# CO-EXISTENT MENTAL HEALTH DISORDERS AND INFERTILITY: A UNIQUELY VULNERABLE POPULATION

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## BACKGROUND

- Anxiety and depression are disproportionately common co-morbidities within the group of people seeking fertility treatment, with rates estimated to be five times higher compared to the general population
- Both anxiety and depression and fertility treatment have been associated with increased risks of adverse maternal outcomes and fetal complications including preterm labor, diabetes, preeclampsia, fetal growth restriction, and neonatal death
- Despite these interactions, the specific impact of both having a history of anxiety and/or depression and conceiving with fertility treatment has been poorly studied

## PURPOSE & OBJECTIVES

To quantify the additional obstetric risks of having anxiety and/or depression and conceiving with fertility treatment beyond each of these risks individually.

## MATERIAL & METHODS

- Retrospective population-based cohort study
- Linked database of hospital discharge data (*California Department of Health Care Access and Information*) and vital statistics (*California Department of Public Health*)
- Inclusion criteria:
  - Singleton, non-anomalous births
  - Gestational age 23-42 weeks
  - January 1, 2008 through December 31, 2020
- **Exposures:**
  - **Having anxiety and/or depression**
    *Identified via anxiety- and/or depression-related ICD-9 or ICD-10 codes recorded in hospital discharge data*
  - **Pregnancy conceived with fertility treatment**
    *Captured in the California Vital Statistics database*
- **Primary outcome:** Severe maternal morbidity (SMM)
- Secondary outcomes:

| Maternal | Neonatal |
|---|---|
| • Gestational diabetes<br>• Hypertensive disorders of pregnancy<br>• Placental abruption<br>• Postpartum hemorrhage | • Preterm birth (<37w)<br>• NICU admission<br>• Hypoglycemia<br>• Respiratory distress syndrome<br>• Small for gestational age<br>• Apgar score <7 at 5 min<br>• Infant death |

- Data analysis:
  - Demographics and perinatal outcomes compared using chi-square tests
  - Multivariable Poisson regression models of exposure groups and perinatal outcomes; neither fertility treatment nor mental health diagnosis as reference
  - All models adjusted for maternal race and ethnicity, age, education, pre-pregnancy BMI, insurance, parity, number of prenatal visits, chronic hypertension, pre-existing diabetes and substance use
  - Statistical significance was set at 0.005 because of multiple comparisons

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Maternal history of anxiety and/or depression and use of fertility treatment together have an outsized effect on the risk of severe maternal morbidity and other critical maternal and neonatal outcomes

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## RESULTS

Table 1: Demographics of birthing individuals in linked California database

| Exposure | Neither | Anxiety and/or depression only | Fertility treatment only | Both | p-value |
|---|---|---|---|---|---|
| N | 4,649,977 | 137,487 | 33,474 | 2,076 | |
| **Maternal age (Years)** | | | | | <0.001 |
| <20 | 6.4% | 3.6% | 0.1% | 0.1% | |
| 20-34 | 73.9% | 70.2% | 37.4% | 33.4% | |
| ≥35 | 19.6% | 26.2%) | 62.4% | 66.5% | |
| **Pre-pregnancy BMI** | | | | | <0.001 |
| <18.5 | 3.9% | 3.0% | 3.4% | 2.1% | |
| 18.5-24.9 | 47.1% | 41.9% | 57.9% | 50.0% | |
| 25.0-29.9 | 26.4% | 26.4% | 23.0% | 25.6% | |
| ≥30 | 22.6% | 28.7% | 15.7% | 22.3% | |
| **Anxiety/depression** | | | | | <0.001 |
| None | 100.0% | -- | 100.0% | -- | |
| Anxiety | -- | 43.3% | -- | 52.6% | |
| Depression | -- | 40.5% | -- | 30.9% | |
| Both | -- | 16.2% | -- | 16.5% | |
| **Fertility treatment** | | | | | <0.001 |
| None | 100.0% | 100.0% | -- | -- | |
| Fertility-enhancing drugs | -- | -- | 24.5% | 26.2% | |
| Assisted reproductive technologies | -- | -- | 68.1% | 64.4% | |
| Both | -- | -- | 7.4% | 9.4% | |

