Reviewer's report

**Title:** Identification of losses to follow-up in a community-based antiretroviral therapy clinic in South Africa using a computerized pharmacy tracking system

**Version:** 1  **Date:** 25 May 2010

**Reviewer:** Alessandro Cozzi-Lepri

**Reviewer's report:**

The authors present an interesting analysis aimed at investigating the ability of an open-source electronic pharmacy system (the intelligent dispensing of ART – iDART) to identify patients who are likely to drop out or die in a community-based ART cohort in Cape Town, South Africa. Although the objective is clear and the analysis is potentially useful there are aspects of the nature of the data collection and of the analysis design which are unclear and which limit the interpretability of the results.

**Major compulsory revisions**

1. 583 patients who started ART after enrolment in the cohort and who did not take part of the survey at April 2008 were excluded from this analysis. Were iDART data available for these patients? If so, it is unclear why these were excluded as it seems crucial to know whether the delay in pick up of pharmacy prescription could predict the risk of these patients dropping out by April 1 2008. Indeed, I would focus the analysis on all 3,384 patients who started ART, if possible, to avoid selection bias.

2. The definition of patients who failed to pick up ART based on iDART is unclear. Was this based on the time difference between the date of the survey and the time at which medication was last dispensed? If so, could the high sensitivity of the >=6 weeks and >=12 weeks definitions simply reflect the fact that it was too early for the 85 patients to come back to the clinic as they had sufficient drug supply? I suggest to define potential LTFU on the basis of the frequency of medication pick-up over, say, the first year of ART and to exclude patients who started ART within 12 weeks of the date of survey.

3. For the given prevalence of LTFU, one key parameter here seems to be the positive predictive value (how many of those defined as failures on the basis of iDART were truly LTFU). These percentages seem to be reported on the first line of Table 1 (15%, 44%, 45% and 50%) although not defined as such. I suggest to remove Table 1 (and Figure 3 which seems to show the same results) and present a 2x2 table with the raw data, sensitivity, specificity, PPV and NPV for all four definitions of “predicted LTFU” used. These could be done separately for the April 2008 and April 2009 surveys. People who were dead as of the date of the survey should be removed from the analysis related to the survey in question. Why were people who had transferred to a clinic outside of the cohort-network not defined as LTFU? It seems to me that they should be, as long as their last
clinical visit at the site in which they were originally enrolled was >3 months prior to the date of the survey? The only difference with the other patients defined as LTFU is that the reason for the drop out is known.

4. It is unclear how many of the patients included in the survey of April 2008 could be assessed a year later (April 2009?) and how did the authors handle patients who were not included in the second survey? This comment applies also to the analysis with death as an endpoint. Also, how many patients of those who were defined as “truly LTFU” by April 2008 came back to the clinic between April 2008 and April 2009? I am not sure if it makes sense to call these as LTFU.

5. The methods used to ascertain deaths have not been explicitly stated. Given that this is likely to be a major reason for patients not coming back for a visit “notification from any source” seems too vague.

6. There is not attempt to perform multivariable analyses. Were any of the other parameters collected in these patients, say, at the time of ART initiation predictive of LTFU? Could any of this (e.g. enrolment in the cohort when ART-naïve, gender, etc.) confound the association between iDART and risk of LTFU or death?

Minor essential revisions

1. The adopted definition of true LTFU needs to be stated in the abstract

2. Page 6 of Results. These patients had been receiving ART for a median of 1.9 years (IQR, 1.0-2.9). Does this sentence refer only to the 24% of patients who were enrolled when ART-experienced?

3. Page 6 of Results. In total, there were 85 patients who were true LTFU, representing 3.3% of the overall cohort. The real percent of patients LTFU in the cohort by April 2008 seems much higher: (85+334+249)/3384 =20% and more consistent with the rates observed in the resource limited settings.

4. Page 7 of Results. The proportions who were true LTFU ranged from 44-50% and did not differ statistically between groups (p=0.282). Test used is unclear. It is incorrect to test the difference between PPV of the 4 definitions using a standard chi-square because groups are not mutually exclusive. Authors should consider calculating areas under the ROC-curves and compare them using an appropriate t-test instead.

5. Page 7 of Results. Similarly, higher proportions of those with pharmacy delays had died after one year (3.8%, 7.7%, 10.3% and 8.8% versus 0.02%, respectively; P<0.02 for comparisons of #12 weeks group and #18 weeks groups with no delay group). Suggest that raw data used to calculate these proportion are shown – see major point #3 above

6. Page 7 of Discussion. Within each of these groups the proportions of patients who were true LTFU was similar (approximately one half). However, the #18 and #24 weeks cut-offs had substantially lower sensitivities for true LTFU (62% and 47%, respectively) compared to the #12. On this basis, we identified the #12 weeks delay as the optimal cut-off. Optimal cut-off is generally chosen on the basis of the trade-off between sensitivity and specificity and not sensitivity and
7. Page 7 of Discussion. We conducted the cross-sectional study at a single time-point and we cannot be sure that results would be the same at other time-points. Time-points seem to be two, April 2008 and one year later?

8. Table 1. There is no footnote referring to the “a” next to 95% CI – suggest to modify the table as described in major point #2.

9. Suggest to replace Figures 1,2 with ROC-curves and AUC, remove Figure 3 and replace Figure 4 with a cross-tabulation of survey results at April 2008 vs. April 2009.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests