Reframing DOT Symposium
NAR Conference 2025

Historical Perspective DOT

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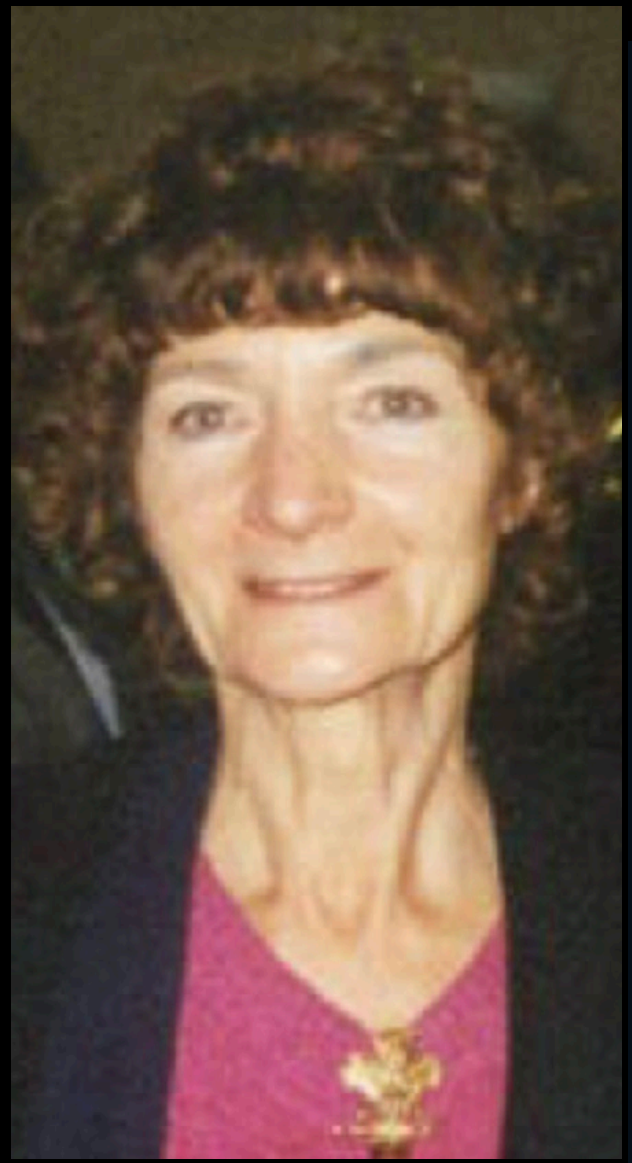
Conflict of Interest

- I have no relevant Conflicts of Interest.

- TB Staff Physician for Hawaii DOH
- Consultant for the Global TB Institute at Rutgers – consult line
- Consultant for the training department The Union-Principles of TB Care and Prevention Course
- Board of Directors
  - The American Friends of The Union
  - Health and Education for All (Bangladesh)
  - IRB of Dopasi Foundation (Pakistan)



Annik Rouillon, Karyl Styblo and The Union

- 1976 Initiative request from Tanzania, following the meeting of the African Region of The Union, to assist in integration of health services from a network of charitable organizations into a national framework to control TB and Leprosy
- 1989 WHO turned to Styblo for advice
- 1991 World Bank funded testing of the strategy in several countries

Karyl Styblo and The Union Model 1991-94

Although there were detailed recommendations, the strategy was summarized with five tenets:

1.) Government commitment

2.) Case detection

3.) Administration of standardized treatment under proper case management conditions

4.) Establishment of a regular drug supply

5.) Establishment and maintenance of a monitoring system for programme supervision and evaluation

TB treatment regimen in Styblo's model

- At this time, HRZE2 HR4 regimen had been demonstrated as highly effective through the British Medical Trials (1976)
- Cost of rifampin was high for most countries
- Styblo's concern was the development of resistance to rifampin if introduced into a weak program
  - Therefore, observation support was recommended while Rifampin was in the regimen
  - 6 months of Rifampin plus supervision support felt to be cost prohibitive
- The regimen utilized was, therefore, an 8 month regimen of HRZE2 HTh6 (INH + Thiacetozone) – Tanzania 1982

Transition to Rifampin throughout the regimen = Short Course Chemotherapy (SCC)

Table 4 The original treatment recommendations in the Styblo model

Category of case	Treatment regimen*
New smear-positive pulmonary cases	2S[HR]Z/6[HT] or 2S[HT]/10[HT]
Previously treated cases	2S[HR]ZE/1[HR]ZE/5[HR]E
Smear-negative cases	2S[HT]/10[HT] or 12[HT]

* Numbers indicate duration of treatment (months) and square brackets indicate fixed-dose combinations.
S = streptomycin; H = isoniazid; R = rifampicin; Z = pyrazinamide; T = thioacetazone; E = ethambutol.

