Session 3: Access to Medicines and TB

TB State-of-the-Art: Implications for Africa

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INTEREST 2020

TB state-of-the-art: implications for Africa

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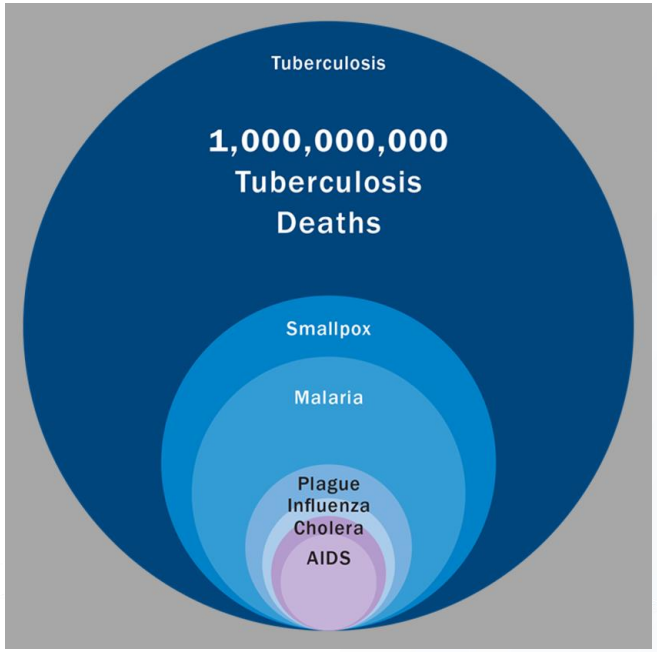
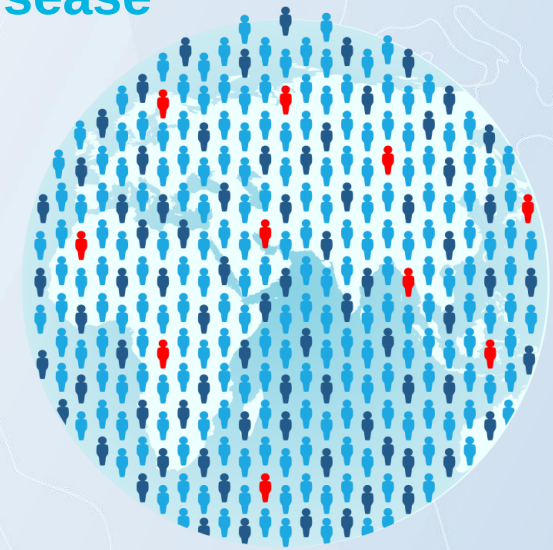
• Tuberculosis remains the number 1 infectious disease killer globally

• TB has killed more people in the last 200 years than any other disease



In 2019:

- ❑ 10 million new cases of TB
  - 3 million undiagnosed/un-treated
- ❑ 1.4 million deaths due to TB
  - Leading killer of People living with HIV
- ❑ 1/4 of all AMR-related deaths
  - ~ 0.5 million new cases of drug-resistant TB



World's population estimated at ~7.4 billion

One-third are infected with Mtb

10% of those infected will develop active TB

Source: WHO Global TB Report 2016

15 of 30 high burden countries are in Africa
Highest incidence of TB disease is in Africa

