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Literature Review of Tuberculosis (TB) Intervention Studies

November 2, 2008

Literature Review of Tuberculosis (TB) Intervention Studies

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KSC Research Series

ABSTRACT: This literature review looks at recent research studies that investigate factors involved in successful tuberculosis (TB) interventions, in particular Directly Observed Therapy Short-Course (DOTS), DOTS +, and incentive programs associated with DOTS programs. The review is based on a bibliography compiled by Christina Blumel and Rebecca Gross, from a search of PubMed and the USAID Development Experience Clearinghouse (DEC).

The USAID Knowledge Services Center is operated by Bridgeborn, Inc. and Library Associates, and funded by M/CIO/KM and M/HR/TE under contract RAN-M-00-07-00003-00. The contents of this document are the sole responsibility of the Knowledge Services Center and do not necessarily reflect the views of USAID or the United States Government.

PN-ADM-018

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This review looks at the literature on successful TB interventions from 2000-2007. Early evaluations of Directly Observed Therapy Short-Course (DOTS) programs were encouraging, although not all the later studies confirmed these findings. In response to these mixed findings, more recent literature has therefore looked beyond simply the effect of DOTS to other factors that led to the failure or success of an intervention package.

Eastern Europe Specific Studies

DOTS program evaluations: Early evidence from Eastern Europe was supportive of the DOTS treatment system. In 1998, a study done by Ruuhonen et al.¹ found that the World Health Organization (WHO) DOTS pilot project in the Leningrad region was moderately effective with patients with high epidemiological and medical risk. This study was followed by a 2003 study in Orel Oblast of a revised DOTS program that also had good results; an 81% cure rate for culture positive patients and a 91% cure rate for clinically diagnosed patients². DOTS + has been successfully implemented for multi-drug resistant TB (MDR-TB) patients as well. A 2005 study from Latvia indicated that 66% of patients were cured or completed therapy under the program. This study included an analysis of risk factors for poor outcome in a multivariate Cox proportional hazards model³.

In 2006, a DOTS program in a prison context was evaluated in Samara Oblast⁴. The study primarily looked at multi-drug resistant TB rates and risk factors among study participants, and concluded that the implementation of DOTS was successful. Also in 2006, a study from Sarajevo examined patient radiographic data from 1998 to 1999 in order to evaluate the effectiveness of the introduction of DOTS. The study found greater chest X-ray partial regression with the DOTS system⁵.

¹ Ruuhonen RP, Goloubeva TM, Trnka L, Fomin MM, Zhemkova GA, Sinitsyn AV, Lichachev AA, Koskela KG. "Implementation of the DOTS strategy for tuberculosis in the Leningrad Region, Russian Federation (1998-1999)." *Int J Tuberc Lung Dis*. 2002 Mar; 6(3): 192-7.

² Kherosheva T, Thorpe LE, Kiryanova E, Rybka L, Gerasichev V, Shulgina M, Nemtsova E, Aptekar T, Kluge H, Jakubowiak W, Grzemska M, Aquino G, Wells C, Kazionny B. "Encouraging outcomes in the first year of a TB control demonstration program: Orel Oblast, Russia." *Int J Tuberc Lung Dis*. 2003 Nov; 7(11):1045-51.

³ Leimane V, Riekstina V, Holtz TH, Zarovska E, Skripconoka V, Thorpe LE, Laserson KF, Wells CD.

"Clinical outcome of individualised treatment of multidrug-resistant tuberculosis in Latvia: a retrospective cohort study." *Lancet*. 2005 Jan 22-28; 365 (9456):318-26.

⁴ Balabanova Y, Drobniewski F, Fedorin I, Zakharova S, Nikolayevskyy V, Atun R, Coker R. "The Directly Observed Therapy Short-Course (DOTS) strategy in Samara Oblast, Russian Federation."

Respir Res. 2006 Mar 23;7:44.

⁵ Paralija, B. "The effectiveness of direct observed treatment short course (DOTS) in tuberculosis treatment." *Med Arh*. 2006;60(5):287-91.

Role of alcohol abuse: Recently, several Eastern European studies have attempted to identify factors associated with unfavorable TB treatment outcomes. Alcohol abuse was found to be a factor in two separate studies. In 2006, Bumburidi et al. used 2000-2002 data from Kazakhstan in a logistic regression analysis to isolate factors associated with outcomes of pulmonary TB (PTB) and PTB+ treatment⁶. Outcomes and cure rates were defined using WHO DOTS guidelines. Unfavorable outcomes were found to be associated with alcohol abuse, homelessness, and previous incarceration. A 2006 study in Tomsk, Russia of MDR-TB patients also identified alcohol abuse as a key factor in poor treatment outcomes⁷.

DOTS and the Russian health care system: In 2007, Marx et al. published an ecological study examining the effects of DOTS implementation on the Russian public health system⁸. The measures used were hospital bed utilization and hospital admission of patients in control and DOTS regions from 2002. The study concluded that DOTS implementation did not lead to fundamental structural changes in the Russian health care system.

Multiregional Studies

Volmink and Garner: In 2006, Volmink and Garner published a Cochrane Database System Review⁹ which contradicted the 2003 Eastern European studies outlined above. The review examined studies from these databases comparing treatment outcomes of DOTS to self administered treatment (SAT) in patients requiring treatment for clinically active tuberculosis or prevention of active disease. The authors searched the Cochrane Infectious Diseases Group Specialized Register, CENTRAL, MEDLINE, EMBASE, LILACS, and other reference lists of articles for studies that met the following inclusion criteria: randomized and quasi-randomized trials comparing a health worker, family member, or community volunteer routinely observing people taking antituberculosis drugs compared with routine self administration. Ten trials, with

⁶ Bumburidi E, Ajeilat S, Dadu A, Aitmagambetova I, Ershova J, Fagan R, Favorov MO; Centers for Disease Control and Prevention (CDC). "Progress toward tuberculosis control and determinants of treatment outcomes--Kazakhstan, 2000-2002." *MMWR Morb Mortal Wkly Rep*. 2006 Apr 28;55 Suppl 1:11-5.

⁷ Shin SS, Pasechnikov AD, Gelmanova IY, Peremitin GG, Strelis AK, Mishustin S, Barnashov A, Karpeichik Y, Andreev YG, Golubchikova VT, Tonkel TP, Yanova GV, Nikiforov M, Yedilbayev A, Mukherjee JS, Furin JJ, Barry DJ, Farmer PE, Rich ML, Keshavjee S. "Treatment outcomes in an integrated civilian and prison MDR-TB treatment program in Russia." *Int J Tuberc Lung Dis*. 2006 Apr;10(4):402-8. Erratum in: *Int J Tuberc Lung Dis*. 2006 Oct;10(10):1183. Mishustin, S [added]; Barnashov, A [added]; Karpeichik, Y [added].

⁸ Marx FM, Atun RA, Jakubowiak W, McKee M, Coker RJ. "Reform of tuberculosis control and DOTS within Russian public health systems: an ecological study." *Eur J Public Health*. 2007 February; 17(1):98-103. Epub 2006 Jul 12.

⁹ Volmink J, Garner P. "Directly observed therapy for treating tuberculosis." *Cochrane Database Syst Rev* 2006 Apr 19; (2) : CD003343

a total of 3,986 participants, met the authors' criteria. The review found no statistically significant difference in patient cure rate or patient cure and completion rate between DOTS and SAT. The authors concluded that DOTS does not have a quantitatively important effect on cure or treatment completion rates.

DOTS vs. Self-Administered Treatment: Region Specific Studies

DOT and DOTS evaluation in Brazil and Ethiopia: A 2005 study in the southern region of Ethiopia¹⁰ indicated that the introduction of DOTS in 1996 and its subsequent expansion to reach a population coverage rate of 75% in 2001 led to an increase in treatment success and decrease in default and failure rates. Treatment success rates for smear-positive patients rose from 38% in 1994 to 78% in 2000, the default rate declined from 38% to 18%, and treatment failure declined from 5% to 1%. These results were echoed by a 2006 study in Rio de Janeiro. Soares et al. demonstrated that patients under DOT were more likely to convert to sputum negative than those under SAT, even when controlled for age, sex, and positive smear or culture upon enrollment.

DOTS and MDR-TB: A 2004 study from India of a standardized multi-drug resistant TB treatment program offered with DOTS to laboratory confirmed multi-drug resistant TB patients yielded mixed results, with a 69% cure rate. The authors noted that serious side effects were a major issue.

Public-Private Partnerships

Other interventions studied in a global context include a review of for-profit private health care provider's involvement in national TB control efforts. The 2006 review by Lonroth et al.¹¹ looked at 15 such initiatives, all but one 'drugs for performance' contracts which included free drugs from the government in exchange for a commitment to dispense the drugs free of charge. In this review, 90% of new smear-positive patients were successfully treated across all 15 initiatives, and case detection rates increased between 10-36%. The authors conclude that this involvement has been successful; however, they do not state any conclusions in relation to the scaling up of private involvement in national TB control efforts. This review follows a 2004 study¹² examining four public-private

¹⁰ Shargie EB, Lindtjorn B. "DOTS improves treatment outcomes and service coverage for tuberculosis in South Ethiopia: a retrospective trend analysis." *BMC Public Health*. 2005 Jun 6;5(1):62.