## RESULTS

Figure 1: Multivariable Poisson regression models for maternal outcomes with adjusted* risk ratio and 99.5% confidence intervals
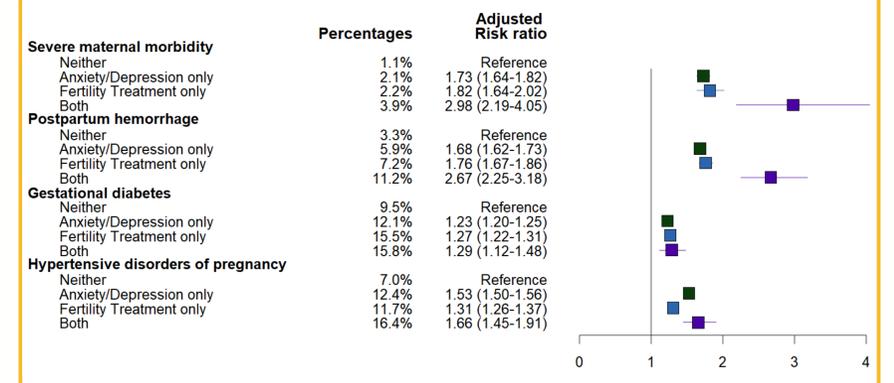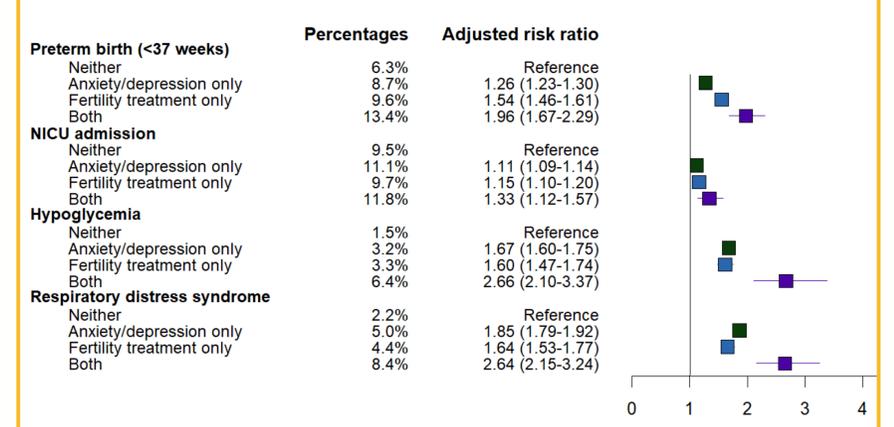
| | Percentages | Adjusted Risk ratio |
|---|---|---|
| **Severe maternal morbidity** | | |
| Neither | 1.1% | Reference |
| Anxiety/Depression only | 2.1% | 1.73 (1.64-1.82) |
| Fertility Treatment only | 2.2% | 1.82 (1.64-2.02) |
| Both | 3.9% | 2.98 (2.19-4.05) |
| **Postpartum hemorrhage** | | |
| Neither | 3.3% | Reference |
| Anxiety/Depression only | 5.9% | 1.68 (1.62-1.73) |
| Fertility Treatment only | 7.2% | 1.76 (1.67-1.86) |
| Both | 11.2% | 2.67 (2.25-3.18) |
| **Gestational diabetes** | | |
| Neither | 9.5% | Reference |
| Anxiety/Depression only | 12.1% | 1.23 (1.20-1.25) |
| Fertility Treatment only | 15.5% | 1.27 (1.22-1.31) |
| Both | 15.8% | 1.29 (1.12-1.48) |
| **Hypertensive disorders of pregnancy** | | |
| Neither | 7.0% | Reference |
| Anxiety/Depression only | 12.4% | 1.53 (1.50-1.56) |
| Fertility Treatment only | 11.7% | 1.31 (1.26-1.37) |
| Both | 16.4% | 1.66 (1.45-1.91) |



Figure 2: Multivariable Poisson regression models for neonatal outcomes with adjusted* risk ratio and 99.5% confidence intervals

| | Percentages | Adjusted risk ratio |
|---|---|---|
| **Preterm birth (<37 weeks)** | | |
| Neither | 6.3% | Reference |
| Anxiety/depression only | 8.7% | 1.26 (1.23-1.30) |
| Fertility treatment only | 9.6% | 1.54 (1.46-1.61) |
| Both | 13.4% | 1.96 (1.67-2.29) |
| **NICU admission** | | |
| Neither | 9.5% | Reference |
| Anxiety/depression only | 11.1% | 1.11 (1.09-1.14) |
| Fertility treatment only | 9.7% | 1.15 (1.10-1.20) |
| Both | 11.8% | 1.33 (1.12-1.57) |
| **Hypoglycemia** | | |
| Neither | 1.5% | Reference |
| Anxiety/depression only | 3.2% | 1.67 (1.60-1.75) |
| Fertility treatment only | 3.3% | 1.60 (1.47-1.74) |
| Both | 6.4% | 2.66 (2.10-3.37) |
| **Respiratory distress syndrome** | | |
| Neither | 2.2% | Reference |
| Anxiety/depression only | 5.0% | 1.85 (1.79-1.92) |
| Fertility treatment only | 4.4% | 1.64 (1.53-1.77) |
| Both | 8.4% | 2.64 (2.15-3.24) |



## CONCLUSIONS

- People with anxiety and/or depression who conceive with fertility treatment have significantly elevated risks of SMM and other adverse maternal and neonatal outcomes
- Further studies are needed to determine whether additional prenatal screening or monitoring may be appropriate within this population.

## SUPPLEMENTARY TABLES



## REFERENCES