INTRODUCTION

Several parenting interventions, which have been delivered during neonatal intensive care, have shown promising results, especially in decreasing postnatal depression symptoms among the mothers of preterm infants. These findings are vital, as the elevated risk of postnatal depression continues to be a significant issue among the parents of preterm infants. A recent review reported that the proportion of mothers of preterm infants exceeding the cut-off for clinical PPD varied from 6.6% to 42.9% suggesting that preterm delivery...
significantly increases the risk of depressive symptoms. The risk of maternal postnatal depression is highest during the first half-year after a preterm birth. However, some vulnerable groups may be at risk of prolonged clinical depression, such as mothers with a history of depression, mothers who experience stress related to their maternal role during their infant’s hospitalization, and mothers with continuous worry about the infant’s health.

We developed an educational intervention, Close Collaboration with Parents, to improve the skills of neonatal staff to provide care in collaboration with parents and to support parenting during an infant’s hospital stay. We previously showed, with two-group design, that the mothers of very low birthweight (VLBW) infants had significantly fewer postnatal depression symptoms after staff education than mothers in the same unit before the education took place. In that study, we measured postnatal depression four to six months after the expected birth date. Correspondingly, other studies on parenting interventions in the neonatal intensive care unit (NICU) environment have evaluated their effect on maternal postnatal depression symptoms at discharge or during the first six months of the infant’s life. A knowledge gap seems to exist concerning the long-term effects of parenting interventions on maternal depression symptoms.

In this study, we aimed to test the long-term effects of the Close Collaboration with Parents intervention on maternal symptoms of depression up to two years after the expected birth date of a VLBW infant. We hypothesized that 1) mothers who delivered after the intervention exhibit fewer depressive symptoms two years after the expected birth date than those who delivered before the intervention; and 2) the intervention effect is consistent at six months and two years after the expected birth date.

2 | METHODS

This study used a quasi-experimental non-equivalent two-group design, comparing mothers who delivered VLBW infants before the intervention, in 2001–2006 (PIPARI follow-up study, www.utu.fi/pipari), and those who delivered such infants after the intervention, in 2011–2015 (the Close Collaboration with Parents Intervention Study). The study protocol has been approved by the Joint Commission on Ethics of the Hospital District (Hospital District of Southwest Finland: ETMK:16/180/2011).

2.1 | Population

All infants of the participating mothers were cared for in the NICU of Turku University Hospital. We included the mothers of infants with VLBW (below 1501 grams), who spoke Finnish or Swedish, who lived in the catchment area of the hospital, and whose child was alive at discharge without major congenital anomalies or syndromes. The pre-intervention group consisted of 126 (59%) and 75 (35%) mothers at the 6-month and two-year time-points, respectively, from a group of 212 VLBW infants who were eligible for the follow-up study. The post-intervention group consisted of 54 (36%) and 45 (30%) mothers at the six-month and two-year time-points, respectively, from a group of 150 eligible VLBW infants. The hospital had an infant mental health team which provided support for all parents of preterm infants in both groups.

In the pre-intervention and post-intervention groups, trained research assistants approached eligible mothers during the infant’s hospital stay. Parents signed an informed consent form after receiving verbal and written information about the studies. Before discharge from the hospital, mothers received a folder that consisted of questionnaires for both six-month and two-year measurement time-points. They filled out the questionnaires at home and returned them by mail to the research assistant.

2.2 | Methods

The depression symptoms were screened using the EPDS. The EPDS is a 10-item, self-report questionnaire for screening postnatal depression symptoms. The maximum score is 30 and the minimum is 0, with a higher score indicating more depressive symptoms. The method is reliable and validated to screen depressive symptoms during the postpartum period. The mean score of EPDS was used as a primary outcome. In addition, the incidence of probable clinical depression was compared between the groups using a cut-off of 13 or more.

2.3 | Intervention

The unit carried out the educational intervention, targeted at its entire healthcare team, from 2009 to 2012. Close Collaboration with Parents is an educational intervention for NICU healthcare teams. The training aims to reach each staff member of the unit to change the unit’s care culture. It provides skills for doctors, nurses, and other neonatal specialists regarding observing and verbalizing infant behaviour, observing infants together with parents, active and

Key Notes
- After the NICU staff had undergone the educational intervention, Close Collaboration with Parents, the mothers had fewer depressive symptoms than the mothers before the intervention in the same NICU.
- After the intervention, the mothers had significantly lower odds of exceeding the cut-off of clinical depression at six-month and two-year time-points than before the intervention.
- The preventive effect of the intervention was similar at six-month and two-year time-points.
empathetic listening to parents’ observations and experiences, and shared decision-making in infant care. The Close Collaboration with Parents training model consists of four phases, each of which builds on the previous one.\textsuperscript{17}

In the study hospital, 49 (96%) of the neonatal nurses and three (50%) of the neonatologists participated in theoretical training, bedside practices with individual mentors, and reflective group discussions led by a psychologist. Each staff member worked with the individual mentor for six work shifts (an average of 49 h). The intervention and implementation has been described in greater detail elsewhere.\textsuperscript{17} A qualitative interview study showed that the staff had changed their practices in infant care and collaboration with parents and reported better parent satisfaction in the study hospital.\textsuperscript{18}

2.4 | Statistical analysis

Linear mixed models for repeated measures analysis were applied to study the variation of the EPDS scores of the pre-intervention and post-intervention groups over time. The multivariable models included the following factors: gestational age, gender, small for gestational age, vaginal birth, singleton/multiple, hospital days, maternal smoking, previous depression, and siblings. We square root transformed the scores prior to analysis to prevent right skew in the residuals of those models. The confidence intervals for differences were then back-transformed using the delta method to yield approximate confidence intervals for median differences in the original scale for the median EPDS scores in the pre-intervention group at six-month and two-year time-points. We calculated effect size as the difference in the average square root transformed scores between the pre-intervention and post-intervention groups, and covariate-adjusted effect size by the corresponding contrast in the multivariable model. We then standardized both effect sizes by the standard deviation of the square root transformed scores pooled over the pre-intervention and post-intervention groups. Generalized estimating equations with binomial distribution and logit link function for repeated measures analysis were used to investigate the association between the intervention and the depression screening cut-off value. We assessed the possibility of attenuation bias by dividing the sample into mothers with and without valid responses at the two-year time-point and searching for differences in the responses at the six-month time-point and all explanatory variables, applying
unpaired t-tests for quantitative variables and Fisher’s exact test for categorical variables.

3 | RESULTS

The infants in the post-intervention group were born earlier \((p = 0.04)\), had lower birthweight \((p = 0.01)\), and stayed longer in the hospital \(<0.001\) than those in the pre-intervention group. Furthermore, the mothers in the post-intervention group had more previous mental health problems \(<0.001\). No other significant differences were found between the groups (Table 1).

Dropout analyses were carried out by comparing those mothers who returned the six-month questionnaire but did not return the two-year questionnaire \((n = 60)\) to those mothers who returned both questionnaires \((n = 120)\). The results of the dropout analyses are presented in the Table 2. The mothers who did not answer the two-year questionnaire smoked more often during pregnancy than those who answered the questionnaire at two years, \(p = 0.009\). The mothers who did not answer at the two-year time-point had also lower education with borderline statistical significance, \(p = 0.05\). No other statistically significant differences were found between these groups.

The EPDS scores of the mothers in the post-intervention group \((M = 3.67, SD = 3.57)\) were lower than of those in the pre-intervention group \((M = 5.63, SD = 4.84)\) two years after the expected birth date of the VLBW infants. The median difference at the two-year time-point was 1.73 (95% CI from 0.03 to 3.43), \(p = 0.024\).

Consistently, the maternal EPDS scores were also significantly lower at the six-month time-point in the post-intervention group \((M = 3.69, SD = 3.50)\) than in the pre-intervention group \((M = 6.41, SD = 4.93)\). The median difference at the six-month time-point was 2.69 (95% CI from 1.58 to 4.22), \(p < 0.001\).

