

# Fully Intermittent, Thrice-Weekly Dose of Anti-Tuberculosis Drugs; Their Efficacy under Routine Program Conditions of India

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**Abstract:** When discovered, anti-tuberculosis drugs were always administered in Daily-doses; it worked wonders! Later, studies claimed these drugs could cure even in thrice-weekly doses (intermittently). Not everyone believed that. Three Reviews (Cochrane, Thorax, Azhar) appear unconvinced! Also, most nations (including 20 High TB Burden Countries) practice time-tested Daily dosing! INDIA adopted a unique low-cost, thrice-weekly regimen around 2000. During 15 years, under national program, Thrice-weekly doses have been administered to 15 million TB patients, self-claiming 85% success. To revisit long-term outcome of all registered patients in a district; identify the one, who didn't achieve long-lasting recovery with a single course, was later found re-registered for a second innings; his name figures twice in national registry (a Repeater). Author heads District Tuberculosis Center, Faridabad, India; monitors thousands of current/ex-patients on Thrice-weekly regimen. By providence, he enjoys unique access to registered patients, data, district TB-workers. Two methods of data collection: 1. Author motivated district work-force; jointly conducted systematic Retrospective Record Review of hand-written registers of past 15 years, one at a time—thus identified over 1,575 Repeaters. 2. Author has been conducting ongoing Clinical Audit in his busy TB OPD for 6 years. He is able to cherry-pick (average) one Repeater per day; thus tracked 3,100 Repeaters—about half come in from Delhi's premier TB institutes, duly diagnosed, referred in for local registration for Re-treatment. Long-term fate of 36,785 registered TB patients could be analyzed. 4,675 patients observed to have returned sick, meriting Re-registration, Re-treatment; thus over 12.7 % registered twice/thrice (names, unique govt. ID's, irrefutable evidence enclosed)—an adverse outcome, unreported thus far—a bubble. Besides, study recorded 1,590 (5%) Deaths; 2,590 (8%) Defaulters. Under India's routine program conditions, Thrice-weekly regimen is ineffective. Too many (12.7%) patients come back sick, which may promote drug-resistance on industrial scale! A global threat!

**Key words:** TB, TUBERCULOSIS, DOTS, RNTCP, NTP, thrice-weekly dose, intermittent regimen, relapse, recurrence, scholarly article.

## Abbreviations

AFB	Acid Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
AIIMS	All India Institute of Medical Sciences, Delhi
ANM	Auxiliary Nurse Midwife
APUR	Anangpur Primary Health Center
ASHA	Accredited Social Health Activist
AWW	Angan Wari Worker
BCG	Bacille Calmette Guérin
BK HOSP	Badshah khan district govt. general hospital Faridabad
BLB	Ballabgarh
BMJ	British Medical Journal
CAT I	A new TB patient who has not taken anti-TB

	drugs in the past
CAT II	A TB patient who has already taken anti-TB treatment in the past
CD OLD	Civil Dispensary Old Faridabad
CHC	Community Health Center
CP	Continuation phase of treatment
DC	Dabua colony slums
DEF	Defaulter
DMC	Designated Microscopy Center
DOT	Directly observed treatment
DOTS	The basic package that underpins the Stop TB Strategy (Directly Observed Treatment Short Course)
DP	DOT provider
DPUR	Dayal pur PHC
DTC	District Tuberculosis Center
DTO	District Tuberculosis Officer
EPTB	Extra Pulmonary Tuberculosis

