

# eDOTS: a new system applied for improving the treatment of pulmonary tuberculosis patients from Kashgar villages and Urumqi streets in Xinjiang, China

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## Research article

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# Abstract

**Background:** Although the direct observed treatment strategy (DOTS) has been used for the control of pulmonary tuberculosis (PTB) in Xinjiang Uygur Autonomous Region for more than 30 years, the disease is still highly endemic in the region. To increase PTB treatment ability and control efficacy, we developed a new electronic DOTS (eDOTS) system for reminding, monitoring and educating PTB patients taking antibiotics.

**Methods:** A total 167 cases with active PTB from Kashgar villages and Urumqi streets in Xinjiang were involved in the study referring to the criteria published by the National Health and Family Planning Commission of the People's Republic of China. All the participants in Kashgar or Urumqi were randomly assigned into eDOTS group or DOTS group. Among them, 81 patients were from Kashgar villages with 43 patients using eDOTS system and 38 patients with traditional DOTS as control. Eighty six patients were from Urumqi streets with 50 patients using eDOTS and 36 patients using DOTS. T test and ANOVA were used to compare the image scores and treatment compliance rates before and after treatment of these patients between groups.

**Findings:** PTB patients from villages in Kashgar treated with DOTS showed only 27.9% the patients took TB antibiotics regularly. However, with help of village and hospital doctors through the eDOTS system, the medical compliance was increased to 77.2%. The treatment compliance of patients from township (100%) using eDOTS was significantly higher than that of those patients from the rural villages (48.8%) in the first 6 weeks ( $t=32.781$ ,  $p<0.001$ ). The comparison of lung X-ray(DR) scores showed that the patients using eDOTS either from the villages or from township had significantly lower scores than these patients using DOTS by 1.81 points [95% CI (0.72-2.90)] and 1.05 points, 95% CI (0.15-1.95) respectively after 25 weeks of treatment.

**Conclusion:** eDOTS is an effective means for treating TB patients through daily reminding and monitoring TB patients taking antibiotics. Easy contact link with doctors and special education programs for encouraging patients finishing their treatment course can increase the treatment compliance, which is more conducive to improving the control efficacy of TB in remote and poor areas.

## Background

Pulmonary tuberculosis (PTB) is a serious public health disease and challenges the population health system around the world, especially in China, accounting for 15% of the global PTB burden [1-4]. Xinjiang Uygur Autonomous Region (Xinjiang) is a high endemic area of PTB in China [5-8]. The prevalence of active PTB in Xinjiang was 1526/100,000 population and the prevalence of smear-positive PTB was 433/100,000 which was higher than the national average level (66, 119/100,000, 495/100,000) in 2010 [5, 9]. PTB cases reported in Kashgar, Hotan, Aksu and Kizilsu Kirghiz prefectures/region in southern Xinjiang accounted for 70% of the total PTB cases in Xinjiang [5, 8]. The prevalence (292/100,000) was 4.8 times higher than the national average (61/100,000) and ranked the highest in China in 2018 [10]. From 2008 to 2018, Yingjisha County in Kashgar Prefecture had an average annual TB incidence of 720.56/100,000 which was the highest in Xinjiang [8].

World Health Organization (WHO) has recommended the Direct Observed Treatment Strategy (DOTS) [11] for stopping TB transmission for decades and the strategy has been introduced into China since 1990s, which had reduced half of TB prevalence by 2010 [12]. However, the strategy did not effectively reduced TB transmission in Xinjiang. A survey performed in 2010-2011 showed the prevalence of active PTB was 1526/100,000, 2.29 times

higher than the prevalence in 1990 (666/100,000) [5]. A report indicated that poor TB treatment outcome in Xinjiang is likely due to the low treatment compliance [13].

To increase patient compliance with treatment, we developed a new electronic DOTS system (eDOTS) based on mobile network technology, which reminds and monitors patient taking medication daily along with providing specific education program. In this study, we show the application of the eDOTS system used for TB patients from villages and streets in areas in Xinjiang. We showed that the system increased the village/street doctor's management ability and treatment efficacy through increasing patient's treatment compliance.