- Africa 226/100 000
- South Africa 615/100 000

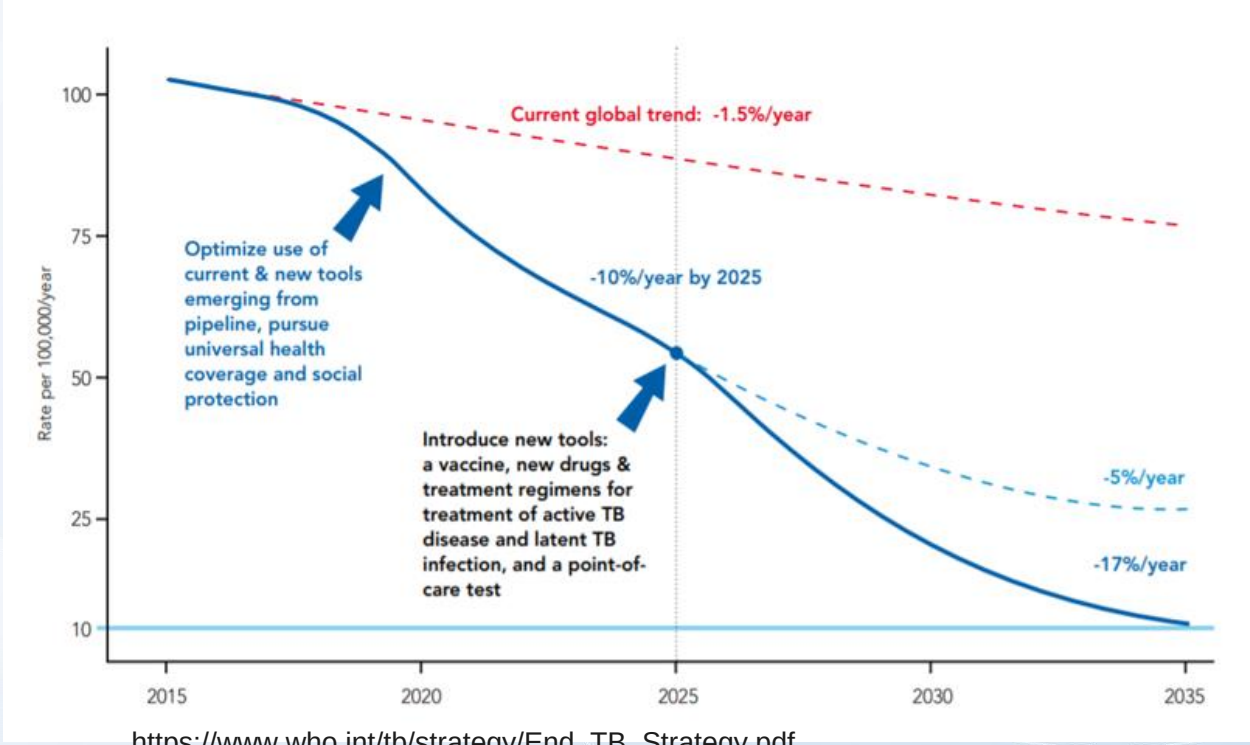
Global tuberculosis report 2020. Geneva: World Health Organization; 2020
https://www.who.int/tb/publications/global_report/en/

NEW TOOLS ARE ESSENTIAL TO END THE TB EPIDEMIC
DRUGS, DIAGNOSTICS, VACCINES

THE END TB STRATEGY

World Health Organization

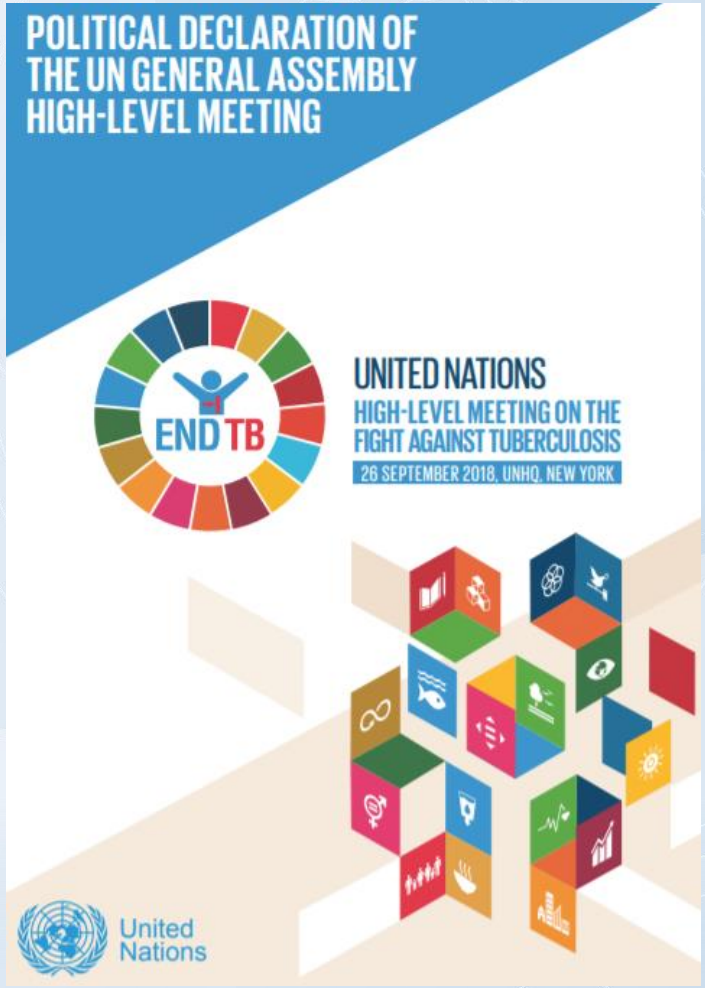
- WHO End TB Strategy targets of a **95% reduction in TB mortality** and a **90% reduction in TB incidence** by 2035
- To attain this target new tools are required to prevent tuberculosis



