Revisiting supervised therapy: Modeling the epidemiology and costs of directly observed therapy in Baltimore

C. Patrick Chaulk, M.D., M.P.H.
Senior Associate,
Annie E. Casey Foundation,

City Chest Clinic
Baltimore City Health Department
Baltimore Maryland,

The Johns Hopkins Schools of Hygiene & Public Health, and Medicine

Mark Friedman, BS
Director
Fiscal Policy Studies Institute
Baltimore, Maryland

Richard Dunning, MSW
Director, Bureau of Disease Control
Department of Epidemiology and Preventive Medicine
Baltimore City Health Department
Baltimore Maryland

Objective.--To estimate the range of pulmonary tuberculosis (TB) cases and treatment costs prevented due to directly observed therapy (DOT) in Baltimore.

Design.--Policy-cost modeling.

Methods: Reported TB incidence (Baltimore, US cities with over 250,000 residents, and, the US) were used to construct a series of scenarios to estimate the number of cases and treatment costs prevented as a result of Baltimore's DOT program: (1) TB patterns between 1978 and 1992 were constructed and compared for Baltimore and all US cities with over 250,000 residents; (2) TB patterns between 1978 and 1996 were constructed and compared for the Baltimore and the US; and, (3) Net cost savings were estimated under each scenario.

Setting: Baltimore; US cities with over 250,000 residents; and, the US.

Results: Our model predicts that in the absence of DOT there would have been between 68% (n = 1,566) and 72% (n = 2,233) more cases of pulmonary tuberculosis in Baltimore than observed with concommitant net savings in treatment costs of between $25.9 million and $27.1 million respectively.

Conclusion: Baltimore's DOT strategy has been accompanied by substantial reductions in TB cases and TB costs in Baltimore. These benefits increased as the proportion of city-wide cases managed under DOT expanded. Wider adoption, at least in high incidence cities, of a community-based DOT strategy similar to Baltimore's could reduce the incidence of tuberculosis beyond current city and national trends.

Background:

Between 1985 and 1992, pulmonary tuberculosis (TB) underwent a dramatic resurgence in the US, with some 64,000 more cases reported by the Centers for Disease Control & Prevention (CDC) than predicted by prior TB trends.[1] However, since 1992, this resurgence has begun to wane, due in large measure to more aggressive national and local TB control targeting several putative causes of this resurgence--physician mismanagement (more education and training), deterioration of municipal TB control programs (greater public investment in TB control), and the failure of patients to complete therapy (greater use of directly observed therapy).

In particular, the increasingly widespread implementation of directly observed therapy (DOT) has been credited with improving local TB control. Recent evidence suggests that in the US, DOT has been effective in achieving high treatment completion rates[2,3] ; in dramatically reducing TB incidence in urban settings where the prevalence of TB risk factors such as AIDS, poverty, substance abuse, and immigration is high ([2],[4]); in preventing and reducing the incidence of multi-drug resistant tuberculosis (MDRTB)[5,2,4]; and, in producing good outcomes for patients even with advanced HIV infection[6]. Additional research suggests that DOT is also cost-effective compared to self-administered therapy.[7,8]

The Baltimore City Health Department's (BCHD) DOT program, implemented 18 years ago, is among the oldest community-based, urban DOT programs in the US. Since immplementation of this program, Baltimore has experienced a steady decline in TB quite distinct from the rest of the nation, particularly as compared to other large

urban centers. For example, in cities with over 250,000 residents, the rate of TB increased 2% between 1981 and 1992, but declined 52% in Baltimore. [2] This decline contrasts with the comparatively high incidence of TB in Baltimore prior to implementing DOT: between 1968 and 1978, Baltimore regularly ranked among the top five incidence cities for TB (BCHD). However, since undertaking a city-wide DOT strategy, Baltimore dropped in rank from second in 1978 to 28th in 1992, while the incidence of TB declined 70.9%. [9,10]

DOT is predicated on the theory that watching patients ingest their TB medications results in higher treatment completion rates. When recommended anti-TB drug regimens are completed, 97% of patients with susceptible organisms should be cured, and the spread of infection to others reduced.[11] Conversely, failure to identify and treat even a single case can have a substantial community impact, resulting in micro-epidemics. [12,13,14,15]

To further explore the impact of DOT on TB in Baltimore, we constructed a series of scenarios using national and US city TB incidence data reported to the CDC between 1978 and 1996 to estimate the number of TB cases that might have occurred in Baltimore in the absence of its DOT program.

