Reviewer's report

Title: Increasing Access to Subsidized Artemisinin-based Combination Therapy through Accredited Drug Dispensing Outlets in Tanzania

Version: 2 Date: 9 December 2010

Reviewer: Catherine Goodman

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General Comments

This paper primarily uses routine data collected in Accredited Drug Dispensing Outlets (ADDOs) to assess the impact of a strategy to introduce subsidised ACT in these outlets in 2 regions of Tanzania. It also presents data from a questionnaire on ADDO dispensers' knowledge of anti-microbial resistance.

The topic area is extremely timely as the subsidy programme has many similarities with the Affordable Medicines Facility-malaria (AMFm) strategy which is just starting to roll out in Tanzania and other pilot countries, and is highly controversial. Moreover, the study has the potential to add important information to the evidence base on the operation of private sector drug retailers in general. The paper is generally very clearly written, well structured, provides considerable information on the intervention which is helpful, and the figures are well chosen and presented.

However, there are many inherent limitations with the data used, which weaken the quality of the study:

1. The paper relies on routine records kept by ADDOs, while acknowledging that these are often highly inaccurate. The authors note that these are frequently incomplete because dispensers under-record for tax reasons, and for some reason do not always record drugs purchased based on a prescription. I would have also thought that they may under-record behaviours that they know are not allowed, e.g. sales of artemisinin monotherapy, or wholesale sales of ACTs to other retail outlets. This could go some way to explaining the very large discrepancies between data on drug volumes from regional distributors and those from ADDO drug registers (apparently the latter are only 60% of the former). As their main conclusions derive from the drug register data this is a major limitation.

2. There is no control group, so it is not possible to tell whether there would have been some increase in ACT sales over time anyway without the intervention.

3. Data are only available from those ADDOs that presented their records (around 70%). The authors say that the 30% who did not present their records were not informed about the request to do so. However, it is possible that they gave this reason as an excuse, while there may have been other reasons e.g. they had not been keeping good records, or had been engaging in inappropriate
practices which they did not want to reveal, or the person trained on the ADDO course might have been no longer working there etc etc. It is therefore not clear that the study is based on a representative sample of ADDOs.

4. Data are only available from these ADDO records on drugs dispensed by ADDOs. It is not possible to assess whether the increase in ACT dispensed is additional to baseline ACT use in the community or is substituting ACT use from other sources i.e. it is not clear whether there is a net increase in ACT coverage at the community level.

5. There is no information on who is buying the drugs e.g. age group, socio-economic status of customers, so we have no way of knowing whether the subsidised ACT is being targeted to those most in need

6. There is also no information on whether those treated with ADDO ACT actually had malaria.

7. There is no information on the actual retail prices charged by ADDOs, which may well have differed from those recommended in the strategy.

8. There is no information on how the drugs are actually dispensed e.g. what advice is provided.

These data would have been greatly enhanced if they had been accompanied by other data collection tools such as a household survey, exit interviews, or mystery shoppers. Having noted all these issues, I still feel that the paper could make a useful addition to the literature, especially given its topical nature. However, it would require the following major and minor revisions.

Major Compulsory Revisions

1. All the important limitations of the study noted above should be fully acknowledged and discussed. Currently there is a small paragraph on limitations at the end of methods. I would propose that this be expanded to cover the issues above in more depth (and personally I think it would fit better near the start of the discussion).

2. The authors present a very positive picture of the functioning of ADDOs, particularly of the regulatory and supervisory arrangements. For example, under “Regulatory Oversight and supervision” in Methods you say that district level staff conduct “quarterly supervisory visits”; in the abstract you say the intervention happened in an environment “where the safety and efficacy of the drugs and the quality of services are being monitored and regulated”, and under “Regulatory and supervisory support” in the Discussion it is stated that the supervisory and regulatory systems have addressed concerns about poor drug use. This contrasts with anecdotal information I have heard which has described the regulation and supervision of ADDOs as major challenges. I am concerned that as nearly all authors work for the implementing agencies for ADDOs (MSH and TFDA), they may have been tempted to paint too favourable a picture of ADDO functioning and avoid highlighting any of the problems. Perhaps they could clarify whether they truly believe the systems to be working as well as they suggest in the paper?
3. The timing of the different elements of the intervention and data collection is quite complicated. It would be helpful to add a figure with a timeline to clarify this for the reader (and providing information on the date of training which is currently missing).

4. It would be helpful to provide more information on the pricing aspect of the intervention under “Packaging and price ACTs for ADDOs” in Methods. For example, how were the prices stated in Table 1 promoted or enforced? What was the markup allowed for ADDOs on each pack size, and for the regional and national distributor? It would also be helpful to give the average retail prices for other common antimalarials here (some but not all of this information is provided in the Discussion, but it is all really needed here to help the reader understand the intervention).

5. The ADR system is described but no information is provided on how many reports were actually made, and of what nature and whether they were followed up.

6. The information on the antimicrobial resistance training and associated questionnaire sits oddly within this paper. For a start it is not clear what overlap there is between the ADDOs reporting drug register data and those included in the AMR data. If this is limited, then I suggest that this aspect is removed from the paper, as it cannot be generalised to the whole ADDO population in question and can therefore be misleading. It is also not clear how this “convenient” sample of 71 ADDO staff was selected and why a more rigorous sampling method could not have been used. Furthermore, that data are relatively weak as it is based on reported not actual behaviour, and when ADDO staff report that they give advice on a particular topic it is not clear if this advice was accurate.