https://www.who.int/tb/strategy/End_TB_Strategy.pdf

UN High-Level Meeting 2018

- **UN** General Assembly **high-level meeting on tuberculosis** on 26 September 2018 endorsed an ambitious and powerful **political declaration** to accelerate progress towards End **TB** targets.
- **Declaration** was adopted by the General Assembly 10 October 2018



https://www.who.int/tb/unhlmonTBDeclaration.pdf

Progress

- Still falling behind for four key targets: treatment; preventive treatment; research; and, funding. Especially funding

- How will countries be held accountable to the targets they agreed to?
  - accountability process being led by the WHO
  - "Once we know where accountability stands, then we know how to improve, and where to target improvements."

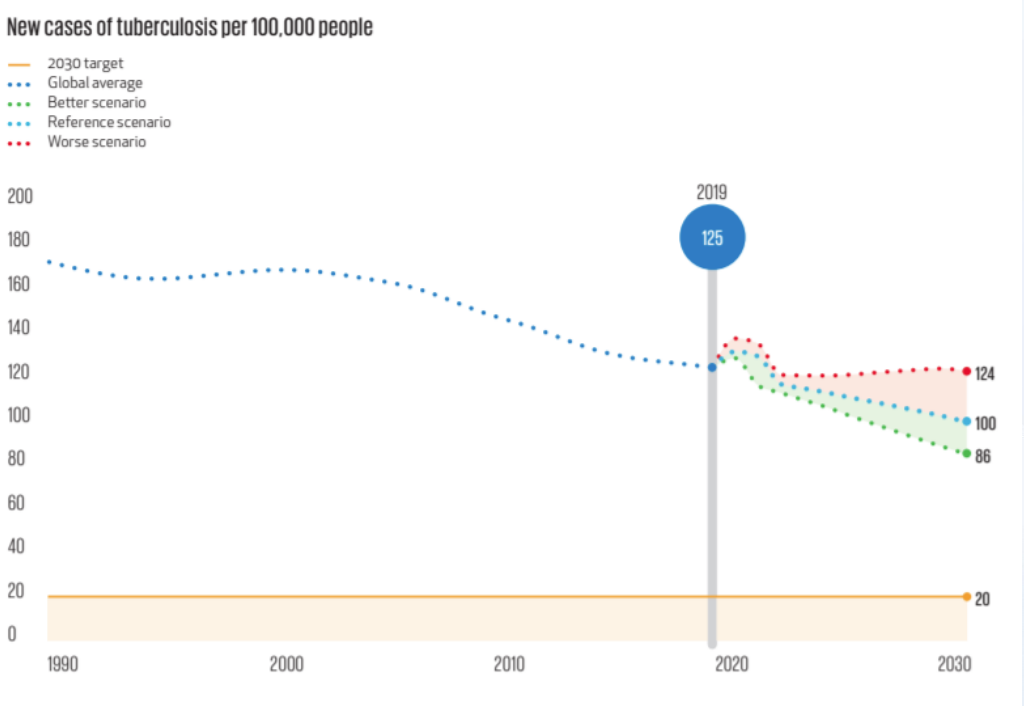
Covid-19 and TB

- Impact on TB
  - Poorer Covid-19 outcomes in patients with TB
  - Impact on TB control programmes; utilizing TB infrastructure for Covid
  - Increased morbidity, mortality, and transmission
  - Impact on TB research programmes
  - Impact on future research funding?

