We assessed whether calculations of reporting rates based on a more conservative estimate of the patient population (ie, patients prescribed extended-release injectable suspension of naltrexone (XR-NTX) for opioid use disorder [OUD]) would affect the overall conclusions of the primary analysis. Here, any adverse event reported as an opioid overdose was considered for each latency group, and patient exposure for OUD was estimated at 50% of the overall patient exposure (ie, 50% of 495,602 patients exposed). Reporting rates were calculated based on the number of opioid overdose events in each latency group relative to the estimated patient exposure for OUD and expressed per 10,000 patients exposed.

\[
\text{reporting rate, opioid overdose (OUD)} = \frac{\text{opioid overdose events}}{\text{estimated overall patient exposure for OUD}} \times 10,000 \text{ patients}
\]

The 95% confidence intervals (CIs) were calculated using the Clopper-Pearson method [1].

Sixty-six cases reporting opioid overdose events were assessable for latency. The estimated reporting rates (per 10,000 patients) for the 66 assessable cases were 1.09 (95% CI, 0.72–1.59), 0.69 (95% CI, 0.4–1.1), and 0.89 (95% CI, 0.56–1.35) for ≤ 28 days, 29–56 days, and > 56 days from the last dose of XR-NTX, respectively (Supplementary Table).

Reference 1. Clopper, Pearson ES. Biometrika. 1934;26:404–13.
### Supplementary Table

Number of cases and reporting rates of opioid overdoses in patients treated for OUD from April 2006 to April 2018

| Time from last XR-NTX dose | Opioid overdoses in patients treated for OUD (estimated) n (per 10,000 patients) |
|---------------------------|--------------------------------------------------------------------------------|
|                           | All cases                                                                       |
| ≤ 28 days                 | 27 (1.09; 95% CI, 0.72–1.59)                                                   |
| 29–56 days                | 17 (0.69; 95% CI, 0.4–1.1)                                                     |
| > 56 days                 | 22 (0.89; 95% CI, 0.56–1.35)                                                   |
| Unassessable cases        | 95 (3.83; 95% CI, 3.1–4.69)                                                    |
| Total cases               | 161 (6.5; 95% CI, 5.53–7.58)                                                   |
|                           | Serious cases                                                                   |
| ≤ 28 days                 | 22 (0.89; 95% CI, 0.56–1.35)                                                   |
| 29–56 days                | 13 (0.52; 95% CI, 0.28–0.9)                                                    |
| > 56 days                 | 22 (0.89; 95% CI, 0.56–1.35)                                                   |
| Unassessable cases        | 58 (2.34; 95% CI, 1.78–3.03)                                                   |
| Total cases               | 115 (4.64; 95% CI, 3.83–5.57)                                                  |
|                           | Fatal cases                                                                     |
| ≤ 28 days                 | 12 (0.48; 95% CI, 0.25–0.85)                                                   |
| 29–56 days                | 8 (0.32; 95% CI, 0.14–0.65)                                                    |
| > 56 days                 | 20 (0.81; 95% CI, 0.49–1.25)                                                   |
| Unassessable cases        | 47 (1.9; 95% CI, 1.39–2.53)                                                   |
| Total cases               | 87 (3.51; 95% CI, 2.81–4.33)                                                  |

Note. Unassessable cases were cases with incomplete information for dates. CI confidence interval, OUD opioid use disorder, XR-NTX extended-release naltrexone. 

N = 247,801 for OUD assuming 50% of patients were treated for OUD; the number of patients exposed to XR-NTX was estimated based on XR-NTX units distributed and an estimated treatment persistence of 3.5 units per patient.