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ESI	Employee's state insurance
ESID	Employee's state insurance Dispensary
ESIH	Employee's state insurance Hospital
F	Failure of treatment
FBD	Faridabad
FRUI	First Referral Unit I Hospital sector 30
FRUII	First Referral Unit II hospital sector 3
GH BLB	Govt. General Hospital Ballabgarh
GH PALWAL	Govt. General Hospital Palwal
GoI	Government of India
HBC	High-burden country, of which there are 22 that account for approximately 80% of all new TB cases arising each year
HIV	Human immunodeficiency virus
IN.DEF	Initial defaulter
IP	Intensive phase of treatment
JC	Jawahar colony slums
KK	Kheri Kalan Community Health Center
KHERI	Kheri Kalan Community Health Center
LNJP	Lok Nayak Jai Parkash Hospital Delhi
LRS	Lala Ram Saroop TB Hospital Mehrauli Delhi
LT	Laboratory Technician
MDR TB	Multi Drug Resistant Tuberculosis
MMPUR	Mewla Maharaj Pur village
MO	Medical Officer
MOTC	Medical Officer Tuberculosis Control
MPHW	Multi-purpose health worker
MPW	Multi-purpose worker
NSP	New Sputum Positive
NTP	National Tuberculosis Program
OPD	Out Patient Department
PHC	Primary Health Center
PHI	Peripheral Health Institution
PMDT	Programmatic Management of Drug Resistant TB
PTB	Pulmonary Tuberculosis
RBTB	Rajan Babu TB Hospital Delhi
RCH	Reproductive child health
RNTCP	Revised National Tuberculosis Control Program (of India)
S/C	Sub center
SCC	Short course chemotherapy (with modern drugs, including Rifampicin)
SCT	Short course therapy
SGM NGR	Sanjay Gandhi memorial nagar
SJH	Safdarjung Hospital Delhi
SKUND	Surajkund civil dispensary
STH	Streptomycin, Thiacetazone, Isoniazide regimen, takes over a year to heal
STLS	Senior Tuberculosis Laboratory Supervisor
STO	State Tuberculosis Officer

STS	Senior Treatment Supervisor
TB	Tuberculosis
TBHV	Tuberculosis Health Visitor
TB UNIT	Tuberculosis Unit (Sub-district)
TU	Tuberculosis Unit
TU3	New TB Unit Sector 30
WHO	World Health Organization.

**Abbreviations coined for understanding Excel sheets (with about 9,600 names of patients):**

1D F	Patient took 1 course of DOTS but failed treatment (under RNTCP)
2D	Patient registered twice under DOTS program
3D	Registered thrice under RNTCP
4D	Patients took four innings of DOTS
5D / 6D	Patient got registered five or six times with DOTS Program.

## 1. Introduction

Some 95% of cases and 98% of (global) TB (tuberculosis) deaths occur in poor countries [1]. India has the highest burden of tuberculosis in the world with over two million incident cases amounting to more than fifth of global burden [2]. Thus, India generates about 12,602 TB patients within two days while US reported only 10,528 cases in a full year in 2011 [3]. Two Indians die of TB every three minutes! Real TB battle ensues (not in the affluent West) but in 22 High TB Burden Countries (HBC's)—like India, China, South Africa, Indonesia, Bangladesh, Pakistan etc.

Discovery of five primary anti-TB drugs (1944-1966) was a miracle for mankind. Those days, these medicines were always administered on a Daily-dose basis. And which worked wonders; TB declined in several Western nations; thus, history itself validates Daily-dosing, which requires no further evidence. Why re-invent the wheel?

Decades later, some studies claimed that anti-TB medicines were equally effective even when administered intermittently—say as Thrice-weekly doses (instead of Daily). However, most scientists were not convinced. 20 (out of 22) High TB Burden Countries continue to practice Daily-dosing schedule [4]. Probably, choosing to exercise caution, they preferred to stick to the traditional, time-tested Daily-dosing.

### 1.1. India

However, India is one of the few exceptions. She switched over to a unique, low cost, Thrice-weekly regimen on a massive scale. Since 1998, Revised National TB Control Program (RNTCP) of India has placed on treatment more than 14.2 million TB patients [2]—all administered three doses per week.

Please remember, if any more evidence is needed, it is for efficacy of Thrice-weekly dose and not for Daily regimen (as stated above).

A Systematic Review in British Medical Journal [5] concluded that despite millions treated in 10 years, few studies examined whether DOTS (directly observed treatment, short course) provides lasting cure or not—just what this present study undertakes.

### 1.2. Objective

To evaluate efficacy of India's TB program under routine program conditions. To quantify Re-registration (Relapse and recurrence etc.), which is a reliable indicator of efficacy.

Aim is to find a registered patient who (at a later date) returned sick and got re-registered again.

Long term outcome of all patients registered during 'thrice-weekly era' was revisited in district Faridabad so as to identify such patients who undertook two cycles of thrice-weekly DOTS. In other words, the study computes re-registration—an unfavorable outcome of treatment.

