

Author's response to reviews

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

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Version: 2 **Date:** 31 October 2006

Author's response to reviews: see over

31st October 2006

Dear Dr Chrissie Kouremenou

**RE: 1543239782103775 Buprenorphine versus dihydrocodeine for opiate detoxification in primary care: A randomised controlled trial [ISRCTN07752728]
Nat MJ Wright, Laura Sheard, Charlotte NE Tompkins, Clive E Adams, Victoria L Allgar and Nicola S Oldham**

Thank you for your e-mail dated 6th October 2006. Please find attached the revised manuscript for publication consideration. The author team would like to thank the reviewers for their comments on the initial manuscript. In light of the comments, the following amendments have been made to strengthen the quality of the paper.

Reviewer: Adrian Dunlop

2 Daily dosing conditions have now been explicitly described.

Two tables have been included to demonstrate the suggested dosing regimes for both buprenorphine and dihydrocodeine.

3 Reasons for lack of final urine collection has been expanded upon within the discussion section.

4 More data has now been provided on prescribed doses (see point 2). The degree to which prescribers followed the recommended dosing regime has been detailed.

5 The sentence regarding recruitment and practitioners has been clarified so as to highlight the distinction between practitioner recruitment and participant recruitment

Timeline inconsistencies have been corrected

The statement in paragraph 3 of this section has been amended

The LEEDS project team recently had a paper published regarding GP experiences of randomising drug users in primary care. (Sheard et al: 2006). Within the paper, there is discussion of GPs views of equipoise between the two medications. We have made reference to the paper in this present manuscript.

6 The abstract has been amended to provide detail on the low adherence rates

Reviewer: Maqi Farre

1 It was suggested that our trial was scientifically unsound due to being non-blind beyond the point of randomisation. We have responded to this in the discussion section. Briefly, the inevitable trade-off between methodological rigour and feasibility when conducting trials in the real-world clinical setting has been considered. Our discussion is supported with reference to other researchers who have used pragmatic RCT methodology in the field of substance misuse. Emphasis has been placed on LEEDS being pragmatic rather than explanatory in design.

2 The reviewer has questioned whether our study was underpowered due to incomplete recruitment. The text has not been edited as we have been explicit that our study had sufficient power to detect difference with respect to the primary outcome. However the paper is already explicit that many of the secondary outcomes are statistically either borderline significant or insignificant due to a lack of power.

3 Planned dosage and number of detoxification days have now been described in the methods section

4 A paragraph has been added in the discussion section regarding the issue of “dose equivalency”. This highlights how it is not possible to make claims regarding dose equivalency as the two medications are not identical in terms of their pharmacological effect upon opiate receptors.

5 In the methods section, it is now stated that the preparation of dihydrocodeine was rapid and not slow release. The tablet strength and preparation of both interventions have been clarified.

6 We have not amended the text on this point as we did not collect information on other drugs prescribed. Whilst some of the participants could have been polydrug users, heroin is the only illicit drug for which there is a pharmacological detoxification intervention. Therefore in this study it was not felt that the prescribing of other drugs for generic medical conditions (e.g. insulin for diabetes) would have a bearing on the primary outcome.

We look forward to hearing from BMC Family Practice regarding publication

Yours

Nat Wright and Laura Sheard (on behalf of the author team)