Impact of directly observed treatment on tuberculosis

Description of the condition

Multidrug-resistant tuberculosis (MDR TB) is defined as Mycobacterium tuberculosis strains with in vitro resistance to at least both isoniazid (INH) and rifampicin (RFP) (Johnston 2009 ; WHO ; WHO 2013). Emergence of this strain since the 1980s has represented a major barrier towards successful TB control (Johnston 2009 ; WHO 2013). Among the newly diagnosed TB patients in 2012, 3. 6% had MDR TB while the percentage was approximately six times higher among those previously treated cases (20. 2%) (WHO 2013). In 2012, it was estimated that 450000 incident cases and 170000 mortality cases of MDR TB occurred globally (WHO 2013). Compared with drug-susceptible strains, treatment of MDR TB is much more complex. According to the WHO guidelines, MDR TB treatment regimen requires a minimum duration of 18 months with two treatment phases, the intensive and the continuation phase (WHO). The first six months of treatment is usually considered the intensive phase since a patient needs to receive both oral and injectable drugs (WHO). After this period, the injectable agent is discontinued and patients receive the oral drugs for another 12-18 months (termed as the continuation phase) (WHO). Management of MDR TB is challenging for that patients are normally in advanced stages of disease with thick-walled cavities and chronic lung lesions which are hard for the drugs to penetrate (Orenstein 2009). Also, the longer treatment duration, high out-of-pocket cost, together with the more frequent adverse reactions that are associated with second line drugs are all contribution factors to poor treatment adherence (Bassili 2013 ; Toczek 2012 ; Volmink 2007). As a result, treatment success rate of MDR TB was much lower compared to drug

sensitive strains. According to the WHO, the pooled treatment success rate of MDR TB patients diagnosed in 2009 was about 48%, whereas it exceeded 85% among non-MDR TB patients (Johnston 2009).

Description of the intervention

Directly observed treatment (DOT) refers to the use of an appointed agent (a professional health worker, a community volunteer, or a family member) to directly monitor people taking their anti-tuberculosis drugs (Mukherjee 2004). Initially, this concept was proposed as a key component of Directly Observed Therapy, Short Course (DOTS) by the WHO in 1994 to ensure cure of TB (WHO). In addition to the provision of standardized 6-8 months short-course directly observed chemotherapy regimen, other components of DOTS include: political commitment, case detection through quality-assured bacteriology, maintenance of an effective drug supply and management system, and evaluation of performance and impact (WHO). Implementation of DOTS in non-MDR TB treatment demonstrates significant effectiveness, as the strategy has helped to treat 37 million TB cases and cured more than 80% of them by 2007(WHO 2013). However, the standardized short-course chemotherapy is usually not applicable to cases of MDR TB.

To improve patients' adherence to MDR TB treatment, in 2000, WHO and its international partners further developed DOTS-Plus strategy by adding the components of MDR-TB diagnosis, treatment and management into the DOTS (WHO 2008 ; WHO 2011). In this DOTS-Plus strategy, DOT is highly recommended by the WHO to be delivered to all MDR-TB patients (WHO 2008 ; WHO 2011). However, treatment of MDR-TB patients requires at least

18 months, therefore, delievering DOT to MDR-TB patients would be more challenge than for drug-suspectible TB patients. There are two types of DOT according to its implementation length. In full DOT, anti-TB drugs were administered under direct observation throughout the treatment duration (including both the intensive and continuation phase) whereas it is directly observed only during the intensive phase for partial DOT (WHO 2008 ; WHO 2011). Effectiveness of DOT is commonly demonstrated through comparison with SAT, a traditional management modality in which anti-TB drugs were self-administered by patients without any observation (WHO 2008 ; WHO 2011). Currently, many countries have incorporated full DOT into their national TB control programs (NTPs) according to suggestions from the WHO guidelines (Bassili 2013). However, there are still countries that adopt partial DOT or even self-administrated treatment (SAT) as the management modality in their NTPs.

How the intervention might work

A better understanding of how DOT improves treatment outcomes of MDR TB could have important management implications. First, knowing the type(s) of DOT provider and location that is associated with a higher treatment success rate could allow one to make evidence-based decisions when designing DOT for MDR TB treatment. Second, studying the influence of other characteristics on successful treatment outcomes of MDR TB could provide a conservative yet more objective conclusion of the effectiveness of DOT. Third, comparing DOT with other strategies for the improvement of treatment adherence could advise policy makers to balance resources

between DOT and these other strategies so that treatment could be delivered in a more cost-effective way.

Why it is important to do this review

Impact of DOT on successful TB treatment has been controversial throughout the years. Previous observational studies suggested that DOT ensured timely adherence management as well as day-to-day monitoring of adverse effects (Orenstein 2009). One meta-analysis revealed that treatment completion rate among pulmonary TB patients could exceed 90% when DOT was implemented throughout the treatment course(Bassili 2013). However, results from a recent meta-analysis of randomized controlled trials showed no significant difference in treatment success rate between DOT and SAT among drug-susceptible TB cases(Mukherjee 2004). Moreover, previous meta-analyses almost exclusively focused on the role of DOT in the treatment of non-MDR TB; little has been examined systematically regarding its role in effective MDR TB treatment.