### 1.3. Why This Study Took 6 Years?

This unintended operational analysis got triggered in 2010 by curiosity and craving for truth, not academics; gathered momentum despite initial doubts, chaos, and confusion; aimed perfection not time-frames or traditional research-frameworks. IN INDIA, RECORDS OF TB PATIENTS ARE HAND-WRITTEN, not computerized or digitized. To search a patient's name in a bulky manual register or to trace him in a thickly populated slum is like finding a needle in a hay-stack. You are literally at the mercy

of 'that' local NTP (National TB Program) worker—who had then performed home-visits, given him doses personally and had scribbled those original entries; no easy shortcuts. 'Harmonious alliance forged between workers of NTP' is the soul of this labor-intensive and time-consuming exercise. Results are therefore reasonably credible, accurate and verifiable.

## 2. Subjects and Methods

### 2.1 Search Strategy

To find a TB patient found registered twice (or more often) under 'Thrice-weekly' DOTS program. Duly registered once, he later reported sick again and was re-registered/re-treated (hence, nicknamed Repeater). Accordingly, his name figures twice in national registry. Government allocated to him (not one but) two or three Unique IDs (called TB Numbers). Once we know his TB No., it takes us straight to that patient's 19-column hand-written DOTS history in the relevant register. Therefore, all 4,675 names and details thereof in excel sheets (enclosed) are easily verifiable.

Pursuing scientific exactitude, most other studies have concentrated on New Sputum smear Positive cases and or Relapse cases, which is a good but indirect indicator of program assessment. Notably, this study is much broader; it doesn't search merely Relapse cases which of course are included. Rather, it enlists everyone who got registered more than once—pulmonary as well as extra-pulmonary; sputum positive and negative; and besides, irrespective of their previous outcome of thrice-weekly DOTS episode—whether cured, failed, defaulted or completed treatment last time over. Thus, it offers a more complete overview under routine program conditions.

Re-treatment patients emerging out of purely private sector pipeline were also identified but were of no interest and were painstakingly excluded/discarded from this study, because private doctors in India

(ironically) use daily dose regimen.

Also, all deaths, and defaulters (who failed to complete medication) were enlisted, quantified and digitized.

## 2.2 *Two Methods of Data Collection (Overlapping)*

### 2.2.1 Retrospective Record Review

Author was intrigued to notice trickle of ‘ex-patients, sick again’ (Repeaters) in OPD. So had been field workers; their frustration served as bonding spirit. Possessed with a unanimous desire to somehow stem the rot, the team formed an informal alliance. They would go out of their way to answer author’s never-ending 24X7 queries. More and more NTP workers, by providence, began voluntarily digging up Repeaters, families, homes falling within their territory and unearthed old dust-laden entries that no one else could have ever retrieved. Author kept inspiring and exhorting them relentlessly—in OPD, monthly-meetings, training-sessions, and (some key ones) on phone. Author cajoled their memory, “did you ever give anyone DOTS twice?” which means 14-month stint with a difficult patient—often hard-to-forget. Names emerged. As mutual trust grew, synchronization and learning curve improved, workers began fetching past registers for joint scrutiny.

Merely procuring a hand-written register without its original author is not much use; it is like a guitar without the guitarist; one invariably got lost in jungle of data. Without willful co-operation of original writer, hand-written DOTS data is impenetrable; no shortcuts possible, hence time-consuming (6 years).

During initial 3 years (2010 through 2012), author systematically perused most district registers (of distant past) kept at TB-Units, PHIs, sub-centers, sputum Labs, one by one—to cherry pick Repeaters, and failures (who indeed require Re-treatment), deaths and defaulters recorded therein. Books were promptly returned, often within a day, as manual entry is a dynamic 24X7 process.

In all, 1,575 Repeaters could be identified from

registers of distant past (about twelve) years.