## Methods

### eDOTs system

The system is composed of several units including an electronic medicine box (eBox) for patient, a mobile connecting system (TB patient management software program I, mobile APP for all participants including patients, doctors, nurses, CDC management staff and patient's relatives using smartphones) and a central processing platform (TB patient management software program II, designed for the Centers for Disease Control and Prevention (CDC)). After registration in mobile phone, the system will be activated immediately. Every day, the eBox alarms at a set time which is convenient for each of patient taking medicine. Once the patient opens the eBox, pictures for taking medicines will be recorded automatically and transfer data into the management system. The system ticks the patient "finish taking medicine". The eBox will alarm for 30 min if the box was no opened. After 30 min the system will automatically send a message to her/his doctor and a relative asking them to remind the patient taking the medicine. If the patient is still not taking the medicine after 5 pm in the day, the system will record as "non-taking medicine" (Figure 1 and 2).

### Patients and adherence strategy

For testing the eDOTS system in village and township, we planed to screen above 100 PTB patients from 14 villages in Yinjisha County of Kashgar Prefecture in southern Xinjiang and screen above 100 PTB patients from 2 districts in Urumqi city area in northern Xinjiang randomly. Approximately half of the cases in urban or rural areas were assigned into the DOTS group and eDOTS group randomly.

All of the PTB patients aged between 15 and 75 were diagnosed and recruited through health check program and the patients showed Digital Radiography (DR) positive with clear and typical symptoms such as night sweats, chest pain, persistent cough and fever for more than two weeks referring to the criteria [14]. Pregnant women and patients with HIV infection or using hormone were excluded.

In addition, we established an X-ray DR score system for evaluating the PTB status based on to X-ray DR chest radiograph features (Supplementary data 1 for the details of classification and scoring methods). Three levels were scored based on lesion image features including level 1 showing exudation (3 scores), level 2 of pathology showing proliferation (4 scores) and infiltration and level 3 showing density of PTB lesion (3 scores) with a total scores of 10 (Supplementary data 1). Three X-ray experts were asked to mark the scores for each of the patients. Examples are shown in Figure S1 and S2.

### Training plan

All doctors from villages and township streets and staffs involved in the study had one-day training for introduction and use of the device and the system of eDOTS. Once a PTB patient was diagnosed and confirmed, he or she was registered as a PTB patient in the study and recorded all relative information for DOTS management including name, ID, age, gender, family location, diagnosis information such as smear results, X-ray and treatment prescription etc. After registered, an eDOTS box and a week of anti-TB medicine were supplied. Doctors saw their patients once a week and added the drugs for the next week.

### **Drug treatment**

Standard anti-TB drug combinations containing isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E) were prescribed for those PTB patients according to WHO recommendation as the first line anti-TB drugs [15]. Two treatment courses for all the cases include a two-month intensive phase with a daily dose of fixed-dose combination tablets containing HRZE, followed by a four-month continuation phase of daily HR.

### **Data records and statistics**

In eDOTS group, the medication data was recorded and uploaded to the server in CDC automatically including taking the antibiotics and contacting between doctors and patients. In DOTS group, doctors provided antibiotics once a week or two weeks and ticked on the record card. We used two parameters, compliance rate and PTB DR scores to compare the efficacy of both managements used in the villages and township. The individual's weekly medication compliance was calculated by dividing the individual's actual number of medications per week by the planned number of medications. T test was applied when DR scores were compared between groups and paired t test was used when DR scores were compared within groups.

## **Results**

### **General information**

A total of 167 active PTB patients were registered in our study from April to June 2016 including 81 cases were from 14 villages in Yinjisha County of Kashgar and 86 cases were from 2 districts in Urumqi City. All the participants in Kashgar or Urumqi were randomly assigned into eDOTS group or DOTS group. Among them, 81 patients were from Kashgar villages with 43 patients using eDOTS system and 38 patients with traditional DOTS as control. Eighty six patients were from Urumqi streets with 50 patients using eDOTS and 36 patients using DOTS (Table 1). In eDOTS group, only 3 (8%) patients fully and completely finished their treatment course by taking antibiotics accordingly to the doctor's prescription. The most patients did not fully take their medicine for some of reasons including neglect of medication, drug side effect, visiting friends, etc. However, the record cards showed the 100% patients from both villages and township streets taking the medicines for the traditional DOTS. However, for applying eDOTS in the villages, we had two weeks of internet out-service, we then immediately asked the village patients using the traditional DOTS one by one. However, we found that when we restarted the eDOTS system, the patient compliance was 27.9%. In the study, we used the data as patient compliance for DOTS in village.

