

## Cohort analysis of directly observed treatment outcomes for tuberculosis patients in urban Pakistan

S. Akhtar,<sup>\*†</sup> S. Rozi,<sup>†</sup> F. White,<sup>†‡</sup> R. Hasan<sup>§</sup>

<sup>\*</sup>Department of Community Medicine and Behavioural Sciences, Faculty of Medicine, Kuwait University, Jabriya, Kuwait; <sup>†</sup>Department of Community Health Sciences, Faculty of Medicine, Aga Khan University, Karachi, Pakistan;

<sup>‡</sup>Pacific Health & Development Sciences Inc., Victoria, British Columbia, Canada; <sup>§</sup>Department of Pathology and Microbiology, Faculty of Medicine, Aga Khan University, Karachi, Pakistan

### SUMMARY

**BACKGROUND:** This quasi-experimental cohort study aimed to evaluate World Health Organization (WHO) defined tuberculosis (TB) treatment outcomes for patients under directly observed treatment at a health facility (clinic DOT) or at home (family DOT) in urban Pakistan.

**METHODS:** We enrolled 582 sputum smear-positive TB patients being treated by either clinic DOT ( $n = 295$ ) or family DOT ( $n = 287$ ) in 11 treatment centres. Patients and/or family members were interviewed for baseline measurements. WHO-defined treatment outcomes were evaluated at the end of treatment. Proportions of ‘cured’ patients were computed. A log-binomial model was used to evaluate the associations of various factors with ‘cured’ status.

**RESULTS:** The proportion of ‘cured’ patients was re-

spectively 66% and 34% in the clinic DOT and family DOT groups (risk difference 0.32; 95%CI 0.24–0.39). Patients on clinic DOT were more likely to achieve cure (adjusted relative risk [RR<sub>adj</sub>] 1.85; 95%CI 1.43–2.39) than those on family DOT, as were patients satisfied with their health care worker’s attitude (RR<sub>adj</sub> 5.73; 95%CI 2.54–12.96).

**CONCLUSION:** Clinic DOT nearly doubled the proportion of cured patients compared to family DOT. Efforts to improve care-provider attitudes to enhance patient satisfaction, and effective implementation of the WHO’s public-private mix approach, may enhance TB control in this and similar settings.

**KEY WORDS:** pulmonary tuberculosis; DOT; cure rate; log-binomial regression model; Pakistan

GLOBALLY, tuberculosis (TB) is a leading cause of morbidity and mortality, with an estimated 8.9–9.9 million incident cases, 9.6–13.3 million prevalent cases and 1.1–1.7 million deaths in 2008.<sup>1</sup> The DOTS strategy remains the cornerstone of global TB control efforts.<sup>2,3</sup> Notwithstanding successes in many regions, global incidence continues to increase, although at a slower rate, and has not fallen even in certain countries that have achieved good results under DOTS.<sup>4–7</sup>

In 2007, with an annual incidence of all types of TB of 181 per 100 000 population, an incidence of sputum smear-positive TB of 81/100 000 and a prevalence of TB all types of 223/100 000, Pakistan ranked eighth among the 22 high-burden TB countries.<sup>8</sup> In 1995, Pakistan’s National Tuberculosis Programme (NTP) adopted the DOTS strategy as its policy for TB care.<sup>9</sup> However, the health system is overwhelmed and cannot cope with caseloads due to a lack of funds and/or dysfunctional politics, resulting in suboptimal implementation of the DOTS strat-

egy and seriously compromising the effectiveness of TB control in Pakistan.<sup>10</sup> So far, in Pakistan and perhaps in other similar resource-poor settings, it has not been practical to apply universal DOTS coverage. Because the majority of patients are very poor, and many are labourers or housewives, parallel non-DOTS modalities are also used to avoid incurring additional costs due to travel to health centres and related loss of earnings. As a result, treatment outcome targets for most TB patients are below target.

All TB patient treatment outcomes should be routinely monitored to assess progress, identify and address deficiencies in the NTP and minimise and control multidrug-resistant disease.<sup>11</sup> To improve patient adherence to treatment, directly observed treatment (DOT), one of the essential elements of the DOTS strategy, has been recommended for implementation in both health facilities and in the community in resource-constrained settings.<sup>12</sup> Elsewhere, DOT at both health facilities and in the family have reached

Correspondence to: Saeed Akhtar, Department of Community Medicine and Behavioural Sciences, Faculty of Medicine, Kuwait University, PO Box 24923, Safat 13110, Kuwait. Tel: (+965) 2498 6542. Fax: (+965) 2533 8948. e-mail: saeed.akhtar@hsc.edu.kw

Article submitted 9 February 2010. Final version accepted 26 June 2010.