ELSEVIER

The Lancet
Volume 337, Issue 8742, 16 March 1991, Pages 627-630

ORIGINAL ARTICLES

Cutaneous hypersensitivity reactions due to thiacetazone in HIV-1 seropositive patients treated for tuberculosis

P Nunn MRCP [a], R Brindle MRCP [a], K Wasunna MB [a], C Gilks MRCP [a], M Omwega MBC [a], J Were [a], M Med [a], P Nunn [b], D Kibuga MB [b], S Gathua MMed [b], A Imalingat MMed [b], P Nunn [c], K Wasunna [c], S Lucas FRCPath [c], K McAdam FRCP [c], R Brindle [d], S Lucas [e], C Gilks [f]

Kraig Klaudt- WHO - 1995

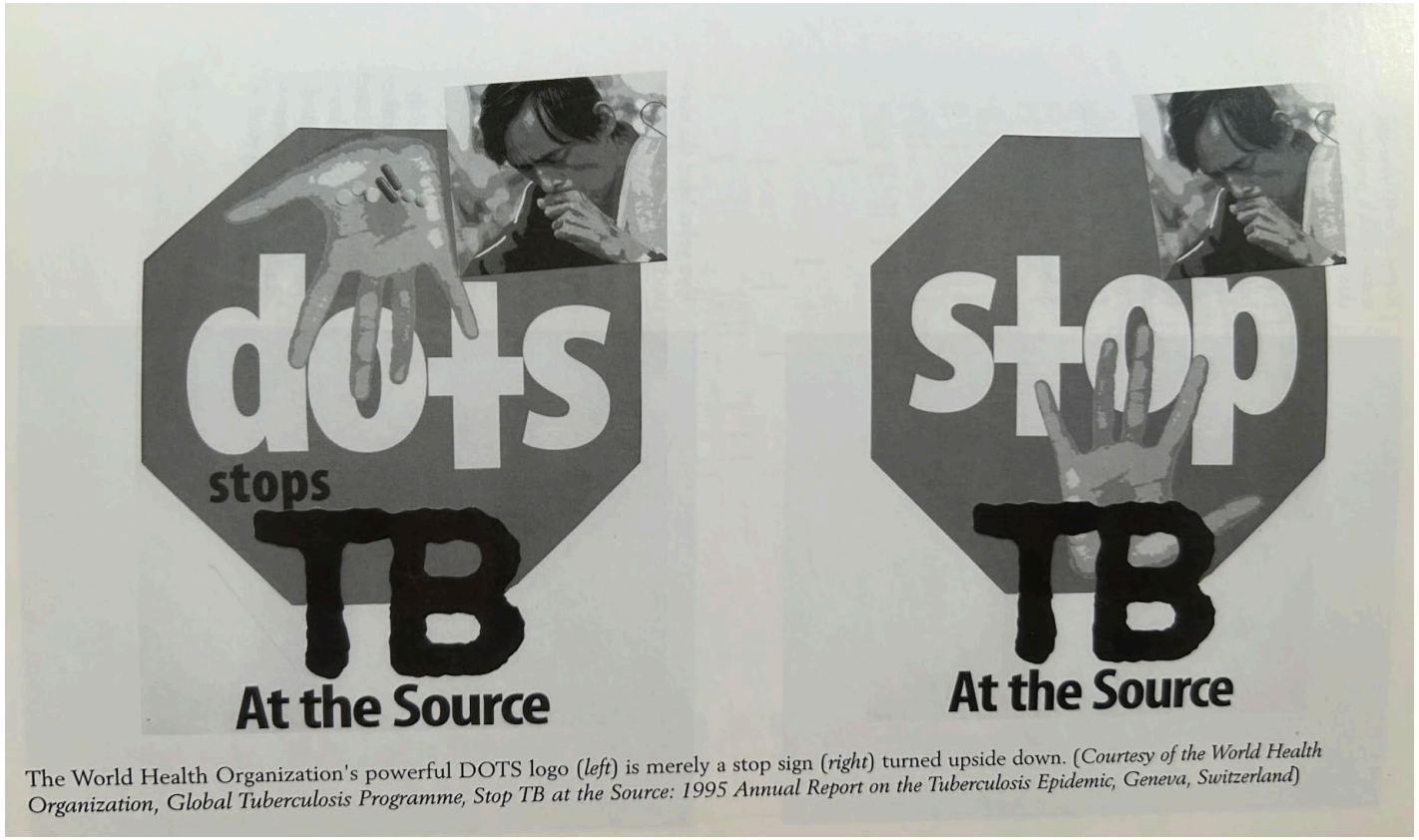
WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTE

DISTR. : LIMITED
DISTR. : LIMITEE
WHO/TB/94.179

WHO TUBERCULOSIS PROGRAMME

FRAMEWORK FOR EFFECTIVE TUBERCULOSIS CONTROL

WORLD HEALTH ORGANIZATION



The World Health Organization's powerful DOTS logo (*left*) is merely a stop sign (*right*) turned upside down. (*Courtesy of the World Health Organization, Global Tuberculosis Programme, Stop TB at the Source: 1995 Annual Report on the Tuberculosis Epidemic, Geneva, Switzerland*)

TUBERCULOSIS IN NEW YORK CITY — TURNING THE TIDE

THOMAS R. FRIEDEN, M.D., M.P.H., PAULA I. FUJIWARA, M.D., M.P.H., RITA M. WASHKO, M.D., AND MARGARET A. HAMBURG, M.D.