- Lessons from Covid-19 for TB going forward
  - Leverage massive Covid-19 innovation on health technologies, social change, behavioral change, policy change
  - Utilise new developments in **digital support systems** for labs and contact tracing
  - **Political understanding that "health is wealth"**

Cost of not ending TB by 2035 will be US$3 trillion and over 28 million deaths*

* The economic cost of inaction - the welfare penalty - of not meeting the target until 2045. THE 51ST UNION WORLD CONFERENCE ON LUNG HEALTH OA-29-680-23- Silva *et al*



“Lost 5-8 years of progress”

http://www.stoptb.org/assets/documents/news/Modeling%20Report_1%20May%202020_FINAL.pdf

https://www.gatesfoundation.org/goalkeepers/downloads/2020-report/report_a4_en.pdf

Four Month Course Therapy for Drug Sensitive TB "A Monumental Achievement"

Since 1980's 6 month TB treatment course.

Shorter courses will improve adherence and reduce costs for the health system and for people with TB.

2516 randomized to one of three regimens:

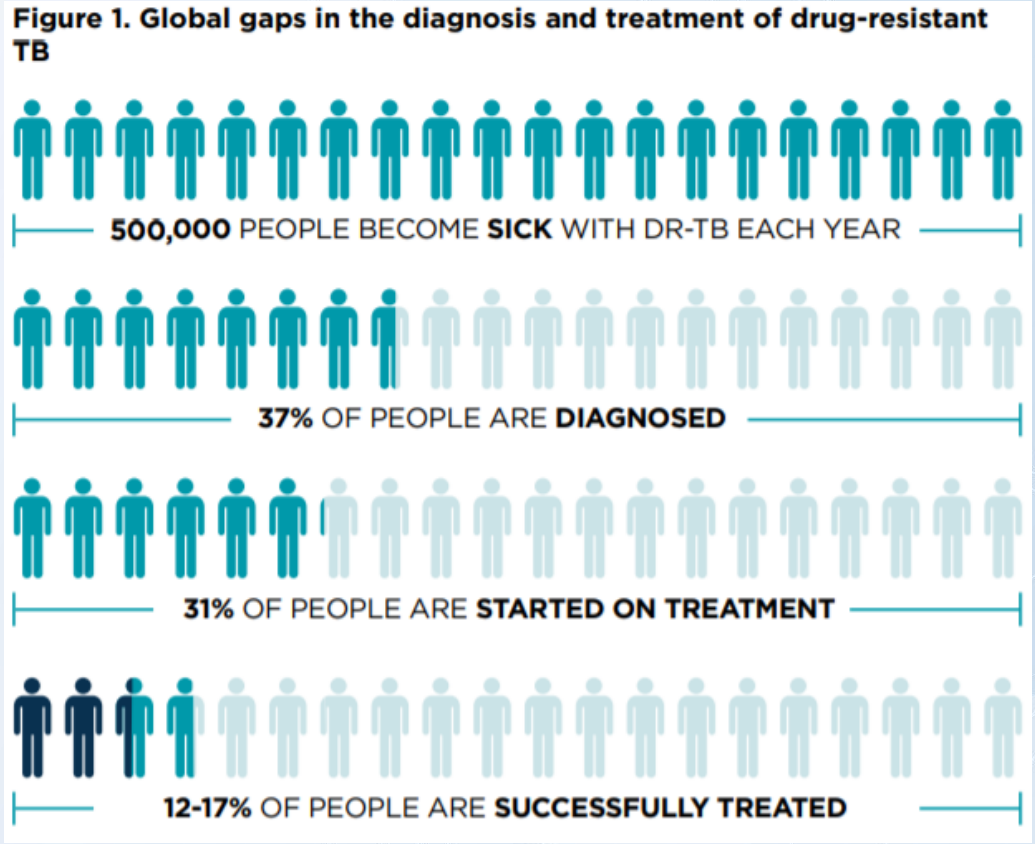
- Standard-of-care (SoC) - 6 months
- Rifapentine substituted for rifampicin as the basis of 4-month treatment (RPT).
- Rifapentine substituted for rifampicin and moxifloxacin is substituted for ethambutol as the basis of 4-month treatment (RPT-MOX).
- Safety similar in all arms
- **<u>RPT-MOX met criterion of non-inferiority</u>**
- RPT was inferior to SoC
- WHO to consider these results when updating treatment guidelines

