

## 論文の内容の要旨

論文題目 Association between perinatal mood disorders of parents and child health outcomes: analysis using an administrative claims database

(両親の周産期気分障害と子どもの健康の関連：レセプトデータを用いた検討)

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### INTRODUCTION:

Perinatal mood disorders are common mental disorders that can occur to both mothers and fathers during a perinatal period during pregnancy and up to one year after childbirth. Perinatal mood disorders can lead to various negative consequences, affecting the physical and psychological health of parents and children. Fathers may influence child health through multiple mechanisms, including parenting, parent-child interactions, genetic factors, environmental factors, marital conflict, and support for mothers. The effect of paternal perinatal mood disorders, however, has not been well investigated in association with adverse outcomes, especially low birth weight, failure to thrive, delayed motor development, dental caries, autism spectrum disorder (ASD), and medical costs of children. The effect of maternal perinatal mood disorders on adverse child outcomes has been investigated in many previous studies, but adjustments for paternal perinatal mood disorders and perinatal antidepressant use have not been considered for most outcomes.

Using an administrative claims database of health insurance in Japan, the study had several aims: (1) The study primarily aimed to examine the association between perinatal mood disorders and low birth weight, failure to thrive, delayed motor development, ASD, and dental caries of children by the age of 36 months, which have not been investigated in previous studies. (2) The study also aimed to examine the association between paternal and perinatal mood disorders and child health outcomes, including preterm birth, language disorders, behavioral and emotional disorders, and child medical costs by the age of 36 months, to improve the generalizability of the previous literature. (3) The study also aimed to investigate the effect of maternal mood disorders on child health outcomes, including low birth weight, premature birth, failure to thrive, delayed motor development, language development disorders, ASD, behavioral and emotional disorders, and medical costs of children by the age of 36 months, after adjusting for paternal perinatal mood disorders and antidepressant use, overcoming the limitations of the previous literature.

### METHODS:

A retrospective cohort study was conducted on mother-father-child triads of Japanese families in the JMDC Claims Database (JMDC Inc., Tokyo, Japan). The JMDC Claims Database is a health insurance claims database that contains inpatient and outpatient medical data (diagnostic codes, diagnostic tests, and

procedures), dental data, and prescription data, which can be linked between parents and their children in the same household.

The study included children born from August 2011 to August 2017 who were registered as family members of health insurance subscribers and their mothers and fathers. Parents with available data from 15 months prior to the child's date of birth to 12 months after the child's birth were included in the study. Children were removed from the sample due to death, as well as the specific conditions of parents (death, retirement from the company, age 75 years or older, change in household status). Paternal and maternal perinatal mood disorders were identified using medical diagnostic codes for mood disorders (ICD-10 codes: F30-39, O993) combined with antidepressant prescriptions (ATC codes: N06A, N05AN01) or psychiatric treatment codes appearing on the same month as diagnostic codes, from 9 months prior to the child's date of birth to 12 months after child's birth. The physical and psychological outcome measures were identified by ICD-10 codes. The cumulative medical costs of children for inpatient and outpatient medical and dental care was calculated for time intervals 0-12 months and 13-36 months of age. For neonatal outcomes, multiple logistic regression analyses were conducted to compute odds ratios (ORs) of parental perinatal mood disorders for outcomes after adjusting for child sex, age of the parent under study at child's birth, and antidepressant use. Multiple logistic regression analyses stratified according to the past history of parental mood disorders prior to pregnancy were also conducted. As some children were removed before the age of 36 months, Cox proportional hazard models were used to consider variation in the observation period to compute hazard ratios of parental perinatal mood disorders for adverse child outcomes by the age of 36 months, after adjusting for covariates. Cox proportional hazard analyses stratified according to the past history of mood disorders were also conducted. Supplemental analyses of ASD considering unmeasured time-invariant factors were explored, including adjustment for parental developmental disorders using ICD-10 codes as covariates, sibling case study, and instrumental variable (IV) analyses. For the medical costs, multivariate negative binomial regression was conducted to compare adjusted means of medical costs per child between children of parents with mood disorder and those without perinatal mood disorders, after adjusting for covariates. A p-value of 0.05 was used to indicate statistical significance.

## **RESULTS:**

A total of 65,804 father-mother child triads were included for analysis, of whom 1,957 fathers (3.0%) and 1,381 mothers (2.1%) were diagnosed with perinatal mood disorders. Some 1,036 fathers (1.6%) and 472 mothers (0.7%) received antidepressants.

In this study, paternal perinatal mood disorders were not significantly associated with adverse childhood outcomes. An unexpected finding was a negative association between paternal perinatal mood disorders and language development disorder (adjusted HR 0.31, 95% CI: 0.13-0.73). The average medical costs of children between 0 and 12 months, and between 13 and 36 months were

significantly lower for children with fathers with perinatal mood disorders than those of fathers with no mood disorders ( $p = 0.019$ ,  $p = 0.025$ , respectively).

Maternal perinatal mood disorders were associated with most of the outcomes, including delayed motor development, language development disorders, ASD, and behavioral and emotional disorders (adjusted HR 2.18, 95% [CI 1.39-3.41]; adjusted OR 3.01, 95% CI [1.90-4.77]; adjusted HR 4.27, 95% CI [2.66-6.86]; adjusted HR 4.24, 95% CI [1.38-13.01], respectively), even after adjusting for paternal perinatal mood disorders and antidepressant use. In stratified analyses, mothers with perinatal mood disorders but no past history of the condition prior to pregnancy were significantly associated with ASD more than were mothers with no perinatal and past mood disorders (adjusted HR 3.10, 95%CI [1.45-6.65]). Due to a limited sample size and weak association of candidate IV variables and disorders, adjustments for parental developmental disorders, sibling case study, and IV analysis were not applied in the study. The average medical costs of children between 0 and 12 months, and between 13 and 36 months were significantly higher for children of mothers with perinatal mood disorders than those of mothers with no mood disorders ( $p = 0.000$ ,  $p = 0.000$ , respectively).

## **DISCUSSION:**

The findings of the study suggested that paternal perinatal mood disorders were not strongly associated with adverse child outcomes. This study provided evidence that paternal perinatal mood disorders were not significantly associated with adverse child outcomes among subscribers of society-managed health insurance for large companies in Japan. Characteristics of the study population may have contributed to the non-significant association observed in most child outcomes. The current study population included father-mother-triads in the same income household (the dependent spouse of a primary insurance payer should not have an annual income exceeding ¥1,300,000) and did not include homes with single or teenaged fathers. Future studies should examine the effect of paternal perinatal mood disorders on adverse child outcomes in participants with different social backgrounds and family structures.

This study showed that maternal perinatal mood disorders were associated with most of the outcomes, including delayed motor development, language development disorders, ASD, and behavioral and emotional disorders, even after adjusting for paternal perinatal mood disorders and antidepressant use. The study confirmed previous findings from limited countries in the sample, extended the findings to a sample of families in Japan, and expanded the generalizability of the findings. The study also showed that maternal perinatal mood disorders were significantly associated with higher medical costs between 0 and 36 months, after adjusting for covariates. The study suggested that maternal perinatal mood disorders imposed an economic burden on society by incremental medical costs by the age of 36 months. This study addressed a need for early identification of mothers with perinatal mood disorders and their children who are at risk for adverse health outcomes. Future studies on maternal perinatal mood disorders should

aim to discover how to alleviate the adverse effect of perinatal mood disorders on child outcomes.

## **CONCLUSION:**

Paternal perinatal mood disorders were not significantly associated with adverse child outcomes observed in the study. Maternal mood disorders were significantly associated with adverse child outcomes of children by the age of 36 months, after adjusting for paternal perinatal mood disorders and antidepressant use. Future studies should explore the effect of paternal perinatal mood disorders with different social backgrounds and familial roles on child outcomes. Future studies on maternal perinatal mood disorders should be directed toward early prevention and intervention strategies to reduce the negative consequences on children.