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Maternal postnatal health and infant development

Thesis presented by

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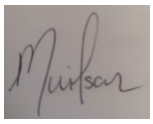
Declaration

This is to certify that the work I am submitting is my own and has not been submitted for another degree, either at University College Cork or elsewhere. All external references and sources are clearly acknowledged and identified within the contents. I have read and understood the regulations of University College Cork concerning plagiarism.

Signed: 

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and bright smile at the end of a hard day provided everything my heart needed. Being your Mum will always be my proudest achievement!

1.Introduction

The overall thesis is underpinned by theories proposed within the field of infant mental health (IMH), namely it draws on the understanding that all infant development takes place within the context of children's relationships, and for many infants, their primary relationship is with their mother. As developmental skills are thought to build on each other in a stepwise, sequential process, any early disturbances in these processes are thought to have a knock-on, cascading, impact on child development (Zeanah, 2019). Given this understanding, early relational variables are likely to play a significant influencing role in later child development outcomes as well as interacting with one another, creating a complex web of early postnatal experiences.

The overarching aim of this research thesis was to take a wide-angled view of the multifaceted postnatal experience, by exploring important early relational variables, namely maternal postnatal depression (PND), maternal-infant attachment, and breastfeeding and their impact on longitudinal child developmental outcomes, specifically cognitive, language, neuromotor and socio-emotional development within the first two years of life. In addition to the empirical paper, this thesis also includes a systematic review looking at the effect of breastfeeding self-efficacy on PND, as research has indicated an association between these factors, but the direction of the relationship is still unclear (Dennis, 2003; Dennis & Faux, 1999).

PND is a mental health problem that is associated with maternal suffering and possible adverse outcomes for offspring (Cooper & Murray, 1998). PND impacts a high percentage of women, with reviews estimating that PND prevalence level is between 13% and 19% (Crotty & Sheehan, 2004; Gavin et al. 2005; O'Hara et al. 1982). As such PND poses a significant

public health risk and is a high research priority as it may present a modifiable variable that could help reduce the long-term risk of child developmental delay/deficit.

The research base on PND and its impact on child development is substantial (Aoyagi & Tsuchiya, 2019; Grace et al. 2003; Parsons et al. 2012). However, there is of yet no consensus regarding whether PND effects children's developmental outcomes in general. The inconsistencies in the research base may be, in part, due to methodological differences between existing studies (Bluett-Duncan et al. 2021). Furthermore, research on the impact of PND on language and neuromotor development has been relatively under-researched in comparison to other areas of development (Aoyagi & Tsuchiya, 2019).

Conversely to PND, breastfeeding in infancy has been shown to have long-term beneficial effects, with research indicating it reduces the risk of infection and morbidity in offspring (Duijts et al. 2010; Sankar et al. 2015). As such, the World Health Organisation (WHO) recommends that all infants are exclusively breastfed till six months (World Health Organization, 2003). A sizeable body of research exists in relation to how breastfeeding impacts long-term neurodevelopment, especially in relation to cognitive development, with results pointing towards a possible significant negative association (Grace et al. 2017; Guzzardi et al.2020; Kramer et al. 2008; Quigley et al. 2012). However, critics have argued that the effects shown are not a result of breastfeeding but rather an artifact of other socioeconomic or environmental factors such as maternal education that may influence breastfeeding initiation, exclusivity, and duration as well as children's neurodevelopmental performance (Jacobson et al. 1999; Malloy & Berendes, 1998; McCrory & Layte, 2011; Wadsworth et al.1998).

Another key critique of breastfeeding research has been the failure of many studies to precisely define the breastfeeding variable (Guzzardi et al. 2020). As breastfeeding is thought to have a dose-response effect, mothers who breastfeed to some extent but 'top-up' with infant formula, versus those that breastfeed predominantly or exclusively, must be identified

accurately to ensure group homogeneity and reliable outcomes. Similarly, to PND, breastfeeding presents another possible modifiable variable to improve neurodevelopment, and therefore further reliable research in this area is warranted.

PND and breastfeeding may affect child developmental outcomes not only directly but also indirectly through their impact on maternal-infant attachment. Attachment theory holds that a responsive, sensitive response by the parent provides the essential criteria for the infant to develop strong, secure attachments (Schore & Schore, 2008). In the context of a secure attachment the infant builds neural connections that facilitate emotional stability, this emotional stability forms the foundation from which a child can explore and learn.

PND symptomology may reduce the likelihood of a mother being an adequate social partner, for example, by reducing maternal responsiveness to infant exploration and maternal attentiveness to the infant's attentional focus, both of which have been shown to negatively impact infant development (Bernier et al. 2012; Hackman et al. 2015; Niedźwiecka et al. 2018). The positive benefits of breastfeeding may also be mediated through maternal-infant attachment relationships as breastfeeding has been shown to provide a more intensified experience of emotional care in comparison to formula feeding or combined feeding (Gibbs et al. 2018).