### **Compliance in rural villages**

In village test, 43 cases were enrolled from 9 villages and treated with eDOTS system and 38 cases from 5 villages using DOTS as control. In the first 6 weeks of treatment in eDOTS group, the average medication

compliance rate was 48.8%, 95% CI (46.5%, 51.1%). At week 7, the network was accidentally disconnected and DOTS had been supplied for those eDOTS patients for two weeks. However, when the system was reused, the compliance rate was 27.9%, 95% CI (22.8%, 33.0%). The compliance rate was increased to 65.1%, 95% CI (59.7%, 70.5%) at week 20 subsequently with using the eDOTS. After we asked a well trained doctor from a hospital to contact with those patients who did not take drugs through the eDOTS system (voice service), the average medication compliance rate was increased to 77.2%, 95% CI (75.1, 79.3%) (Figure 3A).

### **Compliance in Urumqi City**

A total 86 patients were from Urumqi streets with 50 patients using eDOTS who were looked after by one community doctor and 36 patients using DOTS who visited doctors once a week in a hospital in the city. In the first 12 weeks of the intervention, the compliance rate of the patients with eDOTS was nearly 100%. After 12 weeks, the rate was slightly dropped, but the overall compliance rate was kept in more than 80 percent (Figure 3B).

The first 6 weeks of treatment of patients with eDOTS showed that village patients had 45-55% of compliance taking anti-TB drugs, which was significantly lower than the compliance rate of patients in township (99-100%) ( $t=-32.781, p<0.001$ ).

### **DR X-ray score**

There was no statistic difference on PTB scores from patients between Urumqi City and Yinjisha villages before treatment. However, whether DOTS or eDOTS was used, there were significant differences ( $p<0.01$ ) in patient scores before and after treatment (Table 2 and Figure 4). PTB scores were significantly reduced in both downtown and rural area at the end of the intervention period. We analyzed the scores by using Multivariate ANOVA with Tukey's multiple comparisons test after 26 weeks of treatment. PTB score ( $3.46\pm 0.57$  points) of patients from Urumqi applied with eDOTS was significantly lower than those ( $4.52\pm 1.45$  points) with DOTS, and in village, PTB score ( $4.19\pm 1.25$  points) of patients with eDOTS was lower significantly than those ( $6.0\pm 1.48$ ) with DOTS ( $p<0.001$ ). Comparison after using eDOTS, there was no difference between the score of PTB patients in downtown and those in rural areas ( $p=0.51$ ). Comparison only after using DOTS, the PTB score ( $4.5\pm 1.6$  points) of patients in downtown was lower significantly than those ( $6.00\pm 1.5$  points) in village by 1.5 points.

## **Discussion**

Although TB can be cured and controlled, the success of treatment and control depend on the high compliance of PTB patients taking antibiotics constantly and continuously for at least 6 months [16,17]. Failure to meet the compliance as required for DOTS can lead to prolonged the disease duration, drug resistance, relapse and refractory conditions [18-20]. Despite DOTS has improved the TB endemic situation in China, recent studies have shown that DOTS strategy does not increase treatment compliance among TB patients in China as it was considered in some areas [19-21]. In our study, we showed that only 27.9% of these village patients took antibiotics after the internet was off the service for weeks and DOTS was given to these patients in these two weeks of period. We believe the low of compliance for taking drugs with the traditional DOTS is the key for the high prevalence of PTB in rural area in Xinjiang, comparing those in Jiangsu (89%), Anhui (90.5%) and Ningxia (93.3%) in China [21].

From our point of view, the eDOTS system may be a solution for increasing the compliance in these remote and high endemic areas of TB. During the course, TB patients really need an approach for reminding patient taking antibiotics and education program for encouraging TB patients taking the medicine. In addition, as the high endemic areas have so many PTB patients, the village doctor may not observe the all patients taking antibiotics in the way of DOTS management. We believe that eDOTS is a suitable solution for these villages.