Baltimore's DOT Program:

Baltimore's DOT program was selected for analysis because it is one of the oldest and most established urban DOT programs in the US. Since there is comprehensive programmatic, epidemiologic, and cost data available, it has been the subject of numerous reports. [2,7,9,10] Moreover, since Baltimore was annuallly ranked

high for TB prior to implementing DOT, it also provides a unique opportunity to evaluate the impact of DOT in a city historically known for its high rate of TB.

In Baltimore, municipal TB control is the responsibility of the Baltimore City Health Department's Division of Preventive Medicine and Epidmiology. DOT is offered through the city's Chest Clinic located in inner city Baltimore, and is part of BCHD's patient-centered TB control strategy. For example, although patients may receive DOT at the City Chest Clinic, virtually all opt for treatment by visiting nurses at the patient's home, work place, school, shelter, nursing home or other setting. This community outreach strategy obviates the need for extensive incentives and enablers in managing DOT cases. Temporary housing is rented by BCHD for homeless patients during their TB therapy. Where possible, public health nurses visit newly identified cases during their initial hospitalization to review the diagnosis, assess the treatment plan, begin associate and/or contact investigations, and offer DOT services.

The study period begins in 1978, when Baltimore launched its DOT effort as a clinic-based program (Clinic-Based Period) for city-defined "high risk" patients (i.e., unemployed, homeless, and alcoholic patients). Patients were recruited using a limited number of incentives (e.g., free transportation, free medications) to receive DOT at one of the City's five TB chest clinics.

In late 1981, a community-based strategy lasting until late 1987 (Early Community-Based Period) was undertaken whereby all patients in Baltimore with pulmonary tuberculosis were eligible for home-based DOT through the city's program. Community outreach through public health nurses was coupled with existing incentives.

Between 1988 and 1996, Baltimore's DOT program was expanded further into the community (Expanded Community-Based Period) using greater community outreach (including hospital visitations to recruit newly diagnosed cases), community and provider education efforts, additional patient incentives and enablers (housing for homeless TB patients), and assignment of city nursing staff to provide services to high risk populations in Baltimore (jails, substance abuse treatment facilities, a prospective study of injection drug users, and a community-based AIDS service facility).

Methods/Analysis:

Scenarios were developed using Lotus 1,2,3 Version 5 to estimate what the potential number of TB cases (and accompanying costs) would have been had there been no DOT in Baltimore. We assumed that in the absence of DOT, the incidence of TB in Baltimore would likely have followed one of two actual TB patterns other than its own based on annual cases reported by the CDC Division of TB Control for US cities and the nation.[16]

Based on these data, selected TB patterns were used to construct two scenarios. The first scenario was for the period 1978-1992, and compared the TB pattern for Baltimore (Baltimore Pattern-1) with the TB pattern for all US cities with over 250,000 residents (Large City Pattern). We selected this cohort of cities for comparison because it includes only the largest US cities, and as such, is a more suitable comparison to Baltimore. Also, this cohort, which includes Baltimore, is a major focus of the CDC's TB surveillance efforts. We used 1992 as the cutoff year for our large city comparison because the CDC ceased reporting city-specific data in 1993,

and began reporting TB incidence for these cities by metropolitan statistical area (MSA).

Next, using the most current data available (1996), we constructed a second scenario for the period 1978-1996 to compare Baltimore's TB pattern (Baltimore Pattern-2) with the TB pattern for the US (US Pattern).

Finally, net treatment savings (from cases prevented under both scenarios) were calculated based on cost data from the published literature. We used a treatment estimate of $13,515 for DOT from a prior study of Baltimore's DOT program that assumed full drug susceptibility (i.e. no mono or multi-drug resistant cases). [7] Similarly, we assumed the cost per case under non-supervised therapy (non-DOT) equaled $12,672 (again assuming full drug susceptibility).