¹¹ Lonroth K, Uplekar M, Blanc L. "Hard gains through soft contracts: productive engagement of private providers in tuberculosis control." *Bull World Health Organ*. 2006 Nov;84(11):876-83.

¹² Lonroth K, Uplekar M, Arora VK, Juvekar S, Lan NT, Mwaniki D, Pathania V. "Public-private mix for DOTS implementation: what makes it work" *Bull World Health Organ*. 2004 Aug; 82(8):580-6. Epub 2004 Sep 13.

mix (PPM) TB control projects in India and the success factors of these projects. This 2004 study identifies four PPM success factors: orienting both the private providers and the national TB program (NTP) staff; improving the referral and information system; adequate monitoring and supervision of the private providers from the NTP; and free provision of drugs from the NTP to patients treated in the private sector.

In 2007, another study on a public-private partnership in Indonesia was published by Ardian et al¹³. The study found that treatment success rates for smear-positive patients in the province (Papua Province), served by the public-private partnership were similar to Indonesian national figures, in spite of the province's higher rates of TB-HIV co-infection, TB notification rate, and MDR-TB.

Incentives and Enablers in DOT and DOTS Programs

In 2006, DOTS incentive and enabler interventions were reviewed in a Rational Pharmaceutical Management Plus report by Mookherji and Beith¹⁴. The report reviews various incentive and enabler programs that have been implemented in conjunction with DOTS worldwide, and the evidence for their impact on success rates of DOTS programs. It notes that evidence on the impact of incentive and enabler programs is problematic; few of these programs have been evaluated, and when an evaluation is done, isolating the impact of the incentive/enabler aspect of the DOTS program is often difficult, if not impossible. Rather than identify any one enabler/incentive, it outlines some of the variables that need to be considered before implementing an incentive or enabler program alongside DOTS. It also offers a chart detailing incentive and enabler programs worldwide, and any quantitative evidence of their impact from evaluations or other studies. Other studies have focused on specific incentive and enabler interventions below.

Intervention package: A 2007 study from Senegal by Thiam et al.¹⁵ demonstrated the effectiveness of an intervention package which included improved patient counseling, patient choice of DOT supporter, decentralization of treatment and reinforcement of supervision activities. The intervention was studied from 2003-2005. Treatment success rates were 88% in the intervention group as compared with 76% in the control group. Default rates were also reduced from 16% in the control group to 5.5% in the intervention group.

¹³ Ardian M, Meokbun E, Siburian L, Malonda E, Waramori G, Penttinen P, Lempoy J, Kenangalem E, Tjitra E, Kelly PM. "A public-private partnership for TB control in Timika, Papua Province, Indonesia." *Int J Tuberc Lung Dis*. 2007 Oct; 11(10):1101-7.

¹⁴ Mookherji, Sangeeta and Beith, Alix. 2006. "Summary of Current Evidence: Using Incentives and Enablers for Improved DOTS performance." Management Sciences for Health for USAID.

¹⁵ Thiam S, LeFevre AM, Hane F, Ndiaye A, Ba F, Fielding KL, Ndir M, Lienhardt C. "Effectiveness of a strategy to improve adherence to tuberculosis treatment in a resource-poor setting: a cluster randomized controlled trial." *JAMA*. 2007 Jan 24; 297(4):380-6.

Consultants: A 2003 study in India¹⁶ indicated that the assignment of WHO consultants is a factor in the success of DOTS programs. Frieden and Khatri found that rates of sputum conversion were significantly higher in areas with consultants than in the control areas, and that DOTS was implemented faster in areas with consultants than in control areas.

Traditional healers: The use of traditional healers as DOTS supervisors were found to be a positive factor in patient satisfaction rates in a 2003 study from South Africa¹⁷, although patients supervised by traditional healers did not have a statistically significant higher completion rate.

Home visits: Another 2003 study from Baghdad, Iraq found that home visiting by trained personnel improved patient compliance under a DOTS system. The intervention group had a treatment success rate of 94.2% versus the control group rate of 76.7%, a default rate of 0.8% versus the control group rate of 10%, and a smear conversion rate of 92.9% versus 75% for the control group¹⁸.

Nutrition support: A 2002 evaluation of collaboration between the Cambodian National Tuberculosis Program and the World Food Program did not offer a quantitative analysis of the collaboration's effects on cure rate, however, it did offer a positive qualitative evaluation of the program, and offered lessons on possible applications to other DOTS programs.¹⁹

Psychological Counseling

A 2005 Chandigarh, India study by Janmeja et al.²⁰ examined the effects of psychological counseling on TB treatment compliance under an SAT system. The intervention consisted of a total of eight behavior modification psychotherapy sessions, planned to coincide with drug collection visits. Eighty-three percent of the intervention group completed treatment successfully, as compared with 48% in the control group.