World Health Organization (WHO) targets of 85% success.<sup>13</sup> However, there is a paucity of published data on the effectiveness of such approaches in Pakistan.

This cohort study aimed to evaluate WHO-defined TB treatment outcomes with DOT supervised at a health facility (clinic DOT) and supervised by a family member (family DOT) in urban Karachi, Pakistan.

## METHODS

### *Study setting*

This study was conducted at TB treatment centres in Karachi, Pakistan's largest city and the nation's economic hub, with a metropolitan area of 3530 km<sup>2</sup> and a population of 17 million. Pakistan's private sector makes a major contribution to providing health care, particularly in major cities. Although TB control is primarily the responsibility of the government health services, approximately 80% of TB patients consult a private practitioner for initial diagnosis and treatment.<sup>14</sup> Karachi's large private sector treats many TB patients without following the recommended guidelines.<sup>15</sup>

In Karachi, health care is supported by a network of 85 government-approved hospitals and clinics in both the public ( $n = 18$ ) and the private sector ( $n = 67$ ). Health practitioner backgrounds range from fully trained to traditional practitioners.<sup>16</sup> At present, 62 medical centres offer TB treatment: 36 in the public sector and 26 in the private sector. Eleven centres were selected as a convenience sample based on willingness of management to cooperate during the study period, and were regarded as being typical of TB treatment centres in Karachi and elsewhere in Pakistan. Of these, five were run by non-governmental organisations, which use only family DOT, and five were in the public sector, which uses only the clinic DOT strategy. One 'semi-public' centre (regarded as public sector in our analysis) offers both clinic and family DOT. The 11 centres consisted of five tertiary-care hospitals, one Institute of Chest Diseases, one community clinic for chest diseases and four general hospitals.

### *Patients and study design*

We enrolled pulmonary TB (PTB) patients aged  $\geq 15$  years who had started a course of treatment (new or retreatment patient) at any of the 11 centres. A 'new patient' was defined as a TB patient who had never previously received treatment or had received treatment for  $< 1$  month. A 'retreatment patient' was defined as a TB patient who had received treatment for  $\geq 1$  month from any source, and who had returned to treatment after default, i.e., who had not taken anti-tuberculosis drugs consecutively for  $\geq 2$  months and who was found to be sputum smear-positive. The diagnosis of sputum smear-positive TB was made according to WHO/International Union Against Tuber-

culosis and Lung Disease (The Union) criteria,<sup>17</sup> including: 1) two or more initial sputum smear examinations positive for acid-fast bacilli (AFB); or 2) one sputum smear examination positive for AFB and radiographic abnormalities consistent with active PTB determined by a clinician; or 3) one sputum smear positive for AFB plus sputum culture positive for *M. tuberculosis*. Patients were excluded from the study if: 1) they were not residents of Karachi; 2) they exhibited resistance to at least isoniazid and rifampicin; and/or 3) they had severe illness.

The study had a quasi-experimental cohort design (in many respects it conforms to an experimental study, except for treatment randomisation). At the treatment centre offering both strategies, the benefits and limitations of each were explained to each participant, who was then asked to choose either daily clinic DOT at the health centre, to be observed by staff, or family DOT, to be observed at home by a family member of the patient's choice.

### *Treatment regimens and data collection*

At the first treatment visit after diagnosis, eligible patients were approached by a clinic nurse who explained the purpose, process and voluntary nature of the study and sought verbal consent from the patient (or guardian if the patient was aged  $< 16$  years). Clinic DOT patients were advised to attend the clinic during working hours to take their medication under observation by a clinic nurse. Each patient was advised to attend 5 days/week for the first 8 weeks (12 weeks for retreatment patients), followed by 3 days/week for the continuation phase. The treatment regimens used were as recommended by the WHO and Pakistan's NTP guidelines, i.e., an 8-month regimen (2HREZ/6HE for new and 2SHREZ/1HREZ/5HRE for retreatment patients\*). Apart from the difference in DOT, patients in both cohorts received the same case management, and all patients received drugs free of charge. Efforts were made to ensure that care and health education for patients in clinic and family DOT groups were delivered at each visit by the same health centre staff members.