DRUG RESISTANT TUBERCULOSIS

~500 000 developed rifampicin-resistant TB (RR-TB)

- 78% had multidrug-resistant TB (MDR-TB)
- 3.3% of new TB cases and 17.7% of previously treated cases had MDR/RR-TB (Global Tuberculosis Report 2020)

Treatment costs are 8-fold to 15-fold higher than for treating drug-sensitive TB. In LMICs may be unaffordable with consequence of high fatality rates and transmission of drug resistant strains.



https://www.treatmentactiongroup.org/wp-content/uploads/2020/07/activists_guide_dr_tb_treatment_2020.pdf

There is no evidence suggesting that molecular mechanisms of drug resistance in Mtb affect the susceptibility to immune control.

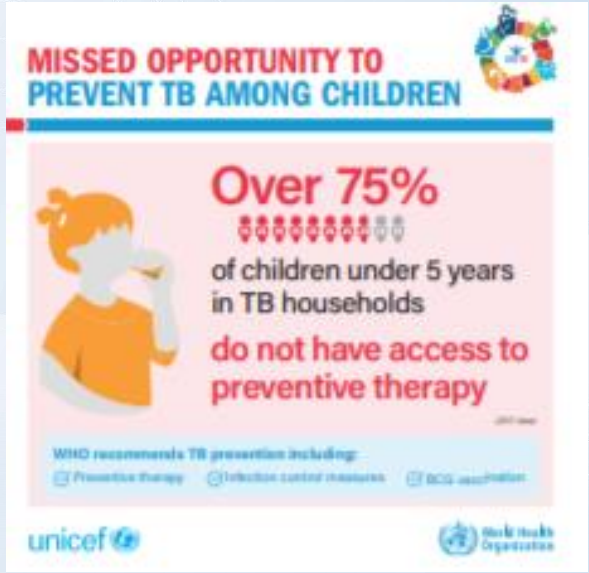
- Therefore, it is likely that vaccine protection against drug-resistant TB will be equivalent to that against drug sensitive TB.

TB Preventive Treatment (TPT)

- Prevention of progression to TB disease critical to reduce burden of ill health and death caused by TB
- Important arm of TB control programmes
- Shorter and better tolerated courses available
- Targets not being met:

Implementation

UNHLM target for TPT	% of target receiving TPT 2018
4 million children under 5yr's	20%
6 million PLHIV	49%
20 million household contacts	2%



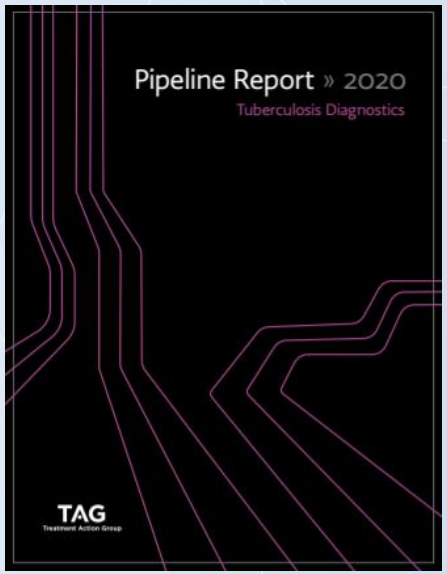
http://www.stoptb.org/wg/dots_expansion/childhoodtb/assets/documents/Social%20Media%20Kit%20Final.pdf

TB Diagnostics

- In 2019, an estimated 10 million people developed active TB. Nearly 30 percent were either not diagnosed or not reported as being diagnosed.
- Outcome - TB continues to spread in households and communities; people with TB are put at greater risk of morbidity and mortality from the disease.
- Improved implementation of available TB diagnostic tools necessary.
- New and better tools are essential to enable low-cost, rapid, and accurate TB screening and diagnosis closer to the point-of-care.

