Reviewer's report

Title: Development and testing of a primary care disease management program for patients with chronic pain

Version: 1 Date: 27 October 2004

Reviewer: Andrew Cook

Reviewer's report:

General

This is a well-conceived study that addresses important clinical questions. The authors are to be commended for tackling very challenging clinical issues with a difficult patient population, using a systematized, multidisciplinary approach. The authors note that this is the first prospective study of its kind in a primary care setting. Particular strengths of the study include: inclusion of commonly excluded subjects (with psychiatric comorbidity and/or substance abuse), an empirically-based treatment incorporating concurrent treatment of pain and depression, use of appropriate assessment measures, comprehensive literature review and bibliography, attention to the crucial issue of opioid misuse, and use of appropriate screening procedures including urine toxicology screening.

There are, however, some significant shortcomings of the study as presented. The most significant are:
1. Absence of a treatment control group.
2. The high dropout rate (27%), which is clearly confounded with the outcome variable of substance misuse (68% of lost subjects were deemed to have misused opioids).
3. Description of the study and its interpretations goes beyond the well-defined but very selective patient population involved.
4. Non-standardization of some treatment components that makes replication and generalization difficult.
5. Cutoffs used for classification of depression.
6. Uncontrolled type I error rate in statistical analyses.
7. Limited attention to the very significant finding of a high rate (31%) of substance misuse.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The study would be strengthened by editing of the title, abstract, introduction and discussion to more closely reflect the design and sample employed: a multidisciplinary disease management approach to opioid therapy for chronic benign pain in a challenging patient population with “a high burden of medical and psychiatric comorbidity”. Important points to focus on: predominantly a program to modify existing opioid therapy (93% on opioids at baseline) in difficult to manage patients (difficult pain management or suspected misuse), unique characteristics of sample (eg, 44% with history of illicit substance use; 51% with history of depression, ave age 51 (SD 9.6), “socioeconomically disadvantaged”), individualized treatment within fairly broad parameters, uncontrolled design.
2. More information is needed on lost subjects given that 15/22 of these were due to discontinuation of opioids. Is the “no important differences” (p.9, line 18) based on grouped means comparisons? What was the prevalence of depression in this dropout group? Given the importance of this group to interpretation of results, I would suggest presenting comparative data in table format.
3. In reference to #2, the comparison of % prevalence of depression pre- and post-treatment (table 3, line 7) may not be meaningful.

4. More attention in the discussion to the limitations on replication/generalization due to individualization of treatment. One difficult issue is the process of selection and adjustment of medications, including short- and long-acting opioids, and adjuvants such as tricyclics and anticonvulsants. Can decision rules be more explicitly stated? How could another group attempt to replicate this program? Also the use of a committee for defining and/or acting on misuse highlights the subjective component of these determinations: can your decision rules be more explicitly stated or are there suggestions for greater standardization in future studies?

5. Because of common overlap in symptoms of chronic pain and depression (particularly neurovegetative components), it is generally recommended that adjusted cut-offs be used with standardized depression scales such as the CES-D, to improve specificity. Geisser et al. (Clin J Pain 1997;13:163-170) recommend a cutoff of 27 for the CES-D. The reported prevalence rates should be adjusted, as well as the description of the sample and the treatment effects. Also clarify use of CES-D scores for guiding antidepressant use in this context (p.7, lines 9-10)

6. Were the research assistants who conducted post-treatment assessments blind to the pre-treatment assessments or were these conducted by the same people? This needs to be clearly stated, with the potential implications for experimenter effects noted.

7. The high prevalence of substance misuse is a very important finding, and would be central in many readers’ evaluations of the feasibility and value of this type of program. The authors provide a good discussion of the issues of misuse, addiction and pseudoaddiction, but do not clearly state their views on whether this misuse affects the success or value of the treatment program. More recommendations on how to minimize and address this problem with the study population are needed. If most patients decline substance abuse referrals, how else can they be treated to avoid the common migration between clinics/providers? The statement on p.14, lines 9-10 is difficult to interpret without knowing baseline rates of misuse in the population. Is this known?

8. The alpha (type I) error rate should be controlled for the multiple statistical comparisons. Though not explicitly stated, it appears the authors are interpreting p<.05 as a significant finding at the per-comparison level. This translates to a multiple comparison alpha of .40 for the main tests in table 3, or a 40% probability of a type I error across these comparisons.

9. Given the uncontrolled design, the potential impact of non-specific treatment effects (placebo) needs to be addressed in the discussion. A fairly robust placebo effect for pain treatments has been demonstrated (e.g., Hrobjartsson & Gotzsche, NEJM 2001;344:1594-1602).

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

10. The sample contract, referred to as appendix A, is missing.
11. Please elaborate on how psychiatric comorbidity was diagnosed (p. 7, lines 5-8). Was this based on clinical interview or were screening tests used?
12. The finding of no demonstrated benefit from substantial increases in opioid doses has significant clinical implications. Recommend greater attention to this finding in the discussion.
13. Polysubstance abuse was often suspected (p.15, line 5). How might this have affected treatment response?
14. The full name of the CES-D is Center for Epidemiological Studies – Depression Scale (p.2, line 12 and other points in manuscript).

Discretionary Revisions (which the author can choose to ignore)

15. Were data on past substance abuse/misuse analyzed as potential predictors of treatment response, substance misuse and/or dropout?
**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

None