The current empirical research paper is a secondary data analysis of an Irish prospective longitudinal birth cohort. The cohort was made up of healthy infants and first-time mothers with key indicators identifying the group as being of high socio-economic status. The current study aimed to investigate the effect of PND and maternal-infant attachment at two months postnatal and exclusive/predominant breastfeeding at two and six months postnatal on infants' cognitive, language, neuromotor, and socio-emotional development at both 12- and 24-months follow-up, while controlling for important confounding variables.

While the empirical study is concerned with the consequences of early relational variables, including PND on neurodevelopmental outcomes, the systematic review investigates whether breastfeeding self-efficacy predicts PND. Breastfeeding self-efficacy is a women's self-belief/ confidence in her ability to breastfeed her child (Blyth et al., 2002). Recent research has highlighted the potential importance of breastfeeding self-efficacy, as a socio-cognitive factor that may be associated with PND (Dai & Dennis, 2003; Minamida et al., 2020). Of the studies examining breastfeeding self-efficacy and PND, the majority show a significant inverse relationship, that is, mothers who experience low levels of breastfeeding self-efficacy are more likely to be at greater risk of PND (Dennis, 2003; Dennis & Faux, 1999; Minamida et al., 2020). While research tends to point towards a significant negative association between PND and breastfeeding self-efficacy, the direction of that relationship is yet unclear. The current systematic review aimedsynthesisese existing empirical research that examined the longitudinal association between early breastfeeding self-efficacy, measured within the first six weeks with postnatal depression whicoccursur later in the first postnatal year.

The layout of this thesis is as follows. Chapter two consists of a literature review providing additional background research. Chapter three consists of the systematic review which was prepared for publication in the *International Breastfeeding Journal*, author guidelines are provided in Appendix A. Chapter four consists of the empirical research paper which was prepared for publication in the *Journal of Experimental Child Psychology*, author guidelines are provided in Appendix B. Chapter five includes the extended methodology, which includes supplementary information relating to the methods and results sections of both the empirical research study and the systematic review. Finally, chapter six includes the overall thesis discussion and conclusions. References are provided at the end of each chapter and are formatted using APA format.

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2. Background

2.1 Conceptual framework

In the mid-twentieth century, there was a growing interest in child development and consequently, research in this area grew. For example, John Bowlby's pioneering work to integrate Sigmund Freud's psychology and Charles Darwin's biology into what we now know as attachment theory helped to model the evolutionary origins of early human development (Schore & Schore, 2008). Bowlby (1973) postulated that infants come into the world biologically pre-wired to form attachments with others, because this helps them to survive. He suggested that an infant has an innate need to attach to one main attachment figure. This view that infants have a powerful influencing effect on their parents contradicted the dominant view at the time of a unidirectional parent-child effect (Zeanah, 2019).

The theory of attachment was expanded by Ainsworth et al. (1978) who suggested that attachment fell into several behaviourally defined categories and that children with sensitive, attentive, and consistent caregiving were more likely to be securely attached than children who did not receive such caregiving. Winnicott (1956) also contributed to the field of early child development by proposing that a mother's ability to *hold* the baby in mind was associated with the infant's emotional development. Furthermore, Escalona (1963) hypothesised that it is not an infant's genetic endowment or the environmental characteristics (i.e., nature versus nurture) that mattered most, rather it is the infant's experience of the world that is most crucial.

These early practitioners and researchers have helped shape the way we think about infant development and the importance of the relationship context in fostering healthy infant growth and development. Contemporary scholars continue to develop and expand on these early theories of child development. For example, interpersonal neurobiological models of attachment have described the central role of attachment relationships on the development of

the infant's brain architecture (Greenough & Black, 2013; Schore, 2000; Schore & Schore, 2008). Theorists suggest that the early structural formation of the infant's right brain, which is dominant for social and emotional development is impacted by the caregiver's psychobiological attunement to the dynamic alternations in the infant's arousal/affective states (Schore & Schore, 2008). These psychobiological transactions that are embedded in the attachment relationship are what researchers have referred to as mutuality or reciprocity. Simply put, these interactions between an infant and its primary caregiver are comparable to the serve and return interaction of a tennis game.

Serve and return occurs when a young infant reaches out to its caregiver through gazing, babbling, or crying and the adult responds by appraising the infant's arousal/ affective state. The caregiver then modulates the infant's arousal/affect before communicating (returning) it back to the infant through the caregiver's vocalisations, posture, and facial expressions (Feldman, 2017). A sensitive, attuned caregiver will modulate the arousal level/affective state before returning it to the infant to ensure it is not at an excessively high or non-optimal low level of stimulation for the infant (Feldman, 2017; Tronick & Weinberg, 1997).