Findings:

The TB incidence patterns for the US, US cities with over 250,000 residents, and Baltimore are displayed in Figure 1. The number of observed cases in Baltimore totalled 3,159 between 1978 and 1992, and 3,583 between 1978 and 1996. (Table 1)

Under the first scenario, replacing Baltimore Pattern 1 with the Large City Pattern results in 2,233 more cases then actually observed in Baltimore between 1978 and 1992. Thus, instead of the observed case burden of 3,159 cases, there would have been 5,392, or 70.6% more cases.

Under the second scenario, replacing Baltimore Pattern 1 with the US Pattern results in 2,160 more cases than observed in Baltimore. And, instead of the observed 3,583 cases there would have been 5,743 or 60.2 % more cases.

Estimated net savings due to cases avoided under these scenarios ranged from $27.1 million (Large-City Pattern), to $25.9 million (US Pattern) (Table 1).

Discussion

After a long history of ranking among the highest cities for tuberculosis. Baltimore experienced a substantial decline in TB following the introduction of directly observed therapy in 1978. The incidence of TB dropped 70.9% between 1978 and 1996, while Baltimore fell from the second highest major city for TB to the 28th (1992). This TB control strategy--watching each patient consume all their TB antibiotics--has been recommended by virtually all leading TB control organizations.[17,18,19,20]

To further explore the impact of this strategy in Baltimore, we developed alternative scenarios based on TB cases reported to the CDC by other large cities and the US to estimate a possible range of TB cases prevented in Baltimore due to its DOT program. Our scenarios benefited from using actual, rather than hypothetical, incidence trends.

Our findings suggest that had the incidence of TB in Baltimore followed either of two other actual major patterns, there would have been substantially more cases--as many as 2,233 more--than observed and additional treatment costs of over $27.1 million. Moreover, as DOT became more widely adopted in Baltimore (expanding from its Clinic-Based Phase to the Expanded Community-Based Phase) the number of TB cases prevented increased (going from roughly 60 cases prevented per year to over 200 cases prevented per year). However, there may be limitations to our model.

First, alternative scenarios notwithstanding, the incidence of TB in Baltimore may

simply have followed the same pattern without DOT. This is unlikely since implementation of DOT in other communities with epidemic TB patterns has been followed by a substantial decline in the subsequent incidence of TB. [4,21]

Second, our approach may overstate the Baltimore effect, since not all TB control programs are equal in terms of resources, priorities, and staffing. Program capacity, apart from DOT, may influence local TB trends.

Third, there clearly are factors besides DOT that influence TB incidence. For example, poor (late) new case identification and reporting would counter even 100% DOT participation since undiagnosed cases would persist and continue producing additional cases in the community. We do not know the extent of any variability in TB reporting among the study cities.

Fourth, the foreign-born account for a disproportionate share of cases in some communities. It might be argued that those due to reactivation, as opposed to new transmission, would not be prevented by DOT. However, TB surveillance is weakest among underserved populations, such as immigrants, and new cases arising among immigrants might therefore actually led to more TB transmission since TB surveillance among such populations can lag behind surveilance in the general community. In these settings, DOT would be effective in reducing TB incidence. Finally, TB declined substantially in Baltimore even during the period of greatest urban immigration and AIDS (case rate 22.9, 1988 and 14.9, 1996; a 34.9% decline, BCHD).

Fourth, scenario modeling, even when based on actual incidence, is still hypothetical. Nonetheless, our findings add to a growing and consistent body of

evidence that supports the general effectiveness of supervised therapy. [2,3,5,6,9,20]

Despite these caveats are model may also be viewed as conservative. First, both the US and Large City Patterns include the Baltimore Pattern, which should, if anything, somewhat dampen the actual effect of DOT.

Second, between 1985 and 1992, AIDS rose in Baltimore 71.5%, and was the leading reported cause of death in Baltimore for men and women 15 to 44 years old.[22] If anything, this rise in AIDS cases should have been accompanied by an increase in TB (as occurred nationally and in the largest cities) rather than the observed decline.

