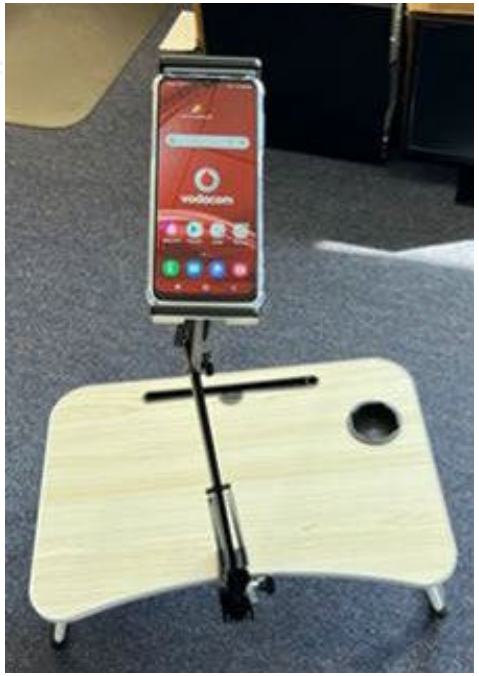
CAGE TB

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

MAKERERE UNIVERSITY

aighd

UNIVERSITÄT GÖTTINGEN



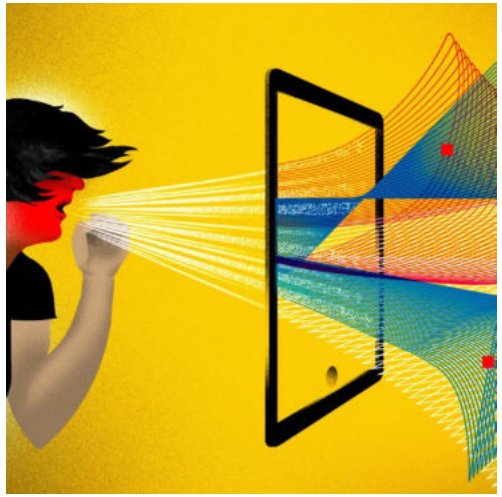
EDCTP

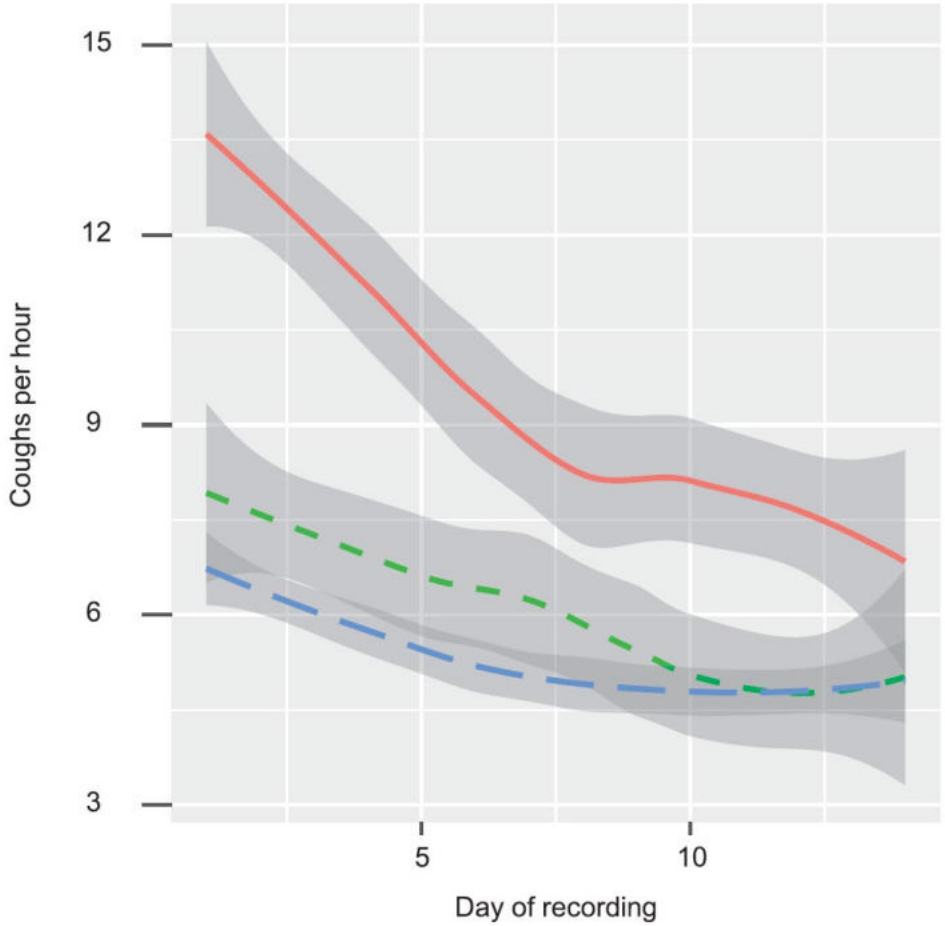
This project is part of the EDCTP2 programme supported by the European Union.

MORE COUGH AUDIO (R2D2)

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

Continuous cough monitoring for diagnosis and treatment response





Diagnosis

Confirmed TB (*n* = 144)

Clinical TB (*n* = 48)

Other respiratory diseases (*n* = 373)

NIH

R2D2 TB Network

PMC9983626

RESCUING DIAGNOSES FROM CONTAMINATED CULTURES

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

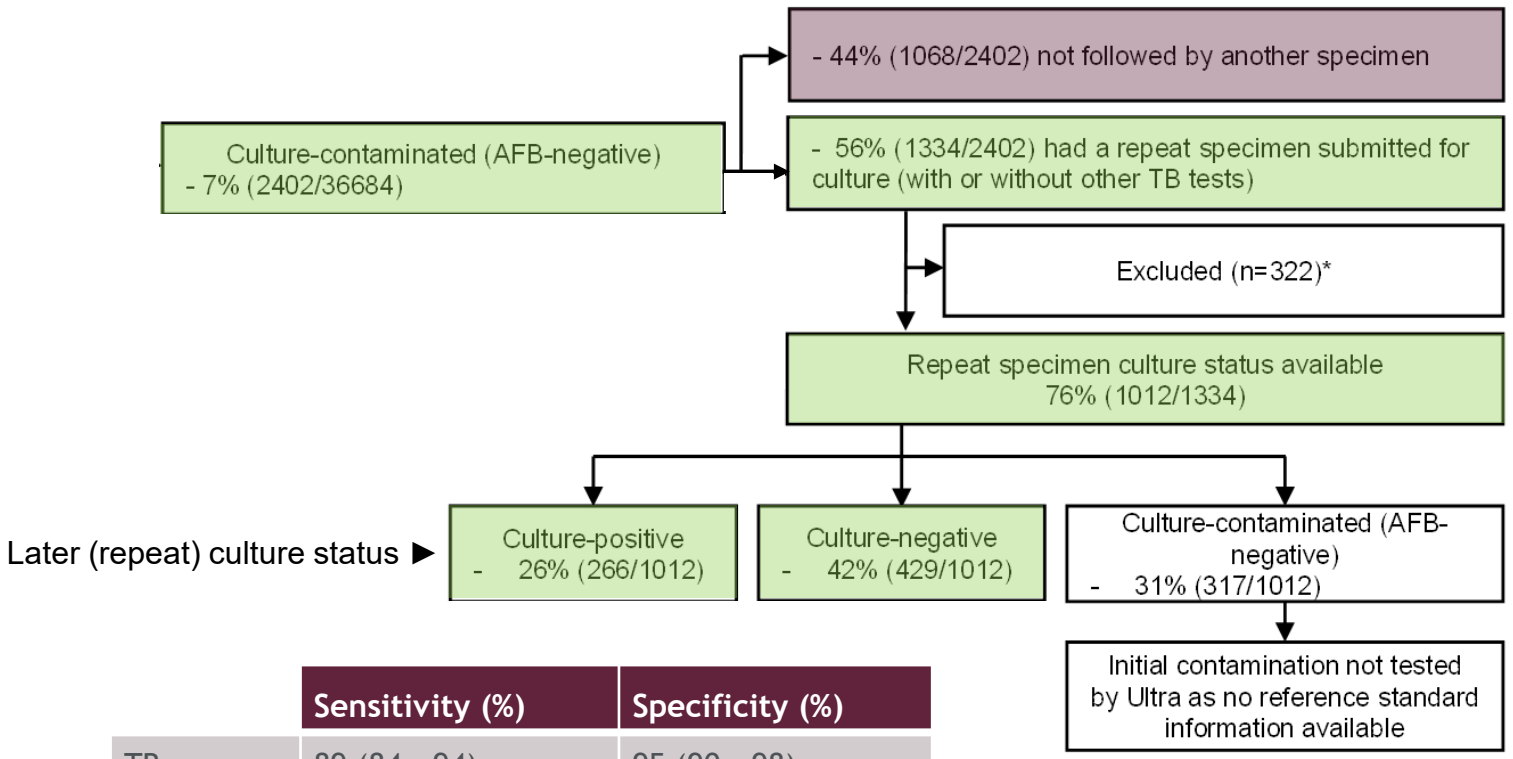
Xpert on to-be-discarded contaminated MGIT960 tubes

- Xpert MTB/RIF Ultra is **widely used on specimens**
- MGIT960 liquid culture is often used as a **diagnostic test** (e.g., PLHIV who test Xpert-negative)
- **Culture-contamination is a common problem** in under-resourced settings
- Growth positive MGIT960 tubes are checked for acid fast bacilli and, if negative, that specimen is **abandoned** and **another specimen is requested**
- This creates **diagnostic care cascade loss and delay**
- Can a molecular test **accurately detect** ***Mtb*** in acid fast negative but growth positive MGIT960 tubes?

RESCUING DIAGNOSES FROM CONTAMINATED CULTURES

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

High diagnostic accuracy of Xpert on contaminated cultures

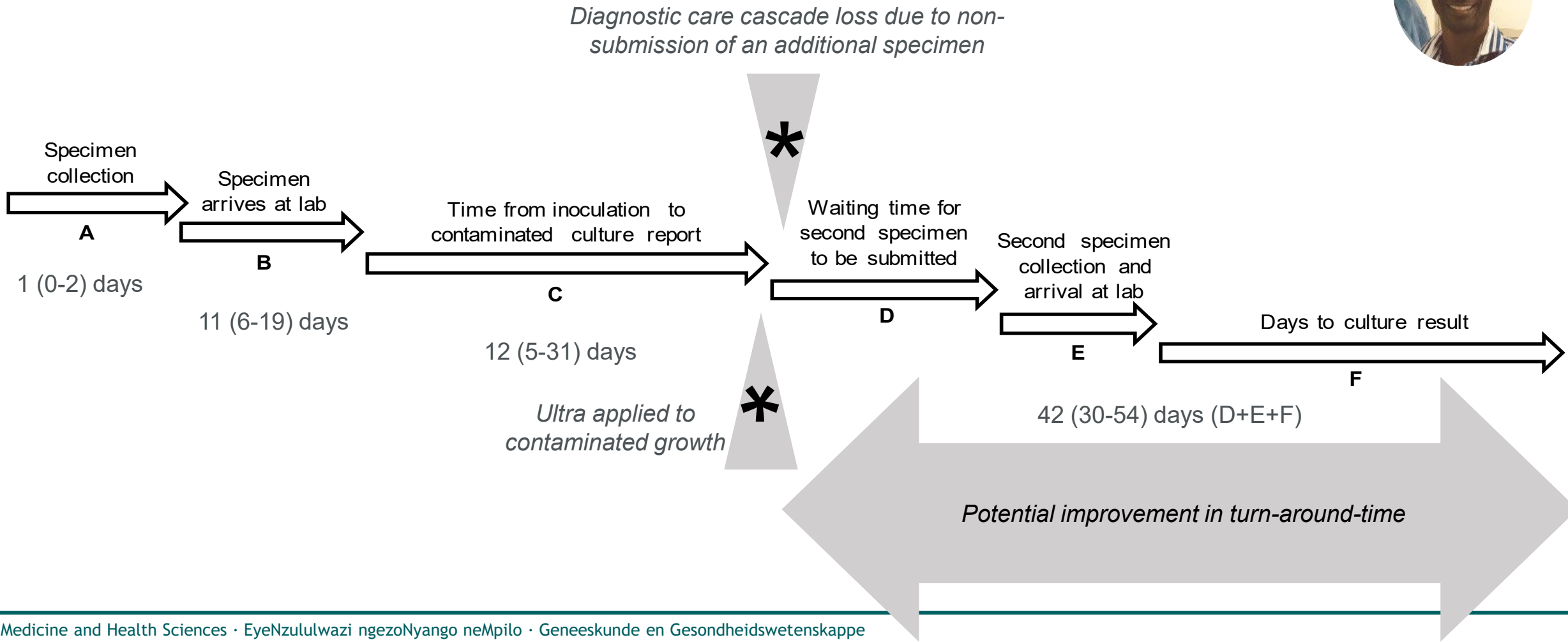


	Sensitivity (%)	Specificity (%)
TB	89 (84 - 94)	95 (90 - 98)
Rifampicin resistance	95 (75 - 100)	98 (93 - 100)

NATIONAL HEALTH LABORATORY SERVICE

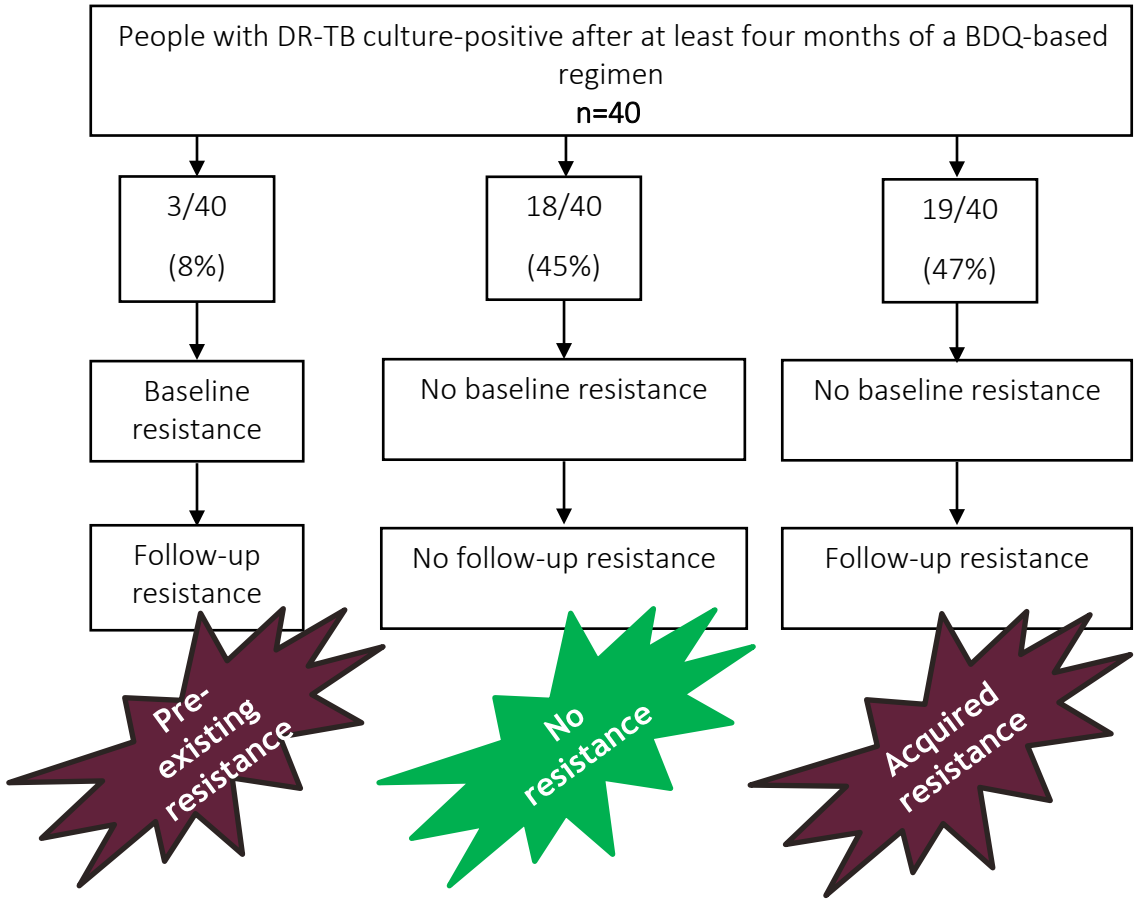
RESCUING A DIAGNOSIS FROM A CONTAMINATED CULTURE

Care cascade improvements



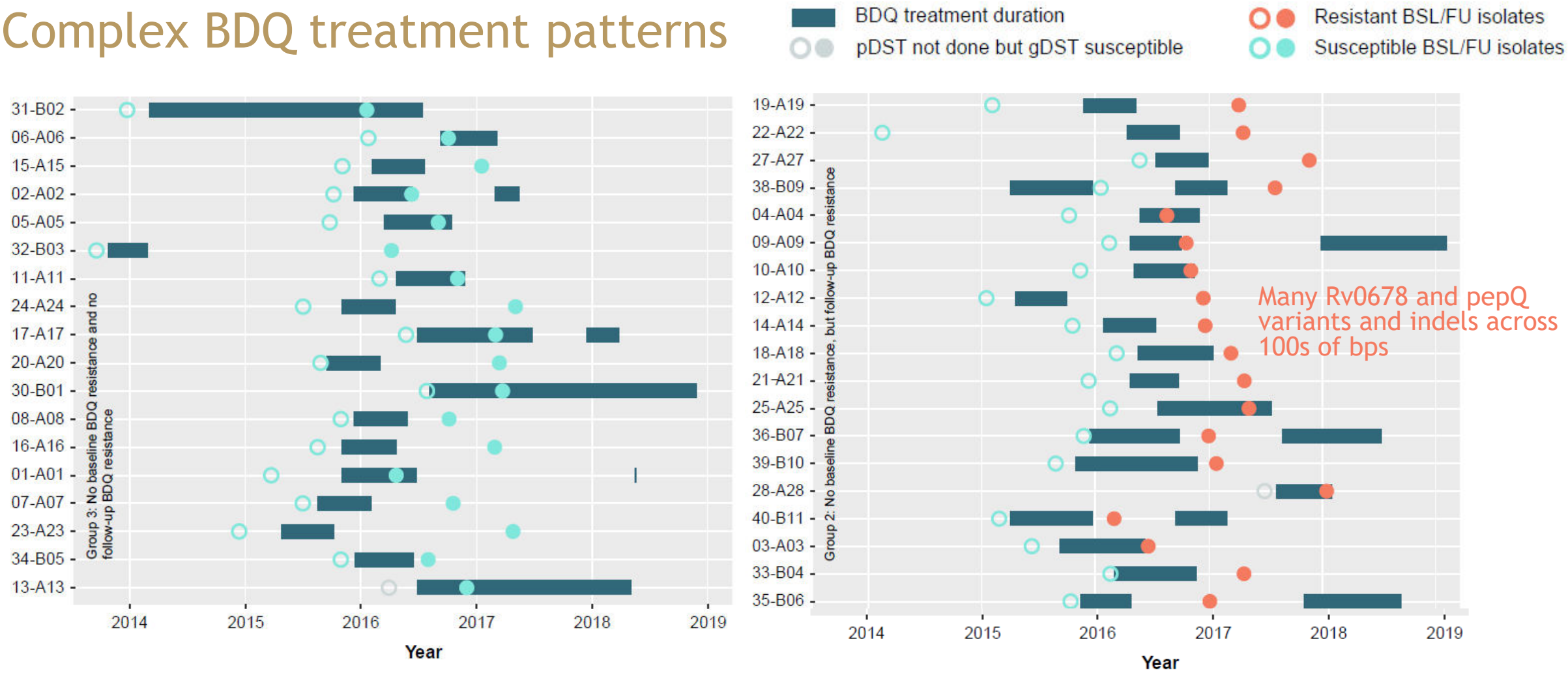
DIAGNOSIS OF BEDAQUILINE RESISTANCE

Patients with second-line resistance and sustained culture-positivity



DIAGNOSIS OF BEDAQUILINE RESISTANCE

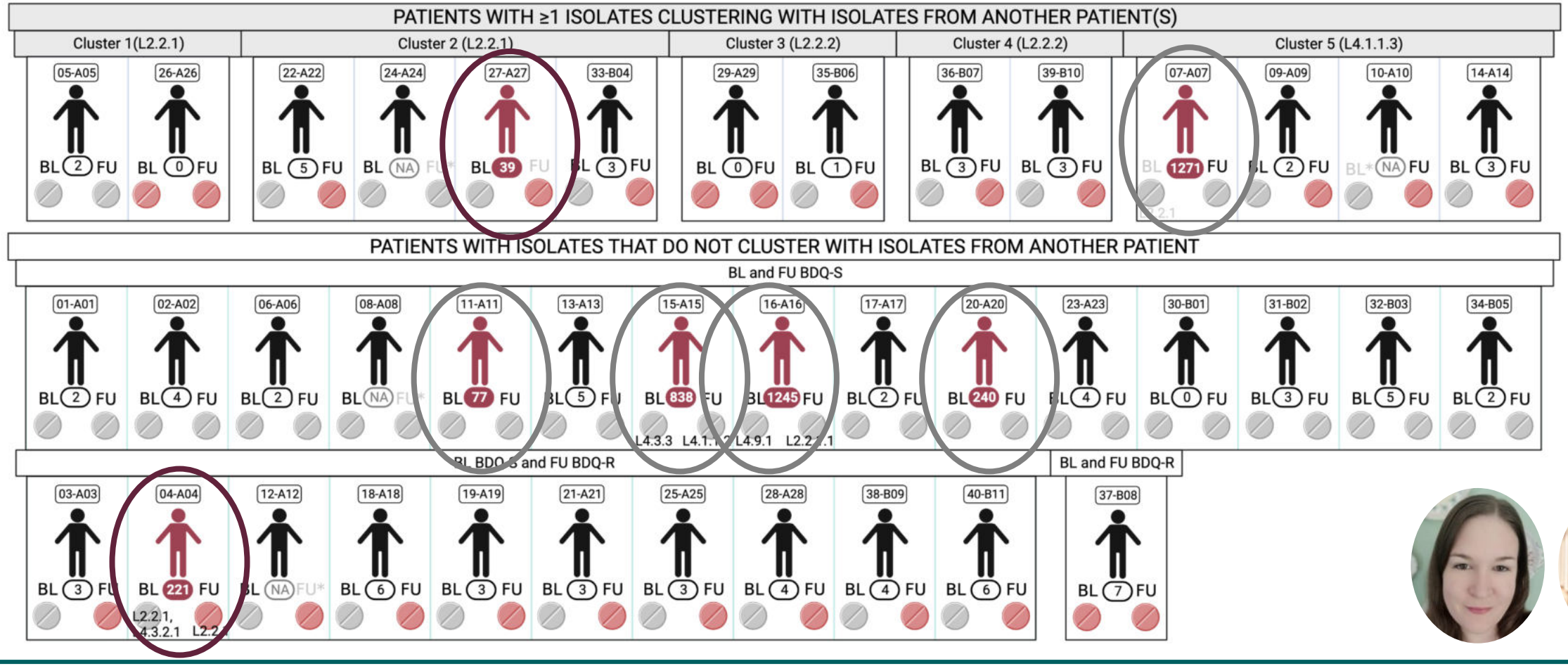
Complex BDQ treatment patterns



BEDAQUILINE RESISTANCE

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

Transmission and reinfection by bedaquiline resistant strains



TONGUE SWABS

Non-invasive and sputum-free

- Scrape tongue dorsum ~5 seconds, eject swab head into transport buffer (or dry)
- Sample = bacterial biofilm, host cells
  - Not saliva
- Tongue swabbing better than other oral sites (Luabeya et al, 2019; Church et al, in preparation)
- Detect *M. tuberculosis* DNA by qPCR or other methods
- Anyone can be sampled in seconds
  - Easy self-sampling
  - TB symptoms (sputum production) not required

TONGUE SWABS

Non-invasive and sputum-free

Tongue swab Ultra, Method 2 (N=183) trace+ for all		
	Sputum Xpert	**Microbiologic reference standard***
Sensitivity	77.8 (64.4-88.0)	73.4 (59.1-83.3)
Specificity	100 (97.2-100)	100 (96.9-100)

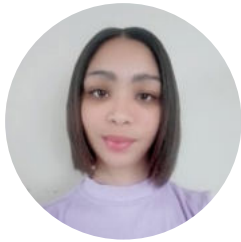
10.1101/2022.02.17.22271147

		Sputum MGIT culture		
		Positive	Negative	Total
Foam tongue swab Ultra N = 10	Positive	9	0	9
	Negative	0	0	0

Sensitivity: 100%

		Sputum MGIT culture		
		Positive	Negative	Total
FLOQ tongue swab Ultra N = 10	Positive	5	0	5
	Negative	4	0	4

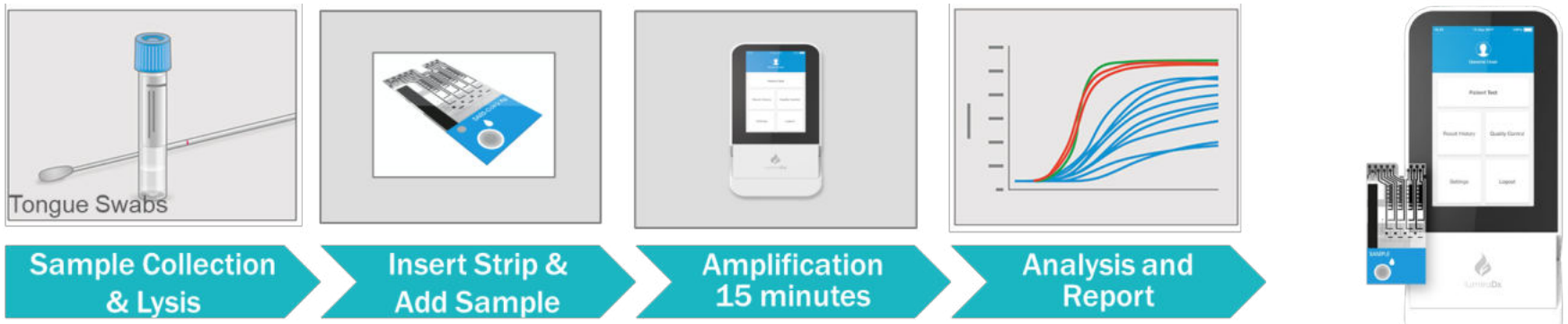
Sensitivity: 56%



TONGUE SWABS

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

LumiraDx TB Molecular: First-in-class swab-based POC detection of TB



LumiraDx Smart Connectivity

- Step-by-step test instructions on screen
- Digital display of results and reporting
- Data analytics and decision support
- Seamless, secure connectivity to the cloud and health IT systems
- Platform launch 2018, in 2021 5k instruments installed in Africa, 20k globally
- TB assay enter policy trial Q1 2023

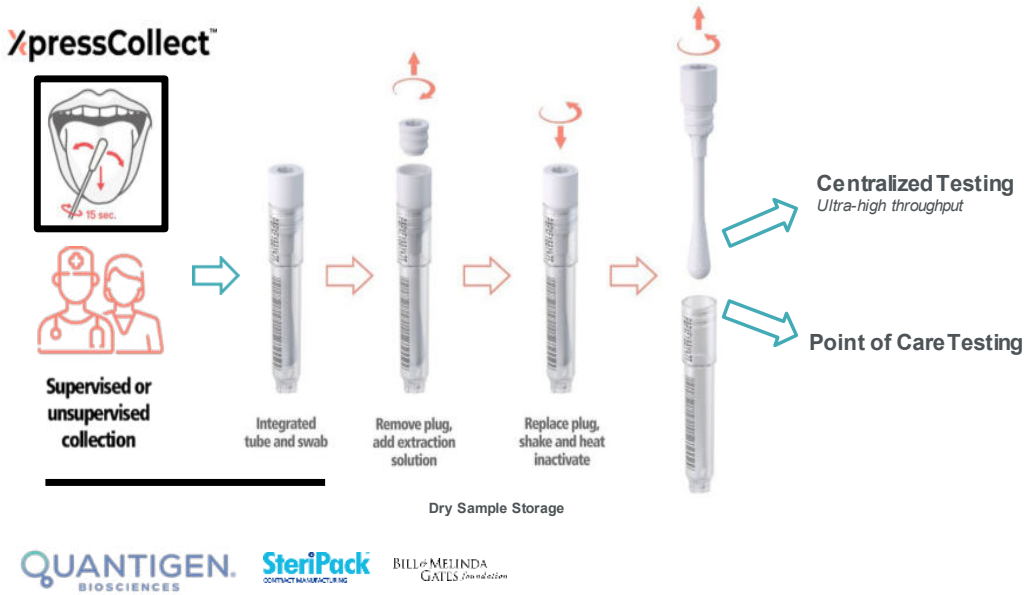
Proprietary process subject to LumiraDx IP protection. Project subject to further development and regulatory approval.