The development of a secure attachment relationship through this interpersonal psychobiological process is growth-promoting. A secure attachment helps develop the infant's self-regulation and social competencies and these competencies provide the foundations for the development of other developmental tasks (Sroufe et al. 2009). Adequate socio-emotional capacities enable the child to adaptively cope with negative emotion and challenging circumstances, engage in meaningful social interactions, rely on others for safety and support, and promotes exploration and play, all of which make learning possible (Simpson et al. 2016).

This modern view of attachment suggests that the young brain is extremely malleable to emotional experiences and as such relational-based stress can have significant and wide-reaching implications for child development (Ammaniti & Trentini, 2009; Siegel, 1999).

Research indicates that even within a relatively secure attachment relationship the caregiver can never be 100 percent attuned (Feldman, 2012). However, temporary attachment ruptures caused by a caregiver's lack of attunement can be adaptive once attachment repair occurs in a timely fashion (Feldman, 2012). These moment-to-moment miss-steps in attunements allow the infant to experience ordinary levels of stress in a manageable way and build the infant's distress tolerance (Schore & Schore, 2008). Through the process of consistent responding by the caregiver to the infant's distress, and through positive play interactions, the infant learns that the caregiver is predictable, consistent, and emotionally available (Schore & Schore, 2008).

However, when a caregiver is emotionally unavailable, rejecting, or hyper-intrusive it can induce extreme levels of arousal/ affective states in the infant. If the caregiver provides no opportunity for repair and the infant is left in an extreme state of stress for prolonged periods, this can lead to biochemical alterations (Koss & Gunnar, 2018). For example, it can lead to excessively elevated levels of stress hormones, creating a hypermetabolic state within the infant's developing brain and body (Schore, 2009). The brain is at its most malleable within the first two years of life. Therefore, disruptions to brain growth during this time can have far-reaching consequences (Zeanah, 2019).

To summarise the above, it is suggested that sensitive, responsive caregiving provides the conditions for infants and children to develop strong attachments. In the context of these attachment relationships, the child builds neural connections that facilitate emotional stability. This emotional stability provides the grounding that facilitates the child to explore its environment, as the infant trusts that their caregiver is there as a secure base. For example, securely attached toddlers tend to be more social with peers and unfamiliar adults than those that are insecurely attached (Booth et al. 1991). As a result of this curiosity and exploration the infant gains experience and acquires competencies. For example, studies have shown that 3–5-

year-olds who are securely attached are more likely to be empathic, resilient, and self-confident (Arend et al. 1979; Elicker et al. 2016). Moreover, the impact of the infant's early attachment relationship has been shown to have long-lasting effects. For example, in a study by Jacobsen and Hofmann (1997), securely attached 7-year-olds were rated by teachers at ages, 9, ,12, and 15 as more attentive and participatory and received better grades than children who were insecurely attached.

IMH theory as described above provides a conceptual understanding of infant development, postulating that all infant development takes place within the context of their relationships. Given this understanding that an infant's relationships are essential for their growth and development, it is important to consider the factors that impact and influence a caregiver's ability to respond in a 'good enough' way to their infants' needs. Postnatal Depression (PND), breastfeeding, and maternal-infant attachment will be considered as the relational variables of interest in the current thesis and their impact on infant socio-emotional and neurodevelopment will be examined. As depicted in Figure 1, the factors of interest are highly inter-related and their relationships with one another will be considered in this research review, other possible related factors will also be considered in the review, some of which will also be controlled for in the empirical papers (see Figure 1).

Figure 1: Postnatal factors contributing to infant social and neurodevelopment.

2.2 PND and Attachment and their Impact on Development

Beck's (1967) stress-vulnerability model has been proposed as a conceptualisation of PND, with childbirth presenting a stressor that triggers depression in individuals who are predisposed to it. Numerous vulnerability factors have been suggested in the research, including poor social support, difficult infant temperament, and low socio-economic status (Leahy-Warren et al. 2012; Robertson et al. 2004). Other factors such as breastfeeding cessation and socio-cognitive factors such as parenting self-efficacy (i.e., self-confidence) may also function as PND vulnerability factors (Brown et al. 2016; Shorey et al. 2015). PND has been defined by the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, fifth edition* (DSM-V) as a major depressive episode (American Psychiatric

Association, 2013). The condition is characterised by low mood, lack of interest, difficulties in day-to-day coping, sleep and appetite disturbances, reduced self-esteem, excessive guilt, and somatic complaints (Cox & Holden, 1994; O'Hara & Swain, 1996).

There is considerable research base on PND and its impact on child development. However, of yet, there is no consensus regarding PND's impact on children's long-term neurodevelopment, the reason for this is both the paucity and inconsistencies of studies (Aoyagi & Tsuchiya, 2019). For example, certain developmental domains, such as neuromotor development and language development have been relatively under-researched (Aoyagi & Tsuchiya, 2019). Of the existing research, findings point totowardND being associated with a slight delay in children's fine motor development and children's expressive language development (Aoyagi, 2019; Keim et al. 2011; Koutra et al. 2013). Thus far, there has been insufficient evidence to suggest an association between PND and children's cognitive development (Slomian et al. 2019). More research is warranted using adequate controls, confounders suggested in the literature include parental education, household income breastfeeding, and attachment (Aoyagi & Tsuchiya, 2019; Slomian et al. 2019).

The symptoms associated with PND are thought to reduce a mother's psychosocial functioning which, in turn, may increase the risk of her being an inadequate social partner for her infant and potentially make her less able to meet the infant's social and emotional needs (Smith-Nielsen et al. 2016). For example, if a mother is preoccupied with her internal world, she is less able or inclined to attend to the infants' communicative attempts, and in turn, an infant may be less inclined to seek maternal attention or engage in the world around them if they are continually met with negative affect or avoidance. If this impaired quality in the early relationship between mother and infant becomes reciprocal in their communicative gestures, then these negative patterns of interaction are believed to have a lasting effect on the infant's functioning developmental trajectory (Rees, 2007).

Infants exposed to maternal depressive symptoms in the postnatal period may be at particular risk as they are entirely dependent on the quality of care and emotional responsiveness provided by others (Murray, 1988). Goodman and Gotlib (1999) provide a model to explain the intergenerational transmission of risk from women with PND to their infants. It highlights multiple interacting mechanisms that transmit the effects of PND between generations, including quality of parenting, the heritability of depression, neuroregulatory mechanisms, exposure to negative maternal cognitions, behavior and affect, sociodemographic conditions, paternal health and involvement, course and timing of depression, and individual child characteristics.

Researchers have suggested that PND should be considered a marker of risk for adverse child outcomes and not a risk mechanism (Rutter, 1997). While numerous risk mechanisms have been considered in the research, the quality of the early maternal-child relationship has received considerable attention as a possible risk mechanism and may mediate the effects of PND on infant developmental outcomes (Rutter, 1997). The association between impaired maternal-infant relationships and adverse infant outcomes in dyads where mothers have PND has not only been noted in high-risk psychosocial populations (Cohn et al. 1986; Field et al, 1990; Lyons-Ruth et al. 1986) but also more recently with lower risk community samples, however, in general, the infant deficits were less extreme in these groups (Lovejoy, 2000; Murray et al. 2003).

While a considerable amount of research supports a significant negative relationship between PND and maternal-infant attachment (Dubber et al 2015 & Grace et al 2003), not all mothers with postnatal depression experience difficulties in the attachment process, nor do all mothers with difficulties in the maternal-infant attachment relationship have postnatal depression. Other factors that have been showing to uniquely impact maternal-infant

attachment outside of postnatal depression include, maternal education, perceived social support, infant temperament, and preterm birth (Doyle et al. 2022; Hanko et al. 2020).

Infant temperament has been found to impact maternal PND, on maternal-infant attachment, and on infant developmental outcomes. In general, a secure attachment relationship helps to buffer the impact of less favourablfavorableal (e.g., prematurity) and temperamental factors on developmental outcomes (Brisch et al., 2005). Researchers have suggested the 'goodness of fit' framework for understanding the interplay between an infant's innate temperament and parenting behaviour in explaining a child's attachment and long-term development (Mangelsdorf, 1990). For example, a child who takes time to warm up may pose a difficulty for a parent who is themselv and needs immediate feedback to feel successful with their baby. As such, the infant's temperament has an indirect effect on their development by influencing the behaviour of the caregiver (Hong, 2012). Research has shown that infant temperament (including measures of infant fussiness, activity level and positive affect) were predictive of conduct problems between the ages of 4 and13 years (Lahey, 2008). However, the risk of conduct disorder was reduced in infants of mothers who were rated responsive to their child's needs in the first year of their lives. It appears that although certain temperamental traits are associated with less favourable outcomes the infant's outcome maybe ameliorated by attuned, responsive parents (Lahey, 2008). Equally, parenting may also negatively influence the developmental trajectory of a child who shows no temperamental risk factors for developing atypical behaviour such as conduct disorder if parents are not able to adjust to their child's temperamental needs (Lahey, 2008).