### 2.2.2 Clinical Audit and Collection of Current Data

At district govt. hospital, in busy, exclusive TB OPD, 6 days a week, author personally conducts clinical audit. He interrogates each TB patient arriving for—diagnosis, follow-up, or diagnosed elsewhere but referred-in for local registration for Re-treatment. His favorite question is “did you ever take Thrice-weekly DOTS from govt. in the past?” If yes, this current TB episode (if now confirmed) is the second innings, making him a Repeater—a suitable candidate for this study. Once so established, author would then record in his diary and laptop all details and retain complete documentary evidence—patient’s name, father’s/husband’s name, address, Lab. No. of sputum-positive report, mobile no.; photos were clicked of patient himself, X-ray (sometimes), previous TB ID card, refer form, discharge slip, relevant FNAC/biopsy reports etc.

Unverified cases were excluded.

During 6 years of intensive clinical audit, author could identify about 3,100 Repeaters (average one repeater detected per day) in OPD.

AUTHOR’S ROLE in these 3,100 cases (Repeaters) was twofold:

Confirmation of first innings: To verify the basic precondition—that the patient had indeed taken ‘thrice-weekly DOTS’ in the past, through skillful history-taking: [Then, medication was free of cost, from a govt. outlet (and not a private doctor), medicine-box delivered somewhere in the neighborhood, health-worker watched him swallow 7 tablets, all at once, on alternate days (thrice-weekly), reclaiming empty blister packs and insisted on repetitive sputum tests etc. Wherever available, author perused, filmed, collected old records (cards etc.). It was ensured that the previous episode was not prior to 2000 (pre-DOTS era)].

Confirmation of second innings: To confirm that now patient has active TB disease at present. In this, help came from numerous quarters:

Half of such Repeaters (about 1,500) arrived ‘already-diagnosed’, ripe and ready to be plucked—from credible sources: (i) Delhi’s premier TB-Institutes/Hospitals [hundreds of original refer-forms from Delhi ordering Re-treatment preserved] (ii) Faridabad’s seven large hospitals (without refer-forms). Patients would come to OPD simply for local registration; author welcoming them like a record-keeper and guiding them on to correct DOTS centers, closely monitoring their future course (by method no.1 above). He would later obtain their new TB No. as and when allotted (usually within a month), and follow till their final outcome.

Simultaneously, author would trigger the process to track down patient’s previous TB No. from past registers, through consistent 24X7 interactions with relevant field-workers (by method no.1 above).

Some Repeaters’ were diagnosed and referred by our own in-house physicians, surgeons, pediatricians, and orthopedicians etc. in district hospital, which has over 40 doctors. They have already clinched the current diagnosis of active TB (2nd innings, necessitating re-treatment now).

Some Repeaters came straight to author’s OPD, where he would confirm that they were indeed sick again and warranted re-treatment; a vast majority being sputum-positive; laboratory no. duly recorded. Some repeaters were also sputum negative PTB. Some were Extra-PTB cases—often FNAC positive or having duly consulted a relevant specialist. Author exercised due restraint while labeling patients.

Also, district’s peripheral army of ‘trained’ doctors (stationed at 9 TB Units, PHCs etc. as detailed under ‘extrapolation’) keeps enrolling Repeaters routinely, dispatching them straight to respective destination DOT centers; author nowhere in the picture. Weeks/months later, some loyal workers would possibly inform the author (method no.1 above).

Like a command-center, author kept multi-tasking—demanding, receiving, applauding, digitizing and indexing incoming information—drop

by drop, so as to complete the big picture, to make sense of it all.

### 2.2.3 Main Results of the Audit

Data of 36,785 TB patients registered in 15 years (since inception of DOTS in April 2000) in district Faridabad could be scrutinized (Table 1). Of them, at least 4,675 (12.7%) patients could be identified as Repeaters (registered twice/thrice); many more remain undetected—actual percentage likely to be higher (Table 2).

## 3. Conclusions

Under routine program conditions, India’s unique fully-intermittent, Thrice-weekly regimen of anti-tuberculosis drugs has not proven effective; it fails to provide reliable, lasting cure/relief. At least 12.7% of registered patients come back—sick again, meriting Re-treatment, which might be promoting multi-drug resistance on an industrial scale, a global threat.

India ought to revert back to the time-tested daily regimen, before it is too late.

Besides, study found 4.9% Deaths, 8% Default.

More fool-proof mechanism for independent data-verification and automatic course-correction, like systematic clinical audits, must be built into the original design of a public health program, run by a single agency; or else, a bubble may form. This study is nothing but incarnation of that (invisible) bubble within RNTCP, run solely by Govt. of India.

