

Annual meeting of the Stop TB Partnership Working Group on New Diagnostics. October 19,2005 Paris, France

**New approaches for the
diagnosis of smear negative
TB among PLWHA in
resource constrained settings**

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Sputum smear negative pulmonary TB

WHO 1991

- At least **two** negative AFB sputum specimens

AND

- Radiographic abnormalities consistent with active TB

AND

- Decision by a **physician** to cure with a full curative course of anti-TB chemotherapy

OR

- A patient with AFB smear negative sputum which is culture positive for MTB.

WHO 2003

- At least **three** negative sputum specimens for AFB

AND

- Radiographic abnormalities consistent with active TB

AND

- No response to **a course** of broad spectrum antibiotics

AND

- Decision by a **clinician** to treat with a full course of anti-TB chemotherapy

Extrapulmonary TB

WHO 1991

- A patient with histological and/or clinical evidence consistent with active TB

AND

- Decision by a **physician** to treat with a full curative course anti-TB

OR

- A patient with one culture specimen from an extrapulmonary site positive for MTB

WHO 2003

- One culture positive specimen

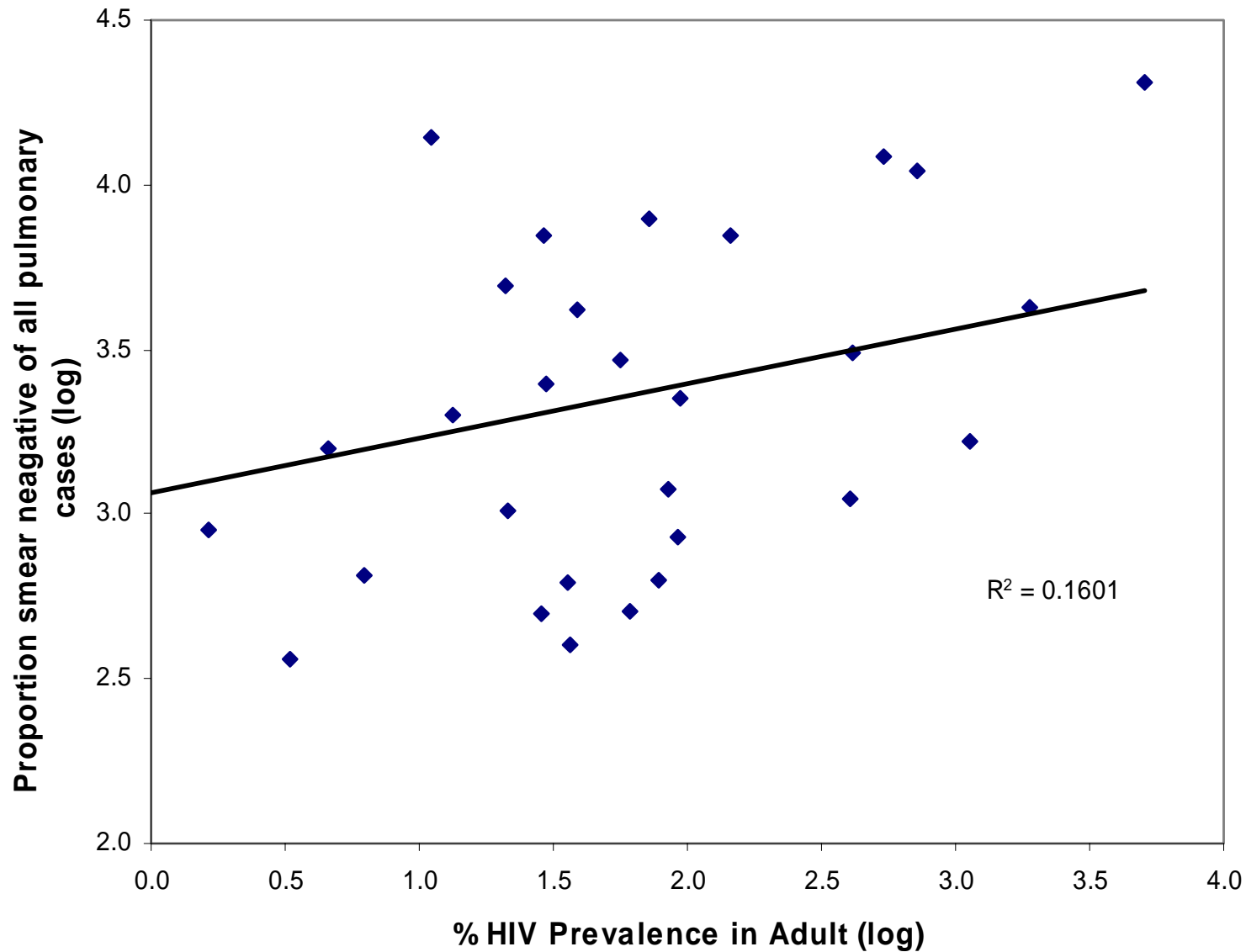
OR

- Histological or strong clinical evidence consistent with active extrapulmonary TB , followed by a decision by a **clinician** to treat with a full course of anti-TB chemotherapy.

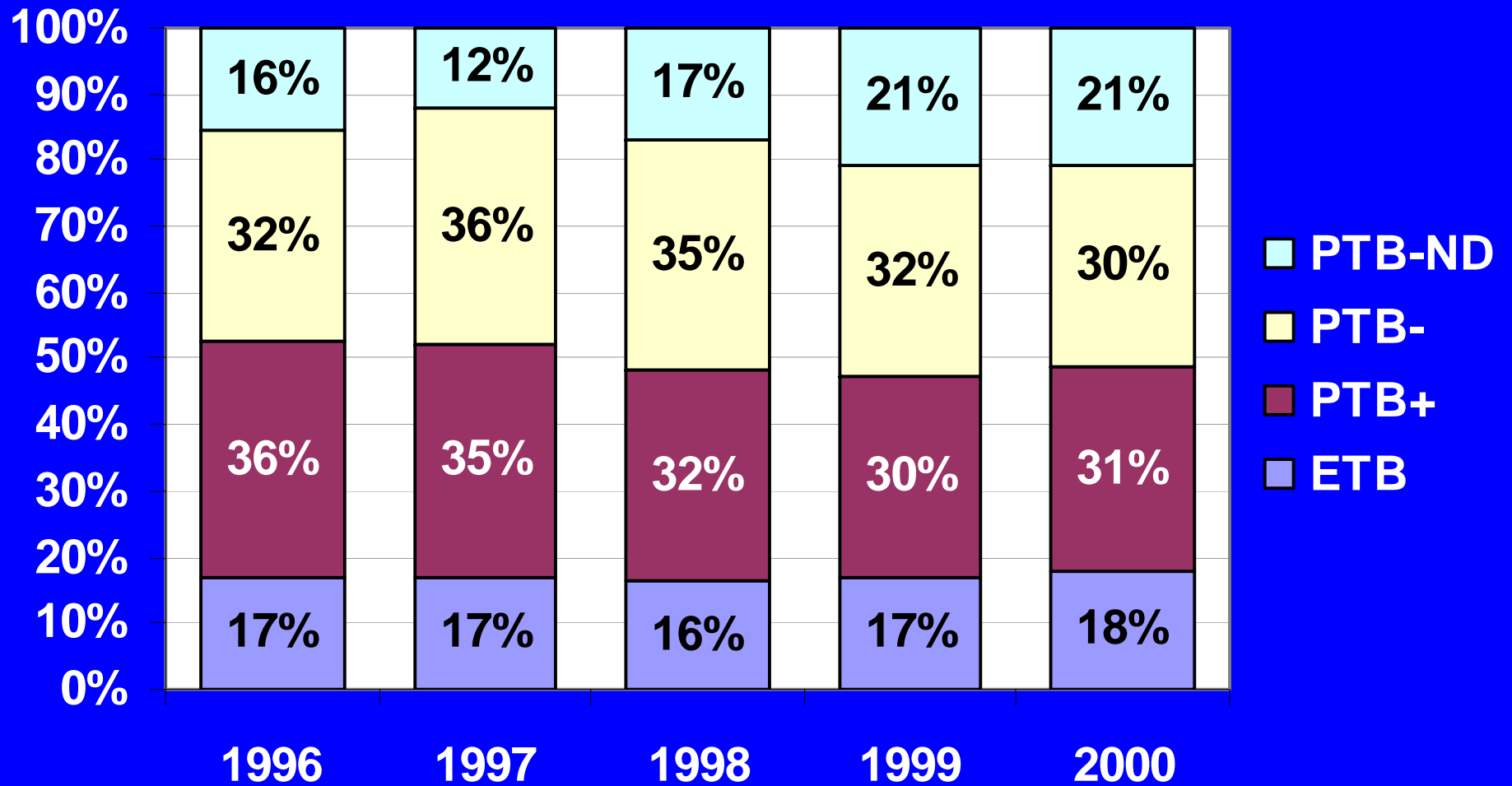
Differential diagnoses of smear negative pulmonary TB in PLWHA