In a systematic review, PND and infant temperament have also been found to be moderately associated with one another (Becks, 2001). In a study by Murray et al (1996) where infant irritability and PND were measured at 10 days old, results indicated that neonatal irritability was the best predictor of the mother's developing depression in a group of women

at high risk of developing PND, irritability was not a risk factor in a low-risk group. PND and infant temperament have been shown to have a bidirectional relationship, with certain infant temperamental traits putting mothers at risk of PND, but also research has shown that an infant's temperament may be affected by maternal PND, for example, Whiffen and Gotlib (1989) found that infants of depressed mothers displayed significantly more negative emotions and were less tolerance than infants of non-depressed mothers.

Furthermore, more recently research has shown that paternal parenting practices may be correlated with maternal mental health and child development. Partners of depressed women have been shown to demonstrate less optimum interactions with their infants. Although less recognised, postnatal depression in men is a significant problem with studies estimating paternal depression to be between 1.2% to 25.5% in community samples (Goodman, 2013). The rate of paternal depression in partners of women who have a diagnosis of PND has been estimated to be as high as 50% (Goodman, 2013). Maternal depression is thought to be the strongest predictor of paternal depression in the postnatal period (Zhang et al. 2016). The influence of fathers' involvement in the neurodevelopment of their children has become of greater research interest in recent years. For example, father-infant play has been shown to offer substantial support for early development in multiple domains, including cognitive development, emotional regulation, and the development of secure attachments (Stein et al. 2014). Paternal PND may pose barriers to father-infant involvement and engagement, if mothers and fathers experience PND at the same time this may further risk the child's developmental potential.

Another factor that has been shown to be correlated with both PND and child development is marital stress (Hanington et al. 2012). Families of depressed mothers report higher levels of stress in comparison to families where mothers are well, marital stress is a particularly important source of stress as it has the potential to impact all family members

(Coyne et al.1990). Levels of marital stress and divorce are must higher in families where the mother is depressed (Coyne, 1990; Johnson et al.1997). Moreover, the significant positive association between marital conflict and child behavioural, emotional, and cognitive problems has been well established in the literature (Cummings et al. 1994, 2002). In addition, marital conflict has been shown to mediate the relationship between maternal and paternal PND and child outcomes (Hanington et al. 2012).

2.3 Breastfeeding and its Impact on Development

Breastfeeding is a significant task of early motherhood. Evidence suggests that it is linked to multiple health benefits, for example, reducing the risk of infection, asthma, obesity, and diabetes (Cushing et al.1998; Stuebe, 2009; Wang et al. 2017). It may also support neurodevelopment (Horta et al. 2018; Sacker et al. 2006). The WHO recommends exclusive breastfeeding for the first six months of life, and continuation of breastfeeding with complementary feedingforo two years and beyond (World Health Organization, 2003). Despite many well-published benefits of breastfeeding, many countries fail to meet the WHO recommendations (Victora et al. 2016). The UK and Ireland have some of the lowest breastfeeding rates in the European region. The latest national Irish figures from 2015-2016 indicate that 60% of mothers breastfeed to any extent at hospital discharge and this drops to 42% at 3 months (Purdy et al. 2017).

There is a growing body of research investigating the effect of breastmilk on neurodevelopment, this is in part because breastfeeding is a modifiable variable that potentially can enhance the physical, emotional, and developmental health of children (Bernardo et al. 2013). One theory regarding the transmission of breastfeeding benefits is that breastfeeding may enhance cognitive development by providing important biological components such as long-chain polyunsaturated fatty acids, certain hormones, oligosaccharides, and phospholipids

that are important for neural functioning (Innis, 2007). Alternatively, researchers have suggested that the positive advantages of breastfeeding on neurodevelopment simply reflect a more advantaged childhood environment and it is these factors that are correlated with enhanced developmental outcomes (Der et al. 2006; Walfisch et al. 2013). For example, mothers who initiate and continue to breastfeed their children tend to be older, have a higher level of education ,and have higher socio-economic status than mothers who never breastfed their children or breastfed for a limited time (Persad & Mensinger, 2008; Thulier & Mercer, 2009) Some studies have shown that the association between breastfeeding and neurodevelopmental outcomes are not statistically significant after adjusting for these confounders (Der et al. 2006; Gibson-Davis & Brooks-Gunn, 2006). Moreover, the positive benefits of breastfeeding may also be linked to an enhanced attachment relationship between mother and infant, this possibility will be considered further below.

In a study where the effect of breastfeeding duration on cognitive and motor development was examined in one- and five-year-old children, an effect of breastfeeding duration was found for cognition but not for motor development (Angelsen et al. 2001; Florey et al. 1995). Of note, infants in the breastfeeding group were exclusively fed. Other studies have also reported no effect of breastfeeding duration on motor development (Moberg & Prime, 2013). On the other hand, Sacker & Quigley (2006) found that breastfeeding was protective against gross motor but not fine motor delay, after controlling for biological, socio-economic, and psychosocial factors (Sacker et al. 2006). Moreover, several studies have found that breastfeeding may positively impact language performance (Guzzardi et al. 2020; Leventakou et al. 2015).