NEJM 1995:333:229-33

1980's -staff and clinic reductions

1989: < 50% starting TB treated completed treatment

1992 – 3811 Persons living with TB disease, represented a tripling over 10 years

1/5 persons with TB had MDR TB

What was the response:

The entire system was rebuilt

In two years, the tide was turned – largely ascribed to the initiation of supervised, supportive therapy (DOT)

Infusion of $ = 4 million to 40 million USD

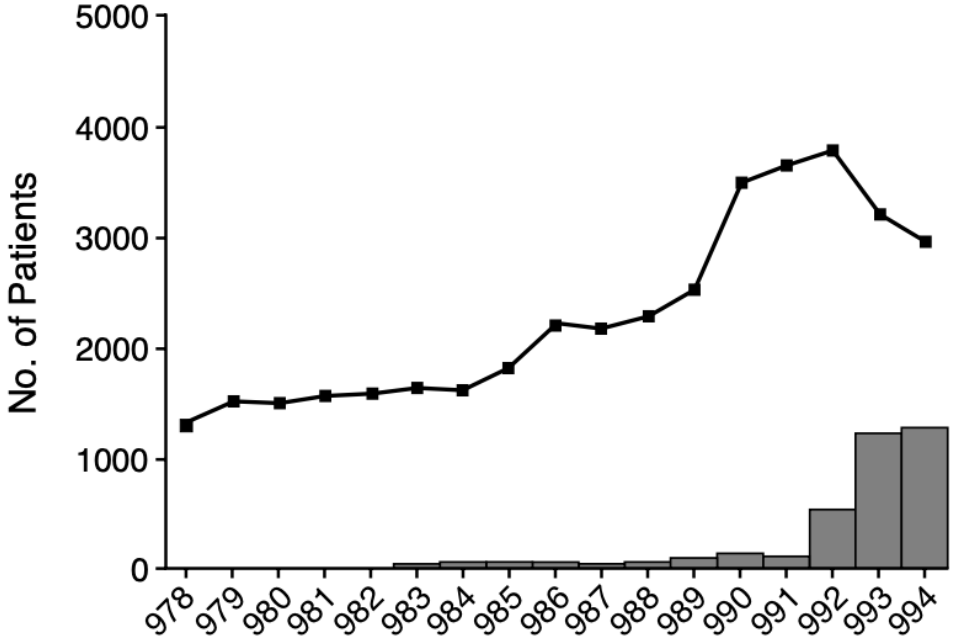


Figure 1. Number of Patients with Tuberculosis in New York City (Solid Line) and Number Receiving Directly Observed Therapy at the End of Each Year (Shaded Bars), 1978 through 1994. Data are from the New York City Department of Health.

For the next decade, terminology/guidance varies….

- Case management with supervision
- Directly observed therapy during the intensive phase
- Directly observed therapy while Rifampin is utilized in the regimen
- Directly observed therapy by ……
  - Health care provider
  - Family member
  - Community member or leader
  - Community outreach worker, volunteer, accompanier
  - Former patients

COMPONENTS OF THE STRATEGY AND IMPLEMENTATION APPROACHES

1. **Pursue high-quality DOTS expansion and enhancement**
   a. Political commitment with increased and sustained financing
   b. Case detection through quality-assured bacteriology
   c. Standardized treatment, with supervision and patient support
   d. An effective drug supply and management system
   e. Monitoring and evaluation system, and impact measurement
2. **Address TB/HIV, MDR-TB and other challenges**
   a. Implement collaborative TB/HIV activities
   b. Prevent and control MDR-TB
   c. Address prisoners, refugees and other high-risk groups and situations
3. **Contribute to health system strengthening**
   a. Actively participate in efforts to improve system-wide policy, human resources, financing, management, service delivery, and information systems
   b. Share innovations that strengthen systems, including the Practical Approach to Lung Health (PAL)
   c. Adapt innovations from other fields
4. **Engage all care providers**
   a. Public–Public and Public–Private mix (PPM) approaches
   b. International Standards for Tuberculosis Care (ISTC)
5. **Empower people with TB, and communities**
   a. Advocacy, communication and social mobilization
   b. Community participation in TB care
   c. Patients' Charter for Tuberculosis Care
6. **Enable and promote research**
   Programme-based operational research