- Target product profiles (TPPs) to guide the development of new TB diagnostic tools developed by WHO and FIND have been developed (https://www.finddx.org/tpps/)

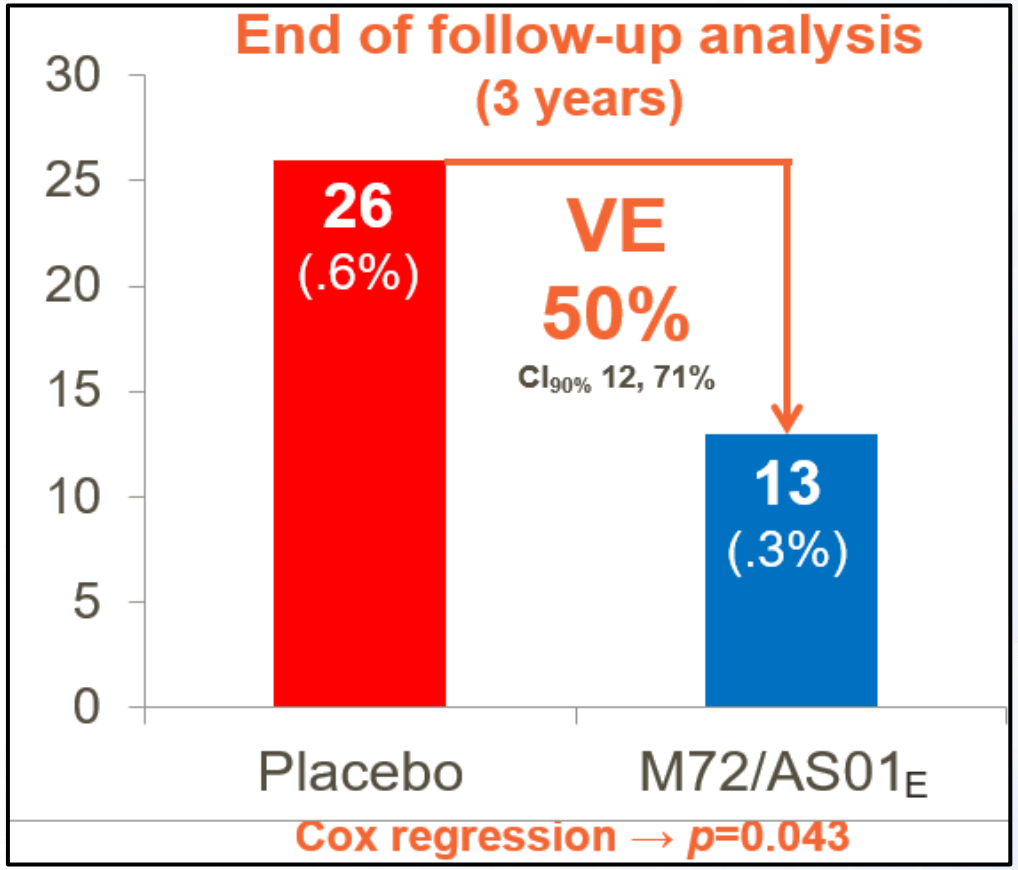
- Pipeline includes:
  - Rapid molecular nucleic acid amplification tests (NAATs) for decentralized TB detection and DST
  - Rapid biomarker-based non-sputum-based point-of-care tests for detecting TB
  - Triage or referral tests for identifying people who may have TB
  - Tests for TB infection
  - Treatment monitoring or test of cure



https://www.finddx.org/wp-content/uploads/2020/11/TAG-pipeline_TB_Diagnostics_2020_final.pdf