TONGUE SWABS

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

Door-to-door sampling and pooling with high throughput platforms

Tongue swab collection for cDST or POC



QUANTIGEN BIOSCIENCES · SteriPack CONTRACT MANUFACTURING · BILL & MELINDA GATES foundation

Abbott


Abbott *m*2000sp


Abbott *m*2000rt

Hain


GenoXtract®96


FluoroCycler® 96

Fluorotype XDR - in trial

BD


BD MAX™

Roche


Roche: cobas® 8800/6800 System

Bioneer


Bioneer: ExiStation™ Universal MDx System

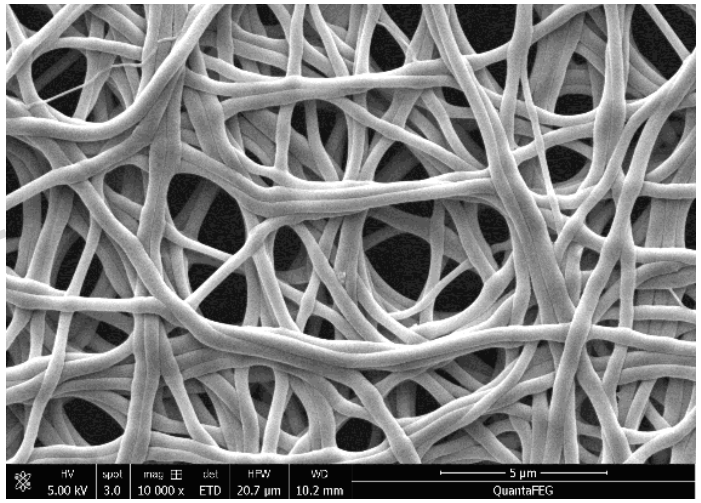
FIND

BIOAEROSOL CAPTURE

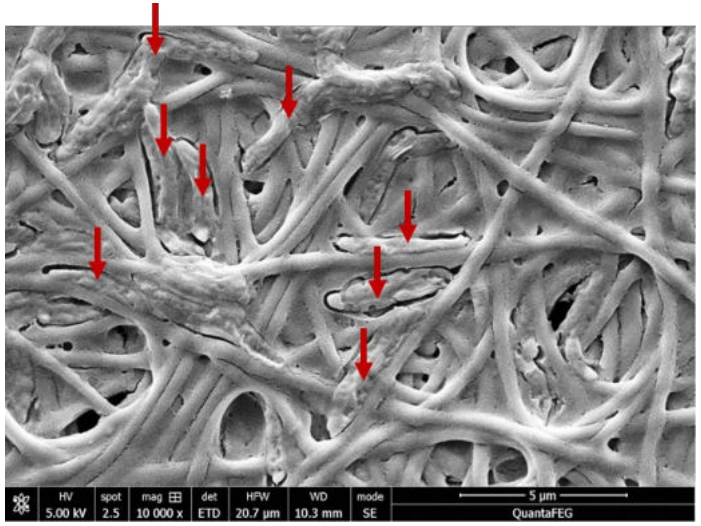
Avelo breath tubes

AveloCollect

Before pathogen collection



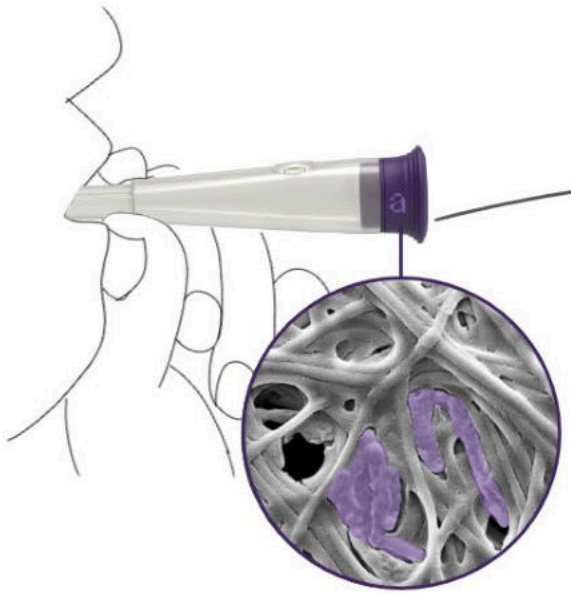
After pathogen collection



BIOAEROSOL CAPTURE

Avelo breath tubes

1. Collect



Cap with Nanofiber Filter Technology (Patent Pending)

2. Dissolve

Standard Lab Tube with Pathogen DNA/RNA

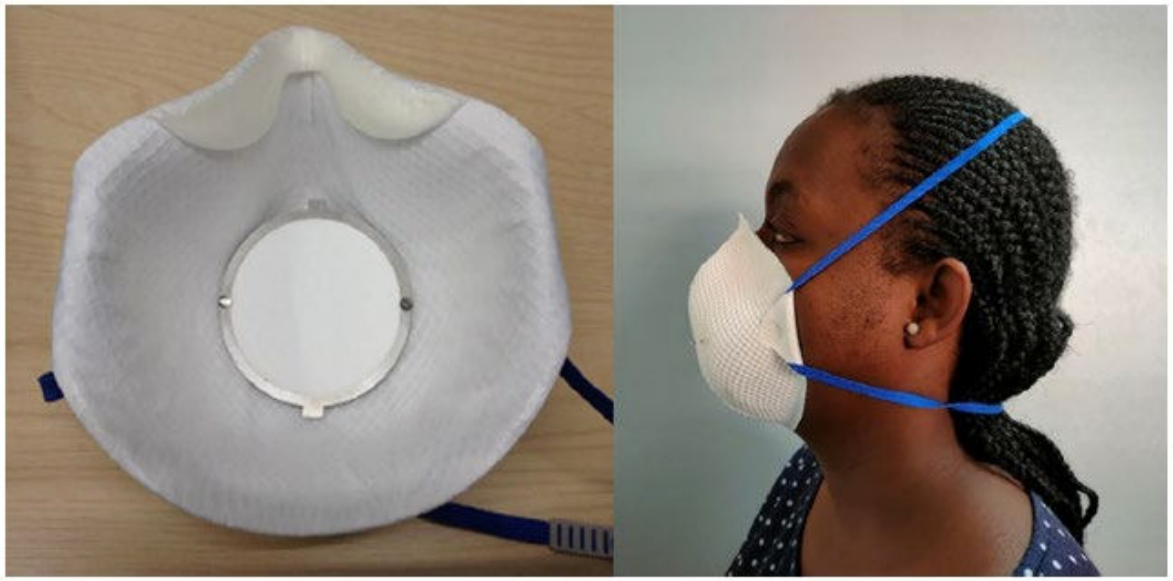
3. Test & Treat

Copyright Cepheid

Standard PCR Test

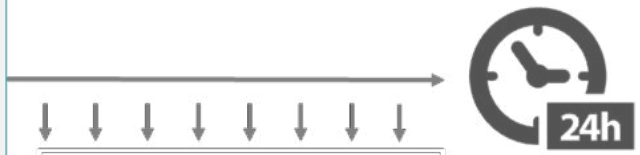
BIOAEROSOL CAPTURE

Facemask sampling



10.1093/cid/ciac455

Pretoria, n=24 micr. conf. in-patients
- 16 Rx naïve
- 6 Rx <24h
- 2 Rx >24h



Mask and sputum every 3h
Total: 192 sampling time points

43 sputum and mask collected at the same time

Sputum \ Mask	+	-	
+	31	7	38
-	5	0	5
	36	7	43

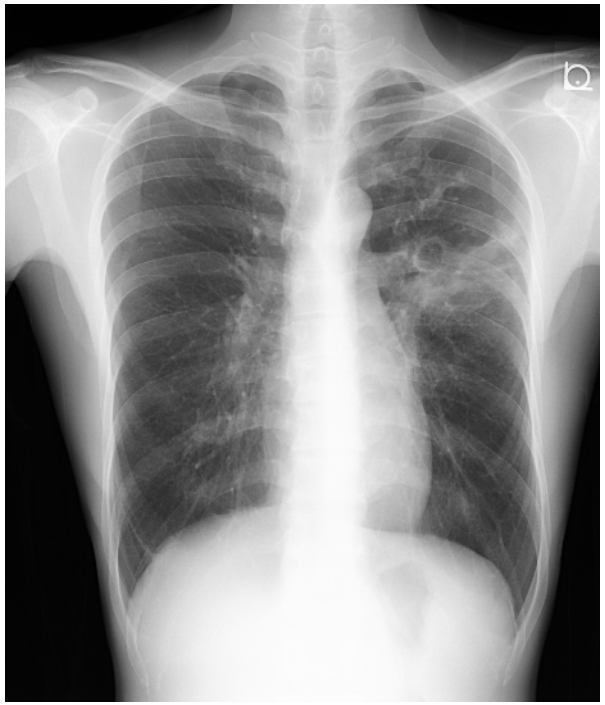
10.1016/S1473-3099(19)30707-8

AI-BASED DIGITAL CXR

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

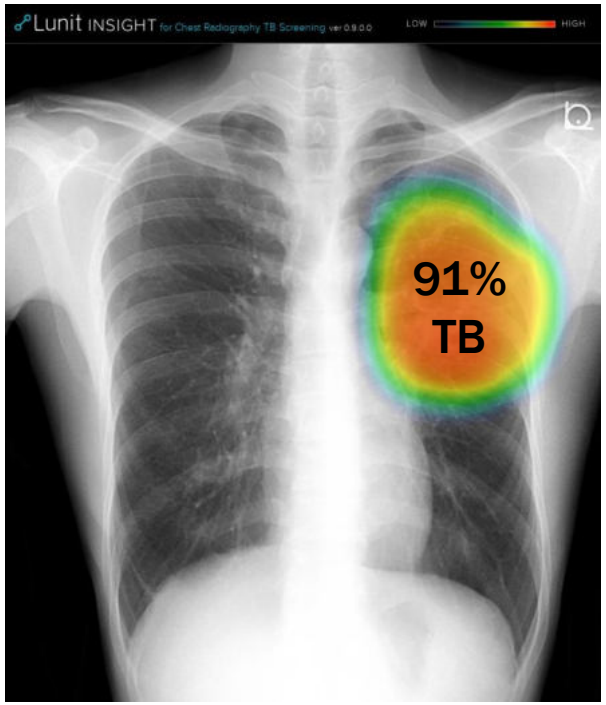
Highly sensitive, permitting subclinical TB detection

Input:
Digital AP CXR



AI algorithm

Output:
Abnormality score & overlay

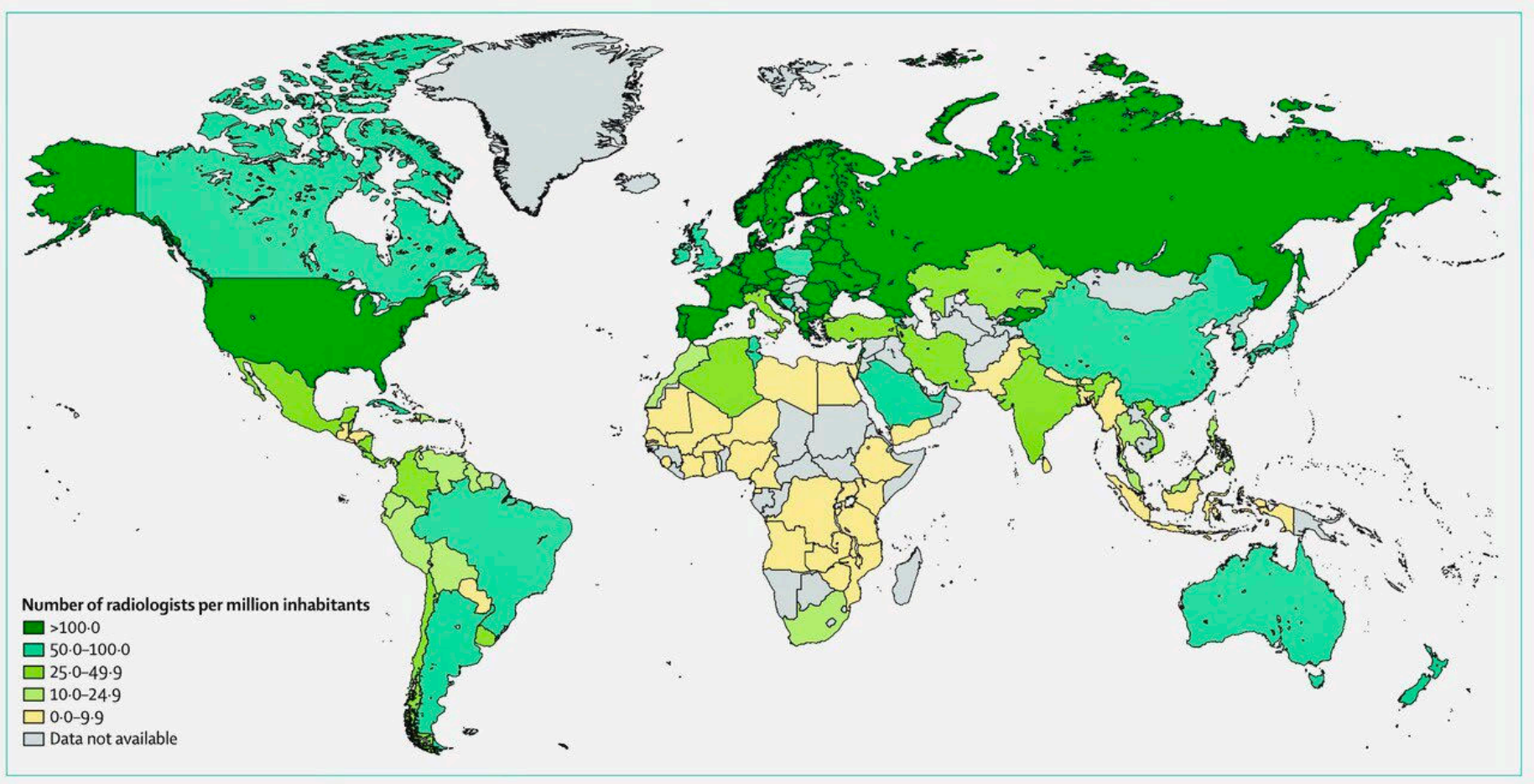


FIND

AI-BASED DIGITAL CXR

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

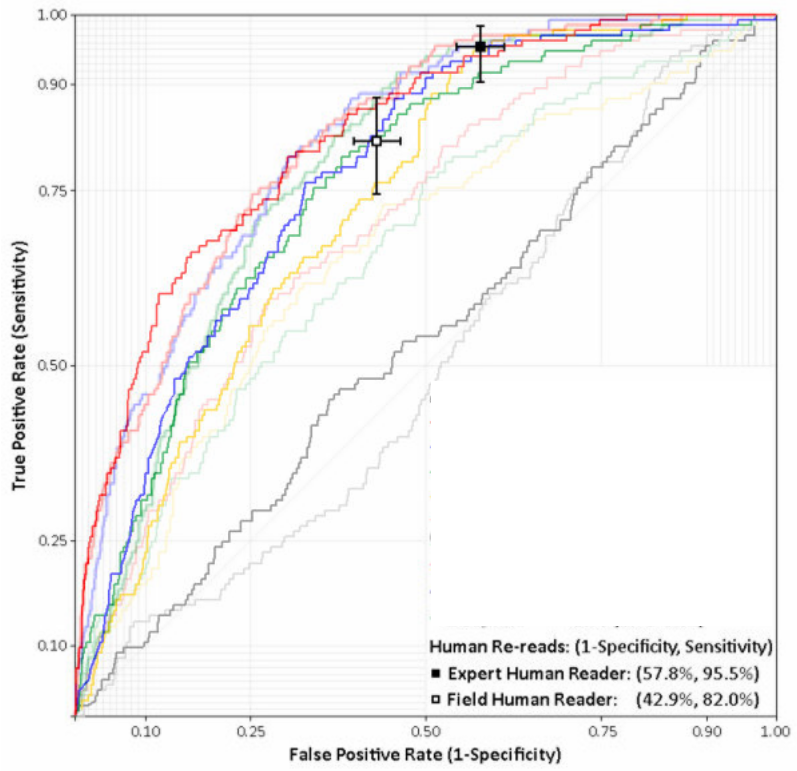
Global shortage of radiologists



AI-BASED DIGITAL CXR

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

(Some) AI's equal the performance of advanced human readers



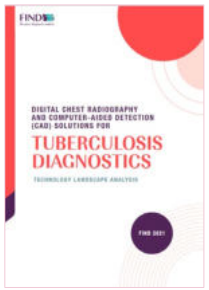
10.1038/s41598-021-03265-0

Study Overview

- X-ray's collected from community ACF in Vietnam (one site)
- 1,032 participants
- 133 TB (Xpert MTB/RIF)
- Compared to human radiologist
  - Expert (>30 yrs experience)
  - Intermediate (5yrs experience)

Findings

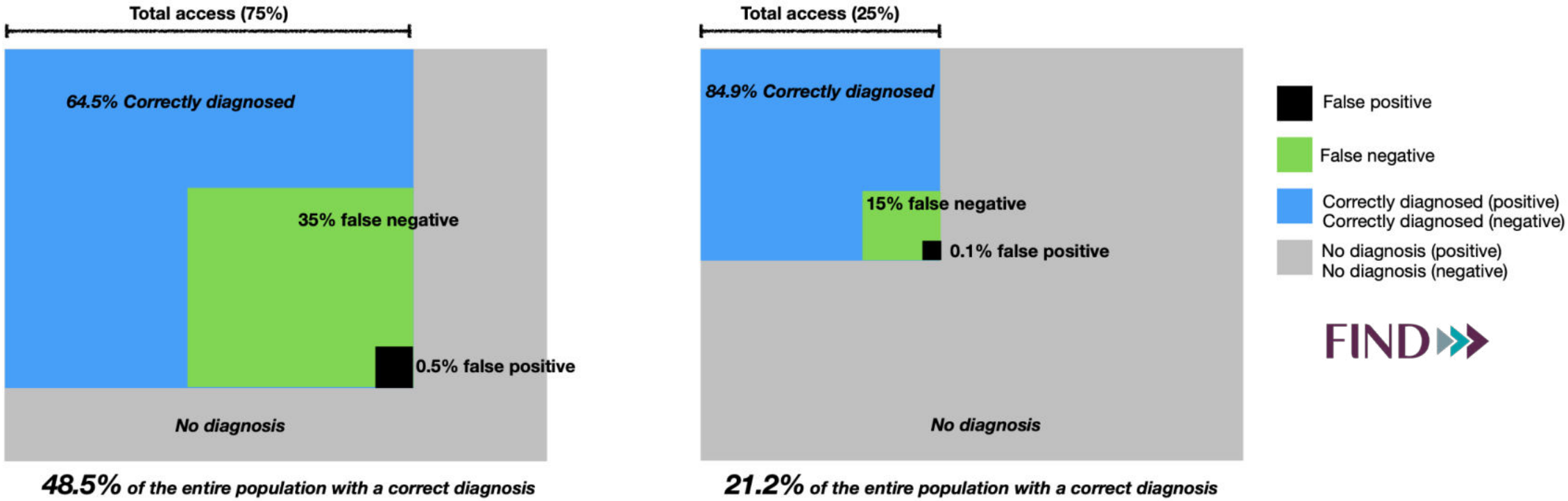
- AUCs 0.82-0.50
- 6 CADs **on-par with Expert** reader (Qure.ai, Delft, DeepTek, Lunit, JF Helatcare, Oxipit)
- 3 CADs **superior to Intermediate** Reader (Qure.ai, Delft, Lunit)



DIAGNOSTIC YIELD

Overly sensitive to sensitivity?

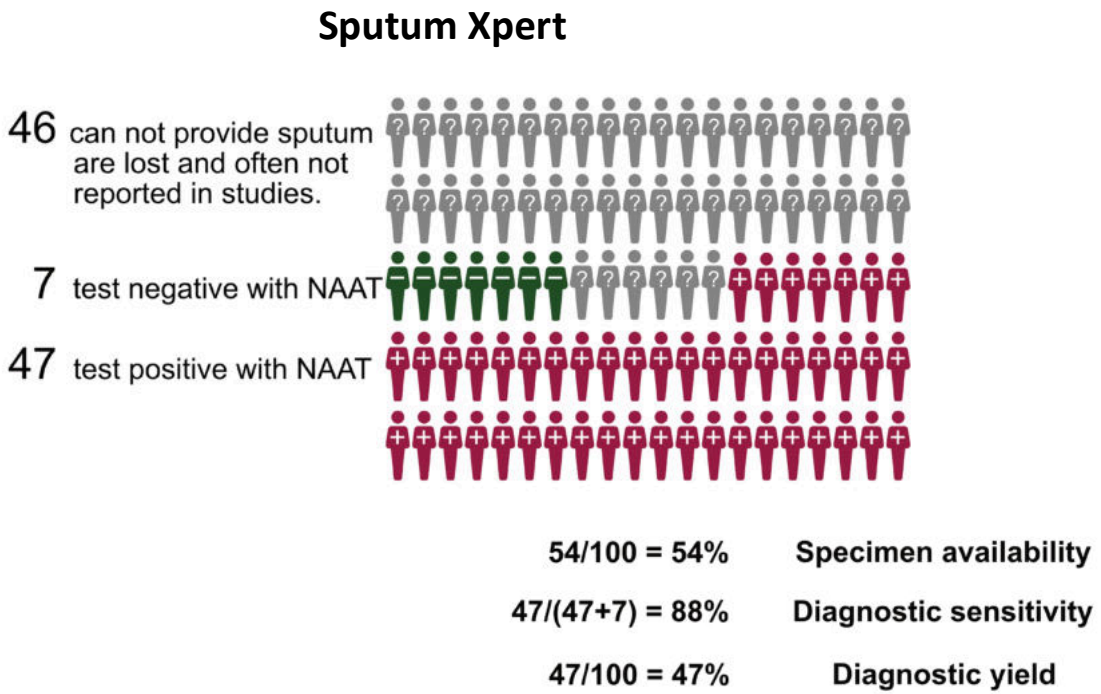
- A less sensitive diagnostic test can be very useful if it has sufficient yield and reaches a large population

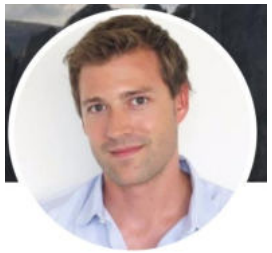


DIAGNOSTIC YIELD

Overly sensitive to sensitivity?

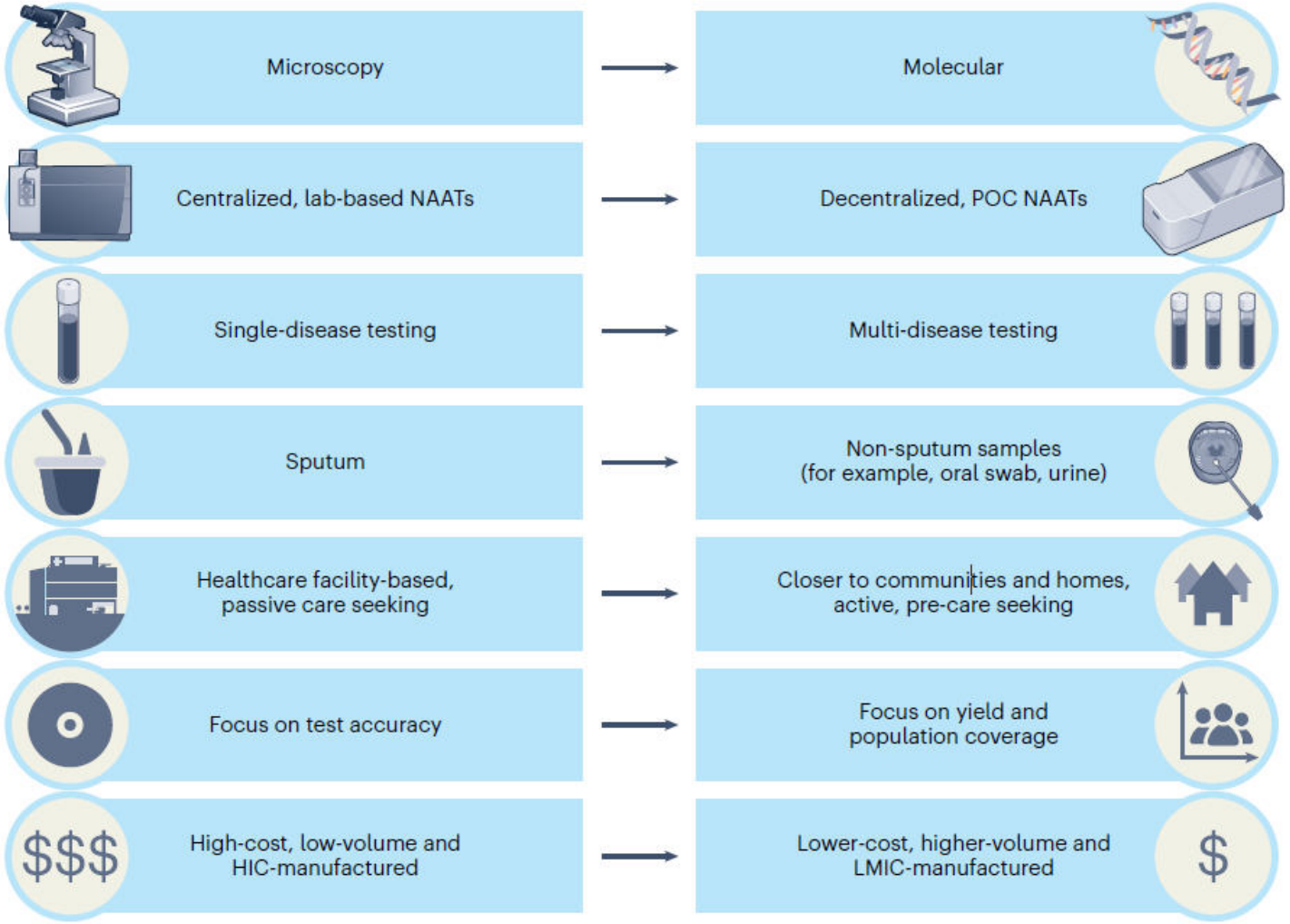
- Amongst all people who had all available confirmatory tests attempted (including if they didn't have a specimen), the proportion positive by a specific test





10.1016/S2214-109X(23)00135-3

TRANSISTIONS TO TRANSFORM DIAGNOSIS?



10.1038/s41564-023-01365-3

OVERALL SUMMARY

- **POC CRP** for facility-based case finding in **PLHIV should be rolled-out**.
- **PreFIT** and **CAGE-TB** are exciting high risk but potentially high reward technologies that could change **how contacts are managed, and how clinic entrants are triaged**
- If you have a **contaminated diagnostic culture**, doing Xpert on it has **high accuracy**
- **BDQ resistance has emerged** in people with weak background regimens and **transmits**. **Rapid DST is a crucial**.
- **Tongue swabs** and **breath sampling** are very promising especially when combined with **high-throughput technologies** are but still early stage
- **AI-assisted CXR is a potential game changer** gaining traction, most needed in Africa
- Diagnostic **yield** can be as important as sensitivity. Do not discount the value of a **less sensitive but more accessible** TB test.

ACKNOWLEDGEMENTS AND THANKS

Stellenbosch UNIVERSITY IYUNIVESITHI UNIVERSITEIT

CLIME

LUNGENLIGA LIGUE PULMONAIRE LEGA POLMONARE

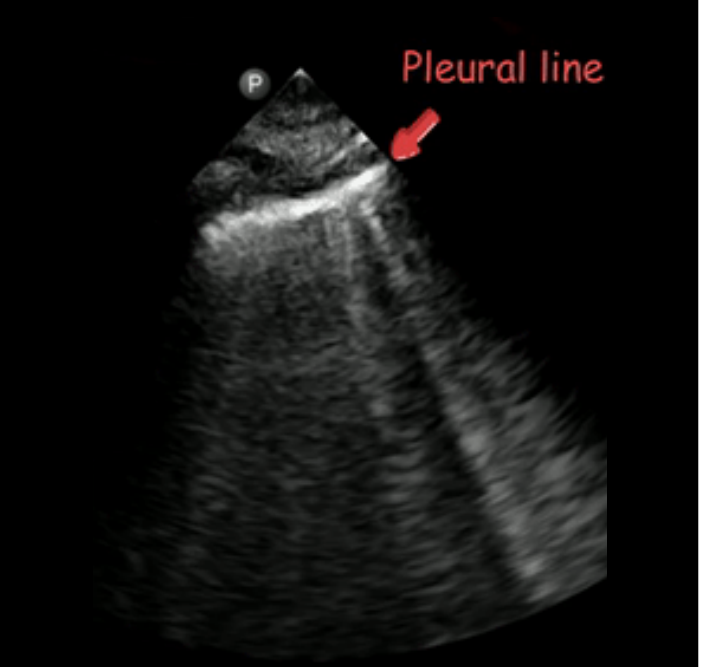
EDCTP

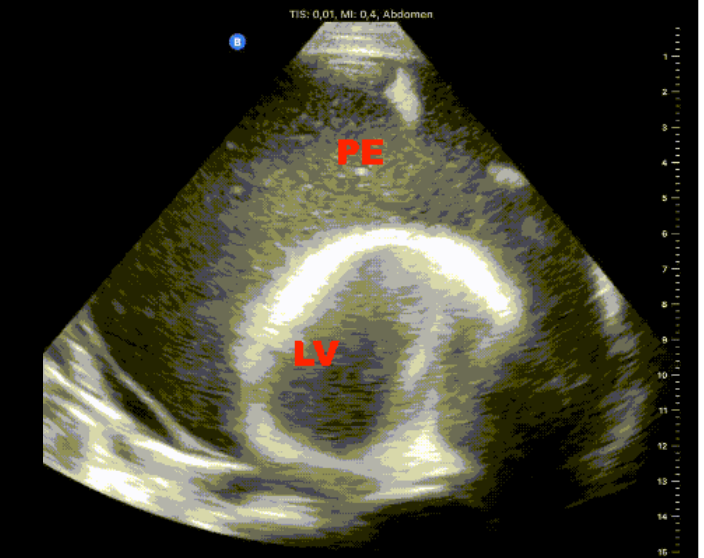
CBTBR DST/NRF

saMRC advancinglife

NIH NRF

LUNGENLIGA
LIGUE PULMONAIRE





Point-of-care thoracic ultrasound for the diagnosis of pulmonary tuberculosis

-

The TrUST study

Véronique Suttels – TB Symposium, June 1, Bern

PhD in life sciences – directed by Noemie Boillat & Annie Hartley

ClinicalTrials.gov Identifier: NCT05423847

LUNGENLIGA
LIGUE PULMONAIRE

Content

- POCUS & PTB: What do we already know?
- Rationale and research question
- Methods
- Interim results of the Benin site
- (Wo)man versus machine
- Conclusion diagnostics
- Scalability and feasibility
- Next steps

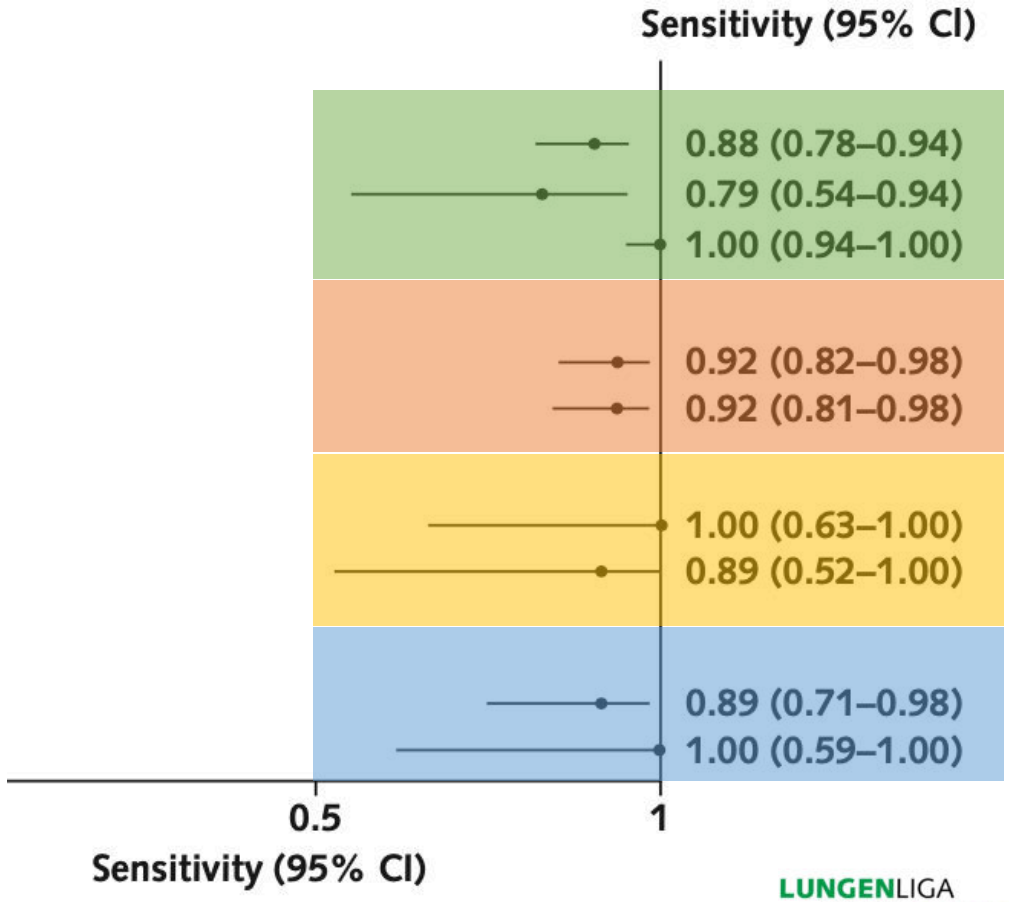
POCUS & TB: What do we already know?