Third, Baltimore is not the only major city to use DOT during the study period.[10,23,24,25] Thus, the DOT effect based on the Baltimore Patterns is again dampened since some cities in the US Pattern employ some level of DOT, although its application in these cities appears to be variable. (CDC) [26,27] Removing the effect of DOT in these cities might generate additional case and cost savings.

Our cost assumptions also are conservative since we excluded indirect costs, did not estimate losses (economic) from TB deaths prevented, and did not account for the economic impact of an increasing proportion of cases nationally that were multi-drug resistant, a fact that is more prominent during the latter portion of these trends, particularly in large cities. Thus cases avoided during the mid-1980s onward (when TB was undergoing its greatest upswing) are more likely to be MDRTB cases which have been shown to be considerably more expensive to treat (averaging as much as $180,000 per case).[28]

We also believe that the full TB control potential of such a community-based

program is not captured by our focus on Baltimore. For example, when we reversed our scenarios, and calculated how may TB cases might have been avoided had the Baltimore Patterns replaced the US or 64-City Patterns we found that there would have been between 192,084 fewer cases with net cost savings of $2.2 billion (nationally), and 54,253 fewer case with net cost savings of $634.6 million (large city cohort).

Finally, the Baltimore Pattern deserves additional comment. Although this pattern declined substantially over time, it appears to be leveling out, assuming an asymtotic shape, i.e, the rate of decline in TB incidence appears to be slowing. We believe this trend reflects two aspects of DOT: the limited capacity for TB eradication solely through DOT; and, the fact that progressive case eradication reduces the denominator from which further cases will be removed, thus making other strategies, particularly early case finding and comprehensive preventive therapy for high risk groups, critical to ultimate TB eradication. Although we could not adjust for this, subsequent adoption of DOT by other communities may shed more light on this effect if they undertake more comprehensive TB control efforts during early implementation of their program.

In this regard, it should be pointed out that it took Baltimore nearly two decades to achieve its TB control results. We believe that the Baltimore Patterns described in this study could be accelerated by early and more aggressive recruitment of patients into DOT therapy, i.e., "going to scale" earlier, thereby yielding the same results sooner.

Meanwhile, our findings under these scenarios provide additional evidence supporting a comprehensive, community-based TB control approach using directly

observed therapy, especially in US cities where the incidence of TB historically has been high. Further research should identify ways to capture treatment savings from cases prevented in order to sustain such community-based interventions, and to identify more cost-effective delivery of DOT across diverse communities.

Making DOT available to as many patients as possible has significant public health and economic implications, dramatically reducing both the incidence and costs of tuberculosis. However, DOT is but one component of effective TB control. Other critical components include effective associate and contact investigations, screening and preventive therapy for high risk populations, and implementing community surveillance, case finding, and disease tracking.[29]

References

1. Expanded tuberculosis surveillance and tuberculosis morbidity--United States, 1993. MMWR 1994;43(12):361-365.

2. Chaulk CP, Moore-Rice K, Rizzo R, Chaisson RE. Eleven years of community-based directly observed therapy for tuberculosis. JAMA 1995;274:945-951.

3. Pozsik C, Kinney J, Dreeden D, Nivin B, Davis T. Approaches to improving adherence to antituberculosis therapy. JAMA. 1993;269:1096-97.

4. Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City -- turning the tide. N Engl J Med 1995;333:229-33.

5. Weis SE, Slocum PC, Blais FX, et al. The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. N Engl J Med 1994;330:1179-84.

6. Alwood K, Keruly J, Moore-Rice K, Stanton DL, Chaulk CP, Chaisson RE. Effectiveness of supervised, intermittant therapy for tuberculosis in HIV-infected patients. AIDS. 1994;8:1103-1108.

7. Moore RD, Chaulk CP, Griffiths R, Cavalcante S, Chaisson RE. Cost-effectiveness of directly observed versus self-administered therapy for tuberculosis. Am J Respir Crit Care Med. 1996;154:1013-9.

8. Burman WJ, Dalton CB, Cohn DL, Butler JRG, and Reves RR. A cost-effectiveness analysis of directly observed therapy vs self-adminsteredt therapy for treatment of tuberculosis. Chest 1997;112:63-70.