### 3.1 Evidence in Literature

To resolve the ‘Daily versus Thrice-weekly’ controversy, three Systematic Reviews are available. Cochrane [6] found ‘insufficient evidence to compare...’ the two Review in Thorax [7] ‘...justifies...Daily... (particularly in initial phase) ...’ India specific review by Azhar [8] stated ‘Relapse rate is high (almost 10%) in India....higher than...international studies.’ He speculates that ‘.... Daily regimen might have lower relapse rates compared to an intermittent regimen’.

### Thrice-Weekly Dose in TB; Does It Work?: Ground Reality

**Table 1 District Faridabad: Total No. of TB patients registered in 16 years (DOTS Era) = 36,785<sup>‡</sup>.**

Year	Total	TB Unit Ballabgarh	TB Unit District TB Centre
2000	0359	0359	Data Untraceable
2001	0746	0746	Data Untraceable
2002	0991	0991	Data Untraceable
2003	0983	0983	Data Untraceable
2004	0999	0999	Data Untraceable
2005	1,110	1,110	Data Untraceable
2006	2,213	1,195	1,018* <sup>@</sup>
2007	1,126	1,126	Data Excluded* <sup>#</sup>
2008	2,572	1,252	1,320*
2009	3,414	1,372	2,042
2010	3,060	1,543	1,517
2011	3,297	1,537	1,491
2012	3,493	1,071	1,079
			TB Unit FRU 1 created in Oct. 2011 0269
			1,343
			Reorganization in Oct. 2013; All 3 TB units dissolved & 9 smaller units carved out.
2013	3,803		
2014	4,202		
2015	4,417		
Total	36,785		

Total = 36,785<sup>‡</sup> Patients (From April 2000 to end of Dec. 2015).

<sup>‡</sup> 36,785 is the number of registered patients whose data could be accessed. Unknown number of patients (whose data was untraceable) obviously stands excluded from study.

\* Original TB Unit Register untraceable. But, a photocopy under Right to Information (RTI) Act obtained by S.K. Dua (a famous social activist) examined.

<sup>@</sup> RTI Photocopy contained partial data from Jan 1 to Sept 30, 2006 (last quarter 2006 missing).

<sup>#</sup> Data from RTI photocopy of TB Unit Register District TB Center for 2007 has been deliberately excluded from study because of bizarre entries in it:

54 Names & details of patients listed at TB No. 1417 to 1471 are found mysteriously re-written verbatim at TB No. 1472 to 1527 (as if copy pasted by hand) enbloc. Similarly, 6 more patients' entries found duplicated.

Out of 934 patients shown registered, 'outcome of treatment' column against 426 patients was found blank (even after two years).

**Table 2 TB Patients found registered twice under DOTS (TB Program) in Faridabad in 16 years.**

Repeaters Identified during Clinical Audit, ongoing since 6 years, in TB OPD of District Govt. Hosp (on an average, 3,100 <sup>#</sup> detected 1 Repeater per day)			
Retrospective Record Review: scrutiny of	TB Unit Ballabgarh	997	
hand-written Registers of distant past (jointly	TB Unit District TB Center	371	1,575 <sup>@</sup>
with key relevant worker)	Miscellaneous	207	
Total Repeaters		12.7%	4,675*
Deaths		4.9%	1,590
Defaulters		8%	2,590

4,675\* Repeaters are the ones that we could find (some possibly remain undetected). Name, Unique ID No.'s, address—clinching and verifiable details of each patient in excel sheets.

<sup>#</sup> More complete details were recorded; some in excel sheets; Some documentary evidence like 16GB Photo albums (with Photos of patient, his X-rays, Sputum +/FNAC/Biopsy reports, refer/discharge slips, TB ID Card etc.) and paperwork not enclosed; work in progress to index data.

<sup>@</sup> Which worker/register is source of information is indicated in 'Source' column of excel sheet.

Repeaters = 4675\*, % age = Repeaters found ÷ Total Patients Registered in 16 yrs × 100

=  $\frac{4675 \times 100}{36785} = 12.7\%$ .