LUNGENLIGA
LIGUE PULMONAIRE

POCUS & TB: What do we already know?

Meta-analysis
Lung US

sensitivity



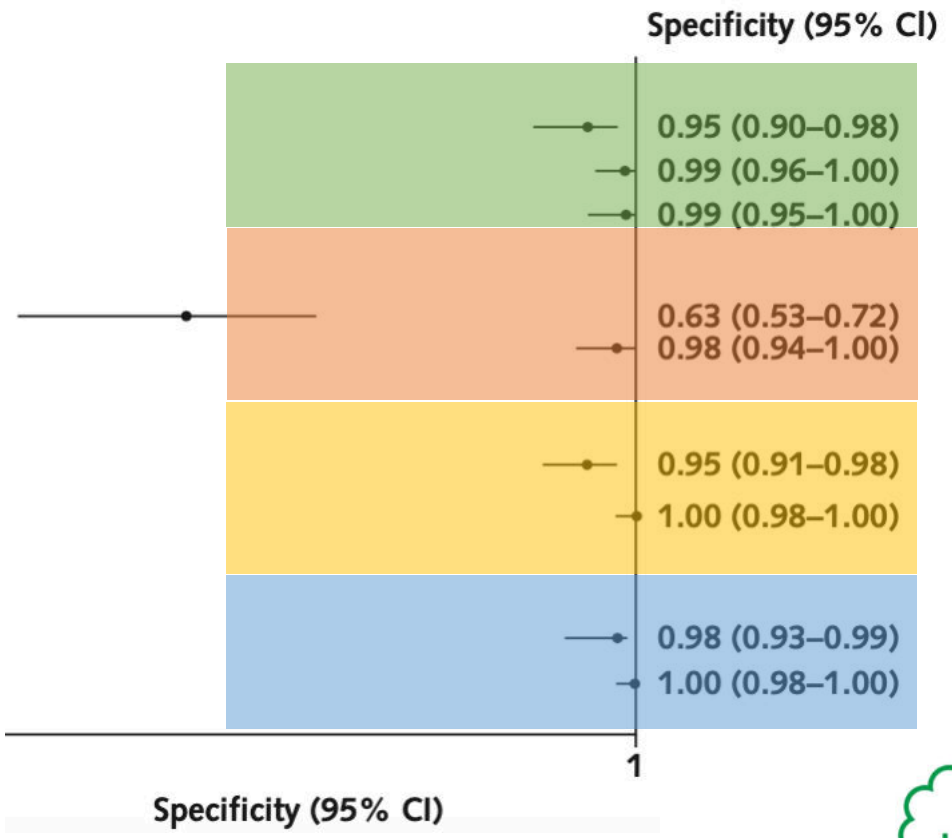
Qaseem A et al. Ann Intern Med. 2021

LUNGENLIGA
LIGUE PULMONAIRE

POCUS & TB: What do we already know?

Meta-analysis
Lung US

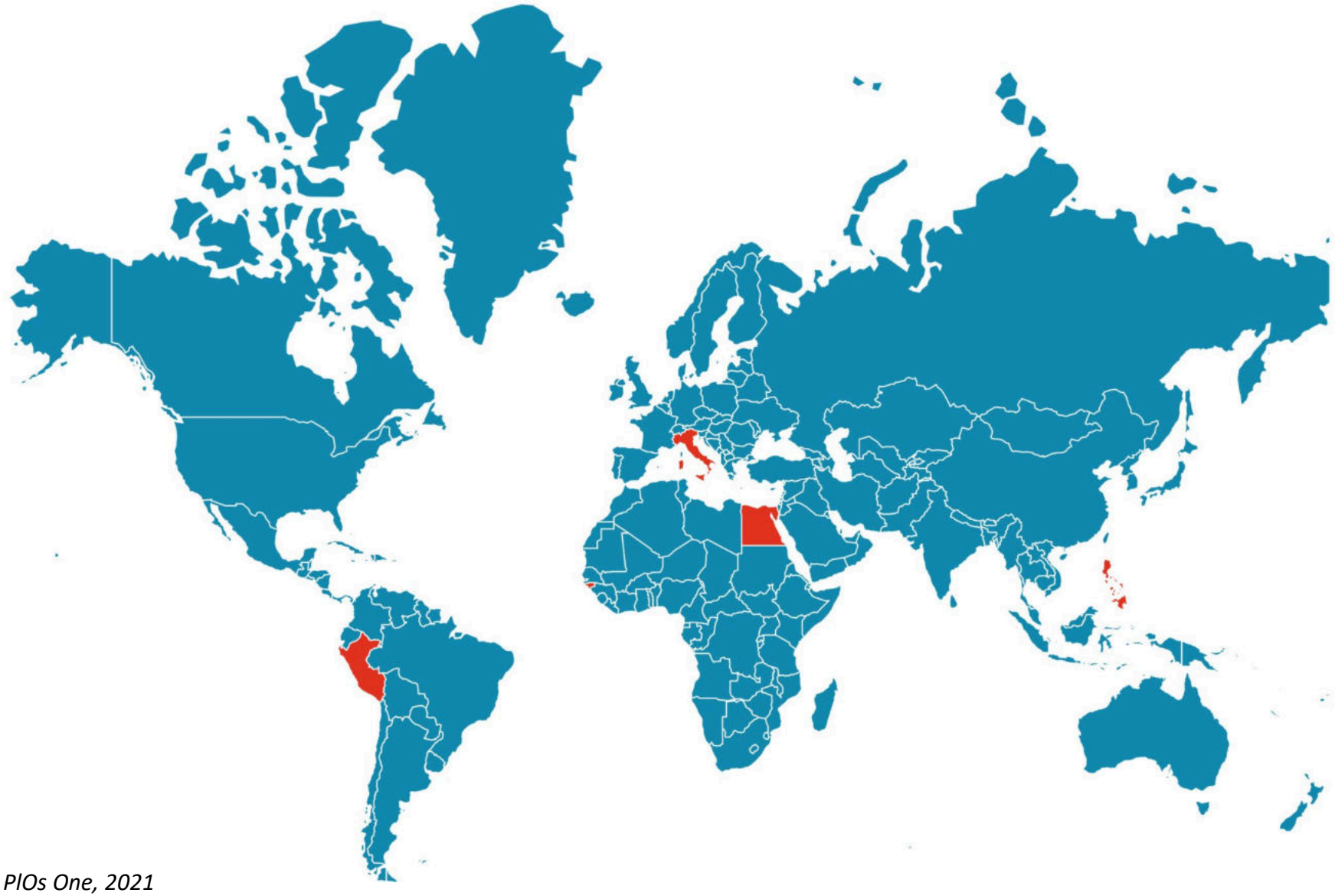
specificity



Qaseem A et al. Ann Intern Med. 2021

LUNGENLIGA
LIGUE PULMONAIRE

POCUS & TB: What do we already know?

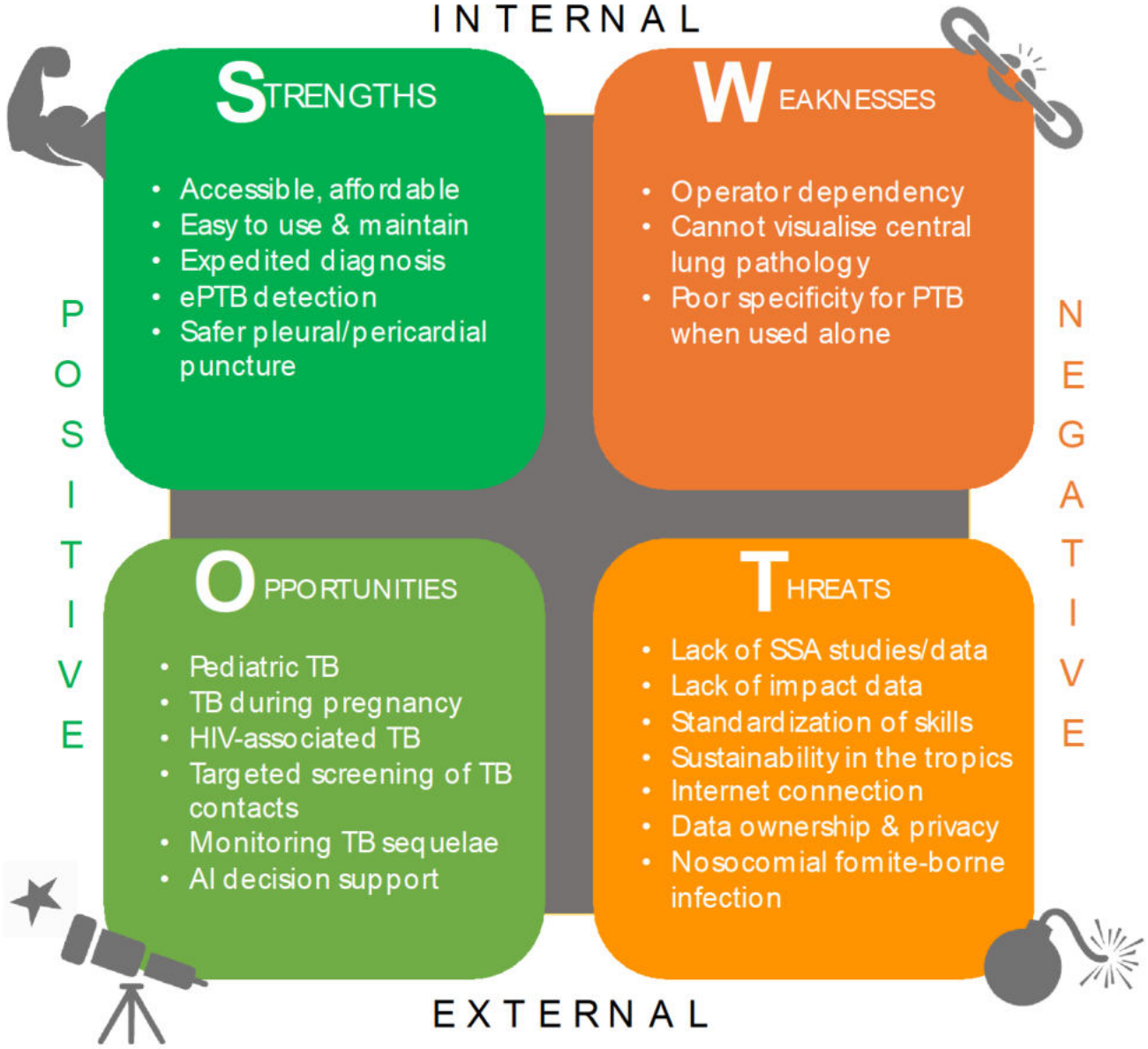


- 5 cross-sectional studies between 2017-2020
- n pts between 50 and 100
- Methodological problems(reference standard!)
- Meta-analysis: SENS 73%-100%

Bigio PlOs One, 2021

LUNGENLIGA
LIGUE PULMONAIRE

POCUS & TB: What do we already know?



Suttels et Al. Int J Infect Dis, 2022

LUNGENLIGA
LIGUE PULMONAIRE

Rationale and research question

LUNGENLIGA
LIGUE PULMONAIRE

Rationale and research question

GenXpert TB

- Global standard of care (WHO 2011)
- Vertical diagnostic approach
- Centralized

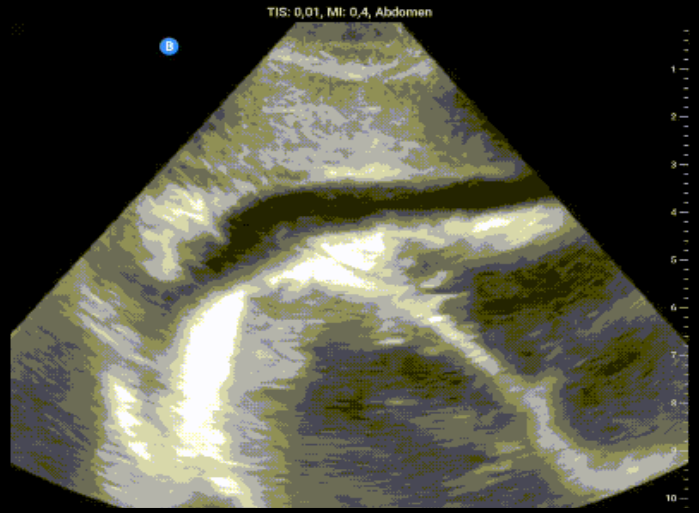
POCUS

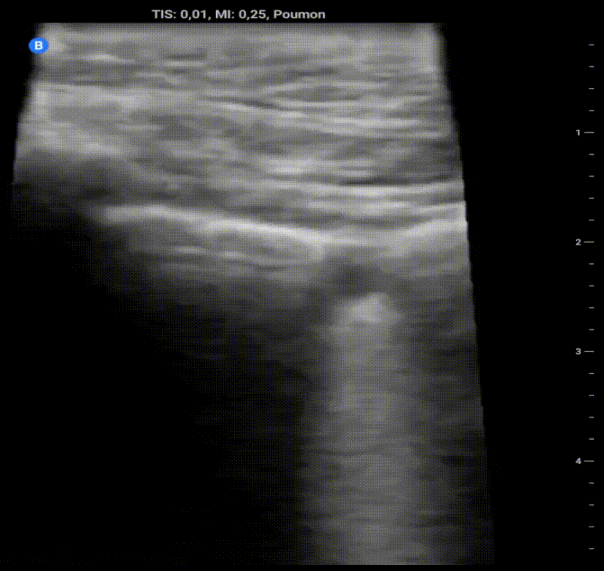
- Role in TB triage or screening?
- POCUS as a rule-out test?
- Horizontal diagnostic approach
- Important potential for decentralization
- Select patients for GenXpert? Cost reduction?

Boehme et Al. Lancet, 2011
Schumacher & Denkinger. Lancet Glob Health.
Thompson et Al. Lancet Glob Health. 2023

LUNGENLIGA
LIGUE PULMONAIRE

Clinical cases make you wonder…





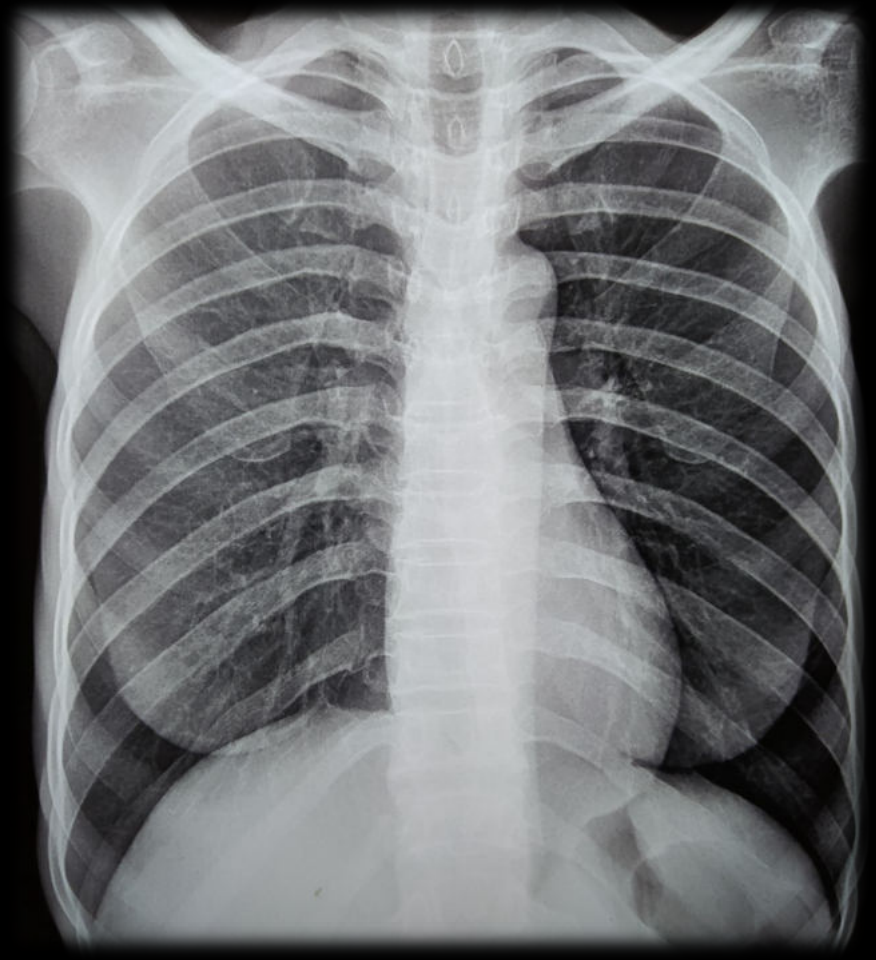
F 39 years old

- Cough
- Dyspnea
- Weight loss
- Since 30 days

HIV pos

26 CD4/mm3

GenXpert TB neg



RX: normal

Clinical cases make you wonder…

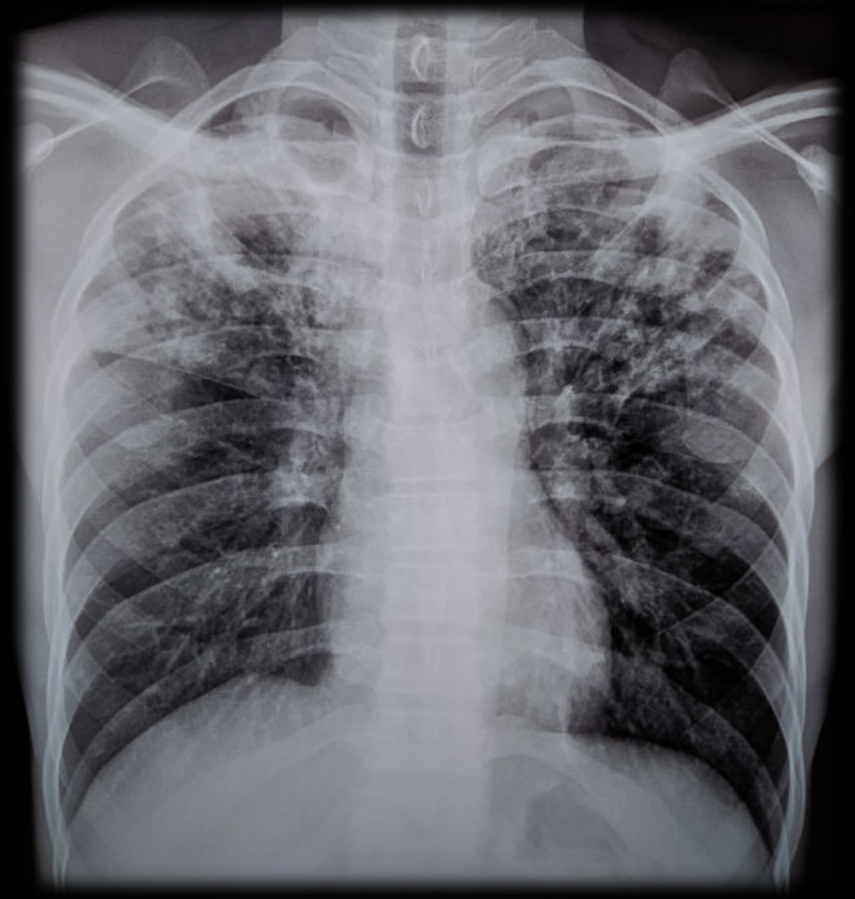
M 41 years old

- Cough
- Dyspnea
- Weight loss
- Since 45 days

HIV neg

GenXpert TB pos

US apex: white lung and small sub-pleural consolidation



RX: infiltrates and cavities

Rationale and research question

Is POCUS a new triage tool for pulmonary TB?

Performance of POCUS for:

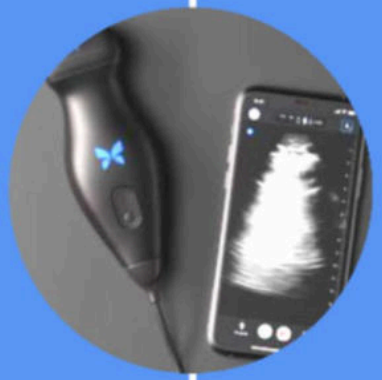
- **The diagnosis of pulmonary TB**
  - versus reference microbiological reference standard GenXpert sputum (low HIV)
  - culture/TB LAM (high HIV)

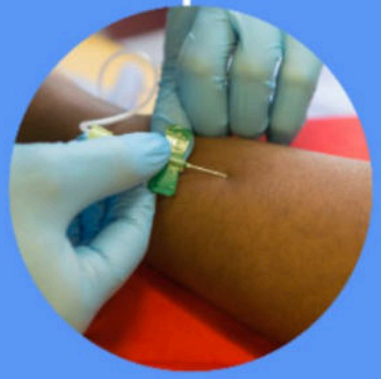
Methods

Multicentric prospective cohort study in Sub-Saharan Africa

Sample size = 1000 patients

- 🇧🇯 *Bénin = 500 patients (Urban, Low HIV, moderate TB)*
- 🇿🇦 *RSA = 500 patients (Rural, High HIV, high TB)*



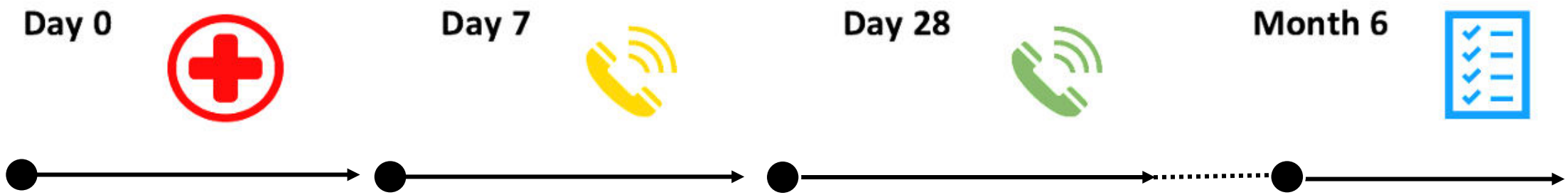


Methods

INCLUSION CRITERIA	EXCLUSION CRITERIA
≥18 years	Suspicion of a non-infectious origin of respiratory symptoms (asthma, heart failure, drugs…)
Presence of cough or dyspnea	Follow-up consultation

LUNGENLIGA
LIGUE PULMONAIRE

Methods



- Symptoms & signs
- Chest X-ray
- Standardized POCUS exam
- GenXpert MTB/RIF® (sputum)
- Sars-CoV-2 XPRESS® (nasopharynx)
- Alere Determine® HIV-1/2 (blood)
- Biobank: whole blood, plasma, urine, oropharynx, sputum, paxgene

- Phone follow-up
- Death/hospitalisation/worsening/ improvement

- TB register for treatment failure

LUNGENLIGA
LIGUE PULMONAIRE

Methods


2 Expectorating zone
1 Waiting room
Triage
Recrutement
3 Lab
Biobank
LABORATOIRE DE REFERENCE
DES MYCOBACTERIES
4 Radiology

Methods

6 **Research consultation US room**

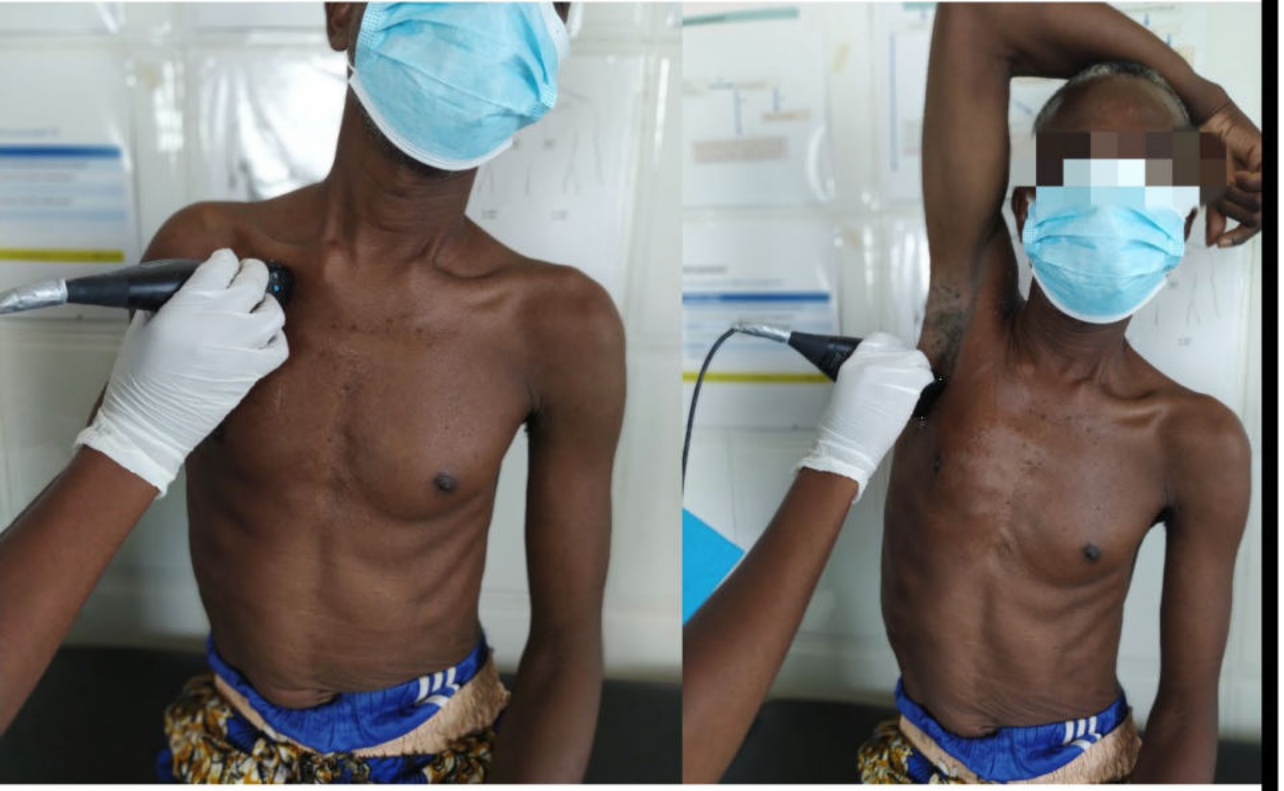
5 **Hospitalisation wards**

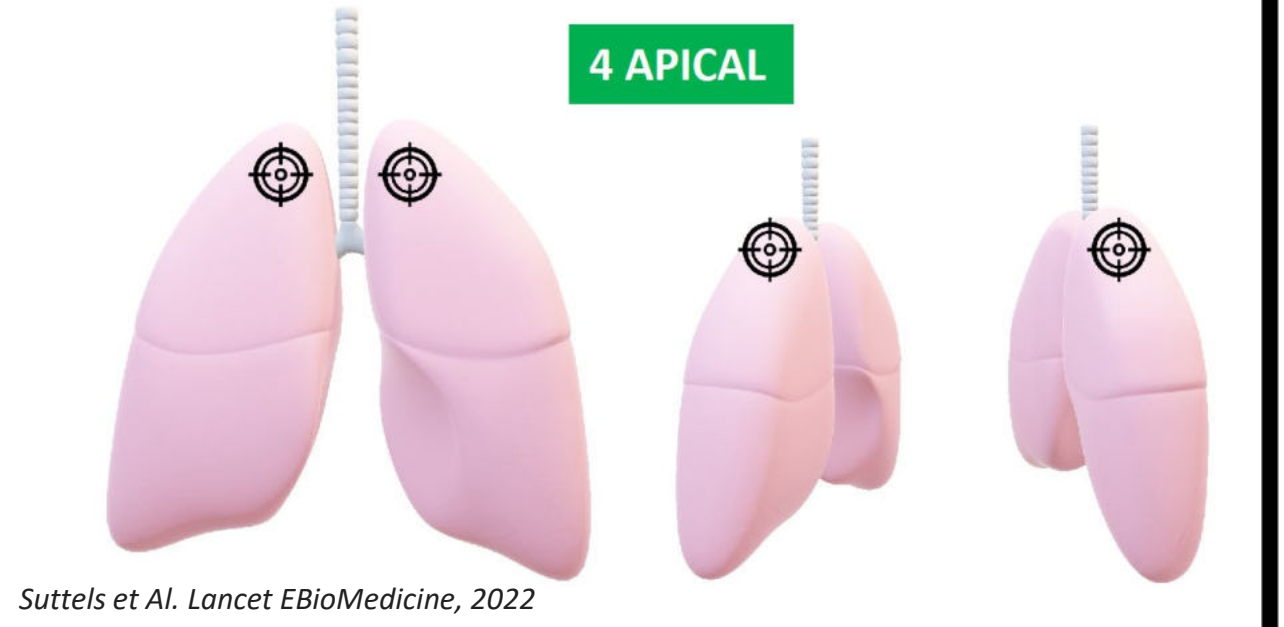
Methods

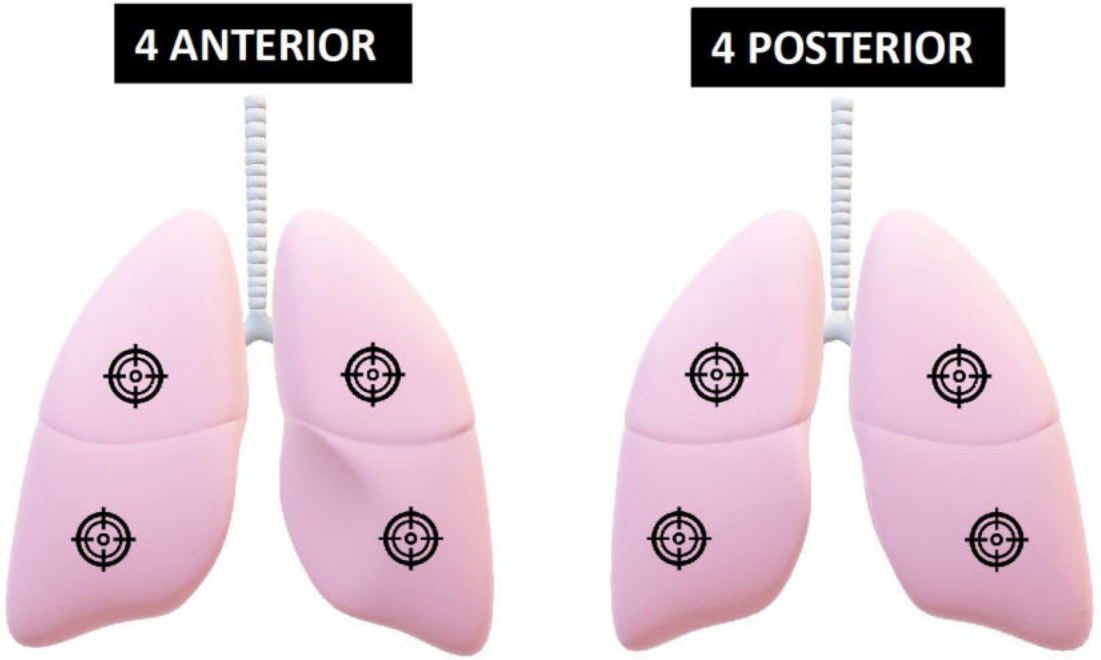
Collection of thoracic POCUS images & videos

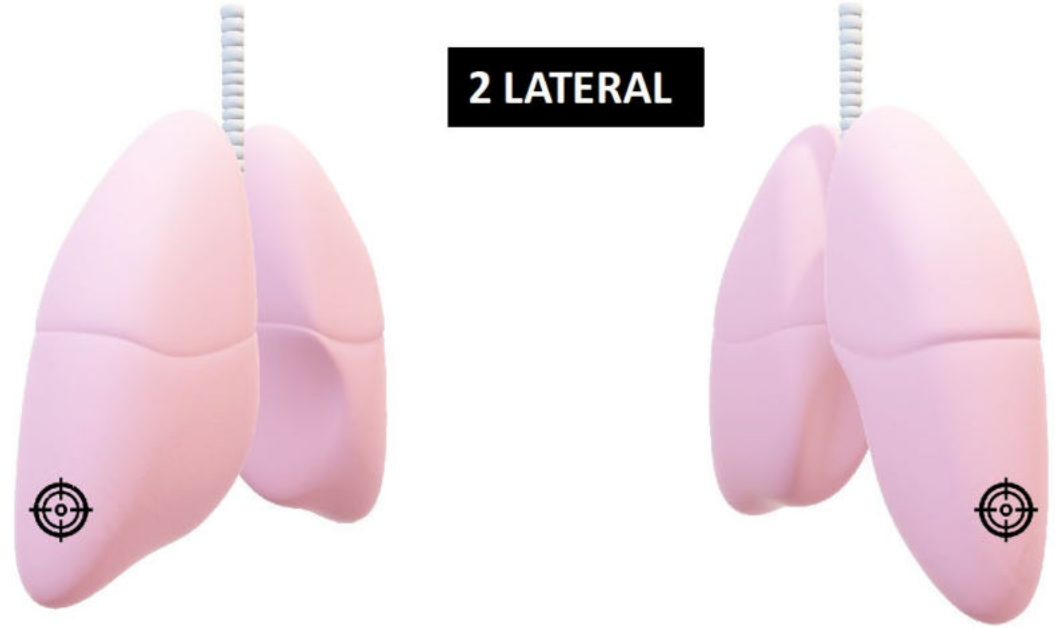
- Standardized LUS protocol
- Subxyphoid pericardial view

LUNGENLIGA
LIGUE PULMONAIRE









Suttels et Al. Lancet EBioMedicine, 2022

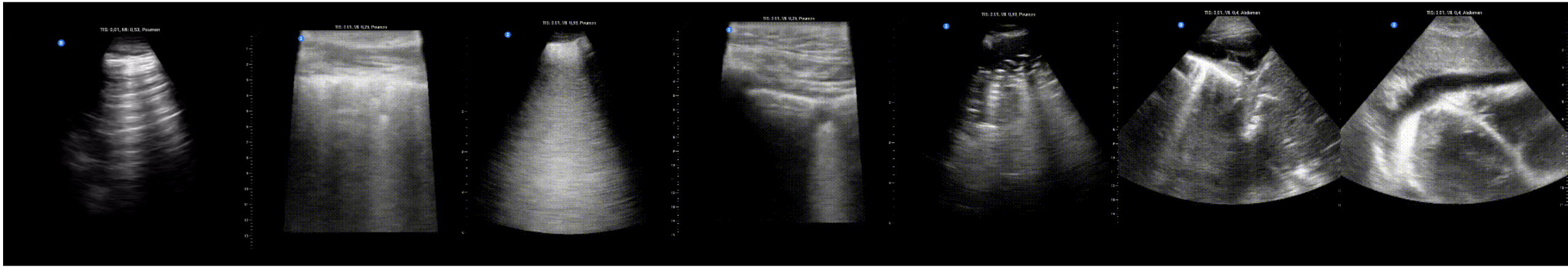
Methods

Standardized interpretation of POCUS images & videos

- 2 blinded expert readers
    - for CXR, clinical and microbiological data
- Third blinded reader in case of disconcordance
- Reading according to prespecified categories

Methods

Dry lung (A lines)	B-lines	White lung	Subpleural pathology <1cm	Consolidation >1 cm	Pleural effusion	Pericardial effusion



DRY

WET

LUNGENLIGA
LIGUE PULMONAIRE

Methods

Benin site = low HIV prevalence

Definitions used

TB+ *= Bacteriologically confirmed pulmonary TB defined as Xpert + cases*

TB- *= Other LRTI, clinically diagnosed TB*

1. **Population characteristics**

→ comparison of TB+ and TB- using Mann Whitney , chi-square, or Fisher tests when appropriate

2. US characteristics & Association of **each individual US sign** with TB+ and TB-

→ univariate logistic regression

3. **Combination of US signs** with the best diagnostic performance

→ multivariate logistic regression score built from 6 LUS features using recursive feature elimination, calculation of sensitivity, specificity, LR+, LR-

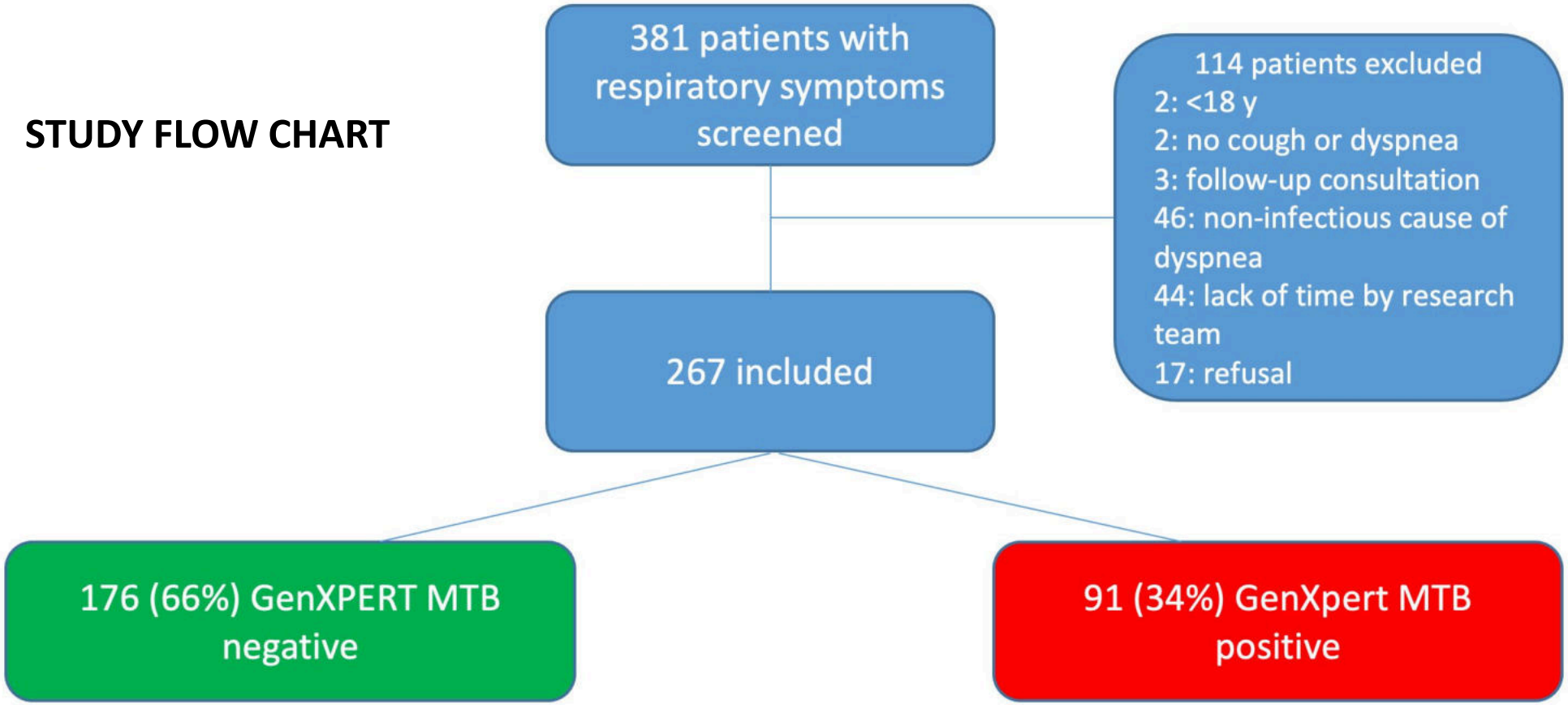
4. Performance of a **(wo)man- versus AI-assisted US interpretation**

LUNGENLIGA
LIGUE PULMONAIRE

Interim results Benin site

14/10/21 – 17/11/22

STUDY FLOW CHART



Suttels et Al. ECCMID 2023

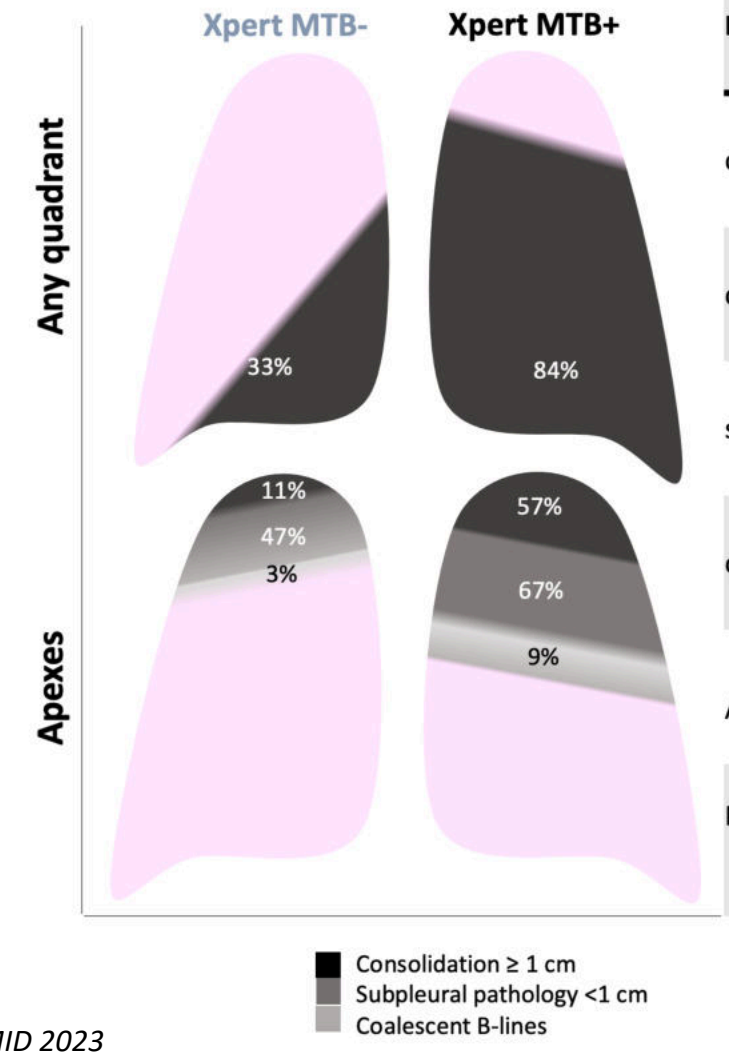
LUNGENLIGA
LIGUE PULMONAIRE

Patient characteristics

	All (n=267)	Xpert MTB – (n=176)	Xpert MTB+ (n=91)	P-value
Demography				
Male N (%)	158 (59)	90 (51)	68 (74)	**<0.001**
Age (years); median (IQR)	40 (29-50)	41 (32-52)	33 (27-47)	**0.003**
Comorbidities				
Former TB N(%)	37 (14)	32 (18)	5 (5)	**0.005**
Co-infections				
COVID positive N(%)	41 (15)	32 (18)	9 (10)	0.069
HIV positive N(%)	57 (22)	48 (28)	9 (10)	**<0.001**
CD4 count; median (IQR)	110 (48-397)	115 (49-397)	83 (48-492)	0.490
Symptoms				
Cough as main symptom N(%)	254 (95)	168 (95)	86 (95)	0.968
Weight loss N(%)	198 (74)	116 (66)	82 (90)	**<0.001**
Hemoptysis N(%)	56 (21)	39 (22)	17 (19)	0.535
Night sweats N(%)	93 (35)	51 (29)	42 (46)	**0.004**
Main symptom duration (days); median (IDR)	30 (14-90)	30 (14-90)	75 (30-120)	0.714
Signs				
BMI <18.5 N(%)	109 (41)	58 (33)	51 (56)	**<0.001**
Temperature >38°C N(%)	17 (6)	6 (3)	11 (12)	**0.005**
Heart rate >100 bpm N(%)	106 (40)	53 (30)	53 (60)	**<0.001**
Respiratory rate > 22 cpm N(%)	209 (78)	131 (74)	78 (86)	**0.023**
Systolic blood pressure <100 mmHg N(%)	53 (20)	28 (16)	25 (28)	**0.022**

Suttels et Al. ECCMID 2023

Univariate logistic regression



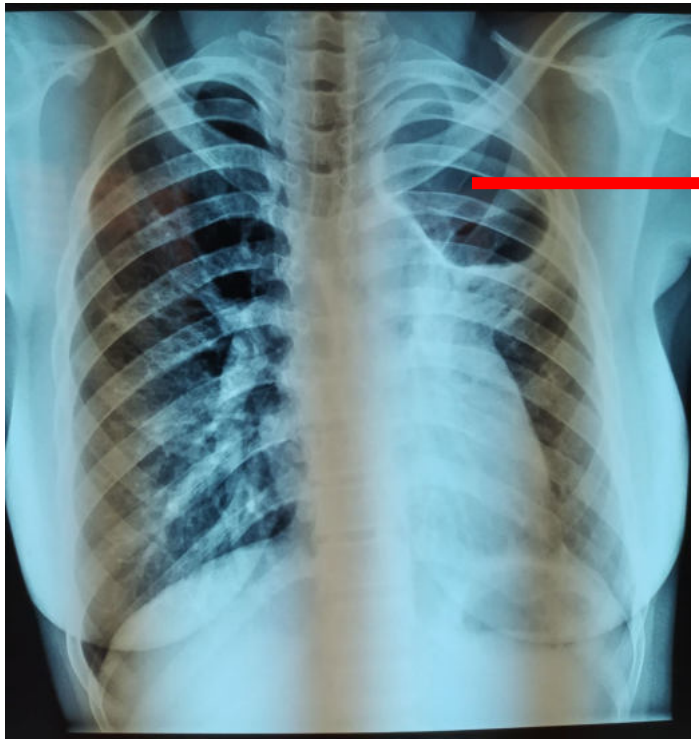
LUS profile & localisation	Xpert MTB- (n=176)	Xpert MTB+ (n=91)	OR (95% CI)	p
consolidation >1cm in any quadrant	58(33%)	76(84%)	10.5 (5.5-19.8)	<0.001
coalescent B-lines apex	5(3%)	8(9%)	3.3 (1.1-10.5)	<0.05
subpleural pathology <1cm apex	84(47%)	61(67%)	2.3 (1.3-3.9)	<0.05
consolidation >1cm apex	20(11%)	52(57%)	10.5 (5.6-19.6)	<0.001
A-lines in both apexes	74(42%)	8(9%)	0.1 (0.1-0.3)	<0.001
Pericardial effusion (any size)	40(22%)	37(41%)	2.4 (1.4-4.1)	0.002

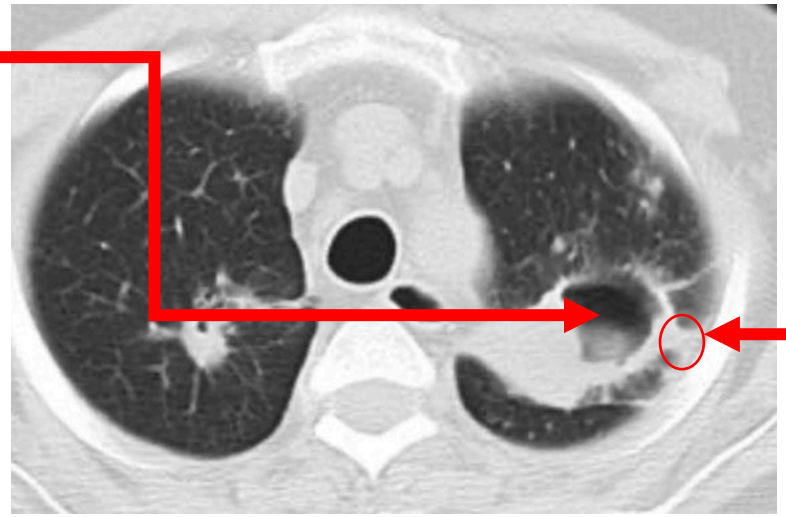
Suttels et Al. ECCMID 2023

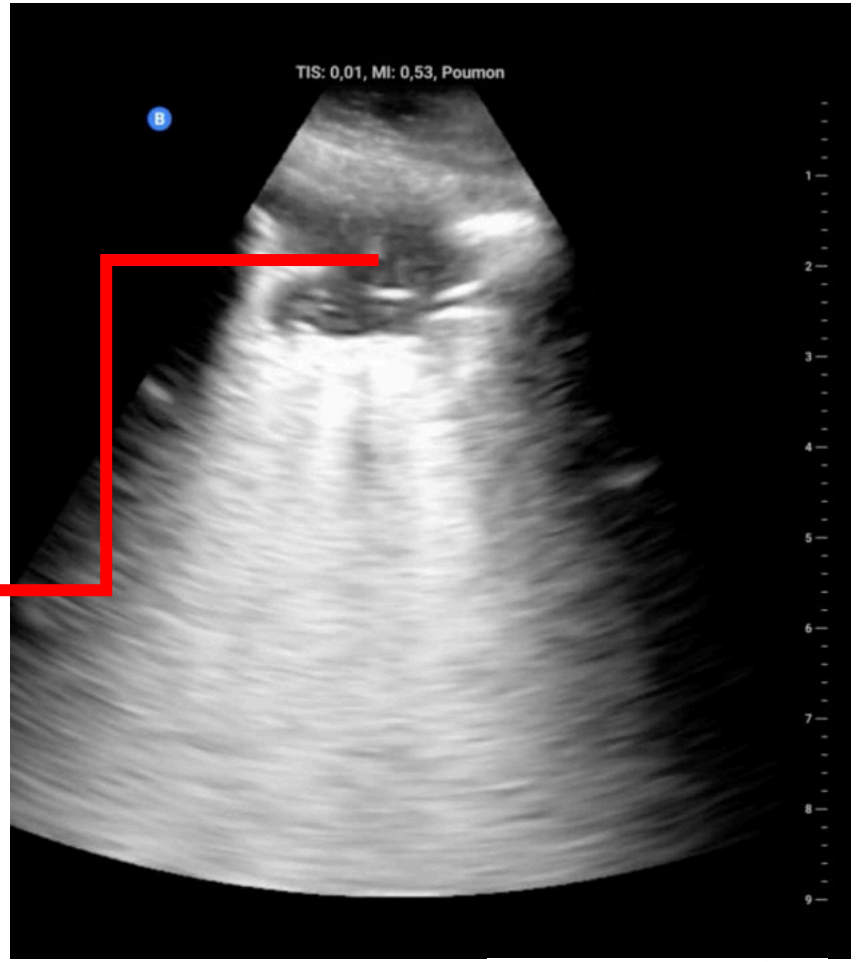
IGA PULMONAIRE

About cavities…

>90% of cavities remain invisible on LUS but surrounding inflammation in contact with the pleura can be easily be detected



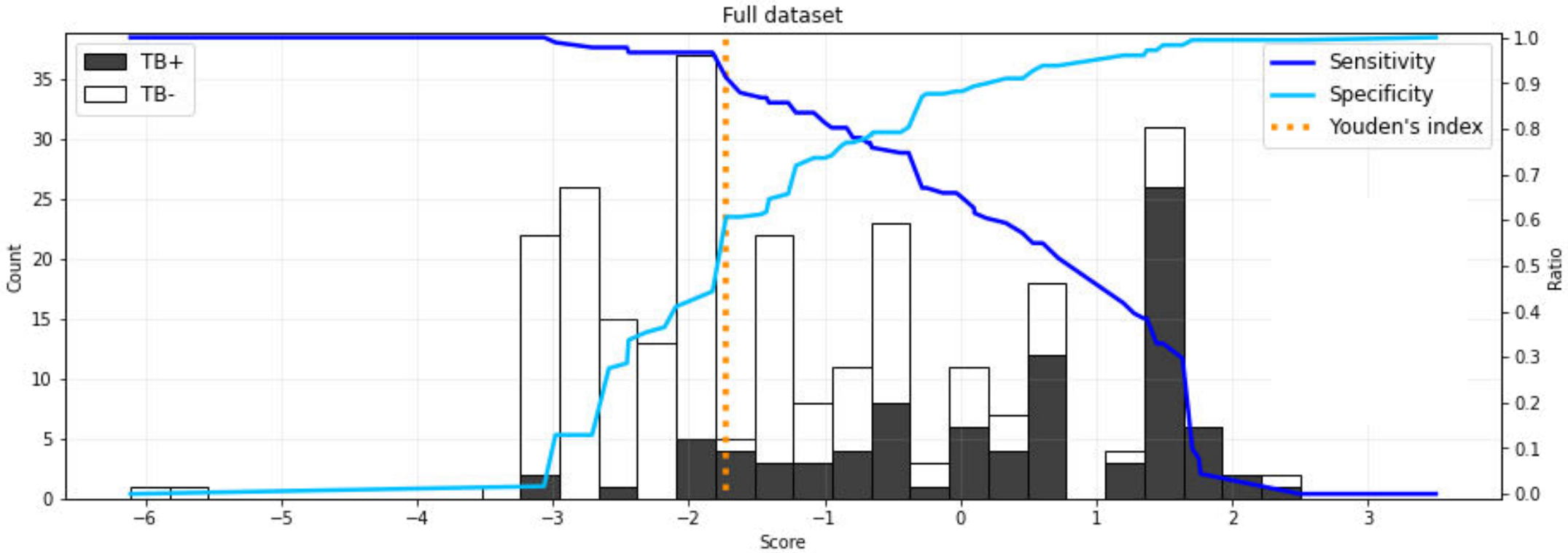




LUNGENLIGA
LIGUE PULMONAIRE

multivariate logistic regression score built from 6 US features

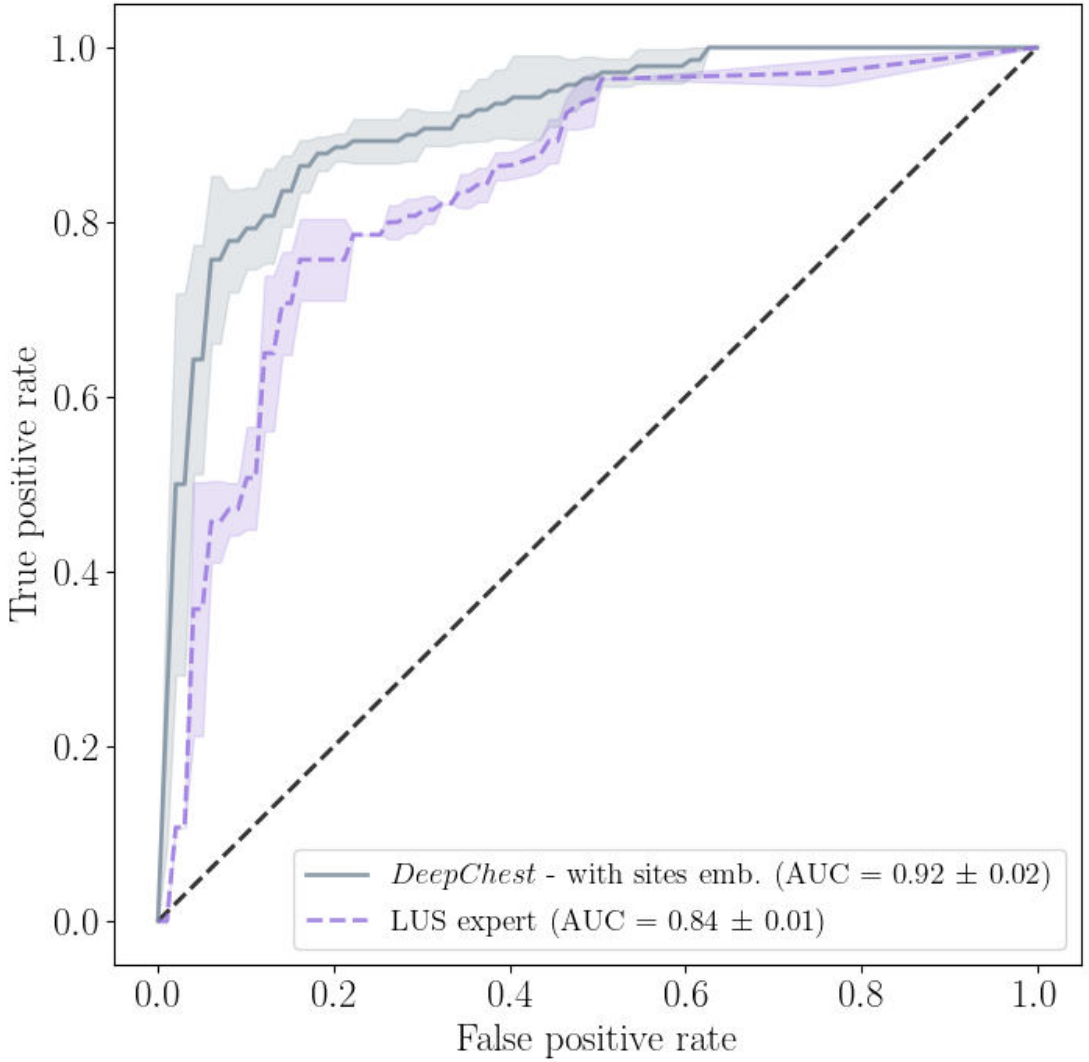
- Desired cut-off chosen with Youden's index
- **SENS 91 % and SPEC 61 %**
- **LR+ 2.3 and LR- 0.1**



