

# Direct observation of tuberculosis treatment did not promote higher cure rates than did self-administered treatment

Walley JD, Khan MA, Newell JN, Khan MH. Effectiveness of the direct observation component of DOTS for tuberculosis: a randomised controlled trial in Pakistan. *Lancet*. 2001 Mar 3;357:664-9.

## QUESTION

In Pakistani patients with tuberculosis, what is the effectiveness of the Directly Observed Treatment, Short-course (DOTS) strategy by a health worker or family member?

## DESIGN

8-month randomized {allocation concealed\*}†, blinded (clinicians and outcome assessors),\* controlled trial.

## SETTING

3 tuberculosis treatment centers in Pakistan.

## PATIENTS

497 patients who were  $\geq 15$  years of age (42% were 15 to 24 y, 22% were 25 to 34 y; 51% men) and were newly diagnosed with sputum-positive pulmonary tuberculosis, had not previously received tuberculosis treatment, and lived in the catchment area. Follow-up was complete.

## INTERVENTION

Patients were allocated to 1 of 3 treatments: self-administered treatment, in which patients received tuberculosis drugs every 2 weeks from the closest health facility ( $n = 162$ ); health-worker DOTS, involving a 2-month intensive phase during which a health worker supervised the treatment and a 6-month continuation phase during which patients received self-administered treatment

( $n = 170$ ); or family-member DOTS, involving supervision of the drug therapy by a chosen family member ( $n = 165$ ). All patients received 2 months of isoniazid, rifampicin, pyrazinamide, and ethambutol and 6 months of isoniazid and ethambutol.

## MAIN OUTCOME MEASURES

Cure rate (sputum-negative test result at 7 or 8 mo and on  $\geq 1$  previous occasion) and treatment completion rates.

## MAIN RESULTS

Analysis was by intention to treat. The study had 90% power to detect a 20% difference in cure rates between groups. The cure rates for the self-administered treatment group did not differ from the health worker-observed group ( $P = 0.73$ ) or from the family member-observed group ( $P = 0.23$ ) (Table). No differences existed for the combination

of cure and treatment completion rates ( $P = 0.75$  and  $P = 0.65$ , respectively). More women than men were cured (71% vs 50%,  $P < 0.001$ ).

## CONCLUSIONS

In Pakistani patients with tuberculosis, no differences in cure or cure and completion rates were seen among 3 tuberculosis treatment approaches. Directly observed treatment by health workers or family members was not more effective than self-administered treatment.

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\*See Glossary.

†Information provided by author.

## Self-administered treatment vs Directly Observed Treatment, Short-course (DOTS) by health worker or family member for tuberculosis at 8 months‡

Outcomes	Self-administered	DOTS health worker	DOTS family member	RBI (95% CI)	NNT
Cure rate	62%	64%	—	2.9% (−8.6 to 12)	Not significant
				RBR (CI)	NNH
	62%	—	55%	10.7% (−26 to 7.3)	Not significant

‡RBR = relative benefit reduction. Other abbreviations defined in Glossary; RBI, RBR, NNT, NNH, and CI calculated from data in article.

## COMMENTARY

By declaring tuberculosis a global emergency in 1993, the World Health Organization (WHO) helped focus attention on the disease and championed the aggressive introduction of the DOTS strategy, which has been hailed as the breakthrough of the century in the fight against tuberculosis. It involves increased commitment by central and state governments, effective diagnosis based on sputum microscopy, standard short-course treatment given under direct observation, a secure drug supply, and systematic monitoring and evaluation (1).

After successes in Tanzania in 1977, when cure rates rose from 43% in 1983 to 90% in 1990, the DOTS strategy was used in several other countries, which resulted in high cure rates. A systematic review done by the South African Cochrane Centre (2) found that the success of DOTS programs might be the result of several components beyond the 5 elements of the WHO's DOTS program, such as the use of education and motivation programs, incentives, home visits, legal sanctions, and additional external funds.

The study by Walley and colleagues seems to confirm that a focus on direct observation as a key factor may be inappropriate. As sug-

gested by the study, dose supervision may be made more user friendly. As it stands, a patient must make 40 visits during 6 months, sometimes traveling up to 5 kilometers a day. The sustainability of such a system is questionable.

Several factors might account for the success of the DOTS programs. It is clear, however, that developing countries cannot sustain the level of resources required for tuberculosis control without support from external agencies. It is important to evaluate the effect of DOTS programs before rates of multidrug-resistant tuberculosis rise to such levels that evaluation is impossible. Subsidizing tuberculosis treatment in developing countries should be a long-term commitment.

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