Reviewer's report

Title: Protocol for a randomized controlled trial to study the efficacy of a brief intervention to reduce alcohol misuse in patients with HIV in South Africa.

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Reviewer: John Norrie

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Discretionary revisions

1. The reported numbers for the per capita consumption of alcohol at 40 litres of pure alcohol for men and 24 for women are astonishing – to the point that you wonder if they are correct – several points:

   a. This is the average amongst those that drink – so what is the overall average per head of adult population (or, what is the estimated proportion of men and women that do not drink).

   b. Even allowing for this, 40 litres of pure alcohol is around 100 litres of whisky – that is around 4 standard bottles of whisky a week – and this is the average, which even allowing for a heavy skew, still will mean that there must be many men drinking more than that?

   c. Is alcohol in South Africa very cheap, because these levels of drinking wouldn’t even seem affordable, particularly in a LMIC context, let alone incapacitating and hugely harmful to health?

   d. The reference given [2] seems to be a WHO datasheet about HIV/AIDS – is this the right reference?

2. It would be useful to have a paragraph or two on how generalisable the findings are likely to be – how these 500 or so recruits from the primary care clinics in townships in Gauteng are likely to be representative of the identified subset of ‘problem drinkers’ with HIV-1 (a) across the rest of South Africa and then (b) across Africa and then (c) globally for all those with HIV-1 who have drink problems?

3. One specific issue about possible selection bias is that the study can only access participants who are attending the clinics – what about HIV-1+ patients who are getting treated but their drinking is contributing to unreliable and sporadic attendance at the clinics, or even more extreme their drinking has meant that they have stopped attending the HIV-1+ treatment clinics? Although their drinking levels may have excluded them from the study anyway, nonetheless there would seem that there may be a possible group of relevance there that could be missed?

4. Page 6 – the aims of the study are a bit confusing to read until you realise that
the study is first a screening study which will capture data on everyone with HIV-1 at the clinics (so for example the study can estimate the prevalence of drinking behaviours), and then having identified the problem drinkers within a certain range on AUDIT, who aren’t in alcohol treatment or have any of the comorbidities listed for exclusion, proceed to randomise just this subset. It would be useful to make this ‘screening -> then randomised trial’ design more explicitly clear.

5. Page 6 ‘... between pre-intervention, 3 months and 12 months after intervention’ – over what period is the pre-intervention defined?

6. The authors introduce the phrases ‘harmful’ and ‘hazardous’ drinking, which seem to have agreed and quantifiably distinct definitions – but by the Discussion are using the term ‘problem drinker’ – useful to define terms and then be consistent throughout?

7. The sample size calculation needs to be explained more carefully – the randomised trial is in a carefully defined subset of problem drinkers, and yet the authors seem to justify the power calculation’s assumed effect size in terms of comparing drinkers with non-drinkers. They need to explicitly discuss what proportion of that difference it would be reasonable to expect a brief intervention would realise, and then justify that reasoning?

8. Page 8 – more specific detail on the randomisation would be helpful (for example ‘... by checking the random numbers which allocate the case to the intervention arm or control arms’ – not clear what this means).

9. Missing data – the study will need to have a comprehensive pre-specified Statistical Analysis Plan worked out in advance, and it would seem that missing data (caused by loss to follow up) could be a major methodological challenge given this patient group – couple of points:

   a. The authors state that extensive efforts (‘at least six individual attempts will be made to contact patients by telephone and letter’) will be made to minimise the attrition, which is good to see.

   b. However, ‘observations with a single follow up point missing ... will be imputed from available follow up’ and ‘data for participants who are lost to follow up at 3 and 12 months will be imputed using baseline values’ looks possibly too simplistic – what about multiple imputation (for missing at random) or even looking at modelling missing data mechanisms assumed to be non-ignorable?

10. Page 13 ‘Trial status – Patients are currently recruited for the trial’ – be more specific i.e. are you saying recruitment is complete?