Suttels, ECCMID 2023

LUNGENLIGA
LIGUE PULMONAIRE

(Wo)man versus machine



Courtesy of Dr. Mary-Anne Hartley

LUNGENLIGA
LIGUE PULMONAIRE

Conclusion diagnostics

- Thoracic POCUS seems a **promising triage tool**

- **Approaching the WHO recommended diagnostic accuracy** *(≥90% sensitivity, ≥70% specificity)* ***better than CXR, symptom screen and CAD4TB***
- to exclude pulmonary TB on an outpatient basis in adult patients with respiratory syndrome in endemic areas
- Subgroups (HIV) to be confirmed

Yoon et al, Lancet resp med, 2019

LUNGENLIGA
LIGUE PULMONAIRE

Scalability & Feasability

- **Qualitative study** on barriers and facilitators of LUS implementation in SSA context
- Standardization of POCUS **training & evaluation** in different SSA sites
- **AI** support

LUNGENLIGA
LIGUE PULMONAIRE

Scalability & Feasability

- **Qualitative study** on barriers and facilitators of LUS implementation in SSA context

LUNGENLIGA
LIGUE PULMONAIRE

EXPERIENCES WITH POINT-OF-CARE LUNG ULTRASOUND

FACILITATORS

EVIDENCE

PRACTICE

BARRIERS

Hospital setting

- Need for free-of-charge POC imaging techniques
- × Lack of resources for tool maintenance and renewal

Physician's perceptions

- Willingness and motivation to appropriate LUS
- Feeling better prepared for technical interventions (e.g., pleural tap)
- Training and building confidence
- × Long examination (when fully labeled and recorded)
- × Lack of experience and/or training
- × Lack of opportunity to use LUS
- × Feeling uncomfortable with certain LUS diagnoses (e.g., pneumothorax)

Tool characteristics

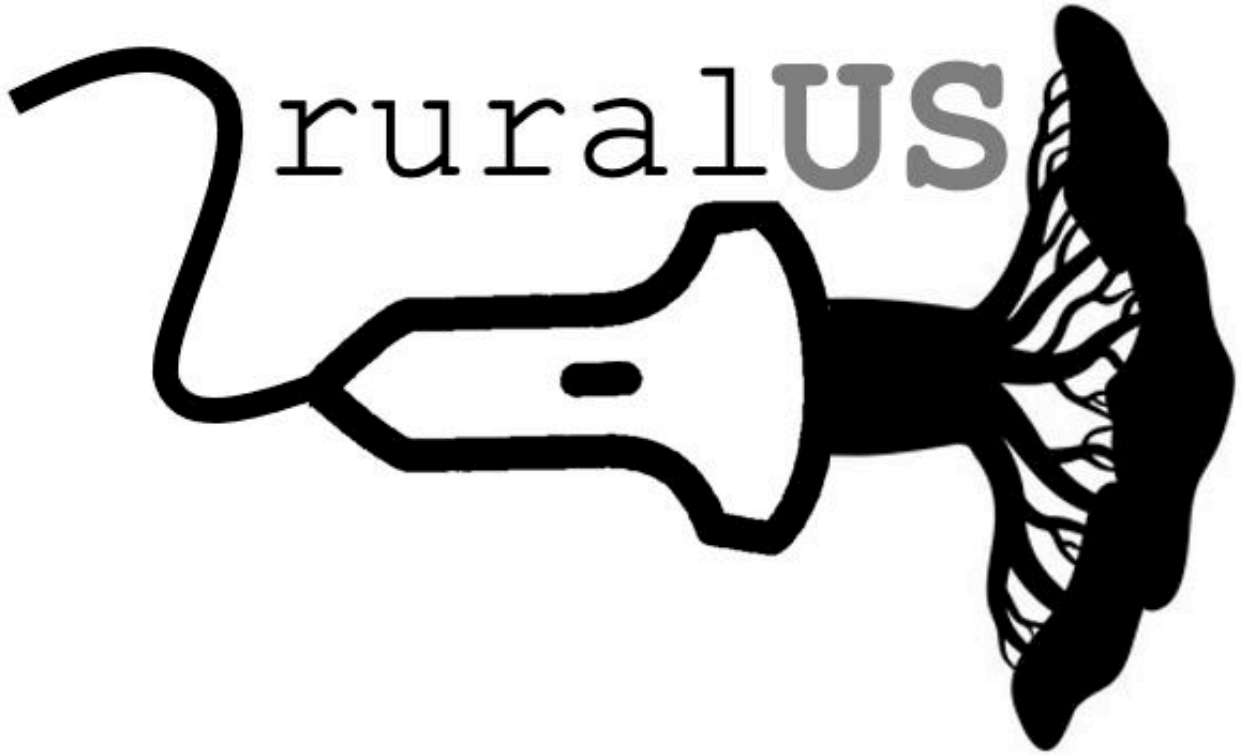
- Easy maintenance
- Affordable purchase price
- Ease of use (portable)
- Faster diagnostic orientation
- Complementarity to chest X-ray
- Non-ionizing
- × Less effective for examining complex central lung pathology (e.g., TB sequelae)
- × Unclear lifespan

Patient's experience

- Confidence and involvement
- Reduction in patient costs
- × Not always suitable for patients in severe distress or pain
- × No analogous image to keep

Scalability & Feasability

- Standardization of POCUS **training & evaluation** in different SSA sites



LUNGENLIGA
LIGUE PULMONAIRE

Scalability & Feasability

Development of a standardized LUS skills evaluation

- ✓ 30 quiz questions
- ✓ 5 practical challenges

Evaluation at 0 and 6 months (Benin), comparison Benin and RSA

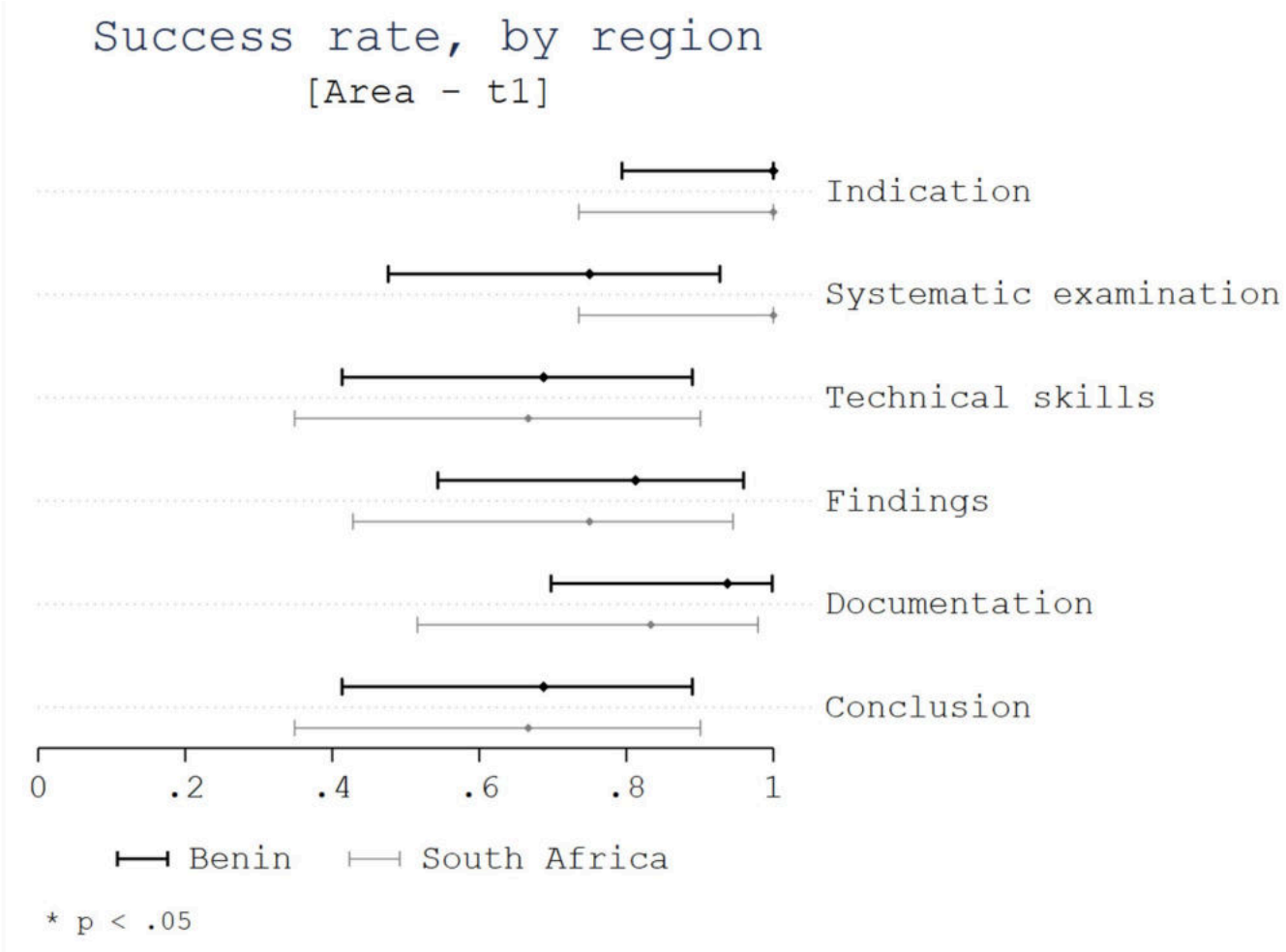
Development of a continuous training platform

ICRC

LUNGENLIGA
LIGUE PULMONAIRE

Scalability & Feasability

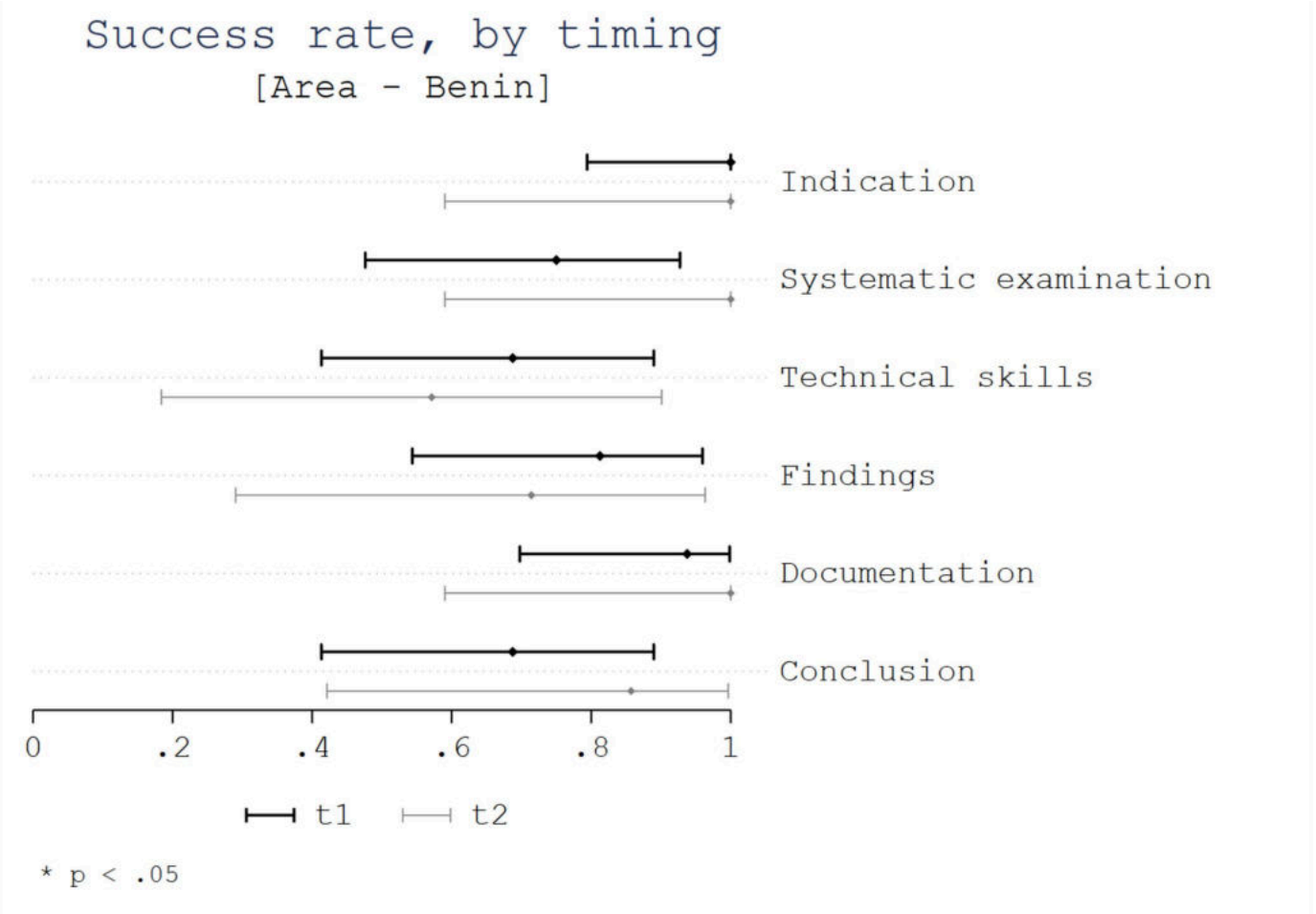
- Standardization of POCUS **training** in different SSA sites



LUNGENLIGA
LIGUE PULMONAIRE

Scalability & Feasability

- Standardization of POCUS **training** over time 0 and 6 months

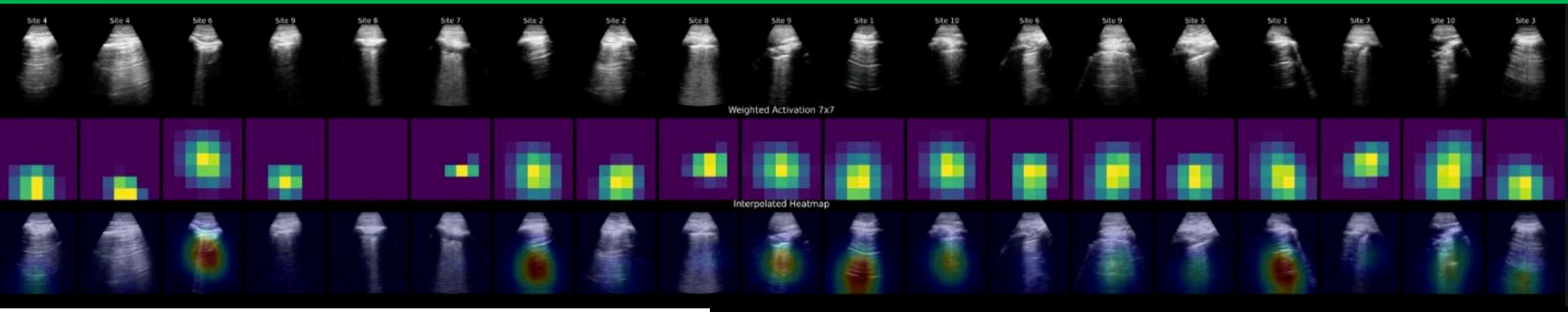


LUNGENLIGA
LIGUE PULMONAIRE

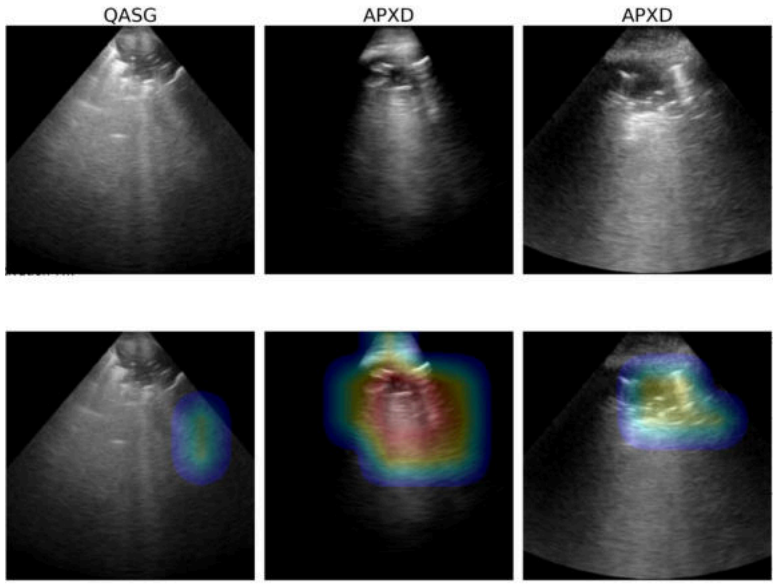
Scalability & Feasability

LUNGENLIGA
LIGUE PULMONAIRE

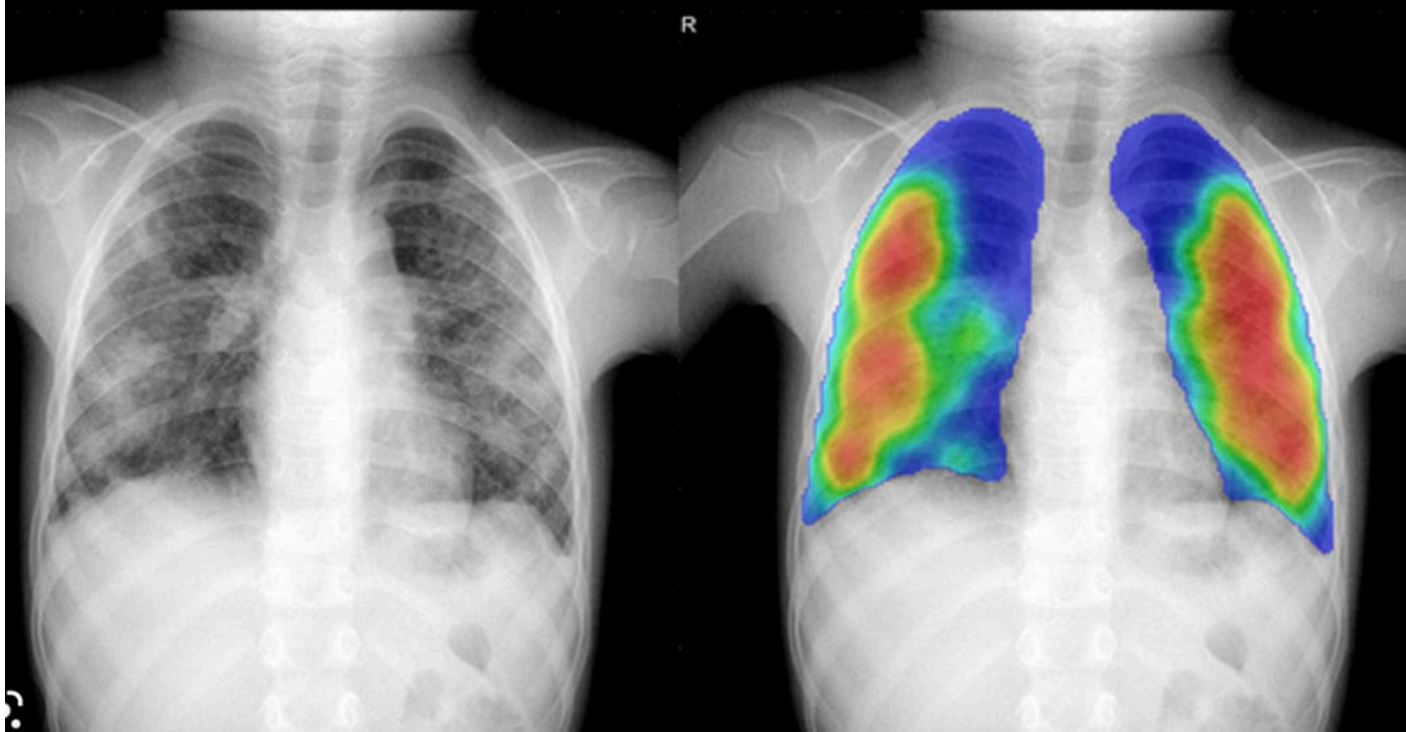
Scalability & Feasability



- AI support



CAD4TB in WHO recommendations since 2021



Next steps

- Maintaining training and research network
- Full analysis of RSA and Benin site (end 2024)
- Sub-group analysis: stratification HIV / former TB
- Biobank analysis (transcriptomics, biomarkers, etiology…)
- Impact evaluation: RCT development

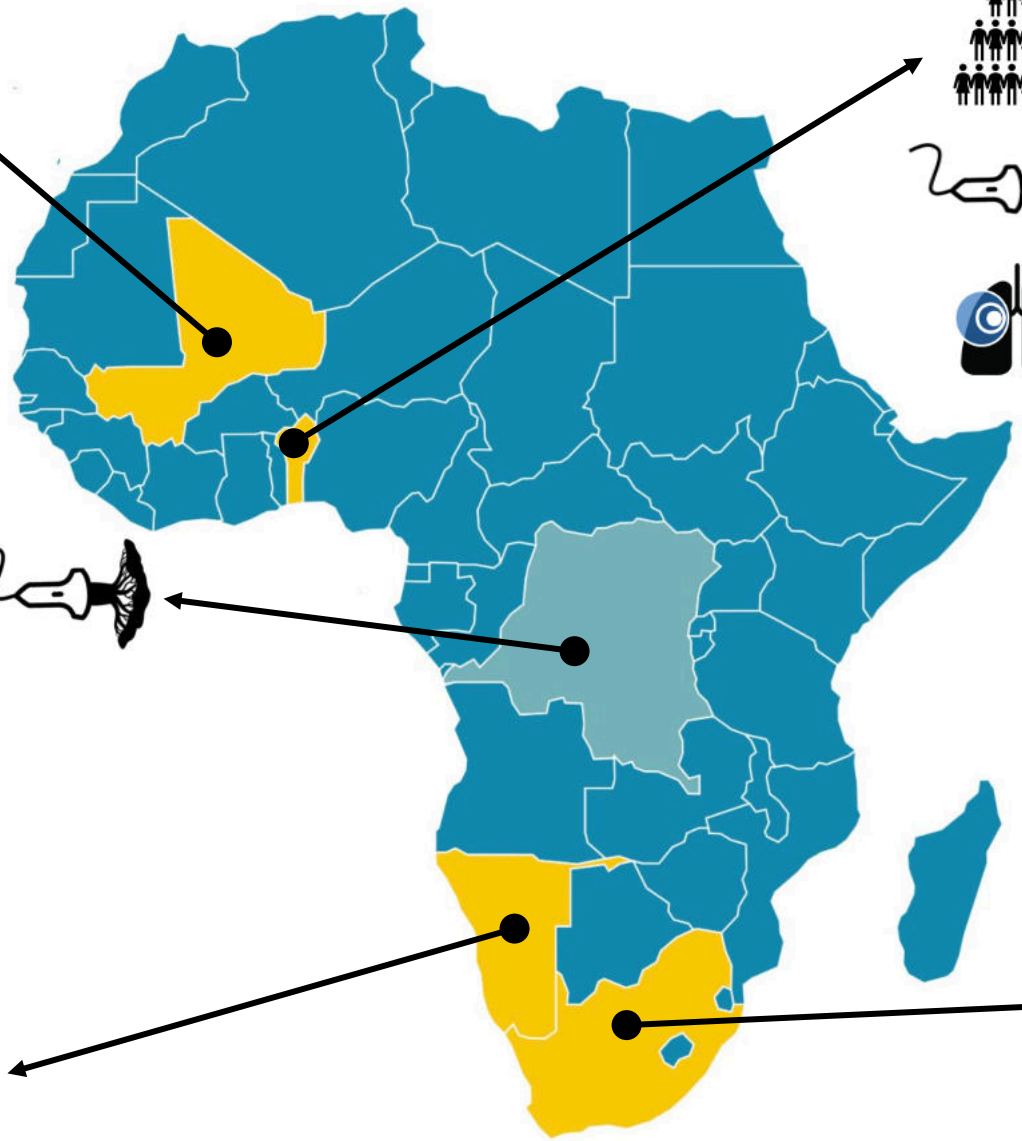
LUNGENLIGA
LIGUE PULMONAIRE

SUMMARY – TrUST study

Adults, urban
Low HIV, low TB

25 HCW trained

Ethics approved



Adults, urban
moderate HIV,
moderate TB

28 HCW trained

450 patients included
Ethics approval paeds

Next training scheduled

Adults, semi-rural
moderate HIV,
moderate TB

5 HCW trained

50 patients included

Adults, rural
high HIV, high TB

41 HCW trained

250 patients included
2nd site opening soon

LUNGENLIGA
LIGUE PULMONAIRE

SUMMARY – TrUST study

2 PI

- Noémie Boillat-Blanco
- Mary-Anne Hartley

TRAINING

- Elena Garcia
- Thomas Brahier
- Brice Guendehou
- Frédéric Alovokpinhou
- Aboudou Hada
- Pierre-André Mans

RESEARCH

2 clinical PhDs

- Jacques Du Toit
- Véronique Suttels

4 master thesis

- Sofia Guedes Da Costa
- Ines Chichignoud
- Orphé Goudjanou
- Maessarath Rafiou

AI TEAM

- 1 Engineer
- 1 PhD
- 2 MSc

Acknowledgments

- Prof Affolabi, SRL, CNHUPPC
- Prof Agodokpessi, CNHUPPC
- Ginette Makpemikpa – assistante de recherche, CNHUPPC
- Laboratoire Supranational de Référence de la tuberculose (SRL) Cotonou
- Programme National contre la Tuberculose (PNT) du Bénin
- Dr Hartley, iGH, EPFL
- Prof Calandra, Maladies infectieuses, CHUV
- Prof Kaufman, Maladies infectieuses, CHUV
- Dr Boillat-Blanco, Maladies infectieuses, CHUV
- Prof Meuwly, Radiologie, CHUV
- Dr Brahier, internal medicine, CHUV
- Dr Garcia, urgences, CHUV
- Dr Didier Le Roy, laboratory, CHUV
- Céline Vicario et le Fonds humanitaire du CHUV
- Dr Keitel, pédiatrie, Inselspital
- Dr Du Toit et son équipe, Tintswalo hospital
- Prof Aubert, Ligue Pulmonaire Suisse
- Livio Glauser Fund 2023

CNHU PPC
Centre National Hospitalier Universitaire de Pneumo-Phtisiologie de Cotonou

SRL COTONOU FOR TB

Programme National contre la Tuberculose

LUNGENLIGA
LIGUE PULMONAIRE

EPFL

CHUV

UNIL | Université de Lausanne

LUNGENLIGA
LIGUE PULMONAIRE
LEGA POLMONARE

Active TB case finding in high burden settings

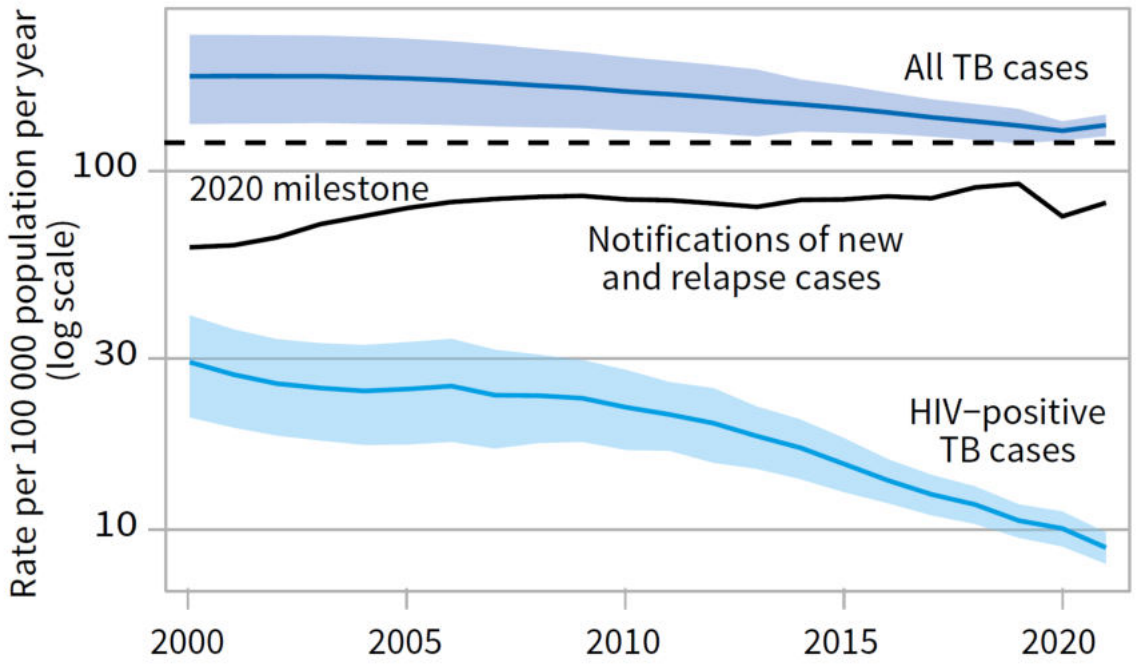
31. hybrides Tuberkulose-Symposium – Lungenliga Schweiz

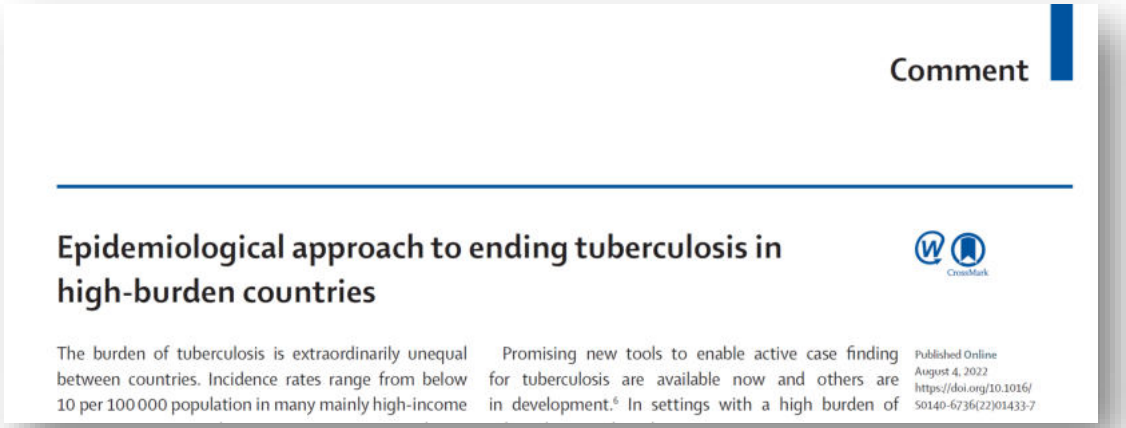
Klaus Reither MD, MSc, PhD
Swiss TPH

Agenda

- Introduction and definitions
- WHO recommendations
- Why active case finding?
- Strategies:
  - Individual-level targeted screening
  - Spatially targeted screening
  - General population screening - high intensity and coverage
  - General population screening - hard-to-reach, high risk populations
- Conclusions

Global trend in the estimated TB incidence rate 2000–2021





Comment

Epidemiological approach to ending tuberculosis in high-burden countries

The burden of tuberculosis is extraordinarily unequal between countries. Incidence rates range from below 10 per 100 000 population in many mainly high-income

Promising new tools to enable active case finding for tuberculosis are available now and others are in development.[6] In settings with a high burden of

Published Online August 4, 2022 https://doi.org/10.1016/S0140-6736(22)01433-7

"We propose that substantial progress towards ending tuberculosis in high-burden settings will require **a focus on community-wide active case finding for tuberculosis with symptom-agnostic tests, followed by effective treatment to stop endemic transmission.**"

Marks GB et al Lancet 2022

Covid-19's Devastating Effect on Tuberculosis Care — A Path to Recovery

Madhukar Pai, M.D., Ph.D., Tereza Kasaeva, M.D., Ph.D., and Soumya Swaminathan, M.D.

"**Targeted active-case–finding initiatives** (…) could help identify people with undiagnosed tuberculosis. This approach will require learning from Covid-19 testing experiences by **bringing tuberculosis testing closer to where people live and work** and engaging communities, private providers, and community-based health workers and civil-society organizations."

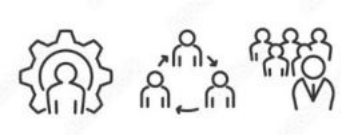
Pai M et al N EngJ Med 2022

Case detection strategies

Passive case finding: TB patients **self-presenting** to routine health services

Enhanced case finding: **Health information or education** to encourage health-seeking behaviours, with or without increasing access to diagnostic services

Active case finding: **General population screening** using any test/procedure, in communities (e.g. door-to-door) or at health facilities

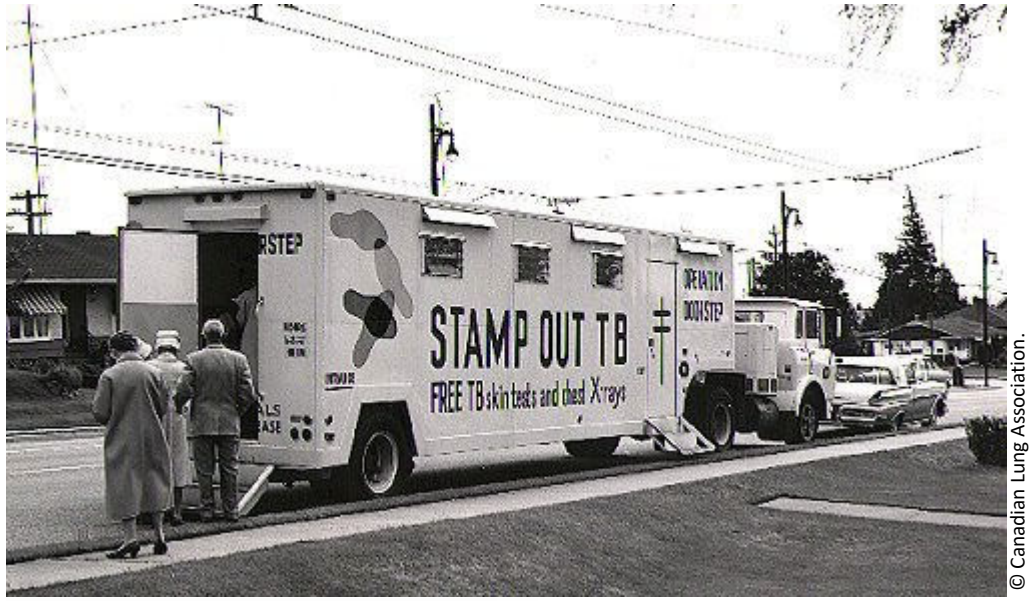


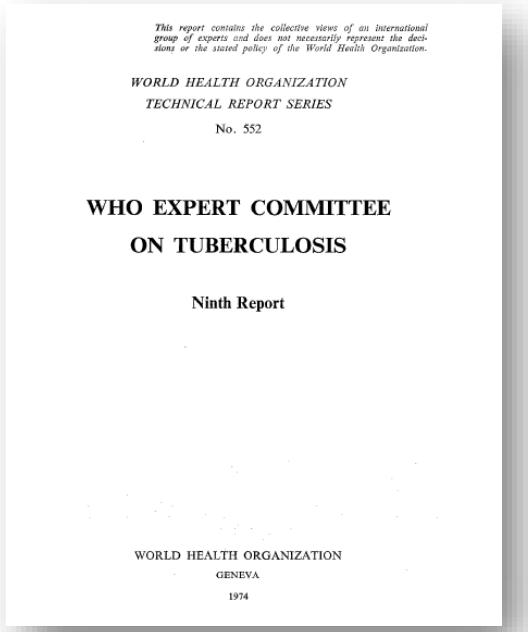
Individual-level targeted screening, e.g. PLHIV, household contacts of a TB case, workers exposed to silica

Spatially targeted screening, within geographically restricted populations (e.g., neighbourhoods or sub-districts) based on surveillance data

Short history of active case finding

- Example for ACF: **large scale mass radiography campaigns** in industrialized countries between the 1930s and 1960s
- Paradigm shift: focus more on **detection of symptomatic TB** patients in the 1960s
- 1974: WHO concerns about accuracy, logistics and personnel requirements for mass radiography: “indiscriminate TB case finding by mobile mass radiography **should be abandoned**”
- In the last 10 years, renaissance of active case finding; e.g. TB REACH / Stop TB Partnership, implementation of innovative case finding strategies at country level, including active case finding




This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization.

WORLD HEALTH ORGANIZATION
TECHNICAL REPORT SERIES
No. 552

WHO EXPERT COMMITTEE
ON TUBERCULOSIS

Ninth Report

WORLD HEALTH ORGANIZATION
GENEVA
1974

Stop TB Partnership
TB REACH

WHO - Systematic TB screening

Recommendations:

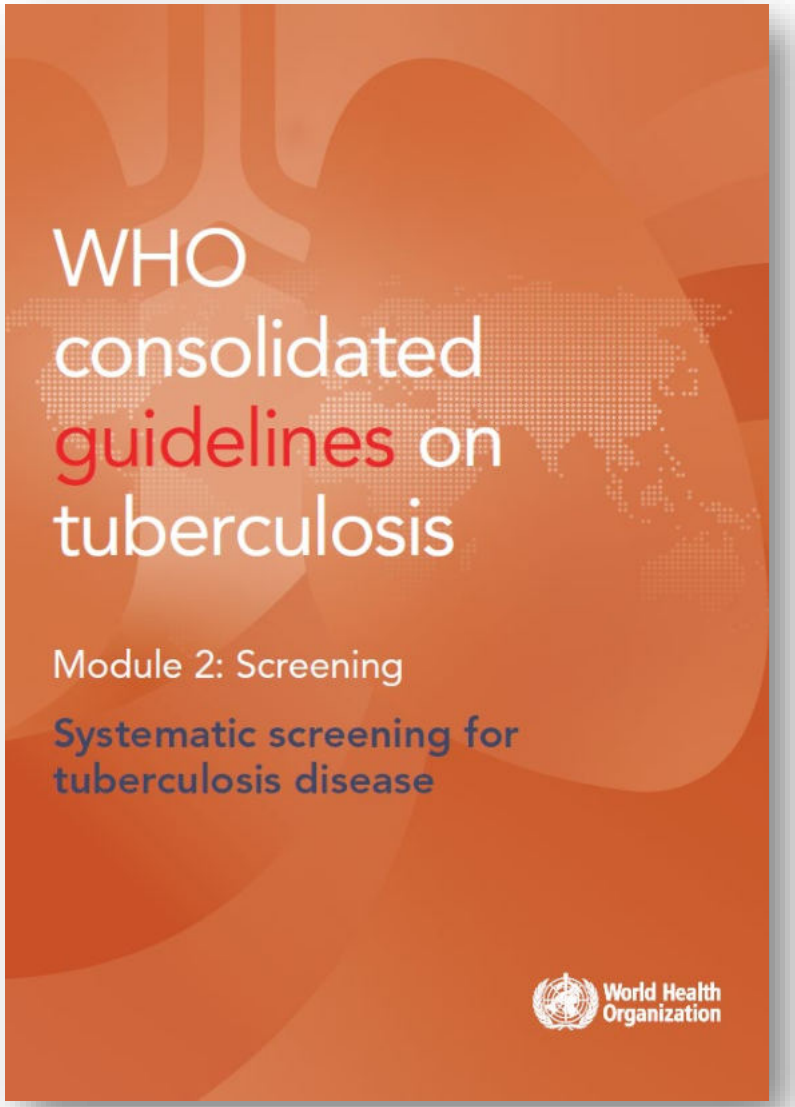
General population

- in areas with an estimated **TB prevalence of 0.5% or higher**

Subpopulations/areas

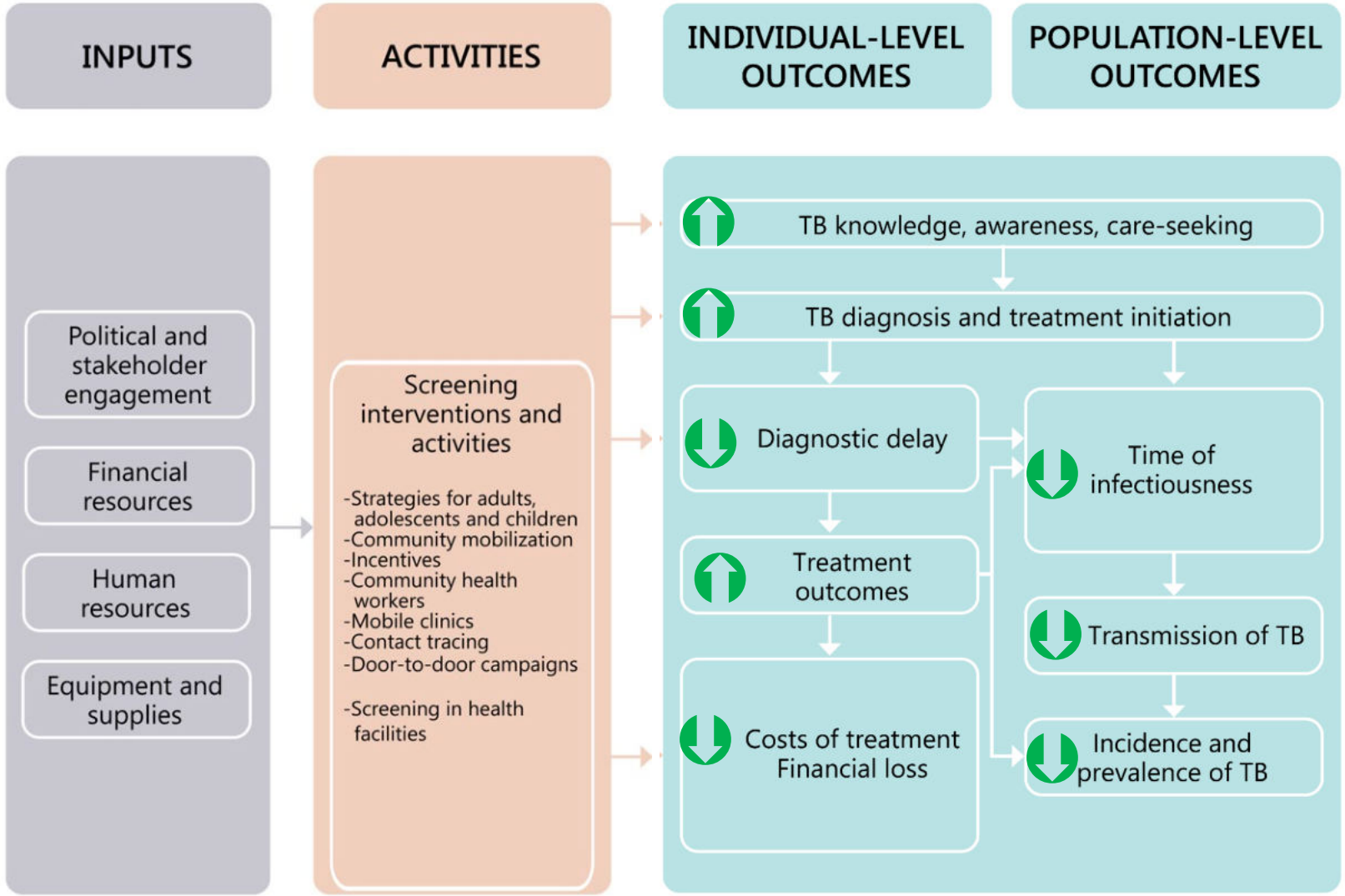
- with structural risk factors for TB
  Such as urban poor communities, homeless communities, communities in remote or isolated areas, indigenous populations, migrants, refugees, internally displaced persons and other vulnerable or marginalized groups with limited access to health care

- PLHIV
- Household contacts of TB cases (including children and adolescents)
- Prisoners
- Miners
- People with risk factors and 100/100’000 TB prevalence
- People with untreated fibrotic lung lesions



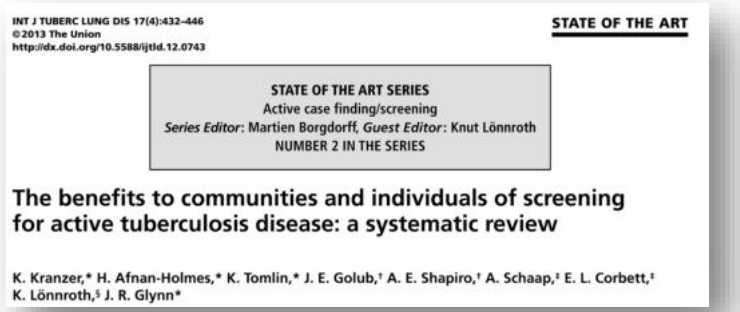
WHO - Systematic TB screening

Framework



WHO, 2021 (modified)

What are the individual and community benefits of active case finding?


INT J TUBERC LUNG DIS 17(4):432–446
©2013 The Union
http://dx.doi.org/10.5588/ijtld.12.0743

STATE OF THE ART

STATE OF THE ART SERIES
Active case finding/screening
Series Editor: Martien Borgdorff, *Guest Editor*: Knut Lönnroth
NUMBER 2 IN THE SERIES

The benefits to communities and individuals of screening for active tuberculosis disease: a systematic review

K. Kranzer,* H. Afnan-Holmes,* K. Tomlin,* J. E. Golub,† A. E. Shapiro,† A. Schaap,‡ E. L. Corbett,‡ K. Lönnroth,§ J. R. Glynn*

Systematic review (2013)

"**Individual and community-level benefits from active screening for TB disease remain uncertain**. So far, the benefits of earlier diagnosis on patient out-comes and transmission have not been established."

Kranzer K et al IJTLD 2013


Contents lists available at ScienceDirect

EClinicalMedicine

journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

ELSEVIER

Research paper

Does tuberculosis screening improve individual outcomes? A systematic review

L Telisinghe[a,b,*], M Ruperez[a], M Amofa-Sekyi[b], L Mwenge[b], T Mainga[b], R Kumar[b], M Hassan[c,d], L.H Chaisson[e], F Naufal[f], A.E Shapiro[g], J.E Golub[b], C Miller[i], E.L Corbett[a,j], R.M Burke[a,j], P MacPherson[a,j,k], R.J Hayes[a], V Bond[a,b], C Daneshvar[c], E Klinkenberg[a,l], H.M Ayles[a,b]

Systematic review (2021)

"**Very limited data** on the effect of TB screening **on individual outcomes**."

Telisinghe L et al EClinicalMedicine 2021


Community-based active case-finding interventions for tuberculosis: a systematic review

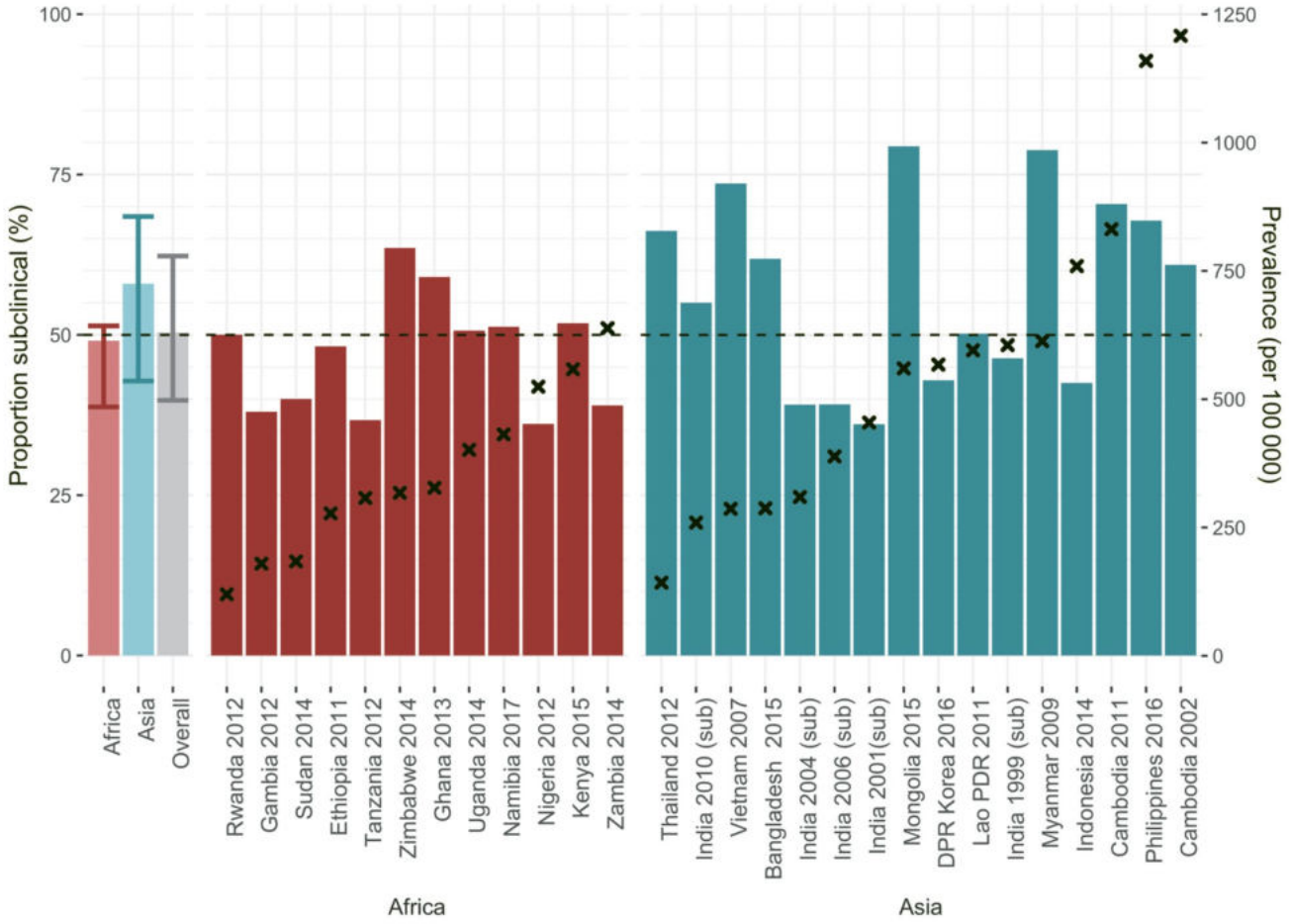
Rachael M Burke, Marriott Nliwasa, Helena R A Feasey, Lelia H Chaisson, Jonathan E Golub, Fahd Naufal, Adrienne E Shapiro, Maria Ruperez, Lily Telisinghe, Helen Ayles, Elizabeth L Corbett, Peter MacPherson

Systematic review (2021)

"Our main findings were that there is **mixed evidence** that active case-finding is effective at initially increasing tuberculosis detection when measured by case notification rates, and that active case-finding **could reduce community prevalence** of tuberculosis **if delivered with sufficient intensity and coverage**."

Burke RM et al Lancet Public Health 2021

Why do we need to pursue active case finding?

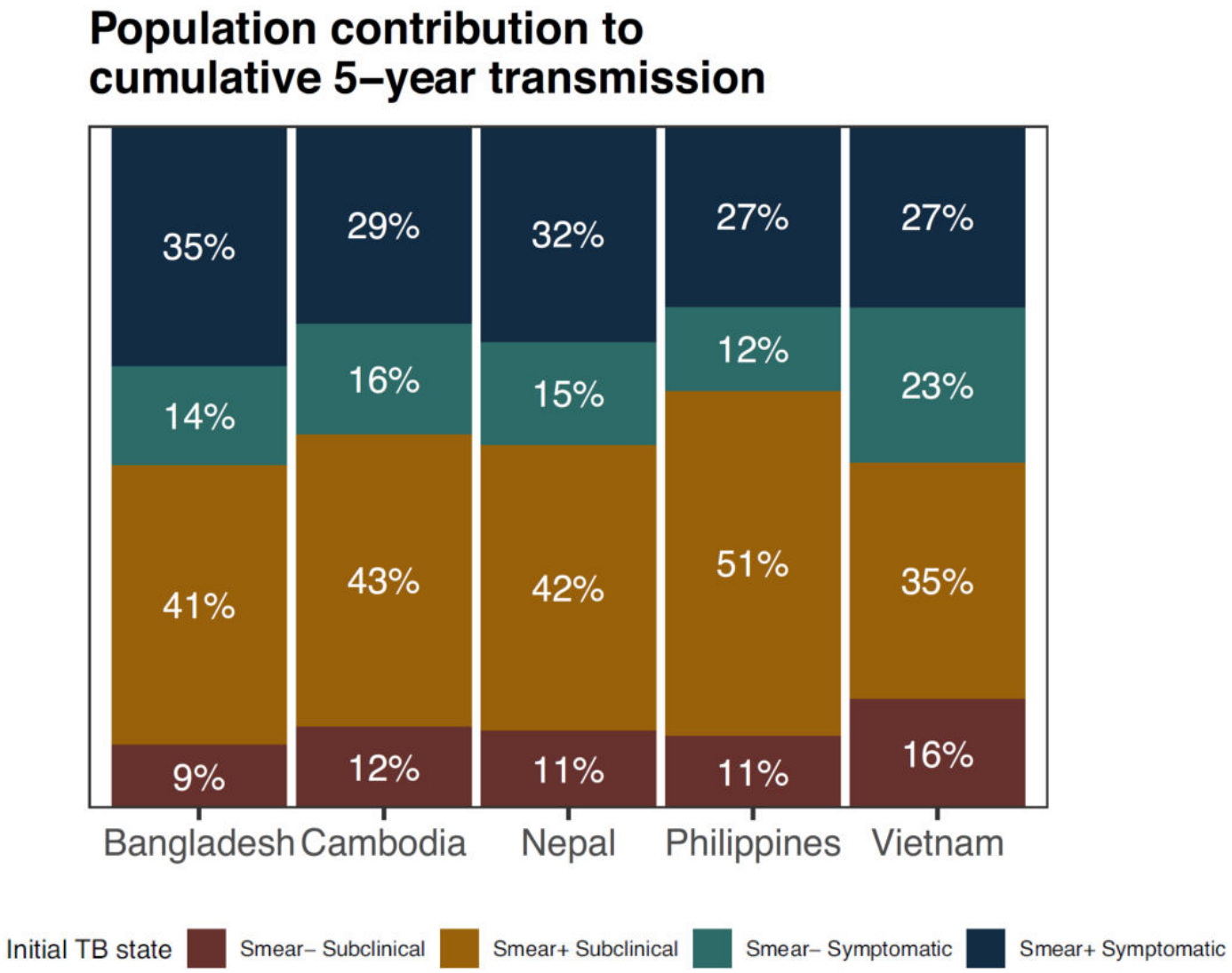


Asymptomatic TB

Prevalence surveys

"Between 36.1% and 79.7% (median, **50.4%**) of prevalent bacteriologically confirmed TB was **subclinical**."

Why do we need to pursue active case finding?



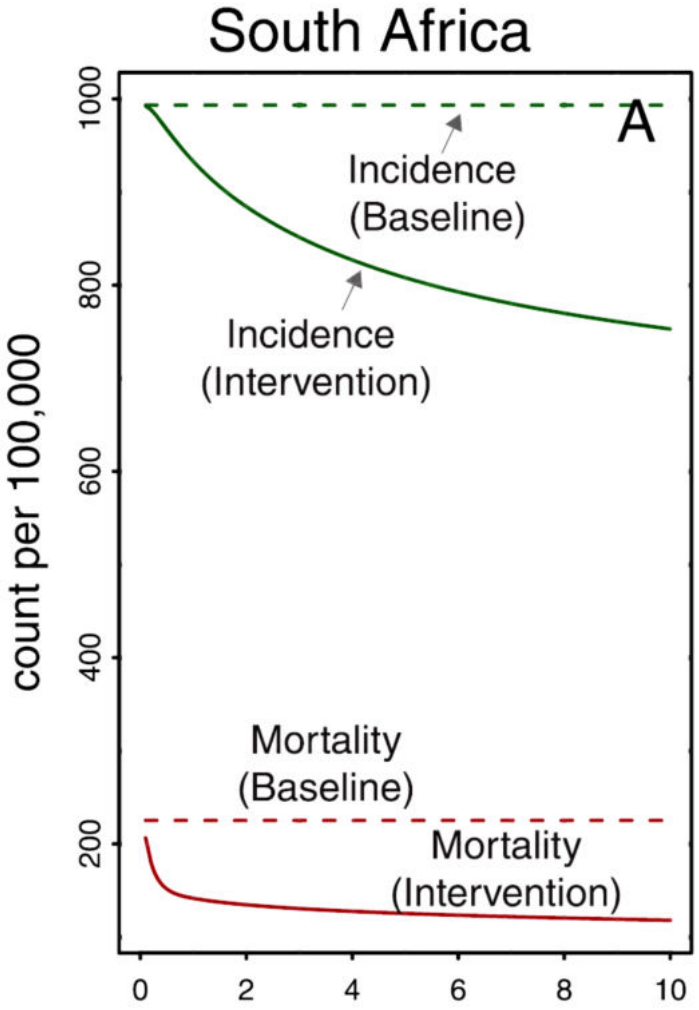
Transmission

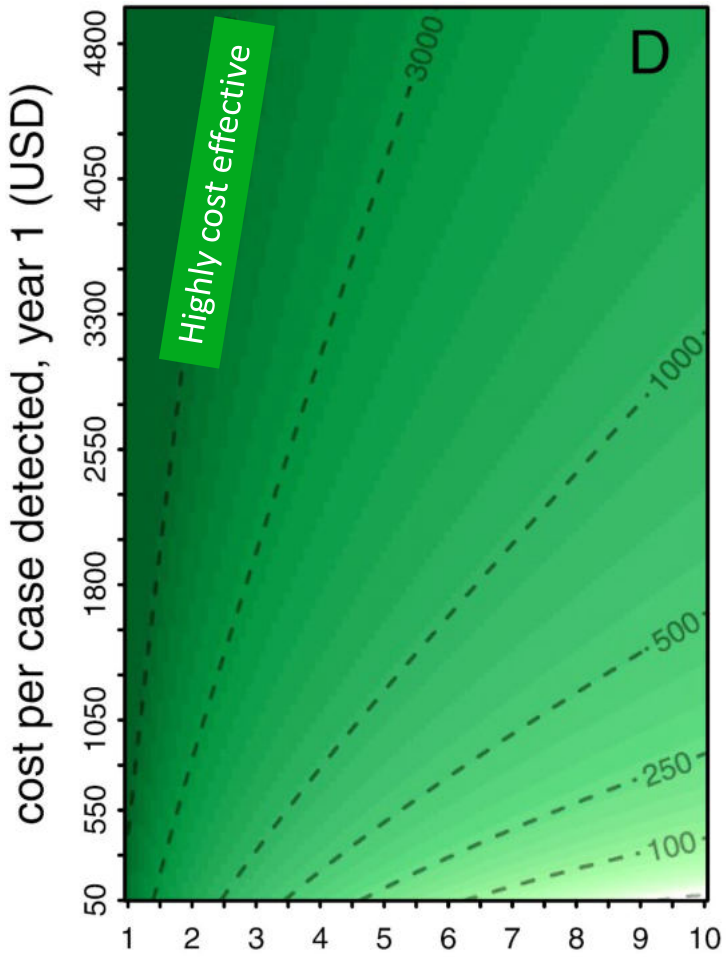
Bayesian modelling

"Despite accounting for only 11 to 19% of prevalent disease, **smear-positive subclinical TB accounted for 35 to 51% of future transmission**—a greater contribution than symptomatic or smear-negative TB."

Ryckman TS et al PNAS 2022

Why do we need to pursue active case finding?





Impact and cost-effectiveness

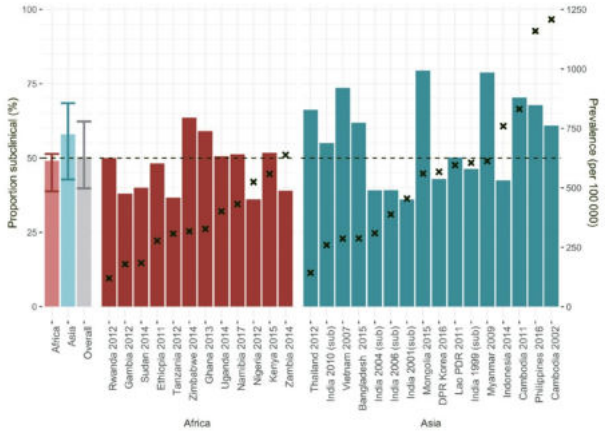
Model: Sustained ACF – 10y

"…**dramatic population impact** on incidence and mortality…

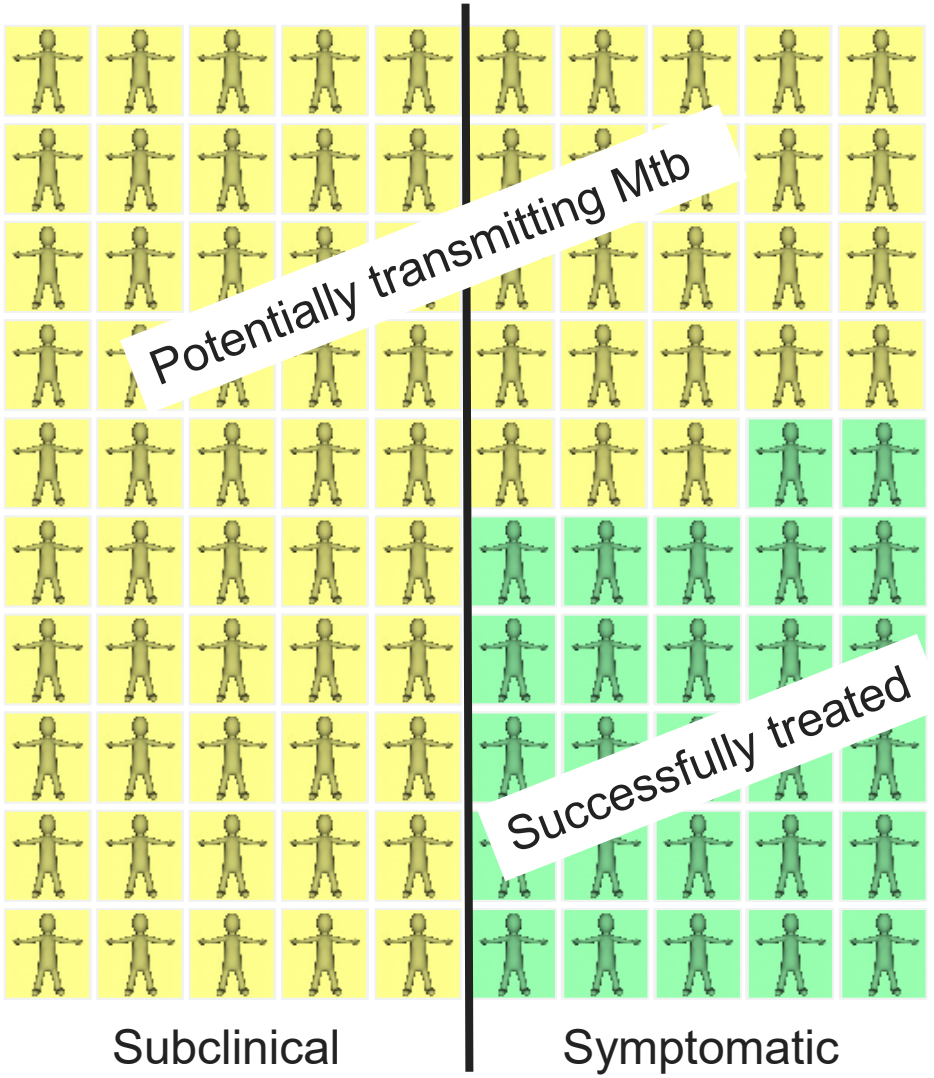
….sustained campaigns costing even $5000 per case detected are projected to be **highly cost-effective** (example: SA)"

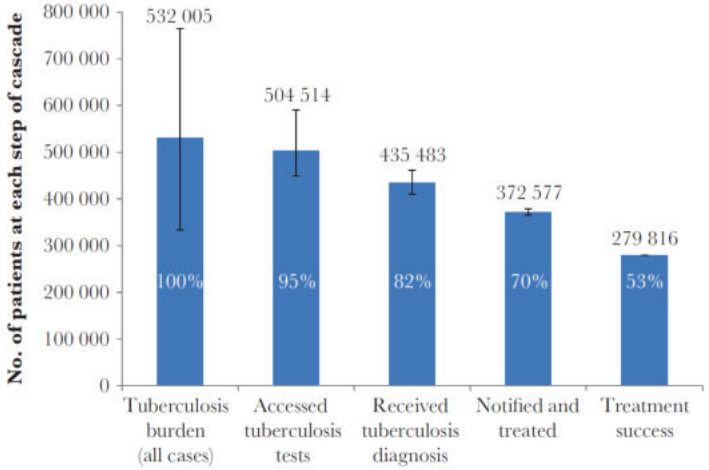
Azman AS et al BMC Med 2014

TB cases in the community



Frascella et al. CID 2021



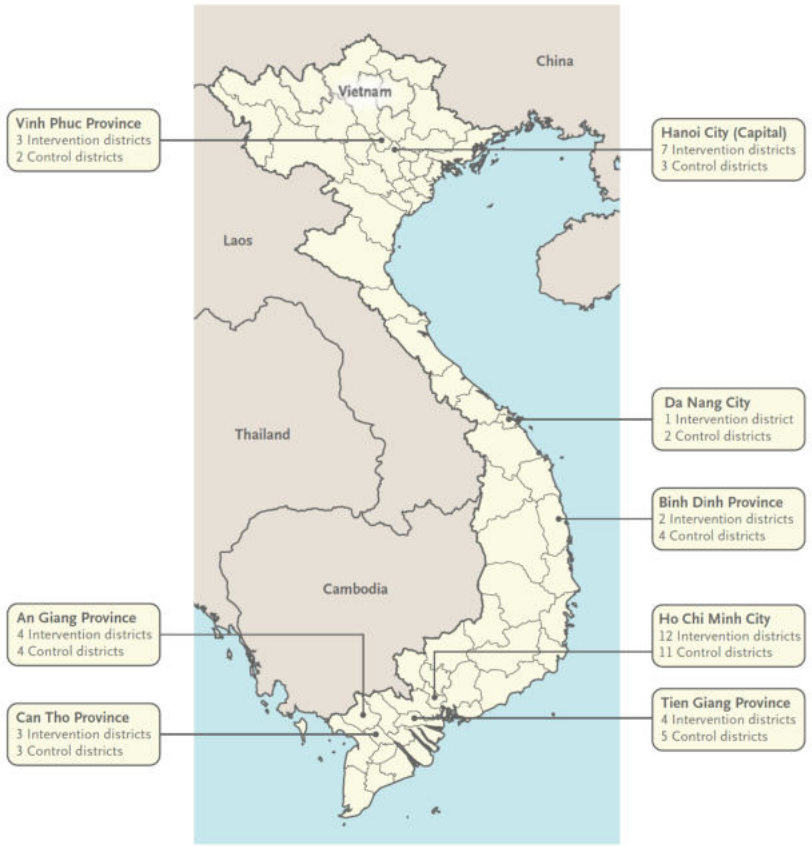


Naidoo et al. JID 2017

→ **symptom-agnostic screening is needed**

Example 1:

Individual-level targeted screening



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 18, 2018 VOL. 378 NO. 3

Household-Contact Investigation for Detection of Tuberculosis in Vietnam

Greg J. Fox, M.B., B.S., Ph.D., Nguyen V. Nhung, M.D., Ph.D., Dinh N. Sy, M.D., Ph.D., Nghiem L.P. Hoa, M.P.H., Le T.N. Anh, B.P.H., Nguyen T. Anh, M.D., Ph.D., Nguyen B. Hoa, M.D., Ph.D., Nguyen H. Dung, M.D., Ph.D., Tran N. Buu, M.D., Ph.D., Nguyen T. Loi, M.P.H., Le T. Nhung, B.P.H., Nguyen V. Hung, B.P.H., Phan T. Lieu, B.P.H., Nguyen K. Cuong, M.D., Pham D. Cuong, B.A., Jessica Bestrashniy, Ph.D., Warwick J. Britton, M.B., B.S., Ph.D., and Guy B. Marks, M.B., B.S., Ph.D.

- Cluster randomized controlled trial (districts: unit of randomization)
- 25,707 **household contacts** of 10,964 patients (smear-positive PTB)

Intervention: **household-contact intervention** (0/6/12/24m: clinical assessment and CXR) plus standard passive case finding
Control: passive case finding

Registered contacts with TB during the 2-year follow-up:
Intervention: 180 (1788/100,000)
Control: 110 (703/100,000)

Relative risk 2.5 (2.0-3.2, P<0.001)

Fox GJ et al. NEJM 2018

Example 2:

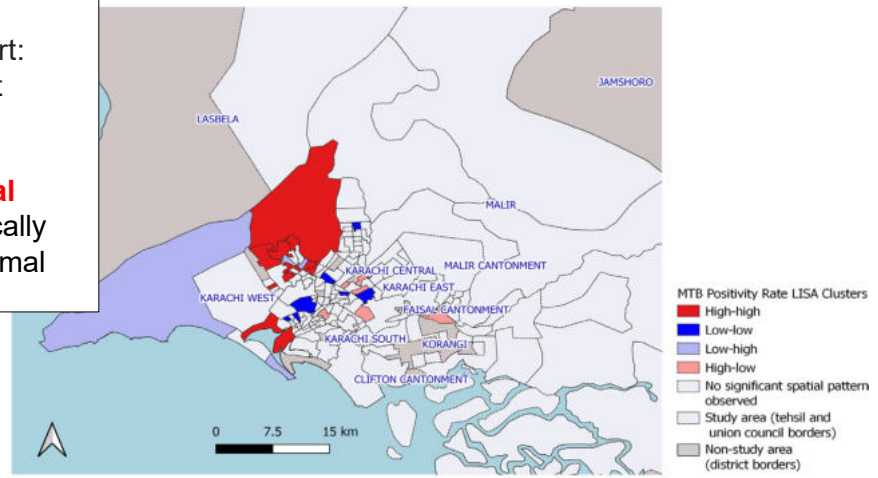
Spatially targeted screening

Evidence from randomized controlled trial on spatially targeted active case finding in high burden settings is still scarce

- **High-quality surveillance data required**
- Identification of TB incidence hotspots through spatial and pathogen genetic analyses
- Mathematical model suggest:
  Targeting hotspots reduces TB incidence in the area and transmission spillover

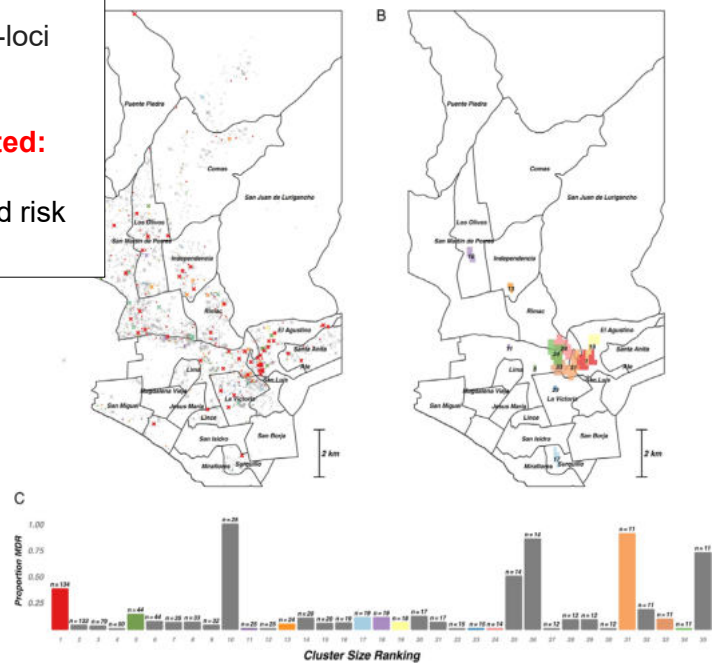
Example: Karachi, Pakistan
Screening: CXR: 197,693; Xpert: 6,571 in 1543 community chest camps

Statistically significant spatial variation: yield of bacteriologically positive TB cases and in abnormal CXR



Example: Lima, Peru
3286 culture positive, DST, 24-loci MIRU-VNTR

MDR-TB spatially concentrated: Risk of MDR-TB in hotspot comparable to MDR associated risk due to previously treated TB.

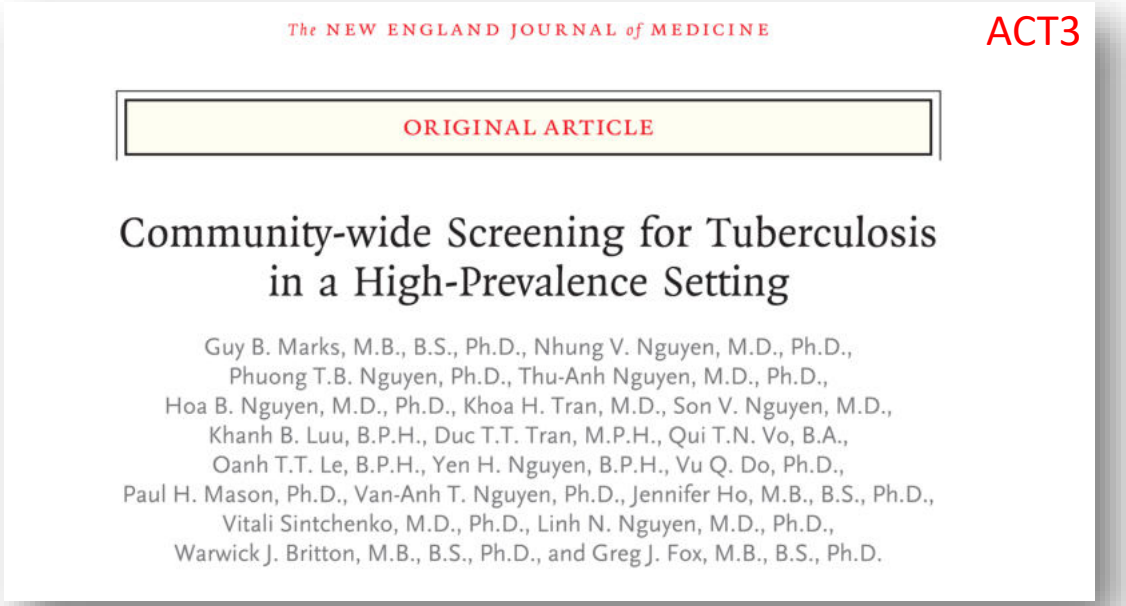


Cudahy PG et al. Lancet Infect Dis 2019

Zaidi SMA, et al. Sci Rep 2023
Zelner JL, et al. JID 2016

Example 3:

General population screening
high intensity and coverage



The NEW ENGLAND JOURNAL of MEDICINE

ACT3

ORIGINAL ARTICLE

Community-wide Screening for Tuberculosis in a High-Prevalence Setting

Guy B. Marks, M.B., B.S., Ph.D., Nhung V. Nguyen, M.D., Ph.D., Phuong T.B. Nguyen, Ph.D., Thu-Anh Nguyen, M.D., Ph.D., Hoa B. Nguyen, M.D., Ph.D., Khoa H. Tran, M.D., Son V. Nguyen, M.D., Khanh B. Luu, B.P.H., Duc T.T. Tran, M.P.H., Qui T.N. Vo, B.A., Oanh T.T. Le, B.P.H., Yen H. Nguyen, B.P.H., Vu Q. Do, Ph.D., Paul H. Mason, Ph.D., Van-Anh T. Nguyen, Ph.D., Jennifer Ho, M.B., B.S., Ph.D., Vitali Sintchenko, M.D., Ph.D., Linh N. Nguyen, M.D., Ph.D., Warwick J. Britton, M.B., B.S., Ph.D., and Greg J. Fox, M.B., B.S., Ph.D.

- Ca Mau Province, Vietnam
- Screened for pulmonary TB, regardless of symptoms
- Annually for 3 years
- Intervention - **All participants (43000!)**: eligible to be tested with Xpert MTB/RIF
- Control - No active case finding

Results	**Intervention** TB cases; TB prevalence (Xpert pos)	**Control** TB cases; TB prevalence (Xpert pos)
Year 1	169; 389/100000	
Year 2	136; 308/100000	
Year 3	78; 176/100000	
Year 4	53; 126/100000	94; 226/100000
Reduction in prevalence Y1-Y4: **64%** (Xpert pos/Cult. pos)		

	Xpert MTB/RIF actually done in intervention arm
Year 1	23282
Year 2	22375
Year 3	19890
Year 4	18837
84384 Xpert tests : 436 TB case	

→ Cost-effective?

Example 4:

General population screening
hard-to-reach, high-risk populations

TB TRIAGE+ Project

EDCTP
This project is part of the EDCTP2 programme supported by the European Union

TB TRIAGE+

www.tbtriage.com

Community-based tuberculosis triage testing ~~after symptom screening~~ in hard-to-reach African populations: CAD4TB versus C-reactive protein

Call: Diagnostic tools for poverty-related diseases
Funder: EDCTP
Amount: Euro 3.19 m
Period: 4 years & 1 Year NCE
Start: January 1, 2020

Partners

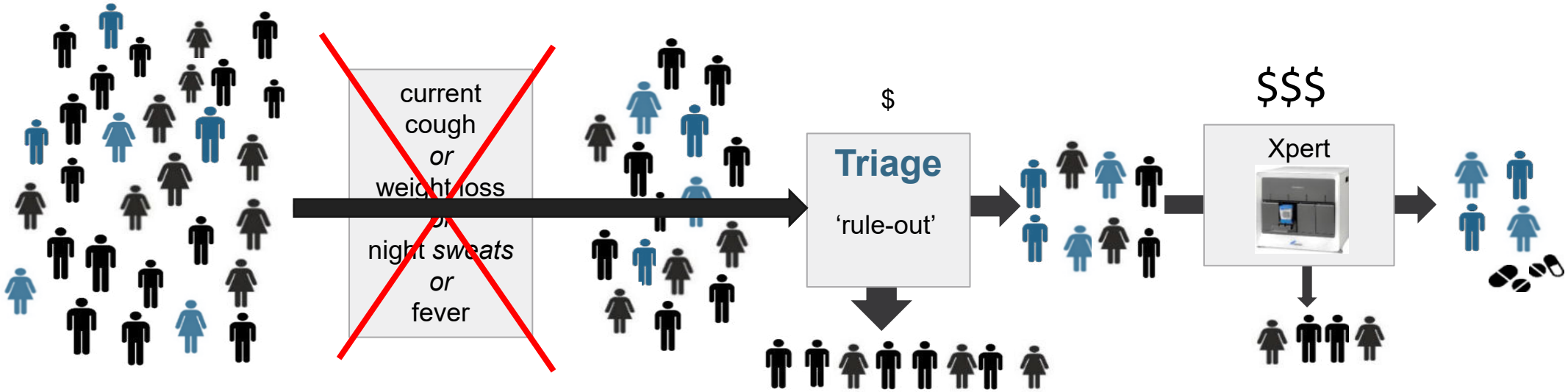
Swiss TPH
SOLIDARMED
HSRC Human Sciences Research Council
INSTITUTE OF TROPICAL MEDICINE ANTWERP
Radboudumc university medical center
University of Basel
CHARITÉ UNIVERSITÄTSMEDIZIN BERLIN

Triage testing can potentially improve active case finding in the community

Target product profiles (TPPs)
for TB triage tests

Sens. >95% min: >90%
Spec. >80% min: >70%

Low costs (<2$), fast, simple, non-sputum



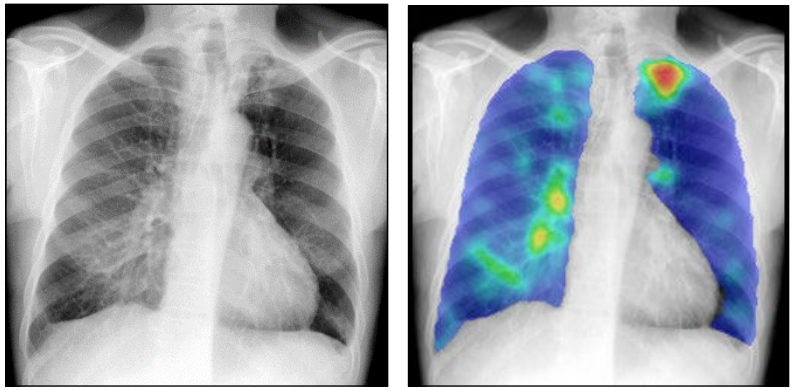
50% of infectious TB cases are asymptomatic

Triage test candidates

CAD4TB

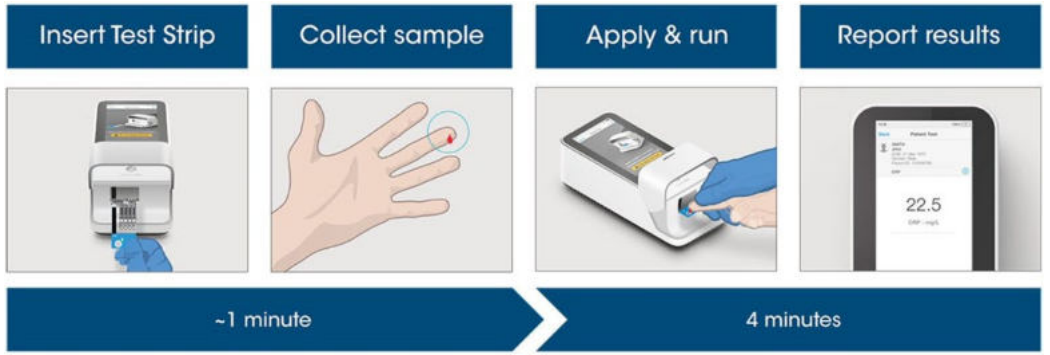
- **Computer-aided detection of tuberculosis using digital chest radiographs**

Deep Learning-Based Software
→ abnormality score (between 0 and 100)

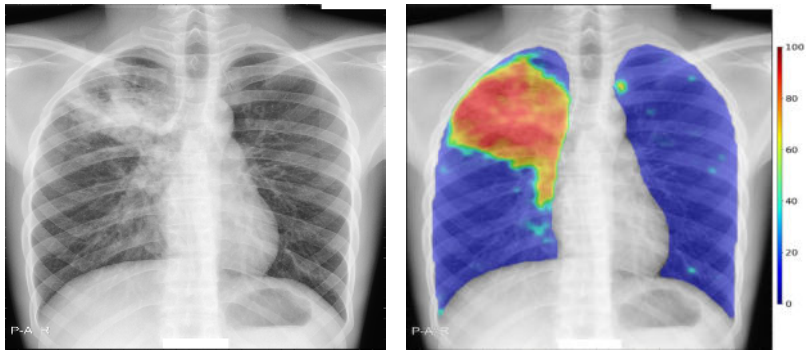


C-reactive protein (CRP)

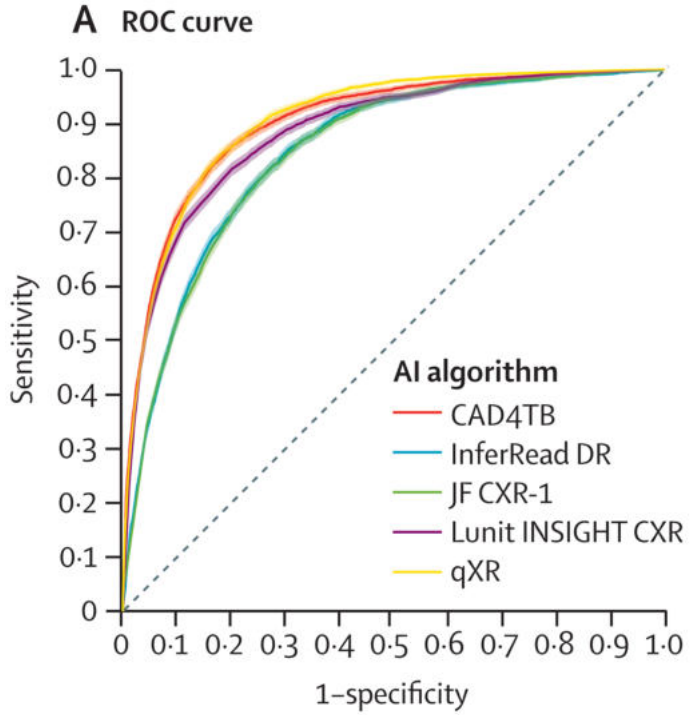
- **Marker for inflammation and infection**
- **Quantitative point-of-care tests available**



CAD: Computer-aided detection software



- High-sensitivity tuberculosis **rule-out test**
- CAD using newest versions of AI algorithms **outperforms experienced radiologists**
- Users need **threshold scores** identified from their own patient populations
- X-ray systems require standardization in terms of **technical properties**

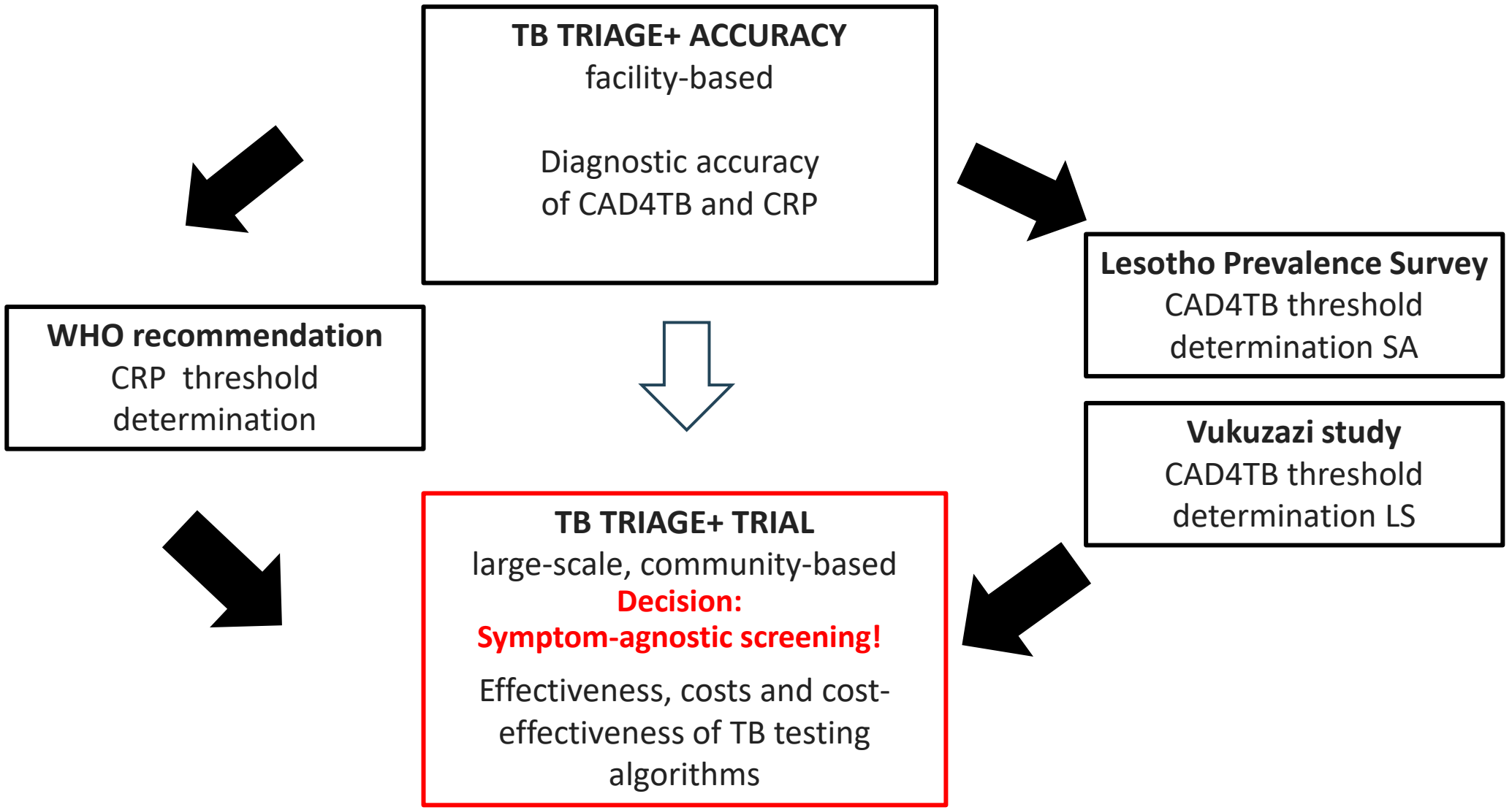


Swiss TPH

Murphy K et al Sci Rep 2020; Qin ZZ et al Lancet Digit Health 2021; Tavziva G et al CID 2022

