Author's response to reviews

Title: Dose patterns in commercially insured subjects chronically exposed to opioids: a large cohort study in the United States

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Abstract

Background

Little data exist on how opioid doses vary with the length of exposure among chronic opioid users.

Methods

To characterize the change in the dosage of opioids over time, a retrospective cohort study using the PharMetrics database for the years 1999 through 2008 was conducted. Individuals exposed to opioids in 2000 who had 2 opioid dispensings at least 6 months apart and were opioid naive (did not receive any opioid 6 month before their exposure in 2000) were included. The date of the first dispensing in 2000 was defined as the index date and had to be for a strong and full agonist opioid. All opioid doses were converted to oral morphine equivalent doses. Exposure was classified as continuous or intermittent. Mean, median dosage, interquartile range, and 95th percentile of opioid dose over 6-month periods, as well as the percentage of subjects who ever received a high or very high opioid dose, were calculated.

Results

A total of 57,345 subjects were included. The mean age was 44 years and 54.5% of subjects were women. Intermittent exposure was observed in 99% of subjects; continuous exposure was observed in 1% of subjects. The mean duration of exposure for the subjects who were continuously exposed to opioids was 477 days. In subjects with no cancer diagnosis who were continuously exposed to opioids, the mean, 25th,
50th, and 75th percentile of dose was stable during the first 2 years of use, but the 95th percentile increased. Seven percent of them were exposed to doses of 180 mg or more of morphine at some point.

**Conclusions**

Dose escalation is uncommon in subjects with intermittent exposure to opioids. For subjects with continuous exposure to opioids who have cancer, doses rise substantially with time. For those without cancer, doses remain relatively stable for the first 2 years of use, but subsequently increase. Seven percent of subjects with no cancer diagnosis will be exposed to daily doses of 180 mg or more of morphine equivalent at some point.