At enrolment, data were obtained on baseline socio-demographic and health centre related variables for each study patient using a structured questionnaire. At subsequent visits (start of treatment, at months 2, 3 and 5 and at the end of treatment), the questionnaire was completed with data on bacteriological test results. Information was also collected on treatment duration and outcome, satisfaction with health services, satisfaction with health care provider's attitude and adherence to treatment. Incomplete entries or suspected reporting inaccuracies by patients

\* H = isoniazid; R = rifampicin; E = ethambutol; Z = pyrazinamide; S = streptomycin. The numbers before the letters indicate the length of each phase of treatment, in months.

and/or health centre staff were addressed in subsequent visits by the research team. An adherence card was signed and dated by a nurse at each visit and retained in the patient's clinic file. Family DOT patients/guardians visited the clinic every week. Responsibility for adherence lay with the patient/guardian; patients completed their own adherence cards for each day of pill taking, and a nurse recorded the weekly collection of drugs during the weekly visit. Based on the treating physician's assessment, adherence to treatment (defined as the number of weeks of treatment completed, and not the number of doses of medication) was also noted. The two WHO/Union-defined outcome variables, i.e., 'cure' and 'treatment success', were analysed.<sup>15</sup> Other possible outcomes considered were also adapted from WHO/Union guidelines.<sup>15</sup>

#### Sample size

The planned sample size was 300 patients in each cohort. This provided 90% power, at 5% significance level, to detect a difference of at least 15% between the proportions of successful treatment and/or cured patients in the clinic and family DOT groups, assuming a rate of 50% of these events in the latter group and approximately 30% refusals and defaults in each cohort.

#### Ethical considerations

At each treatment centre the benefits and limitations of clinic or family DOT supervision modalities were explained to each patient, and verbal consent was sought from all patients/guardians. The study was approved by the Ethics Review Committee of Aga Khan University, Karachi, Pakistan.

#### Statistical analyses

Data were double entered and managed using Epi Info Version 6.04 (Centers for Disease Control and Prevention, Atlanta, GA, USA) and analysed using Stata 9.2 (StataCorp LP, College Station, TX, USA). Type of supervision (clinic vs. family DOT) was the main exposure variable. Two main outcome variables, cure and treatment success (cured plus treatment completed), were analysed. All the analyses were on an intention-to-treat basis. The  $\chi^2$  test was used to compare the distribution of demographic, socio-economic and health care facility variables at baseline between the clinic and family DOT groups. We computed the difference with 95% confidence intervals (95%CI) between proportions of patients with an outcome of 'cured' or treatment success in both cohorts. A univariable log-binomial regression model was used to compute the unadjusted relative risk (RR) and 95%CIs to evaluate the relationship between supervision modality and 'cured' status. To adjust for confounding, factors related to 'cured' status ( $P \leq 0.15$ ) on univariable analyses were considered for inclusion in multivariable log-binomial regression

**Table 1** Baseline characteristics of pulmonary tuberculosis patients in clinic DOT and family DOT supervision modalities in a cohort study, Karachi, Pakistan

Variable	Total	Clinic DOT (n = 295)		Family DOT (n = 287)		<i>P</i> value
		n	%	n	%	
Age (completed years)						0.062
≤20	190	103	34.9	87	30.3	
21–40	254	131	44.4	123	42.9	
41–60	112	51	17.3	61	21.3	
>60	26	10	3.4	16	5.6	
Sex						0.860
Female	282	144	48.8	138	48.1	
Male	300	151	51.2	149	51.9	
Marital status						0.112
Separated	33	11	3.7	22	7.7	
Married	312	159	53.9	153	53.3	
Single	237	125	42.4	112	39.0	
Mother tongue						0.017
Balochi	27	7	2.4	20	7.0	
Sindhi	52	21	7.1	31	10.8	
Punjabi	92	50	17.0	42	14.6	
Pushto	102	56	19.0	46	16.0	
Urdu	224	124	42.0	100	34.8	
Others	85	37	12.5	48	16.7	
Religion						0.056
Non-Muslim	25	8	2.7	17	5.9	
Muslim	557	287	97.3	270	94.1	
Education (years of schooling)						0.002
Nil	330	160	54.2	170	59.2	
1–8	132	82	27.8	50	17.4	
9–10	79	41	13.9	38	13.2	
>10	41	12	4.1	29	10.1	
Household size*						<0.001
>7	283	165	59.9	118	41.1	
≤7	299	130	44.1	169	58.9	
Household income (rupees/month) <sup>t</sup>						0.006
≤6000	448	241	81.7	207	72.1	
>6000	134	54	18.3	80	27.9	
Financial constraints <sup>‡</sup>						<0.001
No	373	165	55.9	208	72.5	
Yes	209	130	44.1	79	27.5	
Patient category						0.234
Retreatment	62	27	9.2	35	12.2	
New patient	520	268	90.8	252	87.8	
Distance (km) from health centre						0.099
>7	539	268	90.8	271	94.4	
≤7	43	27	9.2	16	5.6	
Satisfied with health worker's attitude <sup>§</sup>						0.706
No	70	34	11.5	36	12.5	
Yes	512	261	88.5	251	87.5	
Satisfied with health services <sup>¶</sup>						0.802
No	73	36	12.2	37	12.9	
Yes	509	259	87.8	250	87.1	

\*Number of family members living in the same housing unit and sharing a kitchen.

