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**Retrospective reports of itching with initial opioid misuse are strongly associated with risk of opioid use disorder (OUD), specific OUD symptoms, and more problematic course**

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**Background:** Identifying opioid users with increased risk of opioid use disorder (OUD) has clear clinical importance. **Methods:** Retrospectively assessed subjective effects of initial opioid misuse were examined in opioid misusers including those with limited nonmedical use ( $\leq 60$  times lifetime) and those with a history of daily or near daily use and OUD treatment. **Results:** Individuals who endorsed itching with initial opioid misuse were more likely to meet criteria for OUD [OR 8.74 (6.00 – 12.73);  $p=1.30 \times 10^{-22}$ ] and to first misuse opioid at a significantly younger age [20.2 (SD 6.8) vs 22.8 (SD 9.5);  $p=3.08 \times 10^{-5}$ ]. In those with OUD, report of itching was associated with more frequent endorsement of opioid tolerance, withdrawal, craving, any IV use, and daily IV use; these effects remained significant with addition of mean item scores for five Addiction Research Center Inventory scales to regression models. **Conclusions:** Our findings provide strong evidence that retrospective report of itching with initial opioid misuse is significantly greater in those with OUD. Reports of itching are associated with greater endorsement of tolerance, craving, and withdrawal by those with OUD and with greater progression to IV use and daily IV opioid use. Prior research has implicated specific *OPRM1* isoforms in opioid-induced pruritus; our findings may thus inform future research into OUD pathophysiology including specific OUD symptoms. A prospective examination is needed to determine if assessment of itching and other subjective effects after initial use has predictive utility for identification of those individuals more likely to progress to OUD and daily IV use.