

Reviewer's report

Title: Buprenorphine versus dihydrocodeine for opiate detoxification in primary care: A randomised controlled trial [ISRCTN07752728]

Version: 1 **Date:** 23 September 2006

Reviewer: Adrian Dunlop

Reviewer's report:

Review of Buprenorphine versus dihydrocodeine for opiate detoxification in primary care: A randomised controlled trial [ISRCTN07752728]

1. Is the question posed by the authors new and well defined?

There are no previous randomized controlled trials comparing dihydrocodeine to buprenorphine for the management of ambulatory heroin (or methadone) detoxification. This study is therefore important, particularly, as the authors note, as buprenorphine is being prescribed more frequently for detoxification in the UK.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

An RCT is the accepted gold standard for comparing a new medication to standard treatment. The study is open label. While dihydrocodeine is not indicated for the treatment of opioid detoxification in the UK, it is a frequently used medication. Blinding a study of buprenorphine to dihydrocodeine in a primary health care setting, as one medication is given as a qid dose and the other as a daily dose, is practically very difficult to do and does not detract from the design significantly. However, the dosing conditions (e.g. daily supervised dosing, all take home doses) are not described and require further description in the paper.

While data of suggested maximal dosing regimens is presented in the original publication on this study in BMC, only summary data on total doses is presented in this paper. This makes interpretation of the results very difficult, as it requires some extrapolation to infer what sorts of doses were actually prescribed.

3. Are the data sound and well controlled?

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

The authors comment that retention for the duration of the detoxification period is low, only 23% of the sample attended for the duration of the study and provided a final urine drug screen. This does make interpretation of the data difficult, but, as the authors suggest elsewhere, it can be inferred that the majority of non adherent participants may well have relapsed, indeed imputed data (assuming relapse) has been used in the results section.

The planned dosing regimens, which use moderate doses of buprenorphine during week one, and low doses during week two, may be one reason for the high non adherence rate. Doses in week two may have been too low for dependent opioid users to remain in treatment for that period. There is no discrete discussion on reasons for lack of collection of final drug screens (probably due to drop out).

Follow up data at 3 months is good (~85%) and fair (though quite admirable for a detox study) at 6months (61%).

A principal problems for the study is poor recruitment, only ½ of the original planned sample size was

recruited, this has led to an underpowered study. However, even the large maintenance studies comparing buprenorphine to methadone are underpowered to show significant differences.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

The paper would be improved by providing more data on actual doses prescribed, and the degree to which prescribers followed the recommended dosing regimens.

5. Are the discussion and conclusions well balanced and adequately supported by the data?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

In the conclusion the authors state: "Recruitment was not a substantial problem for practitioners committed to the trial".

The authors should clarify this statement – does this mean that the major problem with recruitment was difficulties in finding committed practitioners (a very important finding for a pragmatic study) or were there additional problems. The low recruitment really limits the degree to which any generalizations can be made from the study, other than a study of this sort is feasible to recruit to (but recruits low numbers).

There is a minor inconsistency with timelines, in the introduction the authors state the timelines were over 18 months but in the conclusion the authors state : ...design, recruitment, analysis and write up taking one year in total.

Further, a minor revision of the statement "...how such studies, undertaken in the context of routine care, even with such potentially problematic clientele, are possible and informative" needs some consideration given the lack of statistically significant differences between the groups. This study essentially demonstrates feasibility of such work.

If any data were collected on GP experiences of prescribing the two medications as part of the study, this would be fascinating. There may be some clinically significant differences for practitioners prescribing the two medications, and while this may not present a robust statistical difference in outcomes, it may practically affect use of buprenorphine (or not) by GP prescribers.

6. Do the title and abstract accurately convey what has been found?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Some more detail on low adherence rates during detoxification should be provided in the abstract.

7. Is the writing acceptable?

Yes

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

Yes

I have received an honorarium from Reckitt Benckiser (manufacturers of buprenorphine and marketers in

the USA and Australia) for speaking at a symposium in Melbourne, Australia in November 2005.

I have no other competing interests.