<sup>t</sup>Total household income from all sources (rupees/month).

<sup>‡</sup>Living comfortably with total household income or hand-to-mouth.

<sup>§</sup>Whether the health care provider was friendly in dealing with and answering questions.

<sup>¶</sup>Availability of free drugs and availability of a health care provider to deal with you during your visit.

DOT = directly observed treatment.

models.<sup>18</sup> The supervision modality, age, ethnicity (mother tongue), education, household size, household income (rupees/month) and financial constraints were always retained in the models, either because of the significant baseline differences between the clinic and family DOT groups ( $P < 0.05$ ), or because of their socio-biological plausibility. Other variables were added to the model using a forward stepwise procedure and were only retained if the log-likelihood ratio test statistic was significant ( $P < 0.05$ ). When the log-binomial model failed to converge, a Poisson regression model with robust variance computation was used. Adjusted RRs and their 95% CIs were used to interpret the final model.

## RESULTS

From 22 January 2003 to 18 January 2005, 582 patients were recruited into the study. No eligible patient refused to participate. Respectively 295 and 287 patients were enrolled in the clinic and family DOT groups. There were significant differences ( $P < 0.05$ ) between the groups with regard to the distributions of some of the demographic- and health centre-related variables, such as ethnicity (defined by mother tongue), education, household size, total household income (rupees/month), financial constraints and distance (km) from the health centre (Table 1).

The overall proportion of 'cured' patients was respectively 66% and 34% in the clinic and family DOT cohorts (absolute risk difference [RD] = 0.32; 95%CI 0.24–0.39). By contrast, the proportion who 'completed treatment' was significantly lower in the clinic (10%) than in the family DOT (40%) cohort (RD = -0.30; 95%CI -0.36–-0.23). However, there was no significant difference between the two cohorts in treatment success (RD = 0.02; 95%CI -0.05–0.09). Also, there were no meaningful differences between the two cohorts in the proportions of patients who defaulted (14% vs. 15%), transferred out (8% vs. 7%), failed (1% vs. 2%) or died (1% vs.

2%; Table 2). Adherence was respectively 85% and 82% in the clinic and family DOT cohorts.

On univariable log-binomial regression analyses, supervision modality, education, financial constraints, satisfaction with health care worker's attitude and satisfaction with health services were significantly associated with 'cured' status ( $P < 0.05$ ; Table 3). The multivariable log-binomial regression model showed that patients in the clinic DOT group were nearly twice as likely to be cured as those in the family DOT group (adjusted RR 1.85; 95%CI 1.43–2.39). Patients satisfied with their health care worker's attitude were about six times more likely to be cured than those who reported being dissatisfied (adjusted RR 5.73; 95%CI 2.54–12.96; Table 4).

## DISCUSSION

In this study, the proportions of patients who achieved 'cure' were respectively 66% and 34% in the clinic and family DOT groups. Clinic DOT patients were nearly twice as likely to be cured, after adjusting for the effects of other variables in the model. Although still short of the WHO target cure rate of 85%, the proportion of 'cured' patients in this evaluation (66%) is comparable with those recorded in randomised controlled trials of DOTS in Northern Pakistan (64%)<sup>10</sup> and in Thailand (62%).<sup>19</sup> While there is evidently room for improvement, the proportion of 'cured' patients in the clinic DOT group in our study was higher than the results obtained from two evaluations of DOT in South Africa (34% and 41%).<sup>20</sup>

The proportion who 'completed treatment' was lower in the clinic than in the family DOT group (10% vs. 40%). There was also no significant difference in treatment success (i.e., 'cured' plus 'completed treatment') in the groups. These findings corroborate those of an earlier controlled trial in Northern Pakistan, where a higher cure rate but lower 'treatment completion' rate were recorded in a health centre-based supervision group than in two other groups.<sup>10</sup>

**Table 2** Treatment outcomes of pulmonary tuberculosis patients by sex and supervision modality in a cohort study, Karachi, Pakistan

Treatment outcome	a			b			c – f
	Clinic DOT (n = 295)			Family DOT (n = 287)			
	Male (n = 151)	Female (n = 144)	Total (n = 295)	Male (n = 149)	Female (n = 138)	Total (n = 287)	RD (95%CI)
<b>Successful</b>							
Cured	100 (66)	94 (65)	194 (66)	51 (34)	47 (34)	98 (34)	0.32 (0.24–0.39)
Treatment completed	13 (9)	17 (12)	30 (10)	54 (36)	60 (44)	114 (40)	-0.30 (-0.36–-0.23)
All successful	113 (75)	111 (77)	224 (76)	105 (70)	107 (78)	212 (74)	0.02 (-0.05–0.09)
<b>Unsuccessful</b>							
Defaulted	27 (18)	15 (10)	42 (14)	26 (17)	18 (13)	44 (15)	
Transferred out	15 (10)	9 (6)	24 (8)	11 (7)	8 (6)	19 (7)	
Failed	2 (1)	—	2 (1)	3 (2)	2 (2)	5 (2)	
Died	1 (1)	2 (1)	3 (1)	3 (2)	4 (3)	7 (2)	

DOT = directly observed treatment; RD = risk difference; CI = confidence interval.

**Table 3** Univariable analysis of factors associated with 'cured' status of pulmonary tuberculosis patients treated with clinic DOT or family DOT, Karachi, Pakistan

Factor	Total	Cured (n = 292)		Not cured (n = 290)		Crude RR	95%CI	P value
		n	%	n	%			
Treatment supervision								<0.001
Family DOT	287	98	33.6	189	65.2	1.00	—	
Clinic DOT	295	194	66.4	101	34.8	1.93	1.61–2.31	
Age, completed years								0.137
≤20	190	104	35.6	86	29.7	1.58	0.92–2.72	
21–40	254	121	41.4	133	45.9	1.38	0.80–2.37	
41–60	112	58	19.9	54	18.6	1.50	0.86–2.61	
>60	26	9	3.1	17	5.9	1.00	—	
Sex								0.936
Female	282	141	48.3	141	48.6	1.00	—	
Male	300	151	51.7	149	51.4	1.01	0.86–1.18	
Marital status								0.151
Separated	33	12	4.1	21	7.2	1.00	—	
Married	312	153	52.4	159	54.8	1.35	0.85–2.15	
Single	237	127	43.5	110	37.9	1.47	0.92–2.35	
Mother tongue								0.082
Balochi	27	13	4.5	14	4.8	1.00	—	
Sindhi	52	26	9.0	26	9.0	1.04	0.65–1.67	
Punjabi	92	48	16.4	44	15.2	1.08	0.70–1.68	
Pushto	102	52	17.8	50	17.2	1.06	0.69–1.64	
Urdu	224	123	42.1	101	34.8	1.14	0.76–1.72	
Others	85	30	10.3	55	19.0	0.73	0.45–1.91	
Religion								0.852
Non-Muslim	25	13	4.5	12	4.1	1.00	—	
Muslim	557	279	95.5	278	95.9	0.96	0.66–1.42	
Education, years of schooling								0.005
Nil	330	147	50.3	183	63.1	1.00	—	
1–8	132	83	28.4	49	16.9	1.41	1.18–1.69	
9–10	79	41	14.0	38	13.1	1.17	0.91–1.49	
>10	41	21	7.2	20	6.9	1.15	0.83–1.59	
Household size								0.068
>7	283	153	52.4	130	44.8	1.00	—	
≤7	299	139	47.6	160	55.2	0.86	0.73–1.01	
Household income, rupees/month								0.348
≤6000	448	220	75.3	228	78.6	1.00	—	
>6000	134	72	24.7	62	21.4	1.09	0.91–1.31	
Financial constraints								<0.001
No	373	158	54.1	215	74.1	1.00	—	
Yes	209	134	45.9	75	25.9	1.51	1.30–1.77	
Patient category								0.332
Retreatment	62	33	11.3	29	10.0	1.00	—	
New patient	520	259	88.7	261	90.0	0.94	0.73–1.20	
Distance from health centre, km								0.278
>7	539	267	91.4	272	93.8	1.00	—	
≤7	43	25	8.6	18	6.2	1.17	0.90–1.53	
Satisfied with health worker's attitude								<0.001
No	70	6	2.1	64	22.1	1.00	—	
Yes	512	286	97.9	226	77.9	6.52	3.02–14.06	
Satisfied with health services								<0.001
No	73	8	2.7	65	22.4	1.00	—	
Yes	509	284	97.3	225	77.6	5.09	2.64–9.84	

DOT = directly observed treatment; RR = relative risk; CI = confidence interval.