The multivariable repeated measures model showed a median decrease of 2.56 (95% CI from 1.64 to 3.48) in the mothers’ EPDS scores at the two-year time-point and 3.28 (95% CI from 2.01 to 4.55) at the six-month time-point. The measurement time-point did not affect the difference between the groups, \(p = 0.303\). The difference between pre-intervention and post-intervention groups remained significant, \(p < 0.001\). The covariate-adjusted effect size of the group was 0.740.

We tested our second hypothesis whether the intervention effect was consistent at both time-points. We found no interaction between measurement time-points and the group in the repeated measures model consisting of time-points, group, and their interaction \((p = 0.907\) unadjusted and \(p = 0.844\) with covariate adjustment). This finding indicates that the decrease in the mothers’ EPDS scores from the pre-intervention to the post-intervention group does not depend upon the measurement time-point. Furthermore, no main effect for the measurement time-points was found, \(p = 0.190\).

Mothers with previous depression had 5.97- and 5.06-point higher EPDS scores than those without previous depression at six months and two years, respectively, \(p = 0.004\). There was also a significant interaction between measurement time-point and siblings, \(p = 0.013\), indicating that siblings increase mothers’ depressive symptoms at six months but decrease such symptoms at two years.

| Variables                        | Pre-intervention (N = 126) | Post-intervention (N = 54) | p-value |
|----------------------------------|-----------------------------|----------------------------|---------|
| Infant                           |                             |                            |         |
| Male sex, no. (%)                | 68 (54)                     | 27 (50)                    | 0.62    |
| Gestational age, mean (SD), week | 29.0 (2.93)                 | 28.1 (2.3)                 | 0.04    |
| Birth weight, mean (SD), g       | 1089 (290.0)                | 971 (272.7)                | 0.01    |
| SGA, no. (%)                     | 44 (35)                     | 12 (22)                    | 0.11    |
| Hospital days, mean (SD)         | 59.8 (29.7)                 | 81.7 (41.0)                | <0.001  |
| NDI at 2 years of corrected age, no. (%) | 7 (6) | 4 (10) | 0.47 |
| Has siblings, no. (%)            | 56 (46)                     | 21 (40)                    | 0.62    |
| Mother                           |                             |                            |         |
| Age, mean SD, year               | 31.1 (5.3)                  | 32.6 (5.2)                 | 0.08    |
| Education, no. (%)               |                             |                            |         |
| Low (≤9 years)                   | 12 (10)                     | 2 (4)                      | 0.23    |
| Intermediated (9–12 years)       | 61 (51)                     | 33 (62)                    |         |
| High (>12)                       | 47 (39)                     | 18 (34)                    |         |
| Singleton, no. (%)               | 102 (81)                    | 43 (80)                    | 0.84    |
| Vaginal birth, no. (%)           | 44 (35)                     | 21 (40)                    | 0.61    |
| Smoking during pregnancy, no. (%)| 18 (14)                     | 6 (11)                     | 0.81    |
| Previous mental health problems, no. (%) | 4 (3) | 10 (19) | <0.001 |

*SGA, Small for gestational age; NDI, Neurodevelopmental impairment.
However, the individual differences were not significant at either time-point.

A lower proportion of mothers exceeded the cut-off for clinical depression in the post-intervention group than in the pre-intervention group at the six-month time-point: 10.3% (13/126) in the pre-intervention group compared to 0.0% (0/54) in the post-intervention group, \( p = 0.011 \). However, the decrease in the proportion of mothers exceeding the cut-off was not significant at the two-year time-point: 6.7% (5/75) in the pre-intervention group compared to 2.2% (1/45) in the post-intervention group, \( p = 0.408 \).

The multivariate model, including group, mode of delivery, previous depression, and siblings, and its interactions with the measurement time-points showed that the post-intervention mothers had 0.054 lower odds of scoring above the clinical cut-off at either time-point (95% CI from 0.006 to 0.484, \( p = 0.009 \)) than those in the pre-intervention group. In addition, previous history of depression gave 10.94 higher odds (95% CI from 1.27 to 94.50, \( p = 0.030 \)) of scoring above the clinical cut-off than absence of previous depression.

### 4 | DISCUSSION

We found that the mothers had fewer depressive symptoms after the staff of the NICU had undergone the educational Close Collaboration with Parents intervention than the mothers before the intervention. We also showed that the effect lasted for two years and remained similar from six months to two years after the expected birth date. To our knowledge, this was the first study extending the follow-up of maternal depression symptoms after a NICU intervention until two years after the birth of a very preterm infant.

The mothers in the post-intervention group had, on average, fewer depressive symptoms than those in the pre-intervention group at the two-year time-point, implying that the training of the staff benefitted a heterogeneous group of mothers. Furthermore, the results showed that the mothers in the post-intervention group had a significantly lower likelihood of exceeding the cut-off of clinical depression than those in the pre-intervention group. This is clinically meaningful because it has been shown that mothers’ persistent postnatal depression was related to more adverse child outcomes compared to non-persistent maternal depression.19

Interestingly, the mothers in the post-intervention group had more previous mental health problems than those in the pre-intervention group at the two-year time-point, implying that the training of the staff benefitted a heterogeneous group of mothers. Furthermore, the results showed that the mothers in the post-intervention group had a significantly lower likelihood of exceeding the cut-off of clinical depression than those in the pre-intervention group. This is clinically meaningful because it has been shown that mothers’ persistent postnatal depression was related to more adverse child outcomes compared to non-persistent maternal depression.19

Despite these risk factors, the mothers in the post-intervention group had fewer depressive symptoms and were less likely to score

### TABLE 2 Dropout analyses comparing the mothers who returned the six-month EPDS questionnaire but did not return the two-year questionnaire to those mothers who returned the EPDS questionnaires at both time-points

| Variables                      | Mothers who returned six-month EPDS only N = 60 | Mothers who returned six-month and two-year EPDS N = 120 | p-value |
|--------------------------------|-----------------------------------------------|----------------------------------------------------------|---------|
| Infant                         |                                               |                                                          |         |
| Male sex, no. (%)              | 32 (53)                                       | 63 (53)                                                  | 1.00    |
| Gestational age, mean (SD), week| 28.81 (2.87)                                  | 28.64 (2.57)                                              | 0.70    |
| Birth weight, mean (SD), g     | 1098.1 (278.5)                                | 1031.4 (293.1)                                            | 0.14    |
| SGA, no. (%)                   | 44 (73)                                       | 80 (67)                                                   | 0.40    |
| Hospital days, mean (SD)       | 61.62 (26.63)                                 | 68.80 (38.31)                                             | 0.19    |
| NDI at 2 years of corrected age, no. (%) | 6 (11)                                    | 5 (6)                                                     | 0.19    |
| Has siblings, no. (%)          | 27 (46)                                       | 50 (43)                                                   | 0.75    |
| Mother                         |                                               |                                                          |         |
| Age, mean SD, year             | 31.25 (5.12)                                  | 31.66 (5.41)                                              | 0.63    |
| Education, no. (%)             |                                               |                                                          |         |
| Low (≤9 years)                 | 9 (15)                                        | 5 (4)                                                     | 0.05    |
| Intermediated (9–12 years)     | 29 (49)                                       | 65 (57)                                                   |         |
| High (≥12)                     | 21 (36)                                       | 44 (39)                                                   |         |
| Singleton, no. (%)             | 46 (77)                                       | 99 (83)                                                   | 0.42    |
| Vaginal birth, no. (%)         | 23 (38)                                       | 42 (35)                                                   | 0.71    |
| Smoking during pregnancy, no. (%)| 14 (23)                                    | 10 (8)                                                    | 0.01    |
| Previous mental health problems, no. (%) | 4 (7)                                 | 10 (8)                                                    | 0.78    |
| EPDS, mean (SD)                | 6.37 (0.65)                                   | 5.21 (0.41)                                               | 0.12    |
| EPDS 13 or more, no. (%)       | 7 (12)                                        | 6 (5)                                                     | 0.13    |

*SGA, Small for gestational age; NDI, Neurodevelopmental impairment.*
above the clinical cut-off than those in the pre-intervention group. However, the attrition up to two years was greater among mothers who had low education and smoked during pregnancy.

Our second aim was to study whether the impact of the intervention was stable from the six-month to the two-year measurement point. The absence of both a time effect and an interaction effect between group and time implies that the intervention effect was similar at the six-month and two-year measurement time-points. The overall effect size of the group was 0.74, which can be considered large. The sustainability of the intervention effect on depression symptoms is an important finding but needs to be repeated in other and larger sample sizes and with randomized study designs.

Our earlier results may provide some potential explanations of why, after the intervention was implemented in the unit, the mothers had fewer depression symptoms than before the intervention, even two years after the expected birth date of the infant. First, the Close Collaboration with Parents intervention has been shown to improve units’ family-centred care practices by, for example promoting a mutual partnership between staff and parents, the involvement of parents in the care of the infant and decision-making related to care and the provision of emotional support to parents. Such care practices have been shown to be associated with lower levels of depressive symptoms in parents of preterm infants. Second, the intervention increased maternal presence by 41% and skin-to-skin contact by 38% when we compared pre- and post-intervention groups in nine Finnish neonatal units. Skin-to-skin contact, in turn, has been shown to have a small protective effect on postnatal depression symptoms among the mothers of preterm infants, probably through oxytocin production stimulation and attachment promotion. Finally, a recent review showed that long parental exposure to an intervention in a NICU was one important element in alleviating maternal depressive symptoms. After the Close Collaboration with Parents training for the unit staff, the majority of the staff were capable of providing comprehensive support for parents throughout the NICU stay, which might be an effect mechanism of this intervention. However, more studies are warranted to investigate the effect mechanisms of the interventions and care models decreasing maternal depression in the NICU context.

Our results showed that mothers with a history of previous depression had higher odds ratio of scoring above the clinical cut-off of depression than those without a history of depression. This result is in accordance with previous results showing that mothers who experience a preterm delivery and have a history of depression are vulnerable to prolonged clinical depression. Paradoxically, mothers with a history of mental problems are often excluded from studies of parenting interventions in NICUs even though they are at greater risk of problems in parenting. In future, parenting interventions should be particularly targeted at mothers with a history of depression. Furthermore, the effectiveness analyses of interventions should contain previous maternal depression as an important confounder.

The use of a historical group was a major limitation of our study design as a 5-year time gap between the pre-intervention and post-intervention groups may cause a chronology bias. However, we have already reported that there were no obvious differences between the groups in the standardized neonatal mortality or morbidities, according to Vermont-Oxford Network results. Undeniably, a randomized and controlled trial would have been a more rigorous study design than a pre-post-intervention test, but it was not possible to randomize individuals within one unit as the intervention was targeted at the unit’s entire staff. Furthermore, we could not compare the pre-intervention and post-intervention groups based on the mothers’ initial stress related to their maternal role and mothers’ worry about the infant’s health. This study does not allow us to explore these factors as mediators. The results need to be interpreted with caution, as the representativeness of the sample in both groups was limited, and selection bias is possible. Furthermore, the use of the EPDS as a measurement tool two years after birth can be criticized; however, its use allowed us to analyze the stability of the intervention effect.

The Close Collaboration with Parents intervention seems to have significant and long-term preventive effects on maternal depressive symptoms. After the intervention, the mothers had decreased levels of depressive symptoms even two years after the birth of a VLBW infant. The effect mechanism of the intervention is likely to be related to the staff’s improved abilities to support parents and form a partnership with them in the care of the infant. Research on the effect mechanisms of the intervention is needed.

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CONFLICT OF INTEREST
We declare no conflict of interest.

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