Although the early debate centered on the impact of socioeconomic variables, and how they may accentuate or ameliorate the relationship between breastfeeding and neurodevelopmental outcomes, other socio-environmental factors such as parental nurturance

and maternal-infant attachment may also have an effect (Linde et al. 2020). Breastfeeding might intensify the early mother–infant relationship, by inducing physiological and behavioural changes through the production of hormones prolactin and oxytocin released in response to skin-to-skin contact and suckling (Moberg & Prime, 2013). Breastfeeding has also been shown to have a relaxation effectonr mothers, with studies showing that breastfeeding mothers have lower blood pressure and respond less to stressors than non-breastfeeding mothers (Blincoe, 2005). More relaxed mothers are more able to be responsive and studies have shown that breastfeeding mothers are more socially interactive with their infants (Bernal & Richards, 1970; Wiesenfeld et al. 1985). While this increased responsiveness may be attributed to the impact of the hormones already mentioned, it may also be related to the physical closeness between breastfeeding mothers and their infants (Linde et al. 2020). Studies have shown that breastfeeding mothers seek greater proximity to their infants (Linde et al. 2020). The greater this physical closeness, the more enhanced a mother's responsive caregiving is likely to be, which in turn is likely to develop a positive attachment in the child (Anisfeld et al. 1990). As discussed above, secure attachment reduces infant's anxiety and provides a safe base from which the infant can explore the world around them. Both these outcomes have a positive effect on learning and are likely to enhance neurodevelopment, increasing the likelihood of infants reaching their biological potential.

Studies have also shown the association between PND and breastfeeding with the findings indicating that there is a significant association between these variables, with early exclusive and non-exclusive breastfeeding cessation more likely in the presence of PND symptoms (Bick et al.1998; Dunn et al. 2006; Feldens et al. 2012; McCoy et al. 2008; Taj & Sikander, 2003; Yonkers et al. 2001; Ystrom, 2012; Zubaran & Foresti, 2013). However, the directionality of the association is yet unclear. Although a successful breastfeeding experience is protective against PND (Ystrom, 2012), studies have also indicated that stopping

breastfeeding early in the postnatal period has been associated with an increase in depressive symptoms (Hasselmann et al. 2008; Dennis et al. 2009). This latter association where early breastfeeding cessation has been found to be associated with PND maybe explained by the mother's feeding experience, in particular stopping breastfeeding due to physical difficulties or pain has been found to be associated with PND (Browne et al. 2015). The possible mismatch between positive breastfeeding expectations and the reality of breastfeeding challenges may contribute to feelings of low self-efficacy and guilt, potentially contributing to PND. The direction of the association may also function the opposite way, for example, depressive symptoms may increase the risk of breastfeeding being more challenging or painful. Mothers suffering from depression may interact less with their infants, including reduced touching and skin-to-skin contact (Field, 2010) which may increase the likelihood of breastfeeding difficulties. For example, causing mother to be less sensitive to positioning of the infthe ant on the breast, leading the to poorer latch and lower milk intake ultimately leading to poorer infant weight gain and breastfeeding cessation (Hart et al., 2011).

Moreover, mothers who have had difficult birth experiences are at greater risk of both finding breastfeeding more difficult and developing PND symptoms. Other factors that may contribute to both shorter breastfeeding duration and depressive symptoms include high maternal trait anxiety (Brown, 2014) and low maternal self-efficacy (McQueen et al. 2011). Both of these factors are likely to leave mothers feeling less able to cope with motherhood in general, predisposing them to poorer breastfeeding outcomes and PND.

While considerable research attention has been given to the association between PND and breastfeeding, less research has considered the socio-cognitive factors connected to breastfeeding, including the impact of negative attitudes to breastfeeding and breastfeeding self-efficacy and their impact on PND (Dias & Figueiredo, 2015). Breastfeeding self-efficacy refers to a woman's confidence in her capacity to breastfeed. Self-efficacy influences behaviour

by impacting how much effort someone expends and how long they persist with a task, as well as how they respond when faced with challenges and the nature of their self-talk, (for example, if it is self-encouraging or self-debilitating cognitions) (Dennis & Faux, 1999). The degree to how self-efficacious someone is, is related to their own previous experience of the task, their vicarious experience of the task (viewing someone else completes the task), the encouragement they receive from influential others (social supports,) and their physiological responses (somatic reactions to anticipation or experience of the event) (Dennis, 2003; Dennis & Faux, 1999).

The affect of maternal confidence in breastfeeding has been investigated by several researchers, the majority of which show a significant inverse relationship, meaning that mothers who experience low levels of breastfeeding self-efficacy are more likely to be at risk of PND (Dennis & Faux, 1999; Dennis & McQueen, 2007; Minamida et al. 2020). However, the direction of this relationship is yet unclear. Methodological differences and limitations among the existing research have also led to difficulty in interpreting the overall picture. For example, the association between PND and breastfeeding self-efficacy has rarely been the primary research question in studies that have examined their relationship, therefore the limiting the possibility of examining causal relationships between the factors. There has also been a lack of reporting of confounding variables controlled for, for example, parity, depression hist,ory and obstetric health, therefore existing findings need to be interpreted with caution (Aoyagi & Tsuchiya, 2019).

Proponents of IMH state that infancy is a time of critical importance and an infant's mental health is the foundation of all future development. Attachment, PND, and breastfeeding may directly impact neurodevelopmental outcomes, but indirect effects of attachment and PND may also be mediated through the maternal-infant attachment relationship. The postnatal period is made up of a tangled web of important variables that may impact long-term

neurodevelopment (see Figure 1), however much of the research to date has looked at the impact of these variables on development independently rather than taking a multifactorial approach. Moreover, while a considerable volume of research has looked at the associations between these early postnatal variables and child developmental outcomes, there remains no consensus among the findings. This may be due tovariationsn in the methodological approaches taken between existing studies. There is a need for more longitudinal, prospective studies that precisely define the variables of interest and that control for important confounding variables (Aoyagi & Tsuchiya, 2019; Figueiredo et al. 2013; Slomian et al. 2019).

The complicated interactions between early postnatal factors such as PND, breastfeeding, and maternal-infant attachment makes it important to consider their impact simultaneously on long-term developmental outcomes. What is common amongst these variables is that they are modifiable and a greater understanding of their impact on neurodevelopment, as well as greater clarity surrounding their relationship with one another, could potentially be of great public health importance, as they potentially offer routes to intervention that may reduce long-term developmental delay.

While considering the consequences of these early variables is of high research priority, it is also essential that risk factors for PND are considered so that preventative measures can be investigated. Breastfeeding self-efficacy is a PND risk factor that is recently gaining more research attention. The research, to date, seems to support an association between PND and breastfeeding self-efficacy (Dennis, 2003; Dennis & Faux, 1999; Minamida et al. 2020). However, the direction of the association is of yet, unclear. The next chapter presents a systematic review that investigated whether breastfeeding self-efficacy is associated with later postnatal depression.

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3.Systematic Review

Is breastfeeding self-efficacy associated with later postnatal depression? A systematic review of prospective studies.

Prepared submission guidelines for the

International Breastfeeding Journal

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3.1 Abstract

Aim: To review studies that have examined the association between breastfeeding self-efficacy and subsequent postnatal depression. The longitudinal and concurrent relationship of breastfeeding self-efficacy to PND was reviewed using prospective studies only.

Method: Literature was synthesised from four databases, PsychINFO, MEDLINE, PsychArticles, and CINAHL in October 2020. Two researchers independently assessed the articles for the following inclusion criteria: prospective studies where the relationship between breastfeeding self-efficacy with later postnatal depression, within the first year postnatal was examined. Participants were healthy primiparous or multiparous women who had given birth to a term or near-term singleton and healthy baby. Breastfeeding self-efficacy was measured within the first six weeks postpartum and PND was measured within the first year postpartum.

Results: Five studies met the inclusion criteria (n = 1,299). Bivariate and multivariate associations are described, and a narrative synthesis of the findings is outlined. Results indicated an effect of breastfeeding self-efficacy on postnatal depression. Specifically, low breastfeeding self-efficacy scores at baseline (ranging from one day to six weeks following birth) were predictive of increased risk of postnatal depression symptoms at follow-up (within the first six months postpartum) in all five studies reviewed. The results also indicated that there was a concurrent association between breastfeeding self-efficacy and postnatal depression when the association was examined cross-sectionally at baseline. Moreover, the predictive significance of breastfeeding self-efficacy became weaker and more varied across time in the postnatal period.

Conclusion: Findings suggest that breastfeeding self-efficacy is not just associated with postnatal depression contiguously in time but predicts the extent of PND across time.

Keywords: Breastfeeding self-efficacy; postnatal depression; postpartum depression; systematic review.

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3.2 Background

It is estimated that the prevalence of postnatal depression (PND) is 19.2% within three months post-delivery (Gavin, Gaynes, Lohr, Meltzer-Brody, Gartlehner & Swinson, 2005). PND has a significant impact on maternal health and well-being and the consequences can be wide-reaching, impacting the mother, infant, and wider family. Therefore, PND is an important public health concern. In many cases, PND can be affectively treated, yet many mothers do not seek treatment and it is often missed by primary caregivers (Briscoe & Williams, 1985; Coates, Schaefer & Alexander, 2004). In the UK and Northern Ireland, the rate of perinatal suicide is 3.7%, with approximately half of these mothers, who die by suicide in the postnatal period, not receiving a diagnosis. The American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, fifth edition* defines PND as a major depressive episode, it involves moderate to severe symptoms that begin within four weeks of delivery.

The symptoms of PND are like the symptoms of depression that occur outside the postnatal period (e.g., sleeping and eating disturbances, emotional lability, guilt, shame, and suicidal thoughts) (O'Hare & McCabe, 2013). However, what differs is the critical importance of this period for women and their babies. There is considerable evidence to suggest that PND compromises the maternal-infant relationship and maternal caregiving capacities, the result of which can have long-term negative consequences for children across physical, social, emotional, psychological, and educational domains (see review by Aoyagi & Tsuchiya, 2019). The personal and societal costs of PND are vast, and as such PND constitutes a significant

public health concern. Therefore, more knowledge is needed about risk and protective factors to prevent the effects of PND.

Two of the most powerful PND risk factors are lack of social support and the mother's previous history of depression and anxiety, with depression in pregnancy being identified as one of the strongest predictors of PND (Ghaedrahmati, Kazemi, Kheirabadi, Kheirabadi, Ebrahimi & Bahrami, 2017). Other risk factors identified include low income, less maternal education, young age (13–18-year-old mothers have the highest risk), having more than one child and labour complications (Ghaedrahmati et al. 2017). While many of these risk factors are non-modifiable, one potential PND risk factor that may be amenable to intervention is breastfeeding failure. Whilst the latter has been associated with PND, the direction of the relationship remains equivocal (Dennis & McQueen, 2007; Henderson, Evans, Straton, Priest, & Hagan, 2003). For example, some studies have found that PND emerges because of breastfeeding interruption suggesting that stopping breastfeeding early may be involved in the cause of PND (Mezzacappa & Katkin, 2002; Mezzacappa & Endicott, 2007). However, other studies suggested that PND symptoms precede breastfeeding cessation and therefore PND is involved in the cause of early cessation rates (Dennis & McQueen, 2007; Galler, Harrison, Ramsey, Chawla & Taylor, 2006; Henderson et al., 2003).

While much of the research in this area has focused on the links between PND and actual breastfeeding behaviour, a limited but growing body of research has investigated the association between PND and other features of breastfeeding such as breastfeeding self-efficacy (e.g., Dennis, 2003; Dennis et al., 2007; Henshaw, Fried, Siskind, Newhouse, Cooper, 2015; Minamida, Iseki, Sakai, Imura, Okano & Tanii, 2020;). Self-efficacy is defined as an individual's confidence in his or her perceived ability to perform a task or behaviour (Bandura, 1977). Self-efficacy plays a part in determining how much effort an individual will expend and how long they will persist when faced with a challenge and whether they have more

encouraging or self-defeating thoughts (Dennis, 2003). Bandura (1977) argued that a general measure of self-efficacy was not sufficient when investigating self-efficacy associated with specific behaviours. Therefore, the breastfeeding self-efficacy measure was developed by Dennis & Faux (1999). High rates of breastfeeding self-efficacy have been found to increase the duration and exclusivity of breastfeeding (de Jager, Broadbent, Fuller-Tyszkiewicz & Skouteris, 2014; McCarter-Spaulding & Gore, 2009; Ystrom, Niegel, Klepp & Vollrath, 2008).

As breastfeeding is thought to be a protective factor reducing the risk of PND, it is also hypothesized that social cognitive factors such as breastfeeding self-efficacy would help to offset depressive symptoms in the postpartum period. Of the studies examining breastfeeding self-efficacy and PND, the majority show a significant inverse relationship, that is, mothers who experience low levels of breastfeeding self-efficacy are more likely to be at greater risk of PND (Dennis, 2003; Dennis et al. 2007; Henshaw et al., 2015; Minamida et al. 2020). In the early postpartum period, feelings of low self-efficacy in breastfeeding may make a mother more vulnerable to negative perceptions of the breastfeeding experience. This negative perception may be further reinforced by negative cognitive bias, characteristic of depressive presentations. These negative cognitions may also lead to a mother misinterpreting her infant's signals. Impaired maternal-infant interactions are a feature of PND and may help to explain the dissatisfaction experienced by the mother with her infant feeding method (Dennis et al. 2007).

Although research tends to point towards a significant negative association between PND and breastfeeding self-efficacy, the direction of that relationship is yet unclear (Dennis, 2003; Dennis et al. 2007; Henshaw et al. 2015; Minamida et al. 2020). Moreover, the methodological limitations within the research base mean that results need to be interpreted with caution. