

# Evaluation of the Directly Observed Treatment's Acceptance by Tuberculosis Patients in the Republic of Macedonia

Biljana Ilievska-Poposka\*, Maja Zakoska, Vladimir Mitreski

*Institute for Lung Diseases and Tuberculosis, Skopje, Republic of Macedonia*

## Abstract

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\***Correspondence:** Biljana Ilievska-Poposka. Institute for Lung Diseases and Tuberculosis, Skopje, Republic of Macedonia. E-mail: [biljana.ilievska@yahoo.com](mailto:biljana.ilievska@yahoo.com)

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**BACKGROUND:** Directly observed therapy (DOT) is a specific strategy endorsed by the World Health Organization in 1994 to improve adherence by requiring health workers, community volunteers or family members to observe and record tuberculosis (TB) patients for taking each dose. The implementation of DOT strategy in the National Tuberculosis Programme (NTP) in Macedonia was introduced in 2006 and was realised by 6 nurses engaged through the Project of Global Fund against HIV/AIDS and TB.

**AIM:** This study aimed to evaluate how these visits conducted by the DOT nurses engaged through the GF were accepted by TB patients and to evaluate the impact on the treatment outcomes.

**PATIENTS AND METHODS:** In this prospective study 105 TB patients who started treatment in 2016 and who were supposed to be visited by DOT nurses at their homes were included. All of these patients filled out a questionnaire compiled of 6 questions related to their opinion about the efficacy and usefulness of the visits managed by the nurses when they would come for check-ups at the Institute for Lung Diseases and Tuberculosis. The assessment of the efficacy of the work of DOT nurses was performed by analysis of the answers received by TB patients. The data were analysed with the method of description and was statistically prepared in the program SPSS for Windows, 17.0.

**RESULTS:** The results from the analyses showed that the number of visited patients were not satisfied, because 29.52% were never visited by a DOT nurse at their homes. A lot of patients (61.91%) were not willing to take medicines under the observed control by nurses. Those TB patients who were visited by DOT nurses thought that this type of visit is useful for them: they were satisfied by the attitude of the nurses during the visits, and they received enough explanations regarding TB.

**CONCLUSION:** We can conclude that the DOT visits to TB patients are useful, contribute patients to complete the therapeutic regime without interruption, take care for every individual patient effectively, and protect the rest of society by preventing the development and spread of TB, including drug-resistant strains.

## Introduction

Despite the widespread availability of cheap, effective treatment, tuberculosis (TB) remains a major cause of severe illness and death, with an estimated nine million new cases and two million deaths occurring annually [1]. One barrier to global TB control is the long duration of TB treatment- a minimum of six months- which frequently results in patients taking their medications erratically or not at all [2]. Interruption of the treatment can lead to relapse and even death in individuals, and also has important public health consequences, such as increased TB transmission and development of drug resistance [3]. Directly observing TB patients taking their anti-TB

therapy, either daily or several times per week, was first piloted in the 1950s as a way to ensure adherence and treatment completion [2] In 1994, based on the reported success of directly observed therapy (DOT) in increasing treatment completion rates and preventing drug resistance, the World Health Organization (WHO) adopted DOT as a principal component of its global TB control strategy named as DOTS - Directly Observed Treatment Short-course strategy [4].

DOT is a specific strategy endorsed to improve adherence by requiring health workers, community volunteers or family members to observe and record patients taking each dose. Cure rates in DOTS programs have been reported to be as high as

95%, and the World Bank considers the DOTS strategy to be one of today's most cost-efficient health interventions [5].

Although WHO and other international agencies strongly advocate DOT, controversy remains whether its benefits have been proven. Randomized controlled trials (RCT) have shown either modest or no benefit of DOT in improving TB treatment success rates, and a meta-analysis of 10 RCTs concluded that the evidence base for WHO's DOT policy is insufficient. A recent Cochrane review reports no benefit from DOT on adherence and cure rates when compared with self-administered treatment (SAT) regimens [6]. The effectiveness of DOT, it has been argued, should be judged by how well it prevents drug resistance, specifically to rifampicin, and not by improvements in treatment success rates [7].

The implementation of DOT strategy in Macedonia started in 2004, but all principles and activities in the National Tuberculosis Programme (NTP) were introduced in 2006. In the period from 2006-2016 when the Project of Global Fund against HIV/AIDS and TB (GF) was presented in Macedonia with significant financial support to our NTP, DOT activities were realised in a big proportion from 6 nurses engaged through the GF. A small part of DOT activities was controlled by the nurses from public health institutions. The role of the DOT nurses was to visit TB patients at their homes especially during the continuous phase of treatment regime few times per week with the aim to observe the intake of medicines, to educate TB patients about diseases and to provide social or some other kind of support where it was needed. DOT nurses from the GF covered TB patients from the four biggest cities in the country.

The objective of this study was to evaluate how these visits conducted by DOT nurses engaged through the GF were accepted by TB patients and to evaluate the impact over treatment outcomes.

## Patients and Methods

In this prospective study, 105 patients were included who were considered to be eligible due to confirmed TB disease and who started treatment in 2016. Out of the total number of TB patients who were supposed to be visited by DOT nurses at their homes, this group of 105 TB patients was randomly selected. The general information regarding TB patients was provided from the evidence of DOT nurses engaged through the GF. The data regarding the disease of the patients like treatment outcomes were obtained from the electronic base of the Central Register for TB patients from the Institute for Lung Diseases and Tuberculosis.

All of these patients received a questionnaire

comprised of 6 questions prepared by the doctors from the Institute for Lung Diseases and Tuberculosis. The questions were related to the opinion of TB patients for the satisfaction and usefulness of the visits managed by the nurses.

The patients filled out the questionnaires when they would come for check-ups at the Institute for Lung Diseases and Tuberculosis. This activity was conducted and controlled by 3 nurses from the Institute, who was not part of the DOT activity organised by the GF. So we conducted the assessment of the nurses' engagement in DOT through the questionnaire filled out by TB patients.

### Statistical analyses

The data were analysed with the method of description and was statistically prepared in the program SPSS for Windows, 17.0.

## Results

In the next text, we present the analyses of the patient's answers to all 6 questions from the questionnaire separately:

### Question No1. How many times per month were you visited by DOT nurses?

According to the results, one third 31(29.52%) was never visited by DOT nurses. 74 patients (70.47%) were visited during their TB treatment: 32 (30.48%) were visited less than 3 times per month, the same were visited between 3 and 9 times, and 10 patients were visited more than 10 times per month (9.52%) (Table 1).

Table 1: Number of DOT visits per month to TB patients

How many times per month were you visited by DOT nurses?	n (%)
Never	31 (29.52)
<3 times	32 (30.48)
3 – 9 times	32 (30.48)
>10 times	10 (9.52)
Total	105 (100.0)

### Question No 2. What was the attitude like of the DOT nurses towards you during the visits?

Nearly all TB patients (73-69.52 %) who were visited by a DOT nurse answered that the DOT nurse had a good positive attitude towards them. Only one patient was dissatisfied from the nurse's attitude (Table 2).

**Table 2: The attitude of DOT nurses towards TB patients during the visits**

What was the attitude like of the DOT nurses towards you during the visits?	n (%)
Not visited	31 (29.52)
Good	73 (69.52)
Bad	1 (0.95)
Total	105 (100.0)

### **Question No 3. Do you find the DOT nurses' visits useful for you?**

Regarding the usefulness of DOT nurses' visits except for 2 patients, the others thought that that kind of visits was very useful for them and their disease (Table 3).

**Table 3: Assessment of the usefulness of DOT nurses' visits**

Do you find the DOT nurses' visits useful for you?	n (%)
Not visited	31 (29.52)
Yes	72 (68.57)
No	2 (1.9)
Total	105 (100.0)

### **Question No 4. Were you satisfied with the DOT nurses' answers to your questions regarding your disease?**

As for the question about the TB patients' satisfaction and the answers received by DOT nurses, 73(69.52%) answered positively with "yes (Table 4). Only 1 patient was dissatisfied with the answer to the questions regarding the disease.

**Table 4: Satisfaction of TB patients to the answers regarding their disease received by a DOT nurse**

Were you satisfied with the DOT nurses' answers to your questions regarding your disease?	n (%)
Not visited	31 (29.52)
Yes	73 (69.52)
No	1 (0.95)
Total	105 (100.0)

### **Question No 5: Did you take the medicines under the nurses' control?**

The results showed that most of the visited patients (65 - 61.91%) did not take the medicines under the nurses' control. It was odd that only 9 patients (8.57%) took medicines during the visits of DOT nurses (Table 5).

**Table 5: Were the TB patients observed when they took the medicines?**

Did you take the medicines under the nurses' control?	n (%)
Not visited	31 (29.52)
Yes	9 (8.57)
No	65 (61.91)
Total	105 (100.0)

### **Question 6: Treatment outcomes of TB patients**

At the time when we finished this study, all of the TB patients who started treatment in 2016 and were included in the study, did not finish their therapeutic regime. So, the treatment outcomes of these 105 TB patients were: 36 or 34.29% still on treatment,

treatment completed 64 or 60.95% and those who died 5 or 4.76% (Table 6). If we exclude those 36 TB patients who were still on treatment, the number of patients that remained for assessment regarding the known treatment outcomes was 69.

**Table 6: Treatment outcomes of TB patients**

Treatment outcomes	n (%)
Treatment completed	64 (60.95)
Died	5 (4.76)
Still on treatment	36 (34.29)
Total	105 (100.0)

We performed statistical analyses by applying the Fisher exact test to see if there is a correlation between the number of visits to the patient's home by the DOT nurses and the treatment outcomes. The results showed that there were statistically significant differences between the number of visits and treatment outcomes ( $p < 0.008$ ). Most of TB patients who completed the treatment (24-37.5%) were visited 3-9 times per month, followed by the group of 21 patients (32.81%) that were visited less than 3 times per month. We have to note that among patients never visited at their homes; there were 12 (18.75%) who completed treatment. In regard to the patients who have died, we have information from the medical documentation that those were older patients with comorbidities: these types of patients should be visited more times at their homes, not less than 3 according to the results.

What is characteristic among the active TB patients who are still in treatment, half of them (50%) have not been visited by DOT nurses not even once.

**Table 7: Correlation between the number of visits by the DOT nurses and treatment outcomes**

The number of visits by the DOT	Treatment outcomes		
	Completed	Died	Still on treatment
Never	12 (18.75)	1 (20)	18 (50)
<3 times	21 (32.81)	4 (80)	7 (19.44)
3 - 9 times	24 (37.5)	0	8 (22.22)
>10 times	7 (10.94)	0	3 (8.33)

Fisher exact  $p < 0.008$

## **Discussion**

TB incidence in the Republic of Macedonia has declined during the last ten years and from 27.8/100 000 inhabitants in 2007, dropped to 12.9/100 000 inhabitants in 2016 (absolute number of 267 new TB cases in 2016). In this period the treatment success rate was between 86.3% and 91.3% of all registered cases. Regarding multidrug-resistance TB (MDR-TB), there are only 2-4 new cases per year (2 cases in 2016).

These positive results are due to all activities performed through our NTP in which DOT presents an important portion (part). DOT is designed to promote

proper adherence to the full course of drug therapy to improve patient outcomes and prevent the development of drug resistance.

The results from the analyses showed that the number of visited patients was not satisfactory, because 29.52% were never visited by a DOT nurse at their home at all. The explanation for the reason why DOT nurses did not visit these TB patients was that some of these patients had support from other family member or some patients refused to be visited without reason or because of stigma. It is correct that DOT nurses should assess that of the patients should be visited less than it was recommended, especially in the case when the patients are aware and educated about their disease well enough. We know that stigma in our country is a big problem among TB patients and sometimes can be a barrier for diagnosing TB in time, starting with treatment and curing the disease.

But in those TB patients who were visited by DOT nurses, nearly all cases thought that this type of visit is useful for them: they are satisfied by the attitude of the nurses during the visits, and they received enough explanations regarding TB.

A lot of patients (61.91%) were not willing to take medicines under the observed control by nurses. Only 8.57% of patients answered that they accepted to take medicine when the nurses had visited their homes.

Regarding the treatment outcomes, we found statistically significant differences between the number of visits and treatment outcomes: nearly half of the patients who completed treatment (48.44%) were visited more than 3 times per month. TB patients who died during the treatment were visited less than 3 times per month because the time of death had happened at the beginning of the treatment regime. However, the analyses showed that there was good compliance by the patients, good adherence to the treatment, good cooperation between patients and nurses which led to the completion of the treatment and cure without any patients who interrupted the treatment. Also, to improve patients' adherence to the treatment, packages with food and hygiene products were provided as an incentive by the GF in the RM. In this study, we did not conduct the analysis how DOT strategy influenced to the country economic burden.

The rates of success of different DOT programs reported in the literature shows great variability.

Six trials from South Africa, Thailand, Taiwan, Pakistan and Australia compared DOT with self-administered therapy for treatment. Trials included DOT at home by family members, community health workers (who were usually supervised); DOT at home by health staff; and DOT at health facilities. TB cure was low with self-administration across all studies (range 41% to 67%), and direct observation did not substantially improve this (RR 1.08, 95% CI 0.91 to

1.27; five trials, 1645 participants). Treatment completion showed a similar pattern, ranging from 59% to 78% in the self-treatment groups, and direct observation did not improve this (RR 1.07, 95% CI 0.96 to 1.19; six trials, 1839 participants [8].

A meta-analysis on the efficacy of DOT, which included 32 studies, reported that only 11 of those were prospective, and of these only two were randomised clinical trials. The majority of the TB programs included in that meta-analysis incorporated other components besides the five key elements of the WHO-recommended DOTS strategy, with great heterogeneity within programs [9]. These other components included incentives, facilitators, follow-up of defaulters, legal sanctions, and patient centred-care and health personnel motivation programs [10]. The potential confounding effect of such co-interventions was evident. In general, DOT completion rates are significantly higher for those receiving DOT plus an incentive than for those receiving DOT without incentives [11]. To focus exclusively on supervised swallowing of the pills must be considered as an extremely simplistic approach to a very complex problem. Patient adherence is multifaceted and is affected by several factors that range from the individual's characteristics to the qualities of the social environment [12]. To attain acceptable rates of treatment adherence might require additional social services and economic incentives [9] [13].

The DOTS strategy imposes an additional economic burden on the health system of a country, and also on the patients treated under this regimen due to the need for the system to provide the necessary infrastructure and personnel for the supervision of treatment and the time and costs involved in the requirement for the patient to travel to the health center every day or three times a week. Moreover, the DOT component can potentially intensify the stigma associated with TB and diminish a patient's ability to maintain privacy about their health [14].

Although some TB treatment programs have health workers who conduct DOT in patients' homes rather than health facilities, no official numbers exist on how many programs administer TB treatment through this method [15].

Nonetheless, between 1995 and 2012, an estimated 56 million individuals were successfully treated for tuberculosis under the DOTS/Stop TB strategy in 184 countries [15]. Worldwide, approximately 86% of TB patients complete treatment; however, treatment success and cure rates vary widely by geographic region and per capita income [16]. DOT is only one part of the comprehensive case management of each patient with TB. Rigorous monitoring of all patients who have started treatment and 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.

On the basis of the results from our study we can conclude that DOT visits to TB patients are useful, contribute patients to complete therapeutic regime without interruption, take care for every individual patient effectively, and protect the rest of society by preventing the development and spread of TB, including drug-resistant strains. NTP in Macedonia and public health policy-makers should find the best way how to strengthen and continue with DOT in the future and assess which are the most important ingredients for success in our particular program. The prime responsibility of a TB control programme for patients and the community is to ensure cure while preventing drug resistance. DOT is the only current documented means to meet this commitment.

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