36785

Once diagnosed, a patient is placed on DOTS treatment within a week, formally registered in a month, treated for 6 to 8 months; outcome (result) compiled after one year. So, for calculating % ages of Died and Defaulters, total number of registered patients = 36,785 min 4,417 (Regd. recently in 2015, outcome not yet known) = 32,368.

**Table 3 No. of DOTS cycles taken by each of 4,675\*Repeaters.**

1	No. of patients who got registered twice or more often	4040	528	82	21	3	1
2	No. of Times that each patient got registered under DOTS program (Treatment cycles taken)	Twice	Thrice	Four cycles	Five innings	Six courses	Seven Times

In books, these 4,675 individuals account for a whopping 10,112 registrations; 12.7% patients occupy 27.5% of registrations. Even though district claims 36,785 patients registered, actually only 31,338 persons have been treated; same persons keep coming back, over and over again!

Furthermore, In South India, of 503 patients cured, 9.5% relapsed within 6 months [9]. Out of 657 successfully treated NSP TB patients, 10.85% relapsed and another 5.9% died due to TB within 2 years [10]. Out of 4,905 successfully treated Cat I patients, 442 (9%) presented as relapses [11]. Daily anti-tuberculosis treatment is more effective than thrice weekly treatment for the treatment of tubercular (TB) meningitis [12]. Twice-weekly intermittent SCT is less likely to cure TB in children [13]. In HIV positive, Daily regimen or at least Daily in IP, followed by thrice weekly CP is better [14]. Cavitory tuberculosis is best treated with ...Daily IP... [15]. [Indian program is sputum-smear based; chest X-ray not mandatory; which patient has cavities is unknown. Follow up of even sputum-negative PTB (diagnosed by X-rays) is by sputum-tests alone!]

### 3.2 Discussion

(1) To cure TB, first opportunity is ideal; thereafter, medicines become less effective, results inferior. Favorable outcomes were significantly less in the retreatment group (66.47%) as compared to new smear positive cases (84.28%) [16]. This is possibly due to generation of some degree of drug-resistance.

(2) Each repeat episode is a baby step towards development of drug-resistance. Of 15 million Indians registered so far, 12.7% took two cycles; about 2 million repeat episodes, which amounts to promotion of drug-resistance at an industrial scale; potential threat for the entire world.

(3) DOTS is misnomer—a confusing term. Several national TB programs, even poles apart, are all popularly called DOTS.

Nepal's DOTS is daily-regimen, Indian DOTS is

thrice-weekly. To a retreatment case, both countries offer Injection Streptomycin for initial two months; that comes to 60 injections (one vial daily) in Nepal; 24 injections (three per week for 8 weeks) in India, which appears desperately inadequate, especially in Failure cases, who respond more poorly than relapse cases. The 'Failure' cases of Category I subsequently treated with Category II were observed to have significantly lower success rates ( $P = 0.05$ ) as compared to Relapse cases [11]. The need for re-appraisal of Category II re-treatment regimen for 'Failure' cases among Cat I is suggested [11]. Karma also hinted that Category I failures are more likely to fail Category II (re-treatment) [17].

(4) Under RNTCP, cured patients are not followed up to see if they shall relapse, hence no systematic, precise quantification of relapse!

(5) Betraying total lack of conviction in her own thrice-weekly system, India has recently reverted back to Daily-regimen in dealing with her drug-resistant cases.

(6) WHO frames its future guidelines based upon 'published research', which is scanty. The exercise essentially ignores a mammoth resource—NTP data generated worldwide.

(7) Randomised Controlled Trial versus Audit in Poor Countries:

RCT is needed to prove more Relapse in thrice-weekly than in Daily. Because if proven right, a simple change to Daily dose would be life-saving.

But, RCT requires funds, manpower but first, a high level decision.

RCT for Relapse is likely to take at least 10 years. Because, after initial treatment of a year, one has to wait for 5-7 years to see how many of them relapse.

With MDR breathing down our neck, we don't have 10 years.

Time to do RCT was:

1990s when India was funded big time to adopt thrice-weekly on insufficient evidence.

Or in 2005 when a South Indian study found 12% Relapse.

Or in 2008 when a large Delhi study found 9% Relapse.

Grave Omissions. Typically, no accountability.

At present, Retrospective is the way to go.