9. Chaulk CP, Chaisson RE, Lewis JN, Rizzo RT. Treating multidrug-resistant tuberculosis: compliance and side effects. JAMA. 1994;271:103-104.

10. Chaulk CP, Pope D. Baltimore City Health Department program of directly observed therapy. Clin in Chest Med. 1997;149:154-157.

11. Combs DL, O'Brian RJ, Geiter LJ. USPHS tuberculosis short-course chemotherapy trial 21: effectiveness, toxicity, and acceptability. The report of final results. Ann Int Med. 1990;112:397-406.

12. Braden CR. Infectiousness of a university student with laryngeal and cavitary tuberculosis. Clinical Infectious Diseases. 1995;21:565-570

13. Arneil AS, Batterstill J. A mini-epidemic of tuberculosis in the Upper Fraser Valley Health Unit. Can J Public Health. 1973;64:497-499.

14. Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multi-drug resistant Mycobacterium tuberculosis during a long airplane flight. N Engl J Med. 1996;334:933-938.

15. Sacks JJ, Brenner ER, Breeden DC, Anders HM, Parker RL. Epidemiology of a tuberculosis outbreak in a South Carolina junior high school. Am J Public Health. 1985;75:361-365.

16. Centers for Diease Control and Prevention. *Annual Tuberculosis Statistics: States and Cities*. Atlanta, Ga: Centers for Disease Control and Prevention. Data from annual volumes, 1978 through 1996.

17. American Thoracic Society, Medical Section of the American Lung Association. Treatment of tuberculosis and tuberculosis infection in adults and children. Am J Respir Crit Care Med. 1994;149:1359-74.

18. Center for Disease Control and Prevention. Initial therapy for tuberculosis in the era of multi-drug resistance. Recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR. 1993;42(No. RR-7)(1993):108-.

19. Improving patient adherence to tuberculosis treatment. Centers for Disease Control and Prevention, U.S. Department of Health & Human Services, Public Health Service, Atlanta, Ga, Revised 1994.

20. World Health Organization. WHO Report on the Tuberculosis Epidemic 1997. Kraig Klaudt, Ed. WHO 1211 Geneva, 27-Switzerland.

21. Chaulk CP, Iseman MD. Directly observed therapy. Lancet 1997;350:666-667.

22. Selik RM, Chu SY, Buehler JW. HIV infection as leading cause of death among young adults in US cities and states. JAMA, 1993;263:2991-2994.

23. Fujiwara PI, Larkin C, Frieden TR. Directly observed therapy in New York City. Clinics in Chest Medicine. 1997;18(1):135-148.

24. Weis SE. Universal directly observed therapy: A treatment strategy for tuberculosis. Clinics in Chest Medicine. 1997;18(1):155-163.

25. Schecter GF. Supervised therapy in San Francisco. Clinics in chest Medicine. 1997;18(1):165-168.

26. Fujiwara P, LarkinC, Frieden TR. Directly observed therapy in New York City: history, implementation, results, and challenges. Clin Chest Med. 1997;18(1):135-148.

27. Schecter GF. Supervised therapy in San Francisco. Clin Chest Med. 1997;18(1):165-168.

28. Mahmoudi A, Iseman MD. Pitfalls in the care of patients with tuberculosis: common errors and their association with the acquisition of drug resistance. JAMA. 1993;270:65-68.

29. CDC. Essential components of a tuberculosis prevention and control program. MMWR 1995;44(No. RR-11):1-16.

Figure 1: Tuberculosis incidence (per 100,000 population) for largest US cities (>250,000 residents), the US and Baltimore between 1978 and 1996.