Innovations in digital x-ray

Stationary - Mobile - Portable - Ultra-portable

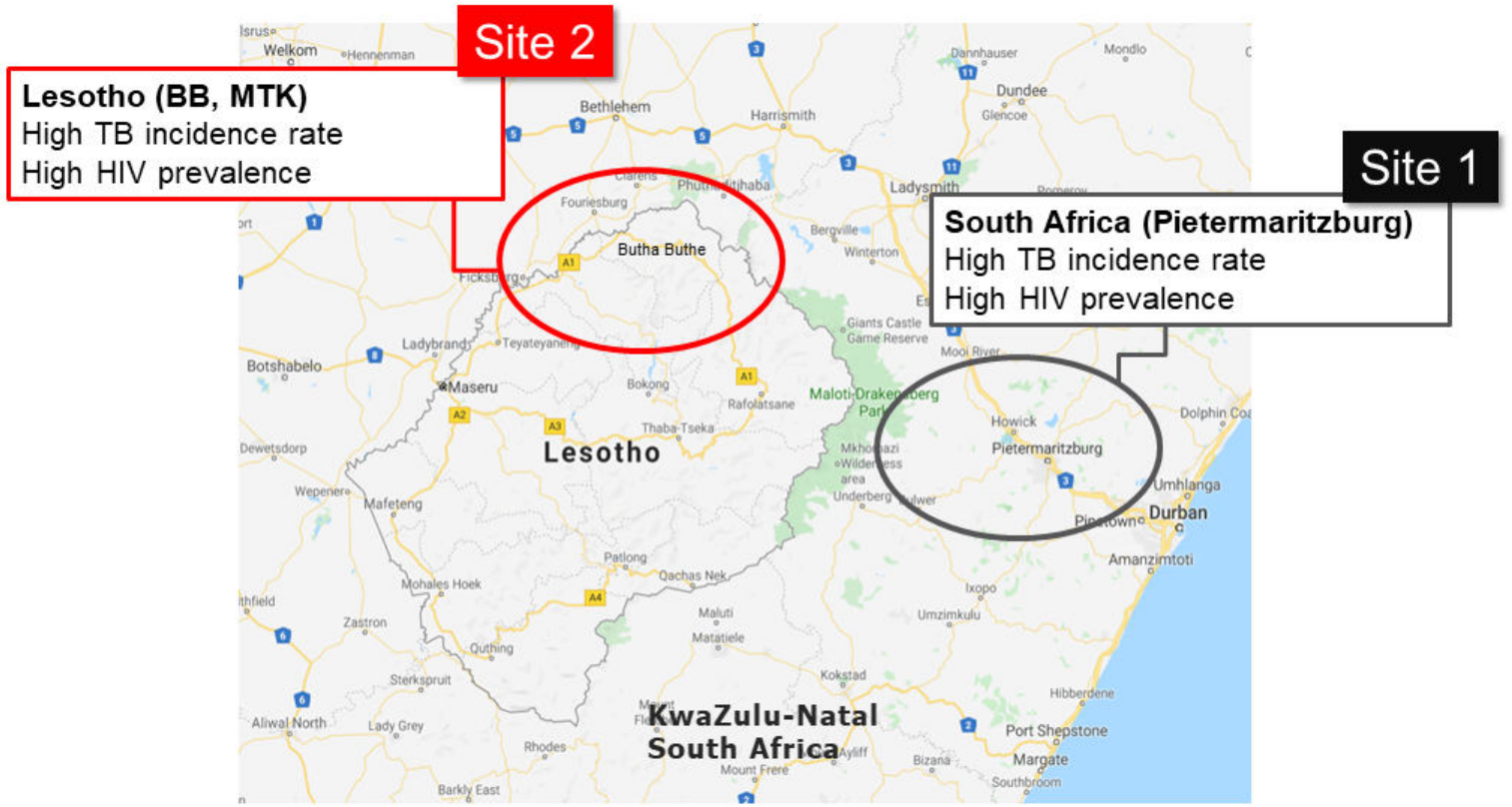

TB TRIAGE+ ACCURACY
facility-based
Diagnostic accuracy
of CAD4TB and CRP
WHO recommendation
CRP threshold
determination
Lesotho Prevalence Survey
CAD4TB threshold
determination SA
Vukuzazi study
CAD4TB threshold
determination LS
TB TRIAGE+ TRIAL
large-scale, community-based
Decision:
Symptom-agnostic screening!
Effectiveness, costs and cost-
effectiveness of TB testing
algorithms

TB TRIAGE+ TRIAL
large-scale, community-based

TB TRIAGE+

Lesotho and South Africa

- Community-based
- Community engagement
- Symptom-agnostic
- **20,000 individuals**
- Health economic analyses
- AHD package in community
- Hypertension and DM screening
- Same day treatment ART, CTX, TPT
- REDcap
- QGIS: geo-referencing
- Internal QC and external monitoring



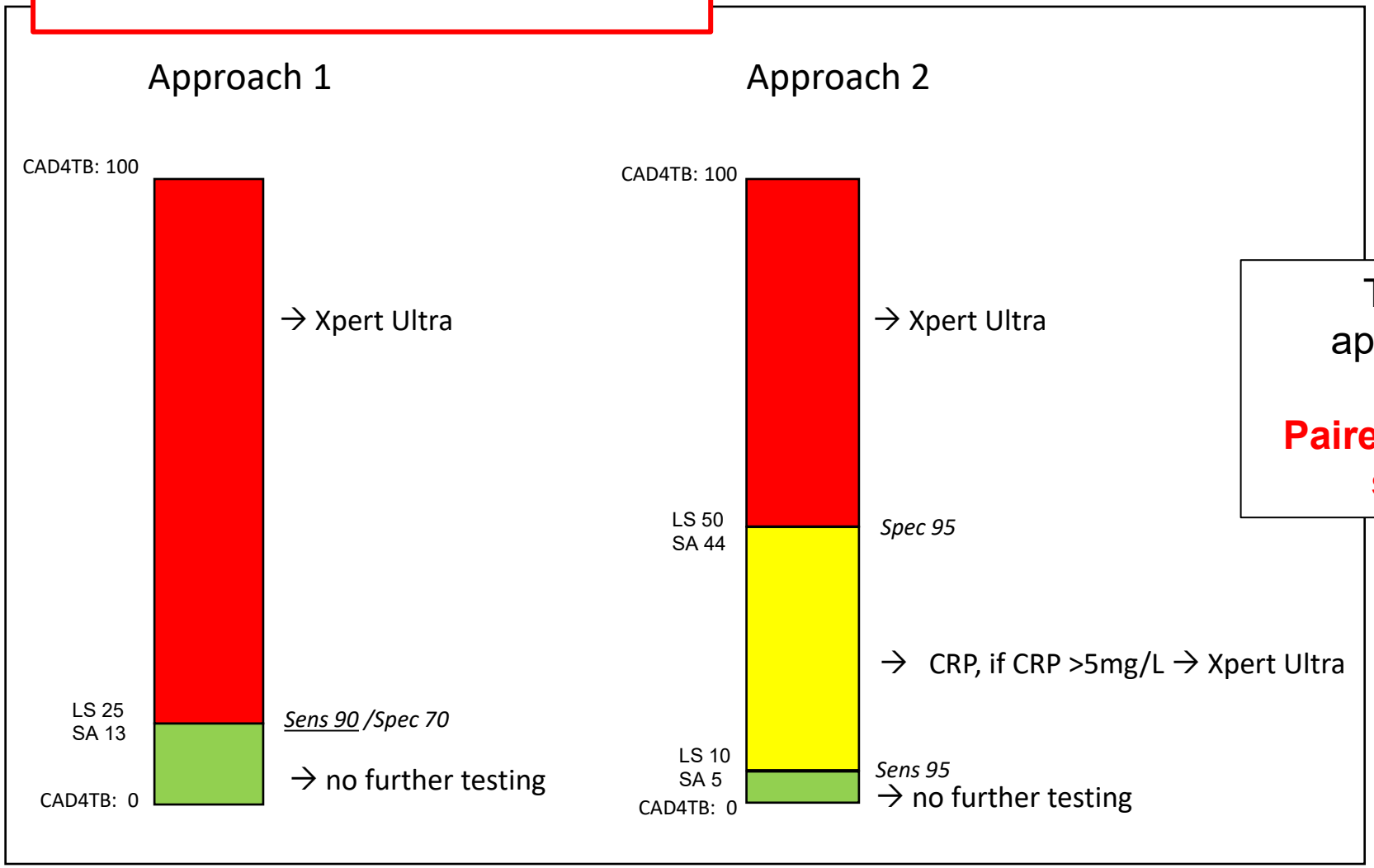
Swiss TPH

TB TRIAGE+

Overall aim:

To investigate the **effectiveness**, **costs and cost-effectiveness** of community-based **TB triage testing** algorithms consisting of CAD4TB screening alone (approach 1) compared to CAD4TB screening with POC-CRP triage testing (approach 2), followed by Xpert MTB/RIF Ultra rapid sputum molecular testing in both approaches

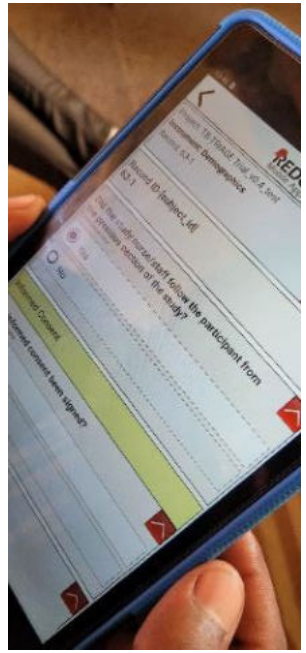
TB TRIAGE+ TRIAL
large-scale, community-based



Two diagnostic approaches in one participant:
Paired screen-positive study design

TB TRIAGE+ TRIAL
large-scale, community-based

South African site

→ Results by end of 2024

Conclusions: Active TB case finding

- New evidence, i.e. on subclinical TB, is fueling the discussion on the relevance of active TB case finding.
- Active symptom-agnostic TB screening has to become a priority if we are serious about "ending TB".
- Significant financial and logistical efforts are required, which cannot be left to national TB programs alone.
- Efficient standardization remains a challenge for the widespread use of CAD software.
- Context-specific research on active screening strategies (individual-level targeted, spatially targeted, community-wide) for both adults and children is of key importance.

Thank you!

EDCTP
Debora Bade

Scientific Advisory Board (SAB)
Christina Yoon
Graeme Meintjes
Sian Floyd
Anja van't Hoog

TB TRIAGE + Collaborators

Swiss TPH
Klaus Reither
Aita Signorell
Tracy Glass
Johanna Kurscheid
Moniek Bresser
Rahel Erhardt
Marina Antillon
Anna Verjans
Fabrizio Tediosi
Franziska Graf
Eric Huber
Christelle Laufenburger

ITM Antwerp
Lutgarde Lynen
Alfred Keter
Bart Jacobs
Tinne Gils

Radboud University
Bram van Ginneken
Keelin Murphy

SolidarMed Lesotho
Irene Ayakaka
Mashaete Kamele
Pauline Grimm
Bulemba Katende

HSRC South Africa
Alastair van Heerden
Shannon Bosman
Thandanani Madonsela
Thulani Ngubane
Philip Joseph

Charité Berlin
Thomas Zoller

University Hospital Basel
Jens Bremerich
Niklaus Labhardt

A short summary of the day and take-home messages

Jean-Paul Janssens, Geneva

LUNGENLIGA
LIGUE PULMONAIRE

Case Management
David Augier – Ligue pulmonaire fribourgoise

- Case history of a Ukrainian patient, former prisoner (several stays), treated for MDR-TB, co-morbid (ENT cancer with PEG, tracheostomy, HIV, chronic HBV, cured HCV).
- Personality disorder, ex drug addiction, non-compliance
- Complex follow-up: non-compliance, refusal of treatment, substance abuse, breach of contract, discussion of restrictive measures (never applied..)
- Death following massive stroke, after 9 months of chaotic treatment
- *Discussion: Challenge of multidisciplinary coordination in a complex case*

LUNGENLIGA
LIGUE PULMONAIRE

Contact tracing for TB in a complex HIV context.
Veronica Maglio - Ligue Pulmonaire Vaudoise.

- MDR miliary TB in a young student of Asian origin, living with HIV since 2019 (untreated); disseminated involvement (including CNS)
- Language barrier, fragile patient, request for anonymity...
- Centrifugal contact investigation: 0 infected cases identified
- *Main problems: language barrier, feeling of guilt related to TB & HIV, very affected by stigma*

LUNGENLIGA
LIGUE PULMONAIRE

Contact tracing
Renate Stumpf-Wüthrich - Ligue Pulmonaire, St Gall

- M 25 years old, Swiss, prisoner, tt for LTBI (INH: 4.20-01.21), history of drug abuse:

  unconfirmed suspicion of case of Pulmonary TB with hemoptysis

- Potential secondary case (unconfirmed): woman living with him

- Case illustrates difficulties in communication, and in obtaining reliable information

LUNGENLIGA
LIGUE PULMONAIRE

International contact tracing after exposure to TB
Philipp Ludin, BAG, Bern

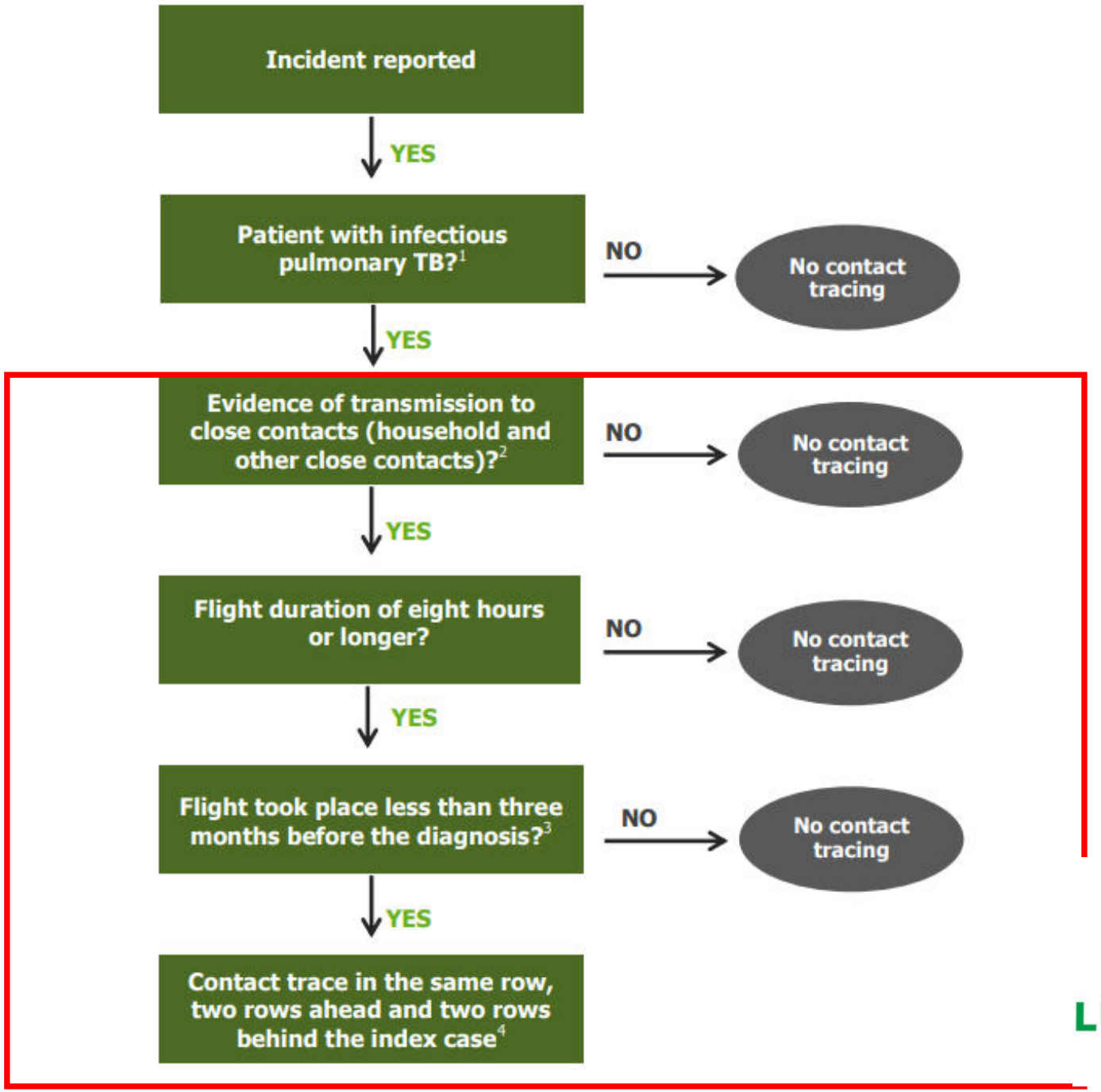
- Only the *national health authorities of the destination country* are competent to determine whether an CTP is carried out after using an international means of transportation.
- Passenger lists are requested by national health authorities
- Exposed persons are reported to the country of residence. The country of residence (or local authorities) decide on any measures to be taken.

LUNGENLIGA
LIGUE PULMONAIRE

International contact tracing after exposure to TB(2)
Philipp Ludin, BAG, Bern

- Risk of transmission considered very low in aircraft ← use of HEPA filters
- Estimated risk: 0.1-1.3% (> 8h flight, highest if seated in close proximity to IC)
- No known active tuberculosis after aircraft exposure reported
- Very high cost for CTP
- Risk in buses or trains estimated higher than in airplanes (but no international recommendations)
- Important decision points (RAGIDA): CTP if evidence of transmission, if flight > 8 hrs, if time since diagnosis < 3 months.
- See *ad hoc forms* for solliciting OFSP/BAG on LPS website

Figure 1. Risk assessment algorithm, TB



LUNGENLIGA
LIGUE PULMONAIRE

Tuberculosis in Switzerland, Nathalie Gasser, LPS, Competence Center for TB

- Reminder of the roles of the TB Competence Center, LPS
- Data on TB treatments, CTPs and treatment for LTBI in CH
- Preventive treatment of LTI is of paramount importance, especially in young exposed children and people at increased risk of progression
- => PERISKOPE calculator (www.periskop.org) : working tool for risk estimation.

LUNGENLIGA
LIGUE PULMONAIRE

Tuberculosis in Switzerland, Nathalie Gasser, LPS, Competence Center for TB

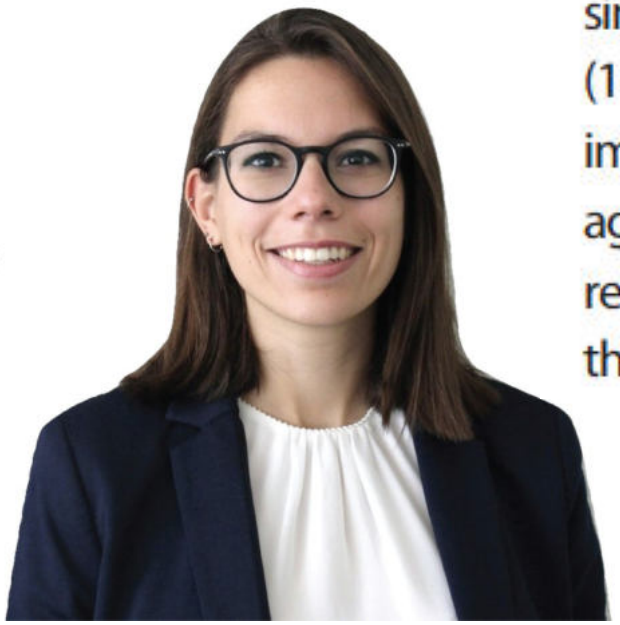
- 2021: 357 cas de TB reported to BAG (-4%/2020)
- Incidence: 4.7/100’000 inhab (low incidence; WHO world: 134/100’000)
- Highest number of cases: ZH>VD>GE>BE
- 67% (239) of TB cases pulmonary, 27% (96) extra-pulmonary
- Most cases aged between 20 and 50 years
- 181 contact tracing procedures: 1023 people tested, 152 infected (14.9%)
- Rate of infection ranged from 10% to 14.9 % between 2017 and 2021
- 73 % (111) of those infected started TB preventive therapy; 52 (47%*) completed preventive therapy (5% of subjects tested)

*: figure debated

LUNGENLIGA
LIGUE PULMONAIRE

Swiss-TB award 2023: Dr Ophelie Rutschmann, EPFL, Lausanne

Preexisting Heterogeneity of Inducible Nitric Oxide Synthase Expression Drives Differential Growth of Mycobacterium tuberculosis in Macrophages (mBio 13: e0225122)



Our finding that preexisting heterogeneity in host cells can have an impact on the growth of intracellular *M. tuberculosis* is particularly relevant for tuberculosis, because even a single bacterium infecting a single permissive host cell may be sufficient to initiate an infection (14, 15). Macrophages have been reported to exhibit heterogeneity in the expression of many immune-related genes due to factors such as circadian rhythm, environmental variation, or age of the host, which could all impact how they respond to an initial infection (44–47). Our results suggest that differences in the expression of even a single antimicrobial gene, such as the gene for iNOS, could be sufficient to influence the outcome of infection. This conclusion

LUNGENLIGA
LIGUE PULMONAIRE

Diagnosing tuberculosis in the light of new technologies

Grant Theron – Stellenbosch University, South Africa

- mmm

Point-of-care thoracic ultrasound (POCUS) for the diagnosis of pulmonary tuberculosis: The TRUST study

Véronique Suttels – CHUV, Lausanne

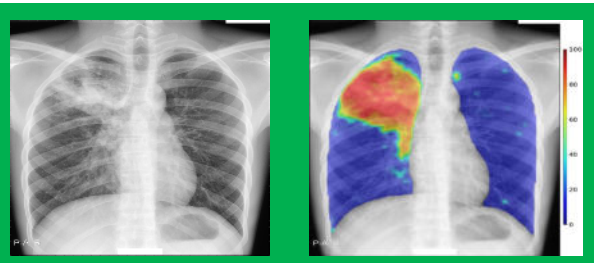
- Is POCUS a new triage tool for pulmonary TB (selecting patients for Xpert testing?
- Multicentric African cohort study (6 month FU; target population n=1000*)
- With its **high AUC (0.84)** and especially **low neg LR (0.1)**, thoracic POCUS seems a **promising triage tool** to exclude pulmonary TB on an outpatient basis in adult patients with respiratory syndrome in endemic areas

*: Mali, Benin, RSA, Namibia

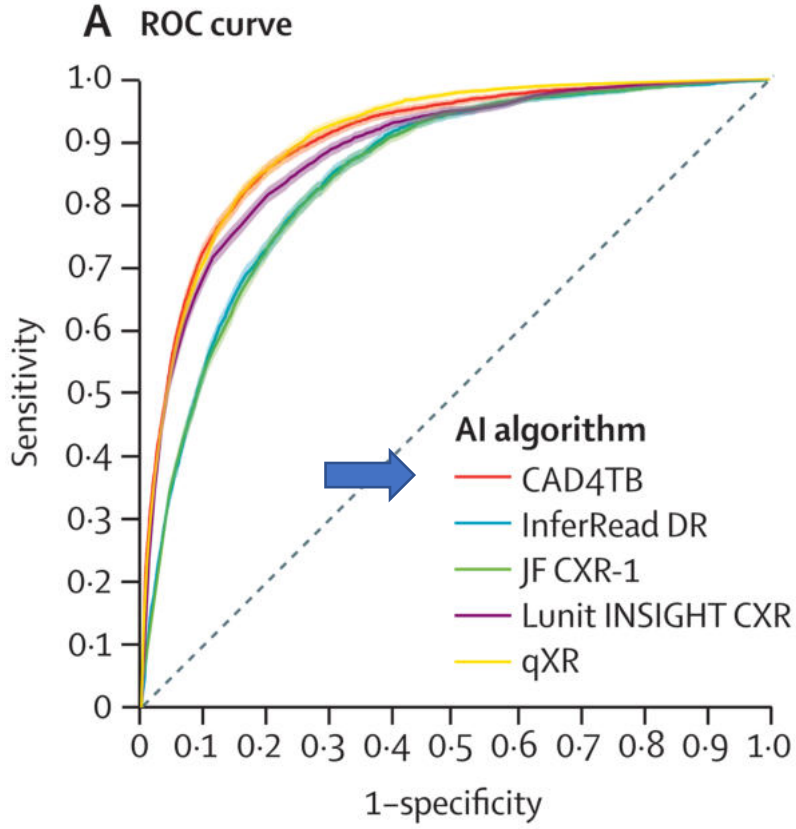
LUNGENLIGA
LIGUE PULMONAIRE

Active TB case finding in high burden settings

Klaus Reither MD, MSc, PhD, Swiss TPH



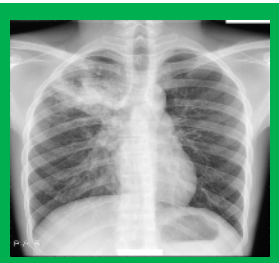
- High-sensitivity tests required to rule out TB
- Computer Assisted Diagnostics using newest versions of AI algorithms outperform experienced radiologists
- Users need threshold scores identified from their own patient populations
- X-ray systems require standardization in terms of technical properties

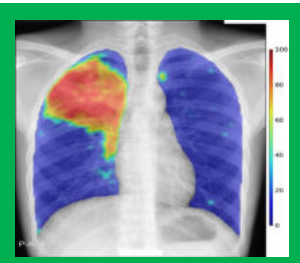


LUNGENLIGA
LIGUE PULMONAIRE

Active TB case finding in high burden settings (2)

Klaus Reither MD, MSc, PhD, Swiss TPH





- **Triage testing** can potentially improve active case finding in the community
- New evidence, i.e. on **subclinical TB**, is fueling the discussion on the relevance of active TB case finding.
- **Active symptom-diagnostic** TB screening has to become a priority if we are serious about "ending TB".
- Significant financial and logistical efforts are required, which cannot be left to national TB programs alone.
- Context-specific research on active screening strategies is of key importance.

Thank you to all the speakers and intervenants and all the participants

A special thank you to Nathalie Gasser, Monika Husi-Hostettler and all those who participated to organizing this meeting

See you next year!

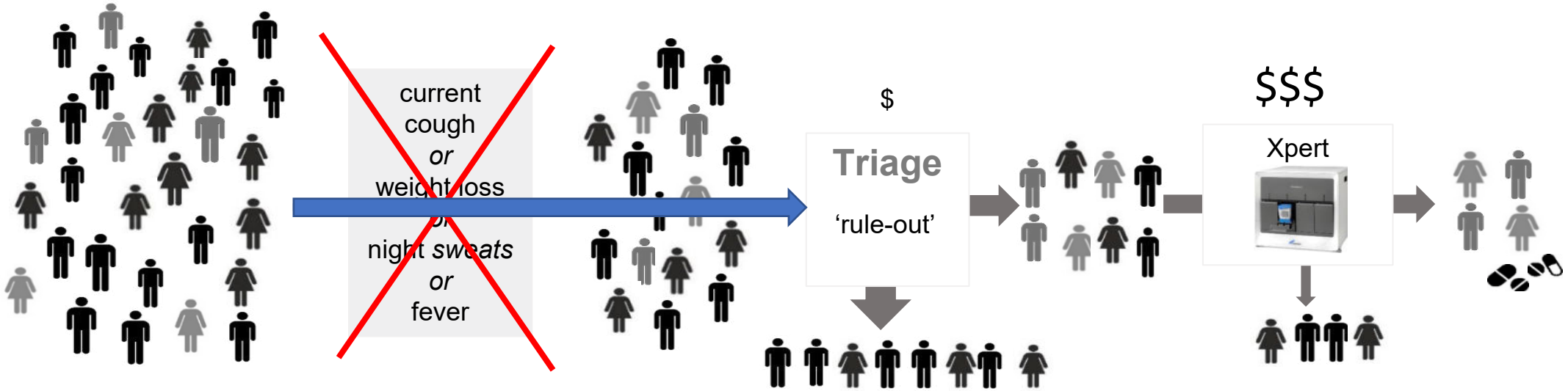
LUNGENLIGA
LIGUE PULMONAIRE

Triage testing can potentially improve active case finding in the community

Target product profiles (TPPs)
for TB triage tests

Sens. >95% min: >90%
Spec. >80% min: >70%

Low costs (<2$), fast, simple, non-sputum



50% of infectious TB cases are asymptomatic

Conclusions: Active TB case finding

- Triage testing can potentially improve active case finding in the community
- New evidence, i.e. on subclinical TB, is fueling the discussion on the relevance of active TB case finding.
- Active symptom-agnostic TB screening has to become a priority if we are serious about "ending TB".
- Significant financial and logistical efforts are required, which cannot be left to national TB programs alone.
- Efficient standardization remains a challenge for the widespread use of CAD software.
- Context-specific research on active screening strategies (individual-level targeted, spatially targeted, community-wide) for both adults and children is of key importance.

LUNGENLIGA
LIGUE PULMONAIRE

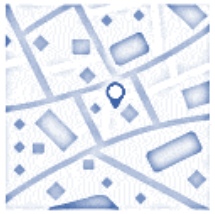
Case detection strategies

Passive case finding: TB patients **self-presenting** to routine health services

Enhanced case finding: **Health information or education** to encourage health-seeking behaviours, with or without increasing access to diagnostic services

Active case finding: **General population screening** using any test/procedure, in communities (e.g. door-to-door) or at health facilities

Individual-level targeted screening, e.g. PLHIV, household contacts of a TB case, workers exposed to silica



Spatially targeted screening, within geographically restricted populations (e.g., neighbourhoods or sub-districts) based on surveillance data

LUNGENLIGA SCHWEIZ
LIGUE PULMONAIRE SUISSE
LEGA POLMONARE SVIZZERA
LIA PULMUNARA SVIZRA

Vielen Dank für Ihre Teilnahme…

Merci pour votre participation…

Mit Unterstützung von
Avec le soutien de

QIAGEN

DiaSorin

LUNGENLIGA SCHWEIZ
LIGUE PULMONAIRE SUISSE
LEGA POLMONARE SVIZZERA
LIA PULMUNARA SVIZRA

…und bis nächstes Jahr

…et à l'année prochaine

SAVE THE DATE
21 / 3 / 2024