Author's response to reviews

Title: Predictors of Opioid Misuse in Patients with Chronic Pain: A Prospective Cohort Study

Authors:

Timothy J Ives (tjives@med.unc.edu)
Paul R Chelminski (paul_chelminski@med.unc.edu)
Catherine A Hammett-Stabler (CStabler@unch.unc.edu)
Robert M Malone (rmalone@med.unc.edu)
J STEPHEN Perhac (john_perhac@med.unc.edu)
Nicholas M Potisek (nicholas_potisek@med.unc.edu)
Betsy BRYANT Shilliday (bbryant@med.unc.edu)
Darren A DeWalt (darren_dewalt@med.unc.edu)
Michael P Pignone (michael_pignone@med.unc.edu)

Version: 7 Date: 22 March 2006

Author's response to reviews: see over
Reviewer’s report
Predictors of Opioid Misuse in Patients with Chronic Pain: A Prospective Title:
Cohort Study
Version: 6 Date: 24 February 2006
Reviewer: James Zacny
Reviewer’s report:
General
The authors have presented a much better manuscript and have addressed most of my concerns. I think we will have to “agree to disagree” on the logic as well as the authors’ definition of opioid misuse. I disagree with urines testing positive for cocaine and amphetamines as part of the authors’ definition of opioid misuse. The authors are being inconsistent in their rationale: they argue it should be considered a measure of opioid misuse because in the contract it states that patients should not be taking illicit drugs while they are on opioid therapy. Yet, if a patient tested positive for marijuana (Schedule I drug, DEA, CSA), this was NOT considered a measure of opioid misuse. Instead urines testing positive for cannabinoids were predictors of opioid misuse. Further I do not understand the authors’ statement that “…concurrent use of cocaine and amphetamines (with opioids) is thought to increase the risk of diversion in order to procure additional stimulants.” (p. 7) Who thinks this – can a reference be provided?

We appreciate the reviewer’s help in improving the manuscript. We relied on the advice of other experts in pain management and substance abuse treatment in creating our definition of opiate misuse. The patterns of use of cocaine and amphetamines, including the extent of cravings and the degree of compulsive use, are different for cocaine and amphetamines than marijuana. Most of our advisors through the Society of General Internal Medicine Pain Interest Group reported that they would consider concurrent cocaine or amphetamine use to be incompatible with continuing opiates, but there was disagreement about whether marijuana use should be similarly sanctioned. This reason, more so than legal issues, led us to treat these conditions differently. We hope that we have made this clear in the manuscript and we appreciate the definitional dilemma discussed by the reviewer.

-------------------------------------------------------------------------------

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

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
Abstract: line 20: delete the word “a”
Corrected

p. 11, line 11: all other differences between non-misusers and misusers are given p values. What is the p value for cannabinoids?
P-Value inserted.

p. 12, lines 20-26: very nice and succinct paragraph
Thanks!

p. 13: the authors appear to be talking about substance abuse in this paragraph although some data specifically address opioid misuse, but I would add the word “substance” in line 2 to set the tone for the rest of the paragraph.
“Substance” added.

p. 14, line 20: are the authors referring to a contract (or medication agreement) that defines misuse and grounds for sanctions as “this pragmatic approach…”? I agree with them if that is what they mean, and ask them just to be more explicit.
The sentence has been edited to read “We believe that our pragmatic approach to monitoring opioid misuse based on the specific elements of the medication agreement can be replicated in primary care settings that do not have the resources to systematically evaluate patients for substance abuse or dependence.” In addition, the succeeding sentence has been deleted as it was essentially redundant.

p. 16, line 3: ref. 53 does not refer to only opioid misuse but also alcohol and sedative dependence. Table 1, 3, and 5 lists “% History of Alcohol Abuse” and Table 6 lists “% History of Ethanol Abuse.” Please choose one or the other term for the substance. Similarly Tables 1 and 3 list “Multiple Drug Convictions,” and Table 6 lists “Multidrug Convictions.”

Thanks for catching this. “Ethanol” has been changed to “alcohol” for sake of consistency.

Discretionary Revisions (which the author can choose to ignore)
P. 7, line 17: the authors and I both worry about nomenclature of words surrounding the issue of misuse/abuse/addiction. Therefore I wonder if the term “serious misuse” muddies up the water by implying there are gradations of misuse.
“Serious” has been deleted.

P. 8, line 17: I hope in the future if the authors conduct similar studies that they will extend their questioning of using non-prescribed or illicit drugs to heroin and benzodiazepines.
We agree and are seeking extramural funding for a follow-up study to investigate these issues.

p. 16, lines 10-11: I agree with the authors but I believe some studies have been done. I would ask the authors to consider integrating their findings with the extant literature. For example their findings seem to be quite consistent with Michna et al. 2004. Also Passik and colleagues and Russ Portenoy have discussed potential aberrant behaviors and I believe have categorized them as more or less likely to be strong predictors.
The sentence was meant to emphasize the need for additional prospective studies in primary care settings and has been edited to reflect this.