TB is highly endemic in Xinjiang, China, especially in these remote and economic no-developed areas. According to the results of the fifth national epidemiological survey on tuberculosis in 2010, the prevalence rate of active tuberculosis among people over 15 years old only in Kashgar is 2, 727/100, 000 [2], which means that the control and treatment of the disease requires a large number of doctors involved in the management. Given an example of Yingjisha County, the data of the sixth census conducted in 2010 showed that the total population was 263, 616 with a total of 231, 336 living in these 122 villages which calculates an average of 1, 896 villagers per village. If using an average prevalence of 2, 727/100, 000 residents, there was an average of 51 PTB patients in each of these villages. Normally one village has one village doctor. It is very difficult for one village doctor to look after so many PTB patients properly using the traditional DOTS. We believe eDOTS can help the village doctors look after so many PTB patients given that one doctor was easily looked after 50 PTB patients in Urumqi.

In addition, PTB patients need an easy way to contact doctors and other society workers for medical and psychological consultation especially when they have difficulty and problem for taking the medicine. While the eDOTS system offers a tool to link patients with doctors especially in rural areas. We believe that proper of doctors contacting with these PTB patients who want to give up taking medicine is crucial important for control of TB. In our study through the eDOTS system, the village doctors called these patients stopping taking antibiotics at week 13 and hospital doctors called these wanting stopping medication patients at week 21, the compliance rate increased to 65.1% and 77.2% respectively. This indicates that regularly communication of doctors with their patients is very importance for encouraging the PTB patients taking medicine.

It has shown that education is important for treatment and control of TB. Retrospective studies have shown that all anti-TB drug induced liver function damage occurred 4-26 days after administration [22]. A study in London showed that 53% of liver damage by anti-TB drug occurred within 2 weeks of the start of treatment, and 87.6% occurred within 8 weeks [23]. Some patients will suffer from side effects such as red urine and tear secretion, facial pigmentation and abnormal liver function accompanied by nausea, vomiting and other gastrointestinal symptoms. As could not understand the problems that arise in the course of medication, they begin to fear treatment and give it up eventually. The eDOTS system has a voice education program which contains 180 key questions and answers about PTB specifically designed and arranged for possible problems appeared duration of taking antibiotics. We believe the voice education program is suitable for taking medicine at home and educates more family members for encouraging the PTB patient to finish his/her treatment course.

Data from China's fifth national tuberculosis epidemiological sampling survey showed that only 14.4% of active tuberculosis patients were smear-positive[9]. In addition, it is well known that once patients take the medicine for few weeks, some cases will become smear negative. Therefore, sputum smear was not used as a parameter for evaluating the treatment efficacy for the whole time course of treatment in our study. DR scores was developed and used for identifying the lesion severity of PTB and speculate on medication adherence indirectly. Through the comparison of DR scores, we found that using eDOTS both in urban and rural areas all showed better therapeutic efficacy than those patients using the DOTS system alone.

## Conclusion

The application of eDOTS in remote villages and city streets showed that the system is effective for improving TB treatment and control through daily automatically reminding and monitoring TB patients taking antibiotics during treatment course, and more conducive in remote and poor areas. The system can also provide health education programs for encouraging patients finishing their treatment course. Most importantly, TB patients can contact with doctors and relatives any time through the system for help and advice. eDOTS is a tool for increasing the control ability of TB through increasing patient's compliance for regularly and consistently taking medicines.

## Abbreviations

DOTS: the traditional direct observed treatment strategy; eDOTS: the electronic direct observed treatment strategy; DR: digital radiography; PTB: pulmonary tuberculosis

## Declarations

### Ethics approval and consent to participate

The study was reviewed and approved by the Ethical Committee of the First Affiliated Hospital of Xinjiang Medical University and in compliance with medical ethics. Informed consents were obtained from participants or guardians of participants under 16 years old.

### Consent for publication

Not applicable.

### Availability of data and materials

The dataset analysed during the current study are available from the corresponding author on reasonable request.

### Competing interests

None.

### Funding

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### Authors' contributions

GG and WZ was the principal writer of the proposals and WZ designed the protocol of investigation and evaluation. GG and LH coordinated the fields survey and data record. LS, QW, BJ, MY, SW, TA, XP, ZL, XM, YC and JZ collected, confirmed PTB samples and applied eDOTS system. LH and YY developed and improved the

eDOTS system. JL and GG collected the data and finalised the statistical analysis. WZ took part in the analyses, interpretation, and critically revised the paper. All authors read and approved the final paper.

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## Tables

**Table 1** Basic characteristics of participants

	Village				Downtown			
	Total	DOTS	eDOTS	<i>P</i>	Total	DOTS	eDOTS	<i>P</i>
Age(years), meanSD	35.716.7	34.816.4	36.717.7	>0.01	34.816.5	35.714.7	33.918.1	>0.01
Male,n(%)	54(66.7%)	25(65.8%)	29(67.4%)	>0.01	58(67.4%)	28(77.8%)	30(60%)	>0.01
Ethnic group, n(%)	81	38	43	>0.01	86	36	50	
Han	0	0	0	>0.01	50 58.1%	24 66.7%	26 52.0%	<0.01
Uygur	81(100%)	38(100%)	43(100%)	>0.01	11 12.8%	411.1%	5 10.0%	<0.01
Hui	0	0	0	>0.01	25 29.1%	822.2%	19 38.0%	<0.01

**Table 2** The results of comparative analysis of patient scores before and after using DOTS and eDOTS in different regions.

	Group	Number of patients	of Scores	of Scores	<i>t</i>	<i>p</i>
			before treatment	after treatment		
Overall	DOTS	74	9.101.22 <sup>†</sup>	5.351.46 *	9.83	0.01
	eDOTS	93	9.230.96	3.580.84 *		
Downtown	DOTS	36	9.141.07 <sup>†</sup>	4.521.45 *	4.70	0.01
	eDOTS	50	9.180.72	3.460.57 *		
Village	DOTS	38	9.071.48 <sup>†</sup>	6.001.48 *	5.96	0.01
	eDOTS	43	9.281.10	4.191.25 *		

**Note:** \* *P* is less than 0.05, compared to DR scores before treatment within the group; <sup>†</sup> *P* is greater than 0.05, compared to DR scores in eDOTS group. *t* and *p* means DR scores significance between DOTS and eDOTs in the same region.