- Bacterial pneumonia
- Kaposi sarcoma
- Pneumocystis carinii pneumonia
- Cryptococcosis
- Nocardiosis
- Penicilliosis
- Melioidosis
- Histoplasmosis
- Etc..

Proportion smear negative of all pulmonary cases with HIV prevalence in selected sub-Saharan African countries, 2003.



TB in Zimbabwe 1996-2000 case-notifications



50% increase in case load

Magnitude among PLWHA

- SN pulmonary= 24-61%
- Extrapulmonary= 4-40%
- Institution based studies under routine programme and skewed towards smear+
- Increased mortality than smear +
 - Hazard ratio SNP (2.2) and EP (1.7)
- Autopsy studies show 14-54% of deaths due to TB (including undiagnosed)

Smear microscopy in PLWHA

- Scanty sputum (<10AFB/100HPF) is common in HIV+
- AFB detected in 80% re-examined scanty sputum (Bangladesh) and 95% of scanty sputum were culture + (Nigeria)
- Considering scanty smears as + would result false positives in less than 1% of the patients (Nigeria)

Smear microscopy in PLWHA

- Fluorescence microscopy
 - improves sensitivity up to 18%
 - Cost effective- \$40 (on 2 sputa) vs \$57(ZN 3 sputa)
 - Reduce time needed (4 mt vs 10 mt)
- Sputum liquefaction and concentration
 - Bleach method: 16-125% improvement
 - Not tested under programme condition
 - Method not standard