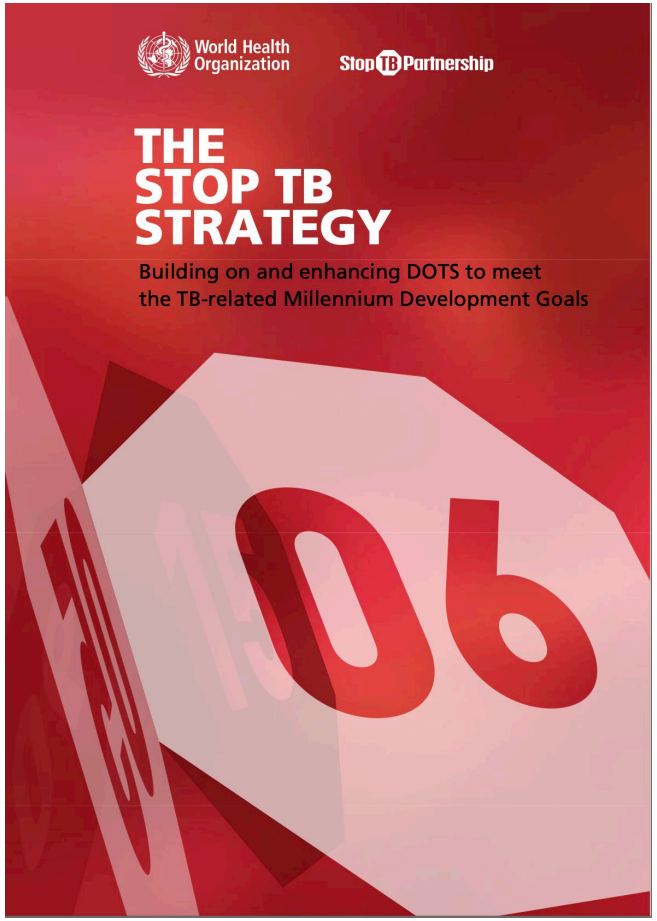
THE STOP TB STRATEGY

Building on and enhancing DOTS to meet the TB-related Millennium Development Goals

WHO 06

2002 WHO guide to DOTS expansion

2002 WHO guide to DOTS expansion



Language in the document calls for a tailored supervisory approach

- Supervised therapy, which may include DOT, helps patients to complete treatment
- Must be carried out in a context specific and patient sensitive manner
- At a facility, workplace, home or in the community
- Treatment partner or supporter acceptable to the patient and supervised by the health system
- Patient peer support groups are helpful
- Selected patients such as those with mental health disorders or drug/alcohol use disorders may need intensive support including directly observed therapty

Digital tool development

- 2015 WHO and Stop TB partnership
- Wave 6 TB reach DAT (digital adherence devices) 2017
- DAT task force in 2020

- Cell phone short messaging service (SMS)
- Digital pill boxes
- Ingestible sensors
- Video recording
- Synchronous or asynchronous
- Recording systems (99 DOTS)

Guidelines – Often focus on Dose Count

	Intensive Phase		Continuation Phase				
Regimen	Drug[a]	Interval and Dose[b] (Minimum Duration)	Drugs	Interval and Dose[b,c] (Minimum Duration)	Range of Total Doses	Comments[c,d]	Regimen Effectiveness
1	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182–130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis.	Greater
2	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	110–94	Preferred alternative regimen in situations in which more frequent DOT during continuation phase is difficult to achieve.	
3	INH RIF PZA EMB	3 times weekly for 24 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	78	Use regimen with caution in patients with HIV and/or cavitary disease. Missed doses can lead to treatment failure, relapse, and acquired drug resistance.	
4	INH RIF PZA EMB	7 d/wk for 14 doses then twice weekly for 12 doses[e]	INH RIF	Twice weekly for 36 doses (18 wk)	62	Do not use twice-weekly regimens in HIV-infected patients or patients with smear-positive and/or cavitary disease. If doses are missed, then therapy is equivalent to once weekly, which is inferior.	Lesser

CDC/ATS/IDSA https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376

Summary 1977 to 2025

- Styblo's model was a programmatic approach
  - Case management -which included observation of dosing - designed to prevent resistance, specifically to the "new" drug Rifampin- not specifically as a tool to ensure COT
- WHO branded the model as DOTS
- Resurgence of TB in the US drove development of Directly Observed Therapy programs
- Directly Observed Therapy programs have no specific, published standardized definition- most guidelines note supportive supervision to include DOT, as needed, should be adapted to the situation and the patient
- Development of DAT emphasizes dose verification rather than case management
- Dose verification is driven by guidelines outlining specific dose counts