Letters to the Editor

Citalopram Discontinuation More Harmful Than Gradual Dosage Reduction?

TO THE EDITOR: We would like to compliment Rector et al. for their article, published in the September 2016 issue of the *Journal*, on the unwanted side effects of citalopram dosage reduction in a veteran population (1). This clinically relevant study justly warns against the precautionary principle, as Rosenheck states in his editorial accompanying the article (2). The results of the article, however, raise a few questions. The authors state that "[s]ubstantial numbers of subjects were censored after a 30-day gap in citalopram resupply." Thus, censored patients were patients who were officially prescribed dosages of 40 mg of citalopram or less, as well as those who ceased collecting their medication. Patients who were censored might also include patients who completely stopped taking citalopram, who conceivably were substantially more at risk for relapse and hospitalization. This detail raises questions about the magnitude of the results and validity of the conclusions. What proportion of the admissions and relapses could be attributed to this group of patients who did not receive citalopram anymore and who likely completely discontinued medication? And was the proportion of patients who did not collect their medication the same as in the group who was already censored, and in the group who was still at risk? How many of these supply-gap patients experienced relapse and hospitalization, compared with the group who followed a prescription of 40 mg or 20 mg of citalopram? Did these patients contribute a greater proportion of adverse events than were noted in the reduced-dosage group?

It would have been more clarifying to show survival curves for time to admission and/or time to relapse and to show separate curves for different levels of dosage decrease and the group of patients censored because of a supply gap (those who likely completely discontinued medication).

In addition, the at-risk population decreases rapidly at day 180, and only 7,058 remain. The true incidence of drug-induced long QT syndrome or torsade de pointes is unknown (3). A German prospective active surveillance study estimated the incidence of drug-induced long QT syndrome or torsade de pointes to be 2.5 per million per year for males (4). As the authors state in the Discussion section, the question is whether the total cohort had enough power to detect a significant difference between groups. Furthermore, as touched upon in the Discussion section, a potential major confounding effect is the survival effect. Patients using high dosages of citalopram might already have died before this study, thus creating a selection bias.

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Petrus J.C. Krijnsen, M.D.
Titus W.D.P. van Os, M.D., Ph.D.
Lex Wunderink, M.D., Ph.D.

From Friesland Mental Health Care Service, Department of Education and Research, Leeuwarden, the Netherlands; the Department of Geriatric Medicine, Medical Center Leeuwarden, Leeuwarden, the Netherlands; and the Department of Psychiatry, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands.

Address correspondence to Dr. Krijnsen (jeroen.krijnsen@znb.nl).

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Clarifying Methods in a Study of Outcomes of Citalopram Dosage Risk Mitigation in a Veteran Population: Response to Krijnsen et al.

TO THE EDITOR: We appreciate the interest in our retrospective cohort study of efforts to reduce the risk associated with the prescribing of higher dosages of citalopram. Initially, all members of the study cohort had citalopram prescriptions for dosages that exceeded a new Food and Drug Administration safety limit of 40 mg/day. All endpoint events that occurred before the first indication we had that the citalopram prescription might have been discontinued (i.e., a 30-day lapse in prescription resupply) were counted in the group or time period when the exceedingly high citalopram dosages were assumed to be continued. As discussed in the article, this possible misclassification of endpoint events into the higher dosage group would bias against finding an increased risk of hospitalizations after the citalopram dosages were reduced. All endpoint events that occurred after subjects were censored because of a 30-day lapse in citalopram resupply were excluded from the analyses. Some of these postcensoring events would have been captured by the sensitivity analysis using a 90-day lapse in resupply before censoring that produced