

Promoting adherence to treatment for tuberculosis: the importance of direct observation

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Since 1993, WHO has recommended a strategy through which national governments can meet their responsibility to treat patients and to prevent the spread of tuberculosis (TB). Four of the major elements of the strategy, which came to be known as DOTS, were political commitment by governments, improved laboratory services, a continuous supply of good-quality drugs, and a reporting system to document the progress (and failure) of treatment for individual patients and of the programme. The fifth element, effective case management via direct observation of treatment by an independent and trained third party, was a response to decades of reports documenting the failure of patients to complete treatment. Put simply: direct observation of treatment is an integral and essential component of DOTS.

WHO has reported that more than 30 million patients with TB have been treated with its five-element DOTS strategy, resulting in cure rates of > 80% and default rates of < 10%.¹ WHO's recently announced Global Plan to Stop TB highlights the need to expand DOTS through "standardized treatment, under proper case management conditions, including directly observed treatment to reduce the risk of acquiring drug resistance, and support of patients to increase adherence to treatment and chance of cure".²

However, the value of the direct observation component of DOTS has been questioned in a recent systematic review, in which it was suggested that direct observation of treatment is unnecessary and disrespectful of patients.³ Both self-administered treatment and treatment observation by a family member have been proposed as acceptable alternatives. We challenge the validity of these assertions.

What is the validity of trials reported to support self-administration of treatment?

The random controlled trial is the gold standard to identify the effect of a single variable on patient treatment. To our knowledge, only three such trials have compared self-administered (i.e. unobserved) dosing with direct observation provided by someone outside the family.⁴⁻⁶ All three trials reported low rates of treatment success in both arms of the study, suggesting that direct observation was not implemented effectively. The reported cure rates of only 38%, 41% and 64% in the patients receiving directly-observed therapy⁴⁻⁶ are far below the relapse-free cure rates of 90-95% consistently reported by other random controlled trials. However, these three trials do confirm that direct observation of treatment can, as with any health initiative relying on human effort, be implemented ineffectively.

To our knowledge, post-treatment relapse rates have not been analysed in any study used to support the elimination of direct observation. In public health practice, failure to ensure treatment observation has been associated with a significantly increased risk of relapse,⁷ often compounded by the emergence of drug resistance; treatment observation has been shown to reduce both relapse and drug resistance.⁸⁻¹¹ In short-term studies reporting no difference in cure rates with or without direct observation of treatment, it is possible that significant numbers of post-treatment relapses and the development and spread of drug-resistant strains are not apparent. If direct observation is to be replaced with administration of treatment by the patient or by the family, the potential community impact of patient non-adherence must be considered.

Direct observation of treatment is only one part of the comprehensive case management of each patient with TB. Rigorous monitoring of all patients who have started treatment and a rapid response to ensure that patients who interrupt their treatment are returned to care are also essential components of effective case management and community-wide TB control.

Because these activities cannot be accomplished effectively in a setting of treatment by self-administration, the full spectrum of TB control services, including direct observation of treatment, must be provided and monitored if public health authorities are to meet their basic and primary responsibility to protect the public by ensuring patient cure.

Family observation is a seductive but risky concept

The suggestion that treatment observation can be performed routinely by family members is a dangerous challenge to WHO's successful TB control strategy. It is a "feel good" idea that can give government leaders and programme managers a false sense of assurance that a greater percentage of patients are being treated successfully under family observation than would have been successfully treated by self-administration. After all, who cares more about sick patients than their immediate relatives? Is not family observation more patient-friendly? It is true that some small pilot projects (none of which have monitored relapse or development of drug resistance) using family observation, combined with intensive supervision and home visits, have achieved high cure rates.¹²⁻¹⁴ However, other studies have reported that family observation yields lower cure rates and much higher default rates than observation by someone outside the family,¹⁵ and results in a substantial proportion of treatment being unobserved and much higher rates of non-adherence.¹⁶

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In practice, where family observation is allowed, patients are often merely handed medicines and told to have their spouse watch them take the pills, a practice that is inconsistent with WHO guidelines specifying that treatment observers be trained and supervised by the health-care system. In cultures with strong matriarchal or patriarchal structures, it is not realistic to believe that any member of the family can insist on any behaviour by the dominant family head.

In our experience, people outside the family structure, who are subject to greater supervision by TB control programmes, are more likely to report valid information to programme managers and take appropriate action when patients decline or forget treatment. Family members may not understand the need to ensure treatment; despite the best educational efforts of health-care staff, there may be limited understanding of, or confidence in, the efficacy of prescribed medicines. And if adherence to treatment creates tension in the family, the simplest way to eliminate the source of that tension is to discontinue treatment observation.

Trials that have investigated the effect of treatment observation by family members are small, non-blinded, usually with enhanced supervision and monitoring, confounded by limited patient selection, have not evaluated relapse or drug resistance and are of questionable generalizability. A recent report from Senegal¹⁷ is an example of this. This well-controlled study reported a 12% higher cure rate among patients allowed to select their own “direct-observation-of-treatment supporter”, but also featured intensive and sustained professional supervision and training and monitoring of the supporter at every level of the study. Such programme conditions are difficult to duplicate and sustain on a large scale, and the study did not evaluate drug resistance or relapse.