Furthermore, the proportions of defaulting patients in the clinic (14%) and family DOT (15%) cohorts were about the same in our study. These proportions were nearly half the magnitude reported in Northern Pakistan among health facility staff (27%) and in home (family member or self; 32%) treatment supervision modalities.<sup>10</sup> A reduction in the proportions of defaulters may be a result of growing

awareness about the benefits of treatment completion among patients and family members, as a result of education received at health facilities or through media campaigns.

In this type of study setting, 100% adherence in a family DOTS cohort is unlikely; however, the majority of defaulting patients are labelled 'treatment completed' with no knowledge of their final bacteriological

**Table 4** Multivariable log-binomial model of factors associated with 'cured' status of pulmonary tuberculosis patients treated under clinic DOT or family DOT supervision modalities, Karachi, Pakistan\*

Factor	Relative risk (95%CI)	
	Univariable	Multivariable
Treatment group (clinic vs. family DOT)	1.93 (1.61–2.31)	1.85 (1.43–2.39)
Health care worker's attitude (satisfied vs. not satisfied)	6.52 (3.02–14.06)	5.73 (2.54–12.96)

\* Multivariable model also included age, ethnicity, education, household size, household income (rupees/month) and financial constraints.

DOT = directly observed treatment; CI = confidence interval.

status. In 2005, treatment outcomes were unknown for an estimated 1.5 million smear-positive non-DOTS patients globally, yet those patients were classified as 'treatment success' after being combined with 'cured' patients, and analysed as one group.<sup>21</sup> This assumption is considered inappropriate due to the public health significance of the unknown bacteriological status of patients classified as 'treatment completed'.<sup>21,22</sup>

In this study, multivariable analysis showed that patients satisfied with their health care worker's attitude were more likely to achieve cure. It is recognised that DOT is more than a mechanical procedure for administering medicine to patients with TB: it is a bond between patient and health care worker, conveying recognition of the value of treatment.<sup>23,24</sup> Staff support and health education are therefore likely to improve adherence to the treatment protocol, including clinic visits and laboratory evaluation.<sup>25</sup> As the model of staff support and health education has been shown to work elsewhere,<sup>26</sup> it should be replicable in Pakistan and similar settings.

Some limitations should be considered when interpreting our results: information on several variables was self-reported by patients/guardians and/or health centre staff, and as such reporting inaccuracies could not be ruled out. Furthermore, the two cohorts may not be truly comparable in terms of all known and unknown confounders, although the multivariable log-binomial regression model did adjust for some covariate effects. Finally, lacking randomisation, we could not evaluate whether clinic DOT performed better at public or private centres, as all patients under clinic DOT received care at public centres.

## CONCLUSION

Although well short of the WHO target of 85%, public sector clinic DOT achieved twice the proportion of cured patients over private sector family DOT. Based on our findings, efforts to enhance patient satisfaction with provider's attitude may improve treatment outcomes. As a large number of TB patients ap-

proach private health care providers for diagnosis and treatment, Pakistan needs to implement the WHO's public-private mix (PPM) approach to engage private providers in TB control.<sup>27</sup> Elsewhere, PPM approaches have yielded evidence of improvement in case detection and treatment outcomes in public sector health facilities,<sup>28–30</sup> and effective implementation is likely to enhance TB control in both Pakistan and other resource-constrained settings.

## Acknowledgements

The authors thank the administration and staff of the TB treatment centres for facilitating this study and the patients for their participation and understanding of the potential benefits of the study. The study was supported by Aga Khan University Research Council's grant no. 01-II/01/CHS.