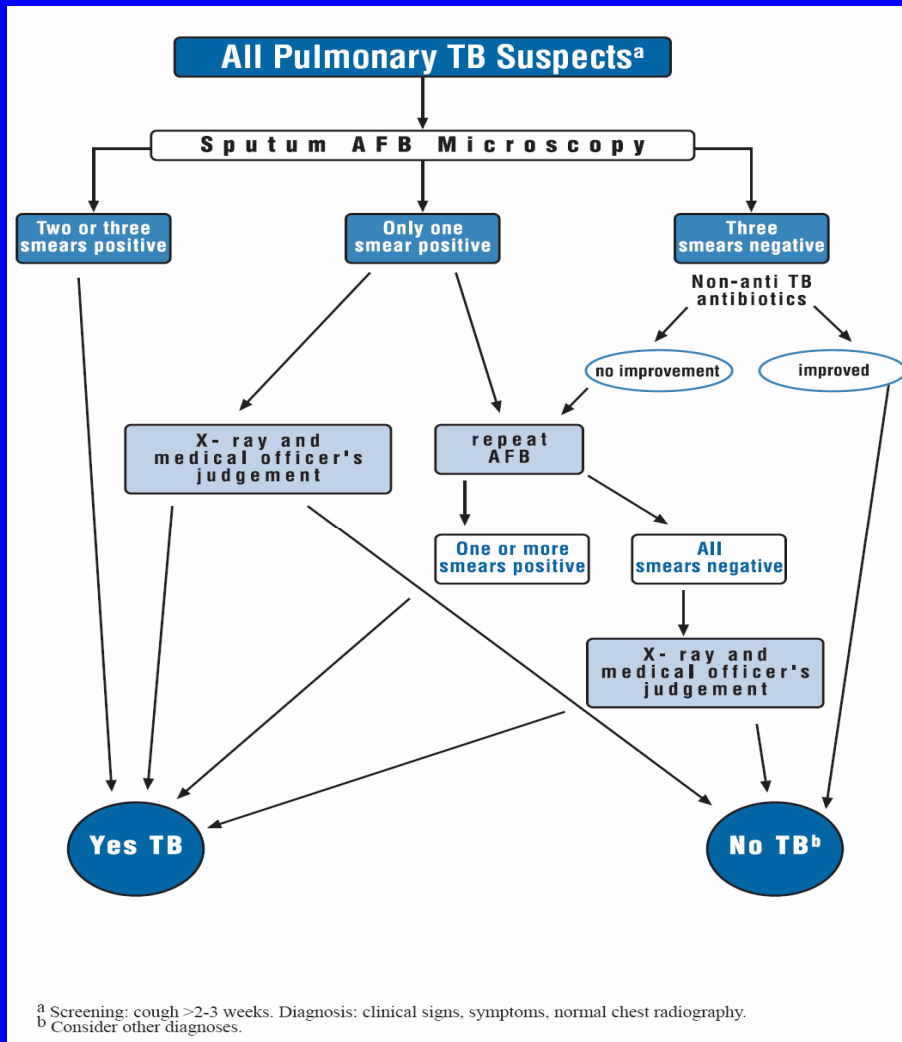
Sputum Culture

- 49% of HIV + TB patients had negative smear on direct microscopy but their sputum was culture positive
- Needs sophisticated infrastructure and expertise and is (?) expensive
- Culture is currently recommended
 - Surveillance of drug sensitivity
 - Treatment failure and relapse
 - Repeated negative smear results

Could this be a barrier?

- Availability at district level vs CD₄ machine expansion

Use of diagnostic algorithm



- Not validated
- Based on consensus

The current WHO recommended algorithm (2003)

Problems with current practice for PLWHA

- Empiric antibiotics trial for up to 4 weeks
- AFB smear (up to 9) even before empiric antibiotics
- HIV status and severity of disease excluded
- CXR not indicated earlier despite being useful
- Duration: min 13 days; max 44 days
- Number of consultations ranging 5 – 7

In the meantime patients die!

The 4th TB/HIV WG meeting in Addis Ababa, Ethiopia September 20-21, 2004

"Improvements in the diagnosis and management of smear-negative and extrapulmonary cases of TB need to be explored and existing guidelines reviewed in the context of emerging new diagnostics."



Key features of revised algorithm

- Increased speed and sensitivity
- HIV test for TB suspects
- Severity of disease
- Presumptive TB treatment for seriously ill patients at peripheral institutions
- Antibiotics to treat a clinical condition rather than a diagnostic step
- AFB, sputum culture and CXR together all at a time and as early as possible

The way forward

- Fast track search for new, easy and rapid tools

The quest should be a political and a human rights agenda

- Advocacy and activism for massive investment for the search (Learn from the HIV community)
- Solar-powered technology for settings where there is no electricity

The way forward

- Improve and expand what is at hand
 - Sputum concentration methods
 - Expand fluorescence microscopy
 - Expand sputum culture capacity
 - Speedy, sensitive and validated algorithm
 - Enhanced utility of CXR

How can the WG ~~on~~ New Diagnostics help?

Way forward

- Improve and expand existing diagnostics **aggressively** along the search for NEW tools.
- Expand the actors and level of scientific interest including in resource limited settings
 - More researchers -Fellowships for young researchers
 - Programme managers- for implementation
 - HIV/AIDS community-activists, researchers etc.
 - Other Working groups

Wish list for what is at hand

- Standardised bleach technique
- Fluorescence microscope: solar powered and with no need for dark room
- District based rapid culture facility
- Solar powered portable CXR
- Effective, efficient and validated clinical algorithms

NOT FOR 2007 or 2010 but for NOW!!!