Is there a place for family observation?

In the Senegal study,¹⁷ direct observation of treatment was delivered by a person selected by the patient. Self-administration was not an option. Patients who selected a family member as their “direct-observation-of-treatment supporter” experienced greater cure rates and less default than those selecting district

health nurses or community health workers. This study, more comprehensive than its predecessors, suggests that family members can potentially be effective treatment observers – but only within the restrictions imposed by the study design, which required close monitoring of all aspects of the treatment delivery system.

Treatment observation must be performed by a person who is accessible and acceptable to the patient, but who is also accountable to the health system. In the Senegal study, the family member was clearly accountable to the system. Public health personnel were responsible for closely monitoring treatment, identifying and responding to patients thought to be in danger of defaulting, and for finding patients who had abandoned treatment. If family members can be transformed into reliable members of the health-care team through careful programme design combined with intensive supervision and monitoring (including accurate, honest and ongoing cohort analysis measuring real outcomes), then any system of treatment observation, including by family members, might be able to achieve acceptable results. However, the lack of monitoring of relapse and drug resistance in published studies of family observation makes this a theoretical rather than an evidence-based possibility.

We have reviewed several large programmes, one published,¹⁶ in which small pilot projects achieved acceptable results with family observation, after which a policy decision was made to implement DOTS using family observation on a large scale. In all these situations, cure rates achieved were well below 60%, and after several years the policy was revised to require direct observation by someone outside the family.

Each culture, each society and each community is unique. Each has particular strengths, and the challenge in implementing direct observation of treatment is to identify and enlist the support of these strengths. About one-third of patients do not take medications regularly as prescribed, and it is not possible to predict accurately which patients will not adhere to treatment.¹⁸ Non-adherence is not related to socioeconomic status, educational level, sex, race, severity of illness, dosage or adverse effects, and is as high with placebo as with active drugs. To address this consistent non-adherence, direct observation of treatment has been given by various members of

the community, including health staff, community workers or volunteers, members of nongovernmental organizations and religious leaders. There is no “best” treatment observer, but for each patient, there is an observer, who must be accountable to the health system, who is the best choice. Self-administration should never be an option.

Direct observation of treatment involves far more than “supervised swallowing” and works best when it builds a human bond between the patient and the treatment observer that acknowledges the value of successful treatment for the patient and for his or her community. It also confirms the responsibility of the programme and the community to ensure successful treatment through respect for the patient by providing treatment at convenient times and in appropriate facilities. Before WHO endorses the inclusion of family members as treatment observers, it must ensure that the programme setting will provide the required system support and close supervision, and will not increase rates of relapse and the acquisition of drug resistance. No large-scale programme without direct observation of treatment has achieved global targets, while most programmes using direct observation of treatment achieve or nearly achieve these targets.

Direct observation is a necessary element of DOTS

Because direct observation requires strong leadership and a lengthy commitment of human resources, it is not yet universally employed. However, the ultimate ethical and legal responsibility for ensuring treatment completion and cure of a communicable disease belongs to the public health system and the community, and not to the individual patient. TB can be controlled when appropriate policies are implemented and continued, even in the absence of an outbreak or media attention. Just as patients may be tempted to change or stop an effective treatment regimen because of the long duration of treatment, public health policy-makers may be tempted to alter key elements of DOTS because of the persistence required to maintain effective programmes.

The stakes in this debate are high. On the basis of three small trials of questionable validity and generalizability, all of which failed to implement direct

observation of treatment effectively, and none of which conducted treatment observation that met minimum international standards, critics of direct observation of treatment are calling to make it an optional rather than a required component of DOTS. In the name of "evidence-based" practice, WHO is being urged to disregard the evidence from 40 years of research on TB control and the data collected from more than 30 million patients treated. In the name of being more patient-friendly, TB programme decision-makers should not be lured into discontinuing direct observation, thereby increasing the number of patients who fail treatment, default, relapse, develop and spread drug resistance, and die.

The key challenge of direct observation of treatment is to implement it well, maximizing convenience of and respectful interaction with patients. Direct observation is necessary both to fulfil society's obligations to care for individual patients effectively, and to protect the rest of society by preventing the development and spread of TB, including drug-resistant strains. Perhaps what is most important is to ensure that the approach is patient-centred, with rigorous monitoring of and accountability for ensuring cure, and rapid intervention to increase cure rates if they are less than 85%. We believe that evidence and experience show that the only way to achieve these high cure rates on a programme

basis is through direct observation of treatment given by a person accountable to the health system and accessible to the patient. The primary responsibility of a TB control programme to patients and to the community is to ensure cure while preventing drug resistance. Direct observation of treatment is the only current documented means to meet this commitment. ■

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