7. This study could have some important implications for the AMFm strategy that is currently rolling out in Tanzania. However, I didn’t find any mention of AMFm in the paper. It would be useful to discuss the implications more directly, and to highlight any differences from the intervention described in the paper and AMFm and explore the likely implications of these. Given that the scale up of ADDOs in Tanzania appears to be happening more slowly than expected, it would also be good to discuss whether and how AMFm or similar strategies should be implemented in districts (or other countries) without ADDOs.

8. Under “Regulatory and supervisory support” in the Discussion, you state that there was “no known leakage of ACTs destined for the public sector to the ADDOs” – however it is not clear how you have assessed this. You also do not comment on whether there may have been leakage of subsidised ACTs meant for ADDOs to other outlet types (e.g. DLDBs).

9. The first sentence of your conclusion does not follow from your results. You cannot say that ADDOs are the “best” mechanism when you haven’t evaluated any others. It is also not clear that the programme ensured quality of services and products, as you haven’t presented any data on this.

10. In the conclusion you note the “substantial human and financial resources” required for ADDOs. It would be good to provide some detail on what the costs are so that readers from other countries can assess the potential to implement
such an intervention elsewhere.

11. Table 2—it seems odd to present data from July when the subsidised drugs were only introduced in Aug in some areas and in November in others. You are therefore mixing baseline and follow up data. I would suggest that instead you present data for the months with subsidised ACT for each district, or that you present all data from November onwards only. You could then present the data prior to the introduction of the subsidised drugs as a “baseline” or omit this.

12. Also in Table 2, the outlets included in the indicators are not clear. From the text it appears that the denominator is the 448 dispensers that provided data, but this figure is not mentioned in Table 2, and the first column actually refers to 660 ADDOs.

Minor Essential Revisions

13. Background, para 6, line 3—state what the price for ACT is at public & mission health facilities. To set the intervention in context it would be also be good to provide some information on the frequency of stockouts of Alu in public facilities during your study period.

14. Background, para 8, line 1-3—provide a reference to back up the claims made about the good functioning of ADDOs.

15. Methods, “Packaging and pricing of ACTs”, para 3, line 1—state whether those prices for public sector ACTs generally adhered to or widely flouted?

16. In a number of places you refer to “malaria” patients or cases (Methods “ACT supply logistics”, para 2; “Uptake and availability of ACTs”, para 1; Table 2), when in fact you mean customers seeking antimalarial treatment. There is of course no way of knowing what proportion of these people actually had malaria.

17. Methods “ACT supply logistics”, para 4, line 7—you refer to “smart push”—I’m not sure what the smart aspect of this refers to.

18. Methods, “Uptake and availability of ACT”, para 1—information should be provided on the data management and analysis for the drug register data.

19. Results, para 2, line 3—be careful not to state what patient perceptions were—you only have ADDO dispensers’ opinions of what patient perceptions were, rather than any direct information from patients.

20. Results, para 2, line 6—you cannot say that dispensers “demonstrated” a high level of compliance with documentation requirements if this is only based on what they reported that they did. Similarly Discussion “Dispenser training”, para 3, line 7, you should clarify that you only know that ADDO staff stated that they provide certain information, not that they provide it.

21. Results, “Level of dispenser knowledge”, para 2, line 7—the figure given for providing information on the relationship between medicine dispensed and the condition differs from that given in Table 3.

22. Discussion, para 2, line 11—it is not clear to me how the efficacy of drugs is being monitored in this programme.

23. Discussion “Sales factors” para 2, line 9—is the price for SP given for an
adult dose?

24. Discussion “Dispenser Training”, para 1 line 13-15– I’m not clear what comparison of interventions is being referred to here – my understanding of the Sabot et al paper is that it only included one intervention.

25. Discussion “Dispenser training”, para 2, line 1 – I’m not clear on how these AMR behaviour indicators were assessed – the data provided only related to knowledge.

26. Competing interests – I would have thought that the employment of nearly all authors by an institution involved in implementing the ADDO programme should be highlighted here.

27. Table 3 – (in general I would suggest removing these data from the paper as discussed above, but if you decide to keep it...) it seems odd to present the 2 indicators on asking patients to repeat instruction, and instructing patients on the importance of returning in the negative form, when all other indicators are “positive”

28. Figure 4 – I assume this is in terms of “customers sold antimalarials”, (rather than antimalarial volumes!)

29. In Table 2 it appears that only these 4 antimalarial types were dispensed. i.e. no artemisinin monotherapies were dispensed. Do you think this is true or reflects a bias in recording? Either way, it deserves comment in the text.

Discretionary Revisions

30. Abstract – it would be good to include the dates of the intervention in the abstract

31. Discussion, para 4, line 2 – it would be good to provide more information on the concept of the “certified wholesaler” and why this is such a long process.

32. You might want to consider citing Alba et al, “Improvements in access to malaria treatment in Tanzania after switch to artemisinin combination therapy and the introduction of accredited drug dispensing outlets - a provider perspective”, Malaria Journal 2010 as it covers some similar issues, and particularly corroborates the reasons you propose for low ALu stocking by ADDOs in Kilombero.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests