Mode of delivery and short-term maternal mental health: A follow-up study in the Danish National Birth Cohort

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Abstract

Objective: To estimate associations between mode of delivery and maternal mental health 6 months postpartum.

Methods: Follow-up of mothers in the Danish National Birth Cohort. Symptoms of anxiety, depression or stress were self-reported at gestational week 30 and 6 months postpartum. Mode of delivery was categorized as spontaneous vaginal birth, instrumental vaginal birth, planned cesarean section and emergency cesarean section. Multiple linear and logistic regression models were used to compute differences and odds ratios (ORs) with 95% confidence intervals (CIs) for associations between delivery mode and mental health indicators adjusted for mental health before and during pregnancy.

Results: Among 54,474 mothers, mental health indicators improved from pregnancy to 6 months postpartum for all delivery modes. Improvement was smallest in mothers with emergency cesarean section. Thus, compared to women with a spontaneous vaginal birth, women with emergency cesarean section more frequently reported symptoms of anxiety (OR 1.11; 0.98–1.24), depression (OR 1.25; 1.09–1.43) and stress (OR 1.14; 1.01–1.29) 6 months postpartum, and women with planned cesarean section more frequently reported symptoms of anxiety (OR 1.15; 1.01–1.29).

Conclusion: Mental health improved from pregnancy to 6 months postpartum regardless of delivery mode. Mothers with emergency cesarean section experienced more symptoms of emotional distress 6 months postpartum.

Keywords
cesarean section, delivery, epidemiology, mental health, mothers, obstetrics, parturition, psychological distress
1 | INTRODUCTION

Obstetric interventions, including cesarean section (CS), have increased worldwide during the past 30 years to a frequency higher than the 10%-15% recommended by most experts, e.g., 25% in Europe and 32% in Northern America. Reasons for the increase include higher maternal age and morbidity, and more CSs on maternal request. CS can be a lifesaving intervention and is underused in some low-income countries. However, it has also been associated with increased risk of obstetric complications, more maternal morbidity and poorer outcome for mother and baby in subsequent pregnancies.

Mode of delivery has also been related to mental health following childbirth. In some, but not all, studies, CS has been associated with an increased risk of symptoms of emotional distress in the first year after childbirth, postpartum depression, and post-traumatic stress disorder. The inconsistent findings may be explained by small sample sizes, and unmeasured factors such as mental health before and during pregnancy.

In this study, we used prospective data from a large ongoing cohort study of Danish mothers to examine the associations between mode of delivery and self-reported mental health 6 months postpartum taking into account mental health before and during pregnancy.

2 | MATERIALS AND METHODS

The study was a prospective cohort study within the Danish National Birth Cohort (DNBC). DNBC is a nationwide ongoing data collection that, between 1996 and 2002, recruited 100 413 pregnancies of 91 381 women, equivalent to approximately 30% of all births in that period. More detailed information about the cohort can be found elsewhere. Women were invited at the first antenatal visit to the general practitioner, and the main data collection consisted of two telephone interviews in pregnancy at approximately gestational weeks 16 and 30 (Interviews 1 and 2) and one interview 6 months postpartum (Interview 3). All questionnaires were pilot-tested and supplemented by a protocol to ensure homogeneity between interviewers. Data were linked to Danish population-based health registries using unique personal identification numbers given to all residents in Denmark. The DNBC was originally approved by all research ethics committees in Denmark and by the Danish National Data Protection Agency (Ref. no 2015-57-0102). All participants provided informed written consent. This study was approved by The DNBC Steering Committee (Ref. no 2018–33).

Information about mode of delivery for the index birth in the DNBC was obtained from the National Patient Register and the Danish Medical Birth Registry. Mode of delivery was classified as: "Spontaneous vaginal birth", "Instrumental vaginal birth", "Planned CS" (CS prior to labor) and "Emergency CS" (CS during labor). All instrumental vaginal births were by vacuum extraction.

The outcome was self-reported mental health from nine questions in Interview 3 approximately 6 months postpartum. The questions referred to the entire period since birth (Table 1). Three questions about symptoms of anxiety and three questions about symptoms of depression originated from the validated Symptoms Checklist-92 (SCL-92). The possible answers were originally classified into five categories, but in the DNBC, a three-point Likert scale was used ("Not at all" = 0, "A little" = 1, and "A lot" = 2). Three questions about stress originated from the validated General Health Questionnaire 60 (GHQ60), where it originally had four answer categories. In the DNBC, possible answers were the same three-point Likert scale as described above. A combined measure of emotional distress 6 months postpartum was generated as a summed continuous score for all nine questions (potential range 0-18). To measure presence of emotional distress 6 months postpartum, the combined score was dichotomized according to an a

| TABLE 1 | Questions on mental health included in interview 2 and 3 |
|---------|----------------------------------------------------------|
| Questions | Item covering symptoms of... | Items originating from | Scale |
| Have you during the pregnancy/since birth... | | | |
| Felt frightened and anxious for any reason? | Anxiety | SCL-92 | 0-2 |
| Felt nervous or at unease? | Anxiety | SCL-92 | 0-2 |
| Felt tense or adrenalized? | Anxiety | SCL-92 | 0-2 |
| Summed (cut-off 90th percentile) | | | 0-6 |
| Felt that the future looked hopeless? | Depression | SCL-92 | 0-2 |
| Felt sad and blue? | Depression | SCL-92 | 0-2 |
| Felt that everything was a big effort? | Depression | SCL-92 | 0-2 |
| Summed (cut-off 90th percentile) | | | 0-6 |
| Felt under a constant pressure? | Stress | GHQ60 | 0-2 |
| Been more touchy and quick-tempered than usually? | Stress | GHQ60 | 0-2 |
| Felt that the demands made on you were too big? | Stress | GHQ60 | 0-2 |
| Summed (cut-off 90th percentile) | | | 0-6 |
| Combined emotional distress (cut-off 90th percentile) | | | 0-18 |

Abbreviations: SCL-92, Symptoms Checklist-92; GHQ60, General Health Questionnaire 60.
prior defined cut-off value closest to the 90th percentile. Specific outcome variables of anxiety, depression and stress were generated by summing the scores for the three questions related to each variable (potential range 0–6), which were then dichotomized according to a cut-off value closest to the 90th percentile. Women exceeding the cut-offs were referred to as having symptoms of anxiety, depression or stress, respectively.

Information on mental health in pregnancy was obtained from Interview 2. The questions in pregnancy were identical to the nine questions asked 6 months postpartum and referred to the entire previous period of pregnancy (Table 1). A combined measure of mental health during pregnancy was generated as a summed continuous score for all nine questions.

Potential confounders were selected a priori using directed acyclic graphs. Calendar year of childbirth, maternal age at conception, and parity were obtained from The Danish Medical Birth Registry. From Interview 1, we obtained self-reported information on body mass index, number of cigarettes per day, number of standard alcoholic drinks per week, minutes of physical activity per week, socio-occupational status (defined by education and occupation in early pregnancy and divided into “Low” [unskilled work or unemployment], “Middle” [skilled manual work and/or less than 4 years of education after high school] and “High” [job as a manager and/or four or more years of education after high school]), chronic disease (metabolic diseases, diseases of the muscles or joints, diabetes, heart disease, epilepsy or other serious illnesses diagnosed by a doctor prior to Interview 1), and pre-pregnancy mental health (self-reported mental conditions or diagnoses that had led to a consultation with a doctor or psychologist prior to the first pregnancy in the DNBC). Self-reported information on breastfeeding duration was obtained from Interview 3 and defined by the total period of any breastfeeding (exclusive or partly) in weeks.

For the present study, we defined a study population initially consisting of the 92,662 live singleton births within the DNBC (Figure 1). Since some mothers participated in the cohort with more than one birth, all births except the first within the cohort were excluded (n = 6452) to ensure independent observations. Mothers not participating in Interview 1 (n = 5520) and Interview 2 (n = 4953) in pregnancy were excluded, as were mothers not participating in Interview 3–6 months postpartum (n = 16,236). Mothers with missing answers on maternal mental health 6 months postpartum (n = 137) were also excluded. Since preterm birth may potentially affect both mode of delivery and postpartum mental health, births before gestational week 37 were excluded (n = 2362). Finally, 2528 mothers were excluded due to missing covariate information, leading to a final study population consisting of 54,474 mothers. Approximately 50% of the final study population were primigravidae.

Linear regression was used to examine the association between mode of delivery and the composite score of emotional distress using the mean individual change in scores from pregnancy week 30 to 6 months postpartum. Furthermore, the associations between mode of delivery and presence of symptoms of emotional distress, anxiety, depression, or stress 6 months postpartum were estimated and presented as crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) using logistic regression.

In the first adjusted model, we controlled for maternal age at conception, parity, calendar year of childbirth, pre-pregnancy BMI, smoking, alcohol intake, physical activity, socio-occupational status, and chronic disease. In the second adjusted model, we further controlled for pre-pregnancy mental health problems and mental health during pregnancy. Maternal age, year of childbirth, BMI, and the combined emotional distress score of mental health in pregnancy were included as continuous variables, other variables as presented in Table 2. Analyses were repeated in first time mothers only, eliminating the possible confounding effects of prior birth experiences on the baseline mental health of the women. To test the robustness of our findings, we performed several sensitivity analyses. First, we tested the robustness of the cut-off used for the mental health variables by altering the cut-off from the value closest to the 90th percentile, as used in the main analysis, to the value closest to the 80th percentile. We also restricted the analyses to mothers with no recorded pre-pregnancy mental health problems. In a third sensitivity analysis, we omitted adjusting for year of childbirth. As breastfeeding was considered a potential intermediate factor, it was not adjusted for in the main analyses, but in a sensitivity analysis. Analyses were performed using STATA (version 15.0 Stata Corp).

3 | RESULTS

Of 54,474 mothers, 41,182 (75.6%) had a spontaneous vaginal birth, 5393 (9.9%) an instrumental vaginal birth, 3650 (6.7%) a planned CS and 4249 (7.8%) an emergency CS (Table 2).

Spontaneous vaginal birth or planned CS were more frequent in multiparous women, in women who smoked, had a higher alcohol intake, or a lower socio-occupational status (Table 2). Planned or emergency CS were more frequent in older women, women with a higher BMI, and women with chronic disease. Instrumental vaginal birth or emergency CS were more frequent in primiparous women. Pre-pregnancy mental health problems were more often seen with planned or emergency CS, whereas symptoms of emotional distress in pregnancy were reported more often by women with a planned CS.

The mean emotional distress score decreased from pregnancy to 6 months postpartum regardless of mode of delivery and prior level of emotional distress (Table 3). At 30 weeks of gestation, women who subsequently gave birth by planned CS had the highest mean emotional distress score. At 6 months postpartum mothers with emergency CS had the highest score. When comparing the mean individual change in emotional distress score using spontaneous vaginal birth as reference, mothers with planned CS had a greater improvement in emotional distress after adjusting for maternal characteristics, life-style factors and chronic disease (Table 4). When additionally adjusting for pre-pregnancy mental health and mental health during pregnancy, the improvement with planned CS was at the same magnitude as seen in women with vaginal births. In
contrast, emergency CS was associated with less improvement in emotional distress score compared to mothers with spontaneous vaginal birth in all models.

Of all mothers, 4059 (7.5%) were categorized as having symptoms of emotional distress 6 months postpartum (Table 5). In the first adjusted analysis, we observed increased odds for emotional distress in mothers with planned CS (OR 1.16; 1.03–1.32) or emergency CS (OR 1.22; 1.09–1.37) compared to mothers with spontaneous vaginal births. When further adjusting for pre-pregnancy mental health problems and mental distress score during pregnancy, higher odds for emotional distress were only observed in mothers with emergency CS (Adj. OR 1.21; 1.06–1.37). When examining specific mental symptoms, higher odds were observed for both anxiety (Adj. OR 1.11; 0.98–1.24), depression (Adj. OR 1.25; 1.09–1.43) and stress (Adj. OR 1.14; 1.01–1.29) in mothers with emergency CS. Increased odds for anxiety were also seen in mothers with planned CS (Adj. OR 1.15; 1.01–1.29).

When restricting the analyses to first time mothers (n = 27057) and after adjustment for maternal mental health before and during pregnancy, higher emotional stress and increased odds for emotional distress were still observed in mothers with emergency CS with similar magnitude of estimates as seen for all mothers (Tables 4 and 5).

The results only changed marginally in sensitivity analyses using a different cut-off for the mental health variable, restricting the analyses to mothers with no pre-pregnancy mental health problems, omitting adjustment for year of childbirth, and adjusting for breastfeeding (results not shown).

4 | DISCUSSION

In this cohort study of Danish mothers, emotional distress decreased from pregnancy to 6 months postpartum regardless of mode of delivery and prior level of emotional distress. Least improvement in emotional distress was observed in mothers with emergency CS.

Compared to mothers with a spontaneous vaginal birth, mothers with emergency CS had more symptoms of anxiety, depression and stress 6 months postpartum, while mothers with a planned CS had more symptoms of anxiety.

Strengths of this study include its large size, prospective data collection and linkage to complete information on mode of delivery. We also had information on important potential confounders such as chronic disease, and mental health before and during pregnancy.

Limitations include the low participation rate, and mothers with poor mental health are expected to be underrepresented. However, in a previous DNBC study, any bias-effect on the internal comparisons were limited after the factors that influenced participation were adjusted for in the analysis. Although non-participation may depend on emotional distress, we find it unlikely that it also related to mode of delivery.
### TABLE 2  Maternal characteristics according to mode of delivery

| Mode of Delivery                        | All mothers | Spontaneous vaginal birth | Instrumental vaginal birth | Planned cesarean | Emergency cesarean |
|-----------------------------------------|-------------|---------------------------|----------------------------|-----------------|-------------------|
|                                         | n           | %                         | %                          | %               | %                 |
| Total population                        | 54,474      | 100.0                     | 75.6                       | 9.9             | 6.7               | 7.8               |
| Maternal age at conception (years)      |             |                           |                            |                 |                   |
| <20                                     | 419         | 0.8                       | 0.8                        | 1.0             | 0.3               | 0.8               |
| 20–24                                   | 6426        | 11.8                      | 11.9                       | 13.9            | 7.3               | 12.1              |
| 25–29                                   | 22,976      | 42.2                      | 41.9                       | 48.3            | 35.6              | 42.6              |
| 30–34                                   | 18,387      | 33.8                      | 34.2                       | 28.0            | 38.2              | 32.7              |
| 35–39                                   | 5,698       | 10.5                      | 10.2                       | 8.0             | 16.3              | 10.6              |
| ≥40                                     | 568         | 1.0                       | 0.9                        | 0.7             | 2.3               | 1.3               |
| Parity                                  |             |                           |                            |                 |                   |
| Primiparous                             | 27,057      | 49.7                      | 43.5                       | 83.8            | 42.3              | 73.2              |
| Multiparous                             | 27,417      | 50.3                      | 56.5                       | 16.2            | 57.7              | 26.8              |
| Pre-pregnancy BMI (kg/m$^2$)            |             |                           |                            |                 |                   |
| <18.5                                   | 2,316       | 4.3                       | 4.4                        | 4.7             | 3.5               | 2.8               |
| 18.5–24.9                               | 36,928      | 67.8                      | 69.3                       | 67.7            | 61.4              | 58.8              |
| 25–29.9                                 | 10,697      | 19.6                      | 18.8                       | 19.9            | 23.0              | 24.7              |
| ≥30                                     | 4,533       | 8.3                       | 7.5                        | 7.8             | 12.0              | 13.7              |
| Smoking in pregnancy (units/day)        |             |                           |                            |                 |                   |
| None                                    | 45,800      | 84.1                      | 83.9                       | 85.7            | 82.9              | 85.0              |
| <10                                     | 6,728       | 12.4                      | 12.4                       | 11.7            | 12.4              | 12.2              |
| >10                                     | 1,946       | 3.6                       | 3.7                        | 2.6             | 4.7               | 2.8               |
| Alcohol intake (units/week)             |             |                           |                            |                 |                   |
| None                                    | 30,016      | 55.1                      | 54.5                       | 57.0            | 55.8              | 58.2              |
| 0–4                                     | 23,916      | 43.9                      | 44.5                       | 42.3            | 42.9              | 40.8              |
| >4                                      | 542         | 1.0                       | 1.0                        | 0.6             | 1.3               | 0.9               |
| Physical activity (minutes/week)        |             |                           |                            |                 |                   |
| None                                    | 34,142      | 62.7                      | 63.1                       | 57.9            | 67.1              | 60.5              |
| 1–119                                   | 11,306      | 20.8                      | 20.6                       | 23.1            | 18.6              | 21.4              |
| 120–239                                 | 6,078       | 11.2                      | 11.0                       | 12.8            | 9.3               | 11.8              |
| 240–419                                 | 2,169       | 4.0                       | 3.9                        | 4.4             | 3.5               | 4.5               |
| ≥420                                    | 779         | 1.4                       | 1.4                        | 1.7             | 1.5               | 1.7               |
| Socio-occupational status               |             |                           |                            |                 |                   |
| Low                                     | 4,860       | 8.9                       | 9.0                        | 7.6             | 9.7               | 8.7               |
| Middle                                  | 20,901      | 38.4                      | 38.6                       | 36.1            | 39.1              | 38.5              |
| High                                    | 28,713      | 52.7                      | 52.4                       | 56.3            | 51.3              | 52.8              |
| Pre-pregnancy chronic disease           |             |                           |                            |                 |                   |
| No previous chronic disease             | 46,293      | 85.0                      | 85.5                       | 85.5            | 80.2              | 83.5              |
| Previous chronic disease                | 8,181       | 15.0                      | 14.5                       | 14.5            | 19.8              | 16.5              |
| Pre-pregnancy mental health             |             |                           |                            |                 |                   |
| No previous problems                    | 50,732      | 93.1                      | 93.2                       | 93.6            | 92.3              | 92.5              |
| Previous problems                       | 3,742       | 6.9                       | 6.8                        | 6.4             | 7.7               | 7.5               |

Mental health during pregnancy

(Continues)
Mental health was measured using questions from validated symptom scores, but women were classified as emotionally distressed by dichotomization, which is crude and may lead to bias toward null. Even then, we observed differences in symptoms of emotional distress 6 months postpartum. We also measured emotional distress as a continuous score, and here we also observed a
|                          | n   | %     | Crude OR | Adjusted OR a (95% CI) | Adjusted OR b (95% CI) |
|--------------------------|-----|-------|----------|------------------------|------------------------|
| **All mothers (n = 54,474)** |     |       |          |                        |                        |
| Emotional distress       |     |       |          |                        |                        |
| Spontaneous vaginal birth| 2995| 7.3   | 1.00     | 1.00                   | Ref                    |
| Instrumental vaginal birth| 387 | 7.2   | 0.99     | 1.01                   | (0.90; 1.13)           |
| Planned cesarean section | 312 | 8.5   | 1.18     | 1.16                   | (1.03; 1.32)           |
| Emergency cesarean section| 365 | 8.6   | 1.20     | 1.22                   | (1.09; 1.37)           |
| Symptoms of anxiety      |     |       |          |                        |                        |
| Spontaneous vaginal birth| 3347| 8.1   | 1.00     | 1.00                   | Ref                    |
| Instrumental vaginal birth| 485 | 9.0   | 1.12     | 1.01                   | (0.91; 1.12)           |
| Planned cesarean section | 369 | 10.0  | 1.26     | 1.22                   | (1.09; 1.37)           |
| Emergency cesarean section| 418 | 9.9   | 1.24     | 1.13                   | (1.01; 1.26)           |
| Symptoms of depression   |     |       |          |                        |                        |
| Spontaneous vaginal birth| 2356| 5.7   | 1.00     | 1.00                   | Ref                    |
| Instrumental vaginal birth| 309 | 5.7   | 1.00     | 1.07                   | (0.94; 1.22)           |
| Planned cesarean section | 241 | 6.6   | 1.16     | 1.15                   | (1.00; 1.32)           |
| Emergency cesarean section| 290 | 6.9   | 1.21     | 1.27                   | (1.11; 1.45)           |
| Symptoms of stress       |     |       |          |                        |                        |
| Spontaneous vaginal birth| 3452| 8.4   | 1.00     | 1.00                   | Ref                    |
| Instrumental vaginal birth| 407 | 7.6   | 0.89     | 0.97                   | (0.87; 1.09)           |
| Planned cesarean section | 321 | 8.7   | 1.05     | 1.04                   | (0.92; 1.17)           |
| Emergency cesarean section| 382 | 9.0   | 1.08     | 1.16                   | (1.04; 1.30)           |
| **First time mothers (n = 27,057)** |     |       |          |                        |                        |
| Emotional distress       |     |       |          |                        |                        |
| Spontaneous vaginal birth| 1280| 7.2   | 1.00     | 1.05                   | (0.93; 1.19)           |
| Instrumental vaginal birth| 333 | 7.4   | 1.03     | 1.05                   | (0.86; 1.24)           |
| Planned cesarean section | 117 | 7.5   | 1.06     | 1.04                   | (0.86; 1.17)           |
| Emergency cesarean section| 269 | 8.7   | 1.23     | 1.26                   | (1.09; 1.44)           |
| Symptoms of anxiety      |     |       |          |                        |                        |
| Spontaneous vaginal birth| 1651| 9.2   | 1.00     | 1.00                   | Ref                    |
| Instrumental vaginal birth| 438 | 9.7   | 1.06     | 1.06                   | (0.95; 1.18)           |
| Planned cesarean section | 159 | 10.2  | 1.12     | 1.08                   | (0.91; 1.28)           |
| Emergency cesarean section| 329 | 10.6  | 1.17     | 1.15                   | (1.01; 1.31)           |
| Symptoms of depression   |     |       |          |                        |                        |
| Spontaneous vaginal birth| 968 | 5.4   | 1.00     | 1.00                   | Ref                    |
| Instrumental vaginal birth| 257 | 5.7   | 1.06     | 1.07                   | (0.93; 1.24)           |
| Planned cesarean section | 81  | 5.2   | 0.96     | 0.95                   | (0.75; 1.20)           |
| Emergency cesarean section| 207 | 6.7   | 1.25     | 1.27                   | (1.08; 1.49)           |
| Symptoms of stress       |     |       |          |                        |                        |
| Spontaneous vaginal birth| 1362| 7.6   | 1.00     | 1.00                   | Ref                    |
| Instrumental vaginal birth| 335 | 7.4   | 0.97     | 0.99                   | (0.87; 1.12)           |

(Continues)
smaller improvement in women with emergency CS than women with spontaneous vaginal birth.

By repeating the analysis restricted to first time mothers, we reduced the possible confounding effects of prior birth experiences on their baseline mental health. However, confounding may still be a limitation, and conclusions on causal relations between mode of delivery and maternal mental health should be made with caution.

Finally, almost all births were in a hospital setting in a high quality free-of-charge Western healthcare system, so our findings may not be generalizable to other settings.

Overall, our findings are in accordance with previous studies, although definitions and measurements of emotional distress vary, and not all studies included measures of the women’s physical and mental health status at the time of birth. In a large Norwegian cohort study including 55,814 women, emergency CS was not associated with more emotional distress 6 months postpartum after adjusting for emotional distress in pregnancy as a dichotomized measure. Further, they did not include the same baseline characteristics as we did, which might explain some of the conflicting results. Another recently published Swedish study of a cohort of 3888 women, including a path analysis, concluded that emergency CS did not have a direct impact on the symptoms of depression at 6 weeks postpartum. However, the study identified several indirect pathways between emergency CS and postpartum depression such as a negative birth experience and self-reported physical symptoms after birth.

Compared to women with spontaneous vaginal birth, we found mothers with emergency CS to have more symptoms of depression and stress postpartum. Planned CS was specifically associated with symptoms of anxiety. When including pre-pregnancy mental health problems and mental health score during pregnancy, associations were more attenuated in mothers with planned CS, indicating that emotional distress in these women is associated with feelings existing or arising prior to giving birth rather than with mode of delivery itself. These women had higher distress scores in pregnancy and therefore probably experienced a greater relief postpartum. Also, when restricting the study to first time mothers, we no longer observed an association between planned CS and symptoms of anxiety 6 months postpartum. This may indicate a possible influence of prior birth experiences that could affect both mode of delivery and mental health before and after birth.

To conclude, mental health among Danish mothers improved from pregnancy to 6 months postpartum. However, mothers with emergency CS had more symptoms of anxiety, depression and stress, and mothers with planned CS had more symptoms of anxiety 6 months postpartum. To provide a better understanding of how mode of delivery affects maternal mental health and to support decision making by women, maternity care providers and policy makers, future research could focus on women’s expectations, choices and birth experiences in different birth settings.

**ACKNOWLEDGMENTS**

We are most grateful to the many women who participated in The Danish National Birth Cohort. The Danish National Birth Cohort was established with a significant grant from the Danish National Research Foundation. Additional support was obtained from the Danish Regional Committees, the Pharmacy Foundation, the Egmont Fonden, the March of Dimes Foundation Birth Defects Foundation, the Health Foundation and other minor grants. The DNBC Biobank has been supported by the Novo Nordisk Foundation and the Lundbeckfonden. Follow-up of mothers and children have been supported by the Danish Medical Research Council (SSVF 0646, 271-08-0839/06-066023, O602-01042B, O602-02738B), the Lundbeckfonden (195/04, R100-A9193), The Innovation Fund Denmark 0603-00294B (09-067124), the Nordea-fonden (02-2013-2014), Aarhus Ideas (AU R9-A959-13-5804), University of Copenhagen Strategic Grant (IFSV 2012), and the Danish Council for Independent Research (DFF - 4183-00594 and DFF - 4183-00152).

**AUTHOR CONTRIBUTIONS**

All authors contributed to the design of the study. JO and EAN were responsible for the data collection. SKS analyzed the data with help from SH. All authors interpreted the results. SKS drafted the manuscript, and EAN, SH, HK, and JO critically revised it. All authors approved the final manuscript.

**CONFLICTS OF INTEREST**

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

**DATA AVAILABILITY STATEMENT**

No. Research data are not shared.
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How to cite this article: Skov SK, Hjorth S, Kirkegaard H, Olsen J, Nohr EA. Mode of delivery and short-term maternal mental health: A follow-up study in the Danish National Birth Cohort. *Int J Gynecol Obstet*. 2022;159:457–465. doi: 10.1002/ijgo.14155