## Figures

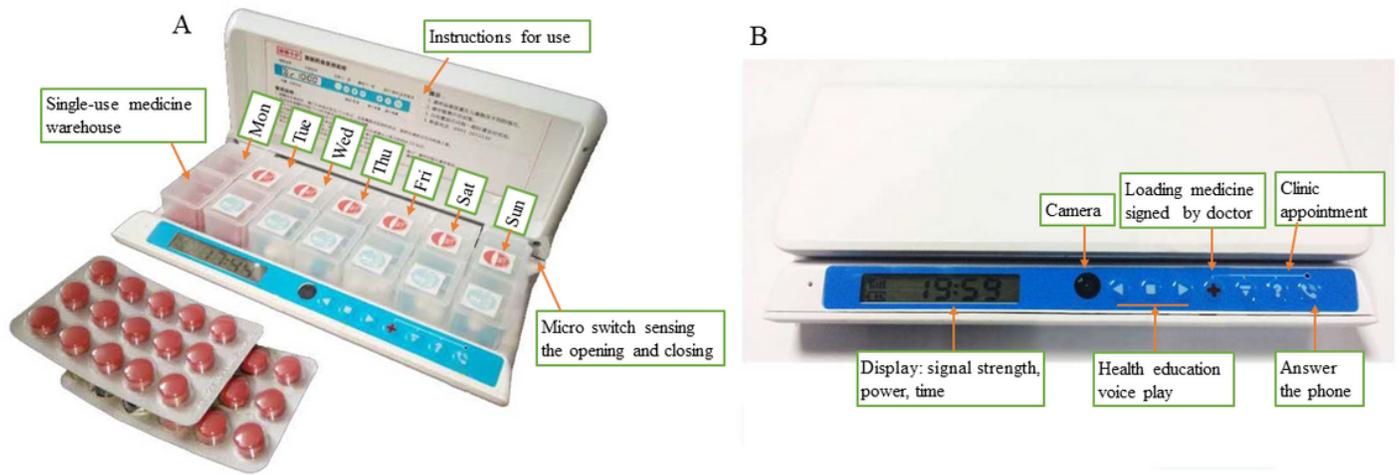


Figure 1

eBox structure A. Open state, B. Close state

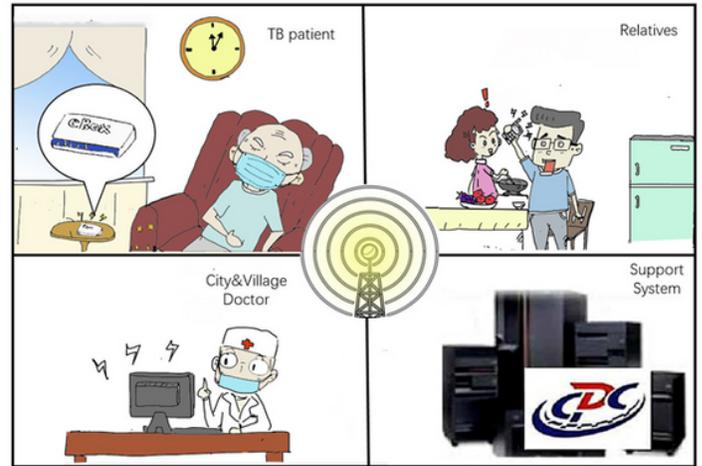
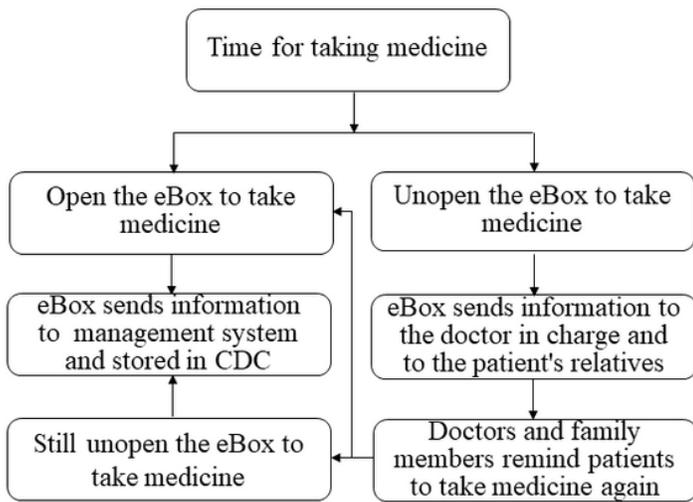
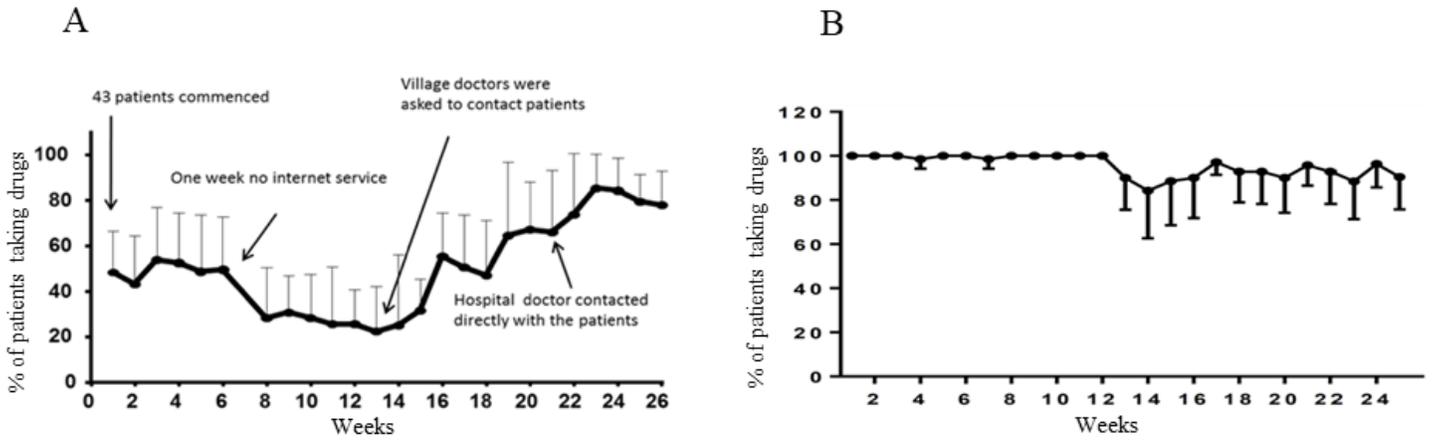