And, outcome of 15 million patients lies buried in Indian Registers; please digitize and share.

No doubt, Audit is a low grade evidence, with risk of bias and fraud. But, here is a clinching, whistle-blower, audit of 35,000 patients—very large, credible and verifiable—as good as RCT.

### 3.3. Constraints

(1) HAND-WRITTEN AND NON-DIGITIZED: India is an ideal laboratory to resolve the 'daily versus thrice-weekly' controversy. Details of 15 million patients fed thrice-weekly doses stand recorded within India's hand-written registers. Their custodian (govt. of India) and technical advisers (WHO) did not timely digitize, share, release, publish or capture this invisible goldmine of retrospective wisdom, which still remains out of reach of potential researchers. What a paradox! The entire world gropes for answers. India began to digitize in late 2012 through case-based Nikshay software, which is still in its infancy, struggling yet to update even the current data.

(2) To search a name in a thick hand-written register is like finding a needle in a hay-stack, more so, retrospectively. Or if patient took DOTS from another TB Unit, district, city or state. Manual entries suffer from bad illegible writing, wrong names/address/spellings, no phone number, faded ink, over-writing, cutting; missing, torn or moth-eaten pages.

(3) OPAQUE: RNTCP is designed to thwart transparency. In each of 2,698 sub-district TB Units of

India, a single contractual supervisor (STS) monopolizes over gathering field-data, compiling reports (unsupervised) and e-mailing them (unverified/countersigned blindly) into public domain! Floods or earthquake, STS must achieve pre-set targets! Or else, he is fired; his children starve; fudging and then safeguarding data becomes a survival-skill. Hence it is no transparency, virtual impenetrability. Inspectors converging from outside (for helicopter surveys), can hardly uncover truth; hence, bubble-formation over time.

(4) NO SYSTEMATIC CATALOGING: 50% TB patients approach private practitioners and receive Daily-dosing, the rest receive govt.'s Thrice-weekly dose; both regimens operate side by side in India. But when a retreatment case presents himself for registration under DOTS, program doesn't ask "Source of previous anti-TB treatment: DOTS or Private sector?" Appropriate cataloging (so easy at entry-point) is not done; he enters untagged; RNTCP data-bank churns up both types, escalating confusion. Hence, the long time taken by this study.

(5) LOW PROFILE: Author worked in silence, quizzed clueless but motivated workers on a mission-to-know basis, in return divulging little. India has no legal protection for whistle-blowers. Govt. is a powerful giant; capable of squashing critics; retribution is quick, efficient. DOTS workers (including author) are on yearly-contract, vulnerable. Once jobs are at stake, entire system may turn hostile, denying data or even resorting to resurrecting brand new fake district registers overnight! For this reason, no names are in acknowledgement section.

(6) UNTRACEABLE PAST DATA: District began to employ ten full-time TBHV's in 2006. Till then, i.e. from 2000 to 2006, PHI registers were almost non-existent. Original DTC TB registers from 2000 to 2008 remained untraceable because Sanjeev STS (the custodian) had since resigned. At Dabwa slums, PHI registers from 2000 to 2009 couldn't be found. Similarly, no past data could be found/examined at:



ESI Hospital NH3 NIT; ESI Dispensaries—sector 19 and 27-B; stone-crushing zone; and several sub-centers—Badkhal (Krishna ANM retired), Mewla Maharajpur (Narbada), Sihi (Sudarshan/Seema), Ajrontha (Anita) etc.

(7) Disillusioned, several patients disappear—to perish, unheard, unwept, unrecorded anywhere in history. Several Repeaters elope before registration; initial default seems considerable and requires investigation. Furthermore, the study may be short of scientific exactitude as it broadly includes all sorts of Retreatment cases—PTB/Extra-PTB, sputum positive/negative. AFB culture is rare in India.

(8) DUPLICATE OR EVEN TRIPLICATE ENTRIES: A patient who defaulted in 2010, re-registered in 2011 and died in 2012, his name appears in all three lists—Default, Repeater and Died. Such duplicity is genuine. Till May 30, 2013, when Puneet Gupta (of Finsys) donated tailor-made software, author clumsily maintained several files and folders; over 40 duplicate (often marked ‘Dupli’) and half-a-dozen even triplicate entries crept in; their deletion was postponed and then given up for fear of erasing hard-earned crucial bits of information! Furthermore, time-overlaps in data collection, percentages need slight refinement. But all that would only have insignificant effect over results of this very large study. But the exercise will guzzle more time; author is already guilty of interminable delay. Noiseless MDR explosion appears imminent, if not already underway. Issue transcends trivia.