2018 Groundbreaking Advances in TB Vaccine Development

First Vaccine since BCG, 100 years go, to demonstrate TB disease prevention



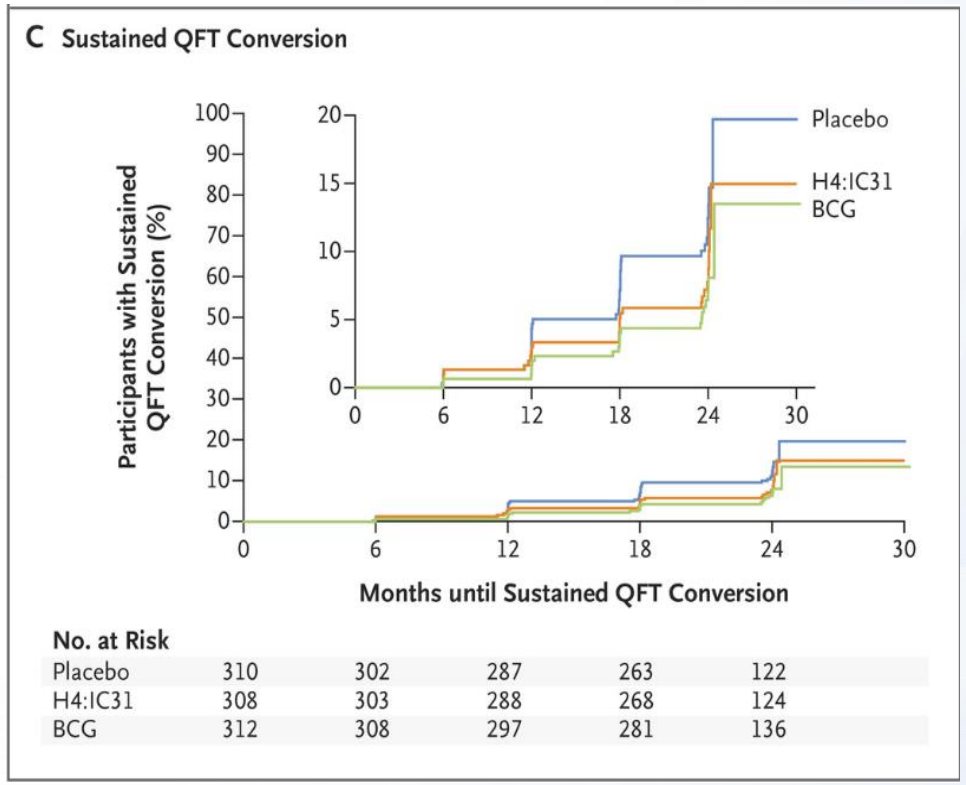
ORIGINAL ARTICLE

Final Analysis of a Trial of M72/AS01$_E$ Vaccine to Prevent Tuberculosis

Dereck R. Tait, M.B., Ch.B., Mark Hatherill, M.D., Olivier Van Der Meeren, M.D., Ann M. Ginsberg, M.D., Ph.D., Elana Van Brakel, M.B., Ch.B., Bruno Salaun, Ph.D., Thomas J. Scriba, Ph.D., Elaine J. Akite, M.Sc., Helen M. Ayles, M.B., B.S., Ph.D., Anne Bollaerts, M.Sc., Marie-Ange Demoitié, M.Sc., Andreas Diacon, M.D., Ph.D., et al.

NEJM October 29, 2019 DOI: 10.1056/NEJMoa1909953

2018 Groundbreaking Advances in TB Vaccine Development
Prevention of TB infection in adolescents



N Engl J Med 2018; 379:138-149 DOI: 10.1056/NEJMoa1714021

ORIGINAL ARTICLE

Prevention of *M. tuberculosis* Infection with H4:IC31 Vaccine or BCG Revaccination

Elisa Nemes, Ph.D., Hennie Geldenhuys, M.B., Ch.B., Virginie Rozot, Ph.D., Kathryn T. Rutkowski, M.Sc., Frances Ratangee, B.N., Nicole Bilek, Ph.D., Simbarashe Mabwe, M.Sc., Lebohang Makhethe, B.Sc., Mzwandile Erasmus, B.Sc., Asma Toefy, B.Sc., Humphrey Mulenga, M.P.H., Willem A. Hanekom, M.B., Ch.B., et al., for the C-040-404 Study Team†

- **Primary** - (QFT conversion) was not met
  - H4:IC31 vs Placebo VE 9.4% (p=0.3169)
  - BCG vs placebo VE 20.1% (p=0.1426)
- **Secondary** - (sustained QFT conversion)
  - H4:IC31 vs placebo VE 30.5% (p=0.08)
  - **BCG vs placebo VE 45.4% (p=0.01)**

Conclusions

- Africa carries a disproportionate TB burden
- Significant loss of progress towards TB elimination due to Covid-19
- Better use of existing tools are needed
- New tools to meet TB eradication goals are essential
- Significant progress with new drug regimens, rich pipeline of new TB diagnostics, and promising TB vaccine candidates progressing to Phase 3 clinical trials
- Honour the commitments made to end the tuberculosis epidemic globally by 2030 as per the United Nations Political Declaration on Tuberculosis.

THANK YOU