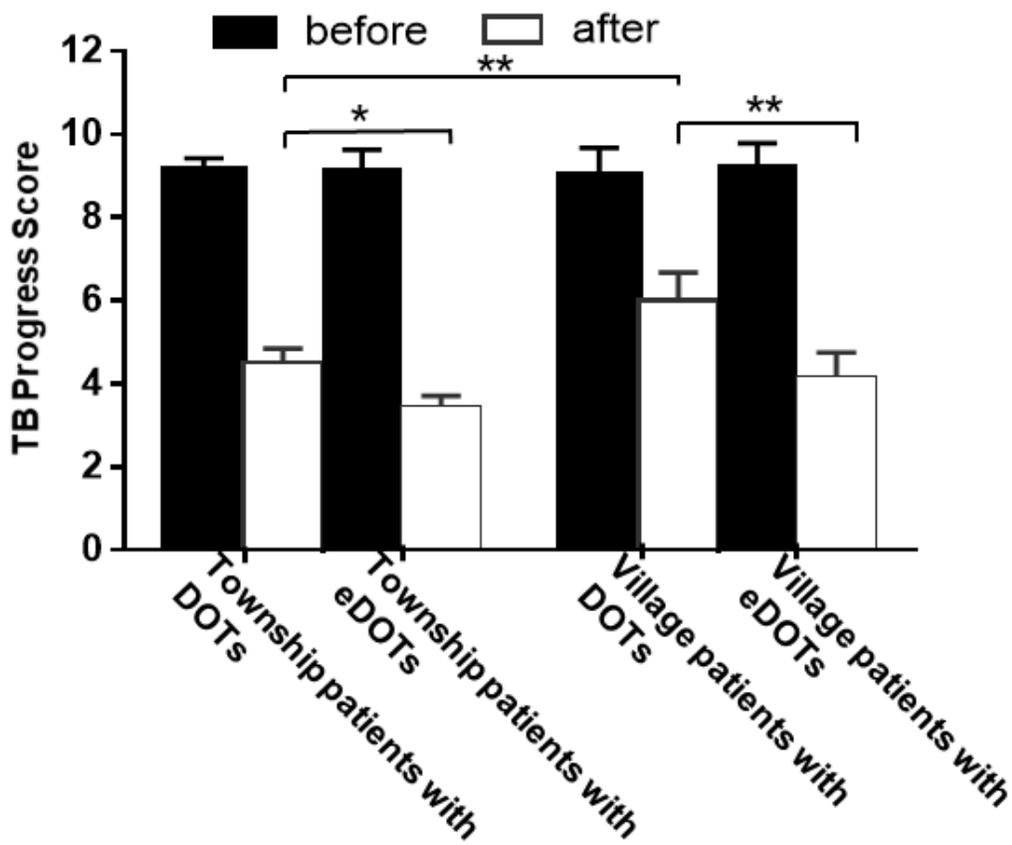
Figure 2

Working flow diagram of eDOTS system



**Figure 3**

The mean percentage of patients taking antibiotics weekly recorded by eDOTS A. In village, B. In city. Dots and error bars denote mean  $\pm$  SD.



**Figure 4**

Comparison of treatment efficacy of patients with eDOTS with these patients treated with DOTS. Data are shown as mean±95% CI. \*p<0.05, \*\*P<0.01

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Fig.S1Divisionoflungs.jpg](#)
- [Fig.S2ExamplesofscoringTBlesion.jpg](#)