

# MI-CRE 2023 Annual Research Symposium and Policy Forum

## *Opioid analgesic exposure during the first trimester of pregnancy and the risk of major congenital malformations in infants: a systematic review and meta-analysis*

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**Is Presenter an HDR Student?** Yes

**Has Research been submitted/presented elsewhere:** No

### **Abstract**

**Background and Aims:** Opioid analgesics are treatment options to manage pain in pregnancy. Previous research has linked opioid exposure during the first trimester to increased risks of major congenital malformations in infants, but uncertainty remains due to conflicting evidence. We aimed to synthesise evidence on these risks for all opioids, and for individual opioids.

**Design and Methods:** In this systematic review and meta-analysis, we searched PubMed, Embase and CINAHL for randomised and non-randomised studies published between January 1, 2000, to May 10, 2022. We log-transformed adjusted risk estimates and standard errors, and then pooled the results using a random-effects meta-analysis. Sensitivity analysis included performing a Bayesian analysis.

**Results:** We included data from eight cohorts comprising a total of 105,500 exposed infants drawn from 5.3 million pregnancies in the meta-analysis. We did not observe a substantial increase in the risk for overall major malformations, cardiovascular malformations, or central nervous system malformations in infants exposed to opioids compared with those unexposed to opioids. We found risks were raised for gastrointestinal malformations (relative risk (RR) 1.40; 95% CI 0.38, 5.16) and cleft palate (RR 1.57; 95% CI 0.48, 5.13) for any opioid exposure, although confidence intervals were wide. Codeine-exposed infants had a 20% increased risk of atrial septal defects (1.20; 95% CI 1.05, 1.36) relative to unexposed infants, although confidence intervals were wider in the sensitivity analysis (1.19, 95% CrI 0.83, 1.71).

**Conclusions:** Opioid exposure during early pregnancy was not meaningfully associated with an increased risk of most malformations examined. Clinicians should be aware of a possible increased risk of gastrointestinal malformations, cleft palate, and atrial septal defects, although these findings require confirmation.

**Impact:** This study provides the most comprehensive evidence to date and informs decisions regarding the management of pain among pregnant women and among women of reproductive age, who might unintentionally become pregnant.