#### (9) No Referees Found

India’s private doctors don’t practice/trust Thrice-weekly; have little first-hand experience; hence can’t be referee here.

Govt. doctors are mortally afraid to (openly) criticize govt. policy; they are brain-washed that ‘DOTS thrives in over hundred countries’, unaware that it is mostly Daily DOTS. Besides, it is backed by WHO, which is considered above suspicion; no one even begins to question.

Easily verifiable, transparent excel-data with names and unique ID’s of about 9,600 patients with clinching evidence is attached. Furthermore, voluminous manual backup, software data containing phone no. of patients, workers, and sputum Lab No.’s, and heavy 16-GB photo-albums (withheld) but remain available with author.

Govt. of India didn’t systematically conduct or encourage any studies over thrice-weekly program. Hence, these remain meager, published locally, circulated poorly, quoted rarely; hence ineffective. Besides, thrice-weekly topic doesn’t directly concern the rest of the world (which largely uses Daily dose). For international journals, subject is low priority, unexciting.

(10) EXTRAPOLATION: This is purely a study of Indian DOTS. Results are India-specific. They can’t be automatically extrapolated over DOTS of other nations (having daily regimen and different field conditions). However, findings ought to be extrapolated over India’s all 662 districts because same model (as per RNTCP guidelines) operates all over! Faridabad represents ‘routine program conditions’ prevailing across India.

To dismiss it as exception would be a dishonest denial. The district offers a large sample; it registers over 3,000 TB cases annually (France does 2,700). Situated near Delhi, monitored intensively, having ten TBHV’s, getting bonus help from infrastructures of ESI, RCH schemes, it consistently ‘achieves’ 85% success. Study reflects years of collective performance of (not just a handful of non-performing individuals but) RNTCP’s routine army—25 PHIs and doctors therein; 10 TBHVs; 19 DMCs, 22 LTs; 300 DOT providers (including ANM, ASHA, AWW, GP’s); 3 TB Units (one headed by the author since 6 years), 3 STSs, 3 STLs; DTO, STO and one WHO Consultant. (As technical advisor to Govt. of India, WHO has perpetually fathered the entire process of conception, birth, expansion, and monitoring of Indian DOTS. Currently, 87 WHO Consultants serve as watchdog).

(11) SIMILAR STORY IN NEIGHBORING DISTRICT PALWAL: Author exhorted some conscientious workers there in mid-2012; result—Repeaters began tumbling out, 532 and still counting (Names, unverified unique IDs in excel sheets)!

India's erstwhile TB Program (1962-97) remained an undeclared disaster; fewer than 30% patients completing year-long antique STH regimen. Belatedly, DOTS ushered in a ray of hope—generational switch to modern, short course chemotherapy. Alas, this too got contaminated with 'thrice-weekly dosing'! Another crime against humanity! No accountability ever for governments or their unions! India's euphoria over self-generated printed papers guarantees little respite in near future. Tuberculosis is blamed to play havoc with poor millions in the third world. Study uncovers the real culprit—gross policy-mismanagement. It reiterates how while seemingly championing governance, equality, justice, human rights and charity, man acts as scavenger on its own race.

### Acknowledgments

Five TBHV's (names withheld to shield them from possible retribution) serve with a missionary zeal; their uncanny knowledge of local patients, meticulous 7-year PHI-records formed valuable data-source. Author salutes them.

He is grateful to the entire district work-force for sustained donation of labor.

Excel sheets detailing 9,700 patients' names reveal their respective contributions under 'Source'. Now, baton has come to rest with the author—to reveal truth, seek justice; no scope for fatigue, fear or failure; to publish or to perish.

Author acknowledges the trust reposed in him by thousands of TB victims, condemned forever to ancient tools; sputum-smear is 132, five primary drugs over 48 and BCG vaccine 91 years old. Little R&D for the poor! Alas, science is neither fair nor universal.

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