## References

- World Health Organization. Global tuberculosis control: epidemiology, strategy, financing—a short update to the 2009 report. WHO/HTM/TB/2009.426. Geneva, Switzerland: WHO, 2009.
- World Health Organization. WHO report on the tuberculosis epidemic: stop TB at the source. WHO/TB/95.183. Geneva, Switzerland: WHO, 1995.
- World Health Organization. The stop TB strategy: building on and enhancing DOTS to meet the TB-related Millennium Development Goals. WHO/HTM/STB/2006.37. Geneva, Switzerland: WHO, 2006.
- Cox H S, Morrow M, Deutschmann P W. Long term efficacy of DOTS regimens for tuberculosis: systematic review. BMJ 2008; 336: 484–487.
- World Health Organization. Global tuberculosis control: surveillance, planning, financing. WHO report 2007. WHO/HTM/TB/2007.376. Geneva, Switzerland: WHO, 2007.
- Dye C, Watt C J, Bleed D M, Hosseini S M, Raviglione M C. Evolution of tuberculosis control and prospects for reducing tuberculosis incidence, prevalence, and deaths globally. JAMA 2005; 293: 2767–2775.
- Huong N T, Duong B D, Co N V, et al. Tuberculosis epidemiology in six provinces of Vietnam after the introduction of the DOTS strategy. Int J Tuberc Lung Dis 2006; 10: 963–969.
- World Health Organization. Global tuberculosis control: epidemiology, strategy, financing. WHO report 2009. WHO/HTM/TB/2009.411. Geneva, Switzerland: WHO 2009.
- Ministry of Health, Pakistan. National Tuberculosis Control Programme. Islamabad, Pakistan: NTP, 2009. <http://www.ntp.gov.pk/about.htm> Accessed June 2009.
- Walley J D, Khan M A, Newell J N, Khan M H. Effectiveness of the direct observation component of DOTS for tuberculosis: a randomised controlled trial in Pakistan. Lancet 2001; 357: 664–669.
- Donald P R, van Helden P D. The global burden of tuberculosis—combating drug resistance in difficult times. N Engl J Med 2009; 360: 2393–2395.
- World Health Organization. What is DOTS? A guide to understanding the WHO-recommended TB control strategy known as DOTS. WHO/CDC/CPC/TB/99.270. Geneva, Switzerland: WHO 1999.
- Newell J N, Baral S C, Pande S B, Bam D S, Malla P. Family-member DOTS and community DOTS for tuberculosis control in Nepal: cluster-randomised controlled trial. Lancet 2006; 367: 903–909.
- National Tuberculosis Control Programme, Pakistan. National guidelines for tuberculosis control in Pakistan. 2nd ed. Islamabad, Pakistan: NTP, 1999.

- 15 Khan J, Malik A, Hussain H, et al. Tuberculosis diagnosis and treatment practices of private physicians in Karachi, Pakistan. *East Mediterr Health J* 2003; 9: 769–775.
- 16 John T J, White F. Public health in South Asia. In: Beaglehole R, Bonita R, eds. Global public health: a new era. 1st ed. Oxford, UK: Oxford University Press, 2003: pp 172–190.
- 17 World Health Organization, International Union Against Tuberculosis and Lung Disease, Royal Netherlands Tuberculosis Association. Revised international definitions in tuberculosis control. *Int J Tuberc Lung Dis* 2001; 5: 213–215.
- 18 Hosmer D W, Lemeshow S. Applied logistic regression. 2nd ed. New York, NY, USA: John Wiley & Sons, 2000: pp 91–142.
- 19 Pungrassami P, Johnsen S P, Chongsuvivatwong V, Olsen J. Has directly observed treatment improved outcomes for patients with tuberculosis in southern Thailand? *Trop Med Int Health* 2002; 7: 271–279.
- 20 Zwarenstein M, Schoeman J H, Vundule C, Lombard C J, Tatley M. Randomised controlled trial of self-supervised and directly observed treatment of tuberculosis. *Lancet* 1998; 352: 1340–1343.
- 21 World Health Organization. Global tuberculosis control: surveillance, planning, financing. WHO report 2008. WHO/HTM/TB/2008.393. Geneva, Switzerland: WHO, 2008.
- 22 Ditah I C, Reacher M, Palmer C, et al. Monitoring tuberculosis treatment outcome: analysis of national surveillance data from a clinical perspective. *Thorax* 2008; 63: 440–446.
- 23 Frieden T R, Driver C R. Tuberculosis control: past 10 years and future progress. *Tuberculosis (Edinb)* 2003; 83: 82–85.
- 24 Volmink J, Matchaba P, Garner P. Directly observed therapy and treatment adherence. *Lancet* 2000; 355: 1345–1350.
- 25 Garner P, Volmink J. Directly observed treatment for tuberculosis. *BMJ* 2003; 327: 823–824.
- 26 Chowdhury A M, Chowdhury S, Islam M N, Islam A, Vaughan J P. Control of tuberculosis by community health workers in Bangladesh. *Lancet* 1997; 350: 169–172.
- 27 World Health Organization. Engaging all health care providers in TB control: guidance on implementing public-private mix approaches. WHO/HTM/TB/2006.360. Geneva, Switzerland: WHO, 2006.
- 28 Dewan P K, Lal S S, Lonnroth K, et al. Improving tuberculosis control through public-private collaboration in India: literature review. *BMJ* 2006; 332: 574–578.
- 29 Lonnroth K, Uplekar M, Blanc L. Hard gains through soft contracts: productive engagement of private providers in tuberculosis control. *Bull World Health Organ* 2006; 84: 876–883.
- 30 Ahmed J, Ahmed M, Laghari A, Lohana W, Ali S, Fatmi Z. Public private mix model in enhancing tuberculosis case detection in District Thatta, Sindh, Pakistan. *J Pak Med Assoc* 2009; 59: 82–86.

**RÉSUMÉ**

**CONTEXTE :** Cette étude quasi-expérimentale a visé à évaluer les résultats du traitement de la tuberculose (TB) définis selon l'Organisation Mondiale de la Santé (OMS) dans les modalités de traitement directement observé (DOT) dans une polyclinique (DOT clinique) et DOT par un membre de la famille (DOT famille) au Pakistan urbain.

**MÉTHODES :** Nous avons enrôlé 582 patients atteints de TB à frottis positif provenant de 11 centres de traitement, soit pour DOT clinique ( $n = 295$ ) soit pour DOT famille ( $n = 287$ ). Les patients et/ou les membres de leur famille ont été interviewés pour toutes les déterminations de départ. Les résultats du traitement définis selon l'OMS ont été évalués à la fin du traitement. On a informatisé les proportions de patients « guéris ». On a utilisé un modèle log-binomial pour évaluer les associations de différents facteurs avec le statut de « guérison ».

**RÉSULTATS :** Les proportions de patients « guéris » ont été respectivement de 66% et de 34% dans les groupes DOT-clinique et -famille (différence de risque = 0,32 ; IC95% 0,24–0,39). Par comparaison avec ceux du groupe DOT-famille, les patients du groupe DOT-clinique ont été plus susceptibles d'être guéris (risque relatif ajusté [RR<sub>aj</sub>] 1,85 ; IC95% 1,43–2,39), tout comme l'étaient les patients satisfaits de l'attitude de leurs travailleurs de soins de santé (RR<sub>aj</sub> 5,73 ; IC95% 2,54–12,96).

**CONCLUSION :** Par comparaison avec la stratégie DOT-famille, la DOT-clinique a quasi doublé le taux de guérison des patients tuberculeux. Des efforts pour l'optimisation des attitudes des pourvoyeurs de soins en vue d'améliorer la satisfaction du patient, ainsi qu'une mise en œuvre effective de l'approche mixte publique-privée préconisée par l'OMS, pourraient améliorer la maîtrise de la TB dans ce contexte et dans des contextes similaires.

**RESUMEN**

**MARCO DE REFERENCIA:** El presente estudio cuasi-experimental tuvo como objeto comparar, con los criterios de la Organización Mundial de la Salud (OMS), los desenlaces terapéuticos entre la modalidad de tratamiento breve directamente observado (DOT) en el dispensario (DOT-dispensario) y DOT en la familia (DOT-familia) en una zona urbana en Pakistán.

**MÉTODOS:** Se incluyeron en el estudio 582 pacientes con tuberculosis (TB) y baciloscopia positiva, tratados ya sea mediante DOT-dispensario ( $n = 295$ ) o DOT-familia ( $n = 287$ ) en 11 centros de atención. Los datos iniciales se obtuvieron en entrevistas a los pacientes o a los miembros de sus familias. Al final del tratamiento se evaluaron los desenlaces terapéuticos con los criterios de la OMS. Se calculó la proporción de pacientes 'curados' y con un modelo de regresión logarítmico binomial se evaluaron las asociaciones entre los diferentes factores con la variable de 'curación'.

**RESULTADOS:** La proporción de pacientes 'curados' fue

66% en el grupo que recibió tratamiento en DOT-dispensario y 34% en el grupo DOT-familia (diferencia de riesgos 0,32; intervalo de confianza [IC] del 95% 0,24–0,39). Comparados con el otro grupo, los pacientes que recibieron DOT-dispensario tuvieron mayor probabilidad de alcanzar la curación (riesgo relativo ajustado [RR<sub>a</sub>] 1,85; IC95% 1,43–2,39) y también los pacientes que afirmaban estar satisfechos con la actitud de su proveedor de atención sanitaria (RR<sub>a</sub> 5,73; IC95% 2,54–12,96).

**CONCLUSIÓN:** El DOT-dispensario casi duplicó la tasa de curación de los pacientes tuberculosos en comparación con DOT-familia. Las iniciativas encaminadas a mejorar las actitudes de los profesionales de salud y la satisfacción de los pacientes con el tratamiento y a optimizar la ejecución eficaz el enfoque de la OMS en la colaboración entre el sector público y el sector privado podrían mejorar el control de la TB en los entornos semejantes.