¹⁶ Frieden TR, Khatri GR. "Impact of national consultants on successful expansion of effective tuberculosis control in India." *Int J Tuberc Lung Dis.* 2003 Sep;7 (9):837-41

¹⁷ Colvin M, Gumede L, Grimwade K, Maher D, Wilkinson D. "Contribution of traditional healers to a rural tuberculosis control programme in Hlabisa, South Africa." *Int J Tuberc Lung Dis.* 2003 Sep;7 (9 Suppl 1): S86-91

¹⁸ Mohan A, Nassir H, Niazi A. "Does routine home visiting improve the return rate and outcome of DOTS patients who delay treatment?" *East Mediterr Health J.* 2003 July; 9(4): 702-8.

¹⁹ Mookherji, Sangeeta and Diana Weil. 2005. "Food Support to Tuberculosis Patients under DOTS: A Case Study of the Collaboration between the World Food Program and the National TB Control Program in Cambodia," December 8-17, 2002. Management Sciences for Health for USAID.

²⁰ Janmeja AK, Das SK, Bhargava R, Chavan BS. "Psychotherapy improves compliance with tuberculosis treatment." *Respiration.* 2005 July-August; 72(4): 375-80

HIV Testing, Voluntary Counseling and Adjunctive Cotrimoxazole

A 2004 study by Chimzizi et al.²¹ evaluated voluntary counseling, HIV testing and adjunctive cotrimoxazole as an intervention to address the HIV/TB epidemic. The study found that this intervention led to better outcomes under the National TB Control Program; a 75% TB treatment success rate in the intervention group as compared with a 61% TB treatment success rate in the control group.

Qualitative Work and Evidence

In addition to the quantitative studies outlined above, there has been qualitative work examining factors influencing the success of TB control efforts.

Eastern Europe: A 2005 *Health Policy* article looked at the attitudes of key TB control stakeholders in the Russian Federation²². Interviewees in the study felt that there were cultural and capacity constraints to DOTS implementation. The authors identified three factors from the interviews: inadequate understanding of DOTS; perceived 'directiveness' of the externally developed strategy; and the standardized nature of the treatment regimes.

A 2003 qualitative study by Harper et al.²³ looked at factors which influence the outcomes of TB control programs in the Gambia. Factors identified include gender, urban/rural residence, knowledge about TB, migration, recourse to traditional healers, and socioeconomic factors. A 2006 review by Noyes and Popjay²⁴ synthesized the qualitative evidence in studies from 1990-2002 on factors affecting the success of DOTS programs. The authors of the study found five themes in the evidence:

- socio-economic circumstances;
- material resources and individual agency;
- explanatory models and knowledge systems in relation to TB and its treatment;
- the experience of stigma and public discourses around TB; and

²¹ Chimzizi R, Gausi F, Bwanali A, Mbalume D, Teck R, Gomani P, Zachariah R, Zuza W, Malombe R, Salaniponi FM, Harries AD. "Voluntary counselling, HIV testing and adjunctive cotrimoxazole are associated with improved TB treatment outcomes under routine conditions in Thyolo District, Malawi." *Int J Tuberc Lung Dis*. 2004 May; 8 (5): 579-85.

²² Rifat A. Atun, Juan Baeza, Francis Drobniowski, Vera Levicheva and Richard J. Coker. "Implementing WHO DOTS strategy in the Russian Federation: stakeholder attitudes." *Health Policy*, 2005 October; 74 (2): 122-132

²³ Harper M, Ahmadu FA, Ogdan JA, McAdam KP, Lienhardt C. "Identifying the determinants of tuberculosis control in resource-poor countries: insights from a qualitative study in The Gambia." *Trans R Soc Trop Med Hyg*. 2003 September-October; 97(5): 506-10

²⁴ Noyes, J.; Popjay, J. "Directly observed therapy and tuberculosis: how can a systematic review of qualitative research contribute to improving services? A qualitative meta-synthesis." *J. Adv. Nurs*. 2007 February; 57 (3): 227-43.

- sanctions, incentives and support, and the social organization and social relationships of care.

In 2003, a qualitative review article by Macq et al. looked at the evolving concept of DOTS programs. Using examples from the international literature, key informant interviews, and statements from participants in a DOTS course, the authors attempted to go beyond the simple dichotomy of SAT versus DOTS. The article examines three key questions: 1) how did DOT work as part of a larger, context specific set of interventions; 2) what were incentives and enablers in DOT programs; and 3) the role of DOT supporter and providers²⁵.

²⁵ Macq JC, Theobald S, Dick J, Dembele M. "An exploration of the concept of directly observed treatment (DOT) for tuberculosis patients: from a uniform to a customized approach." *Int. J Tuberc Lung Dis.* 2003 February; 7(2): 103-9.

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