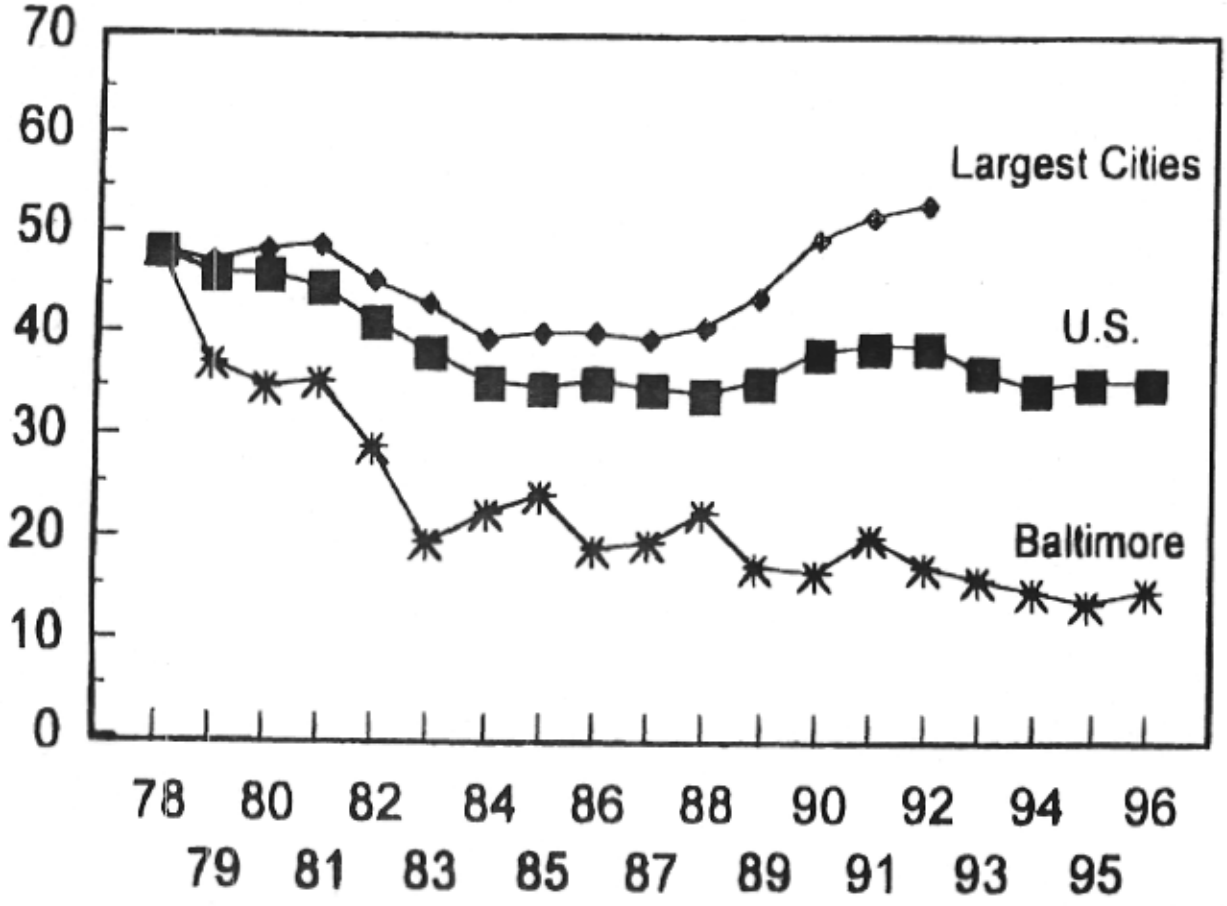

Table 1. Scenarios estimating the number of TB cases in Baltimore when there is no DOT. Estimates derived from substituting actual TB patterns of the US and US cities with over 250,000 residents for actual Baltimore pattern.

Scenarios[1]	Observed Cases[2]	Cases Prevented [3]	New Case Total[4]	Net Savings[5]
Scenario 1: 1978-1992: Replace Baltimore Pattern-2 with Large US City Pattern	3,159	2,233	5,392	27.1
Scenario 2: 1978-1996 : Replace Baltimore Pattern-1 with US Pattern	3,583	2,160	5,743	25.9

[1] For Scenarios: All Patterns based on the respective actual annual incidence of TB in Baltimore, the US, and Large US Cities (populations over 250,000) for the periods 1978-1996 or 1978-1992.

[2] Actual number of cases observed in Baltimore under each respective Baltimore Pattern.

[3] Estimated number of TB cases prevented under each Scenario.

[4] Estimated new number of TB cases based on observed (actual) plus estimated number of cases prevented under each scenario.

[5] Net treatment savings in millions of US dollars (1994) based on estimated number of TB cases prevented.