Drs. Fazel and Grann Reply

TO THE EDITOR: In our article, we investigated the population impact of patients with severe mental illness on violent crime by analyzing national hospital and crime registers in Sweden over a 13-year period. Overall, we estimated a population attributable risk fraction of 5.2%, suggesting that one in 20 violent crimes were committed by patients with hospital diagnoses of severe mental illness. In addition, we reported an increased risk of patients with severe mental illness to commit violent crimes (crude odds ratio=3.8, 95% confidence interval [CI] 3.7–3.9).

Dr. Pinta is right to point out that one of the reasons for this increased risk ratio may be that psychiatric patients are more likely to be criminalized than individuals without such illnesses. For example, psychiatric patients who offend may be more likely to be caught by the police or have poor legal representation when charged with a crime. In Sweden, courts routinely provide mentally disordered offenders with qualified legal representation, so having poor legal advice may not be an important factor. However, it is also possible that there is a greater likelihood that individuals with mental illnesses who commit violent acts are acquitted before charges are pressed or have their charges dropped before trial than the non-mentally disordered. This may be because the police or prosecuting authorities consider that it does not serve the public interest to pursue such criminal investigations. Thus, to summarize, we feel it is unlikely that the higher rate of violent convictions among the mentally ill is simply because of biased criminal justice processes.

Dr. Pinta suggests that it is not possible to draw conclusions about the causative relationship between mental illness and violent crime from our study. We agree—the main focus of our study was to estimate the population impact of patients with severe mental illness to violent crime. We stated in our article that the relationship between severe mental illness and violence is more complex than simple unidirectional causality and that a host of demographic, criminal history, and clinical risk factors will affect the relationship. This is also relevant in studies of the population impact of other mental disorders, such as substance abuse and dependence (1). The relative contribution of these various risk factors remains an important area of future research.

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Comments on "Prescription Drug Dependence and Evolving Beliefs About Chronic Pain Management"

TO THE EDITOR: Jon Streltzer, M.D. and Luther Johansen, M.D. presented a case of an unfortunate woman, a chronic pain patient, who developed an addiction to multiple drugs, including opioids, and finally overdosed. They use this case to develop a position against chronic opioid analgesic therapy, which they describe as a "medical subculture (1, p. 506)."

On behalf of *Pain Medicine*, we would like to take issue with some of the statements in this article that we consider inaccurate, as they are not adequately referenced.

Multidisciplinary pain centers did not develop to treat chronic pain patients with pain out of proportion to objective findings but to treat intractable chronic pain patients who had multiple comorbidities (2).

Treatment usually included detoxification because opioids were thought (with little evidence) to invariably cause addiction and decrease function (2).

Additional evidence (3) now supports the concept of "pseudoaddiction," originally based on one case report.

Contrary to their assertion of little evidence for chronic opioid analgesic therapy effectiveness, there is significant evidence for the efficacy, safety, and improvement in function with chronic opioid analgesic therapy. Two meta-analyses (4, 5) of more than 40 placebo-controlled chronic opioid analgesic therapy pain studies both showed opioids as more effective than placebo, and one (5) demonstrated improved functional outcomes. A structured evidence-based review (6) of 11 studies (2,877 patients) concluded that long-term chronic opioid analgesic therapy can lead to significant functional improvement. Other evidence suggests that chronic opioid analgesic therapy may be associated with low risk of abuse/addiction (2).

Many of the over 50 million American chronic pain patients benefit from management that includes opioids. Addiction disorders occur in 10%–15% of these patients and in the general population without pain. We must train physicians to treat pain effectively and safely based on evidence, including managing risks such as addiction.

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Drs. Streltzer and Johansen Reply

TO THE EDITOR: In our article, we cited current evidence that chronic opioid treatment, particularly in high doses, is associated with adverse physiological and psychological

consequences. Drs. Fishbain and Gallagher cite recent articles that they believe refute our thesis. We do not feel that this is the case.

Multidisciplinary pain clinics did not report that they were formed to prevent addiction, to our knowledge. Rather, the early clinics postulated that behavioral issues contributed to chronic pain complaints, which often seemed out of proportion to medical pathology. By not rewarding these complaints, either socially or with medication, they reported many treatment successes (1, 2).

The reference cited (Lusher et al.) does not describe cases of pseudoaddiction, but rather cases "at risk of pseudoaddiction." The cases selected were not opioid pain medication-seeking chronic pain patients, but rather patients undertreated for acute sickle-cell pain. The article's introduction and discussion reveals how problematic the concept of pseudoaddiction is.

The articles by Eisenberg et al., Furlan et al., and Devulder et al. review studies of opioid treatment for chronic pain. They reveal that the studies have been of short-term treatment, mostly funded by pharmaceutical companies, and the magnitude of pain relief, when present, was often small and of questionable clinical meaningfulness. Subjects in the trials may not be representative of the broader chronic pain population seen in clinical practice. They conclude that adequately designed trials have not been done and long-term studies are needed.

In a recent, detailed review of the pertinent literature, Clark et al. (3) conclude that "there remains no well-controlled, empirically sound evidence supporting the long-term effectiveness of opioid therapy for chronic noncancer pain."

In summary, reasonably well-designed studies of opioid treatment of chronic pain are almost all short-term treatment studies, usually using relatively low doses of opioids. We believe the current state of the evidence is as described by Ballantyne and Mao (4), that long-term, high-dose opioids for chronic pain have not been shown to be safe or effective. The case we presented details many of the problems associated with long-term prescription opioid intake.

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Oxcarbazepine and Pediatric Bipolar Disorder

TO THE EDITOR: In reference to the article by Karen Dineen Wagner, M.D., Ph.D., et al. (1), two issues need clarification regarding 1) generalizability of the study results and 2) issues of comorbidity and combination therapy.

First, in Table 1, the authors reported that the mean number of manic/hypomanic episodes ranged between 15.1–17.1 in the past year of the illness in the groups randomly assigned to oxcarbazepine and placebo, respectively. This seems to be in significant variance with the cohort recruited for the basic descriptive psychopathology study by Geller et al. (2), where, using arguably the best available state-of-the-art diagnostic methods and operationalized definitions of episodes and "cycling," the index episode of mania at intake had a mean duration of 3.5 years, and there were no subjects characterized as "rapid cyclers" (four or more mood episodes per year), but the vast majority of subjects had ultrarapid cycling or ultradian cycling within a single prolonged episode. The average age of the study subjects is not dissimilar, and the male predominance in the two studies is quite similar. Are we left to conclude that the study subjects are in fact composed of different phenotypes of mania or bipolar disorder? Or is there a difference in the way terms such as "episodes" or "cycles" are being used, reflecting disagreement between research groups? Do the authors have suggestions regarding terminology so that interested readers can make informed comparisons between studies regarding the description of basic research subject characteristics?

Second, it is noted that about one-third of subjects in each group remained on "stable stimulant therapy" from screening through the end of the study. Was any consideration given to a concern that stimulant therapy may have been making the mood episode worse or more unstable? If so, why, as a preliminary step, weren't subjects required to discontinue from stimulant therapy prior to randomization to observe the effect of this intervention on the overall mood state? Many clinicians believe that safe and effective use of psychostimulant therapy in pediatric patients with comorbid ADHD and mania requires effective mood stabilization prior to use of stimulant therapy (3). Could the authors review their data and report on whether concurrent treatment with stimulants affected baseline ratings of psychopathology or had a predictive, moderating, or mediating effect on the data through the course of the trial?

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