Reviewer's report

Title: Default from tuberculosis treatment in Tashkent, Uzbekistan; Who are these defaulters and why do they default?

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Reviewer: Douglas Fraser Wares

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Major Compulsory Revisions

The authors present important data and information on what appears to be a weak aspect of the TB programme in Tashkent, Uzbekistan, namely an unacceptably high default rate amongst new PTB patients. The manuscript however needs to be revised in order to give readers a better understanding of the specific setting, namely the setting of TB control in a Former Soviet Union country. There is need of some discussion on why the default rate overall in Uzbekistan is significantly lower than in Tashkent. Also the authors need to make the discussion section clearer and crisper in the presentation of possible interventions and solutions to overcome both the systems and socio-economic issues that they have identified.

Specific comments

“Background” section

1. To give readers a better understanding of the specific setting, it would be useful if the authors provide more details of the actual TB systems in place in Uzbekistan and population data for the country and Tashkent. What TB services and facilities are available generally in Uzbekistan, and specifically in Tashkent? Is it correct that like in many countries of the FSU previously as well as being a vertical service with much emphasis on in-patient care, TB services in Uzbekistan also provided adherence enablers to TB patients e.g. provision of transport vouchers, nutritional support, etc? If correct and if such enablers have now been withdrawn, along with the overall weakening of the health services post break-up of the FSU, this is important background information to be provided to readers.

2. Treatment regimens need to be provided as it is not clear what actually is the duration of the intensive phase treatment.

3. Both failure and death rates in Tashkent are high. Is there data to answer whether these high rates could be due to MDR-TB or HIV co-infection? If known are MDR-TB and HIV rates different in Tashkent to other parts of the country?

“Results” section

1. If the assumption that a 6 month SCC regimen was used, the median of 200 days on treatment for the control group suggests that there was a significant
amount of treatment interruptions even in this control group. The same appears to be true for those who defaulted after completing the intensive phase as median given for this group is 89 days. Or is this an artefact from using median and not mean duration?

“Discussion” section

1. The authors present data which suggest that default rates amongst new smear positive PTB patients are significantly different in Tashkent compared with the other parts of Uzbekistan as for the former it is given as 18% and for Uzbekistan overall as 7%. However the authors do not discuss or suggest any reasons why the default rate is significantly higher in Tashkent and/or why lower in other parts of the country. It would strengthen the paper if this difference was discussed by the authors. Are there differences in the available health care facilities? Is ambulatory care more common outside of Tashkent? Are there other possible reasons such as less unemployment etc?

2. Unlike other studies, males appear not to be significantly at higher risk of defaulting. Also default similar across all age groups. Can the authors suggest why this was the case in Tashkent?

3. It appears from the study that smear positive cases had a lower risk of default. The authors postulate that this could be due to over-diagnosis of smear negative cases. Do the authors have data or information to back this statement up? Alternatively could it be that there more emphasis was given by the system/staff to the smear positive cases compared to those who were smear negative? Or if HIV co-infection is common amongst TB patients in Tashkent, with a resultant greater proportion of smear negative cases amongst those co-infected, could it be that this is the reason that smear negative cases have a greater default rate as they are not improving on TB treatment?

4. Both failure and death rates in Tashkent are high. Could MDR-TB or HIV co-infection be playing a role here? Also could MDR-TB or HIV co-infection be playing a role in default? Such patients may not do well on SCC and may choose to leave treatment if not getting better.

5. The authors state that in a recent systematic review of default in developing countries, default occurs more in the CP. Although not having seen the paper referenced by the authors, this somewhat contradicts findings of many studies that suggests default is common in IP and around the time of the switch to CP. Also routine admission of TB patients is widespread in the FSU countries unlike in the majority of developing countries where treatment is fully ambulatory. The authors highlight that routine admission in a TB hospital is a major obstacle to patient’s adherence to treatment. It is not exactly clear how long the routine hospitalization of TB patients is for TB patients in Uzbekistan. The authors suggest that it “..should be limited to a maximum of 60 days…” suggesting that at present hospitalization is meant to be for longer than 60 days. If this is correct, then is it correct that hospitalization is expected to be for a longer time period than the duration of IP, assuming the IP used is 2 months?

As the authors quite correctly highlight there appears to be “system failure” in
ensuring that patients seamlessly transition from in-patient care to ambulatory care. How would the authors ensure that the referral system is improved?

If the risk of routine hospitalization for default is supplemented by the information given by the “non-DOT SCC” patients, surely this lead to a much stronger push to revise policy and introduce wider patient friendly ambulatory DOT services? Also if in-patient facilities have also been weakened in recent years, does routine admission of patients also not run the risk of higher rates of nosocomial transmission?

Risk factors for default appear to be being homeless, unemployed, a pensioner and alcohol abuse i.e. as a generalization, facets of the poor and marginalized sections of the population. Along with wider use of ambulatory care, what do the authors suggest in respect to addressing the socio-economic factors that they have identified as risk factors for default? If previously enablers and incentives were available to TB patients, should they not be re-introduced? In paragraph 3 on page 7, the authors mention certain groups which may require special attention. This is a crucial part of the discussion and would benefit from further discussion of specific interventions to address the needs of these groups who belong to the poorer and marginalized sections of the community. I here would refer the authors to a recent publication from Keshavjee et al titled “Treating MDR-TB in Tomsk, Russia.” in the Ann NY Acad Sci 1-11(2008) doi: 10.1196/annals.1425.009 in which similar issues are discussed along with the interventions made to address them.

Minor Essential Revisions

“Background” section
1. The flow of the second paragraph needs to be reworked as it jumps back and forth from Uzbekistan to Tashkent, and becomes a little hard to follow.

Discretionary Revisions

“Results” section
1. A flowchart could be provided to show the drop-outs at each stage in the sampling process eg start with 153 defaulters – 144 had records available – 126 had consistent data in TB Register / same for controls.

2. It would be of interest to know how many of the so-called “non-DOTS” group were “refusals of further treatment” during the in-patient period and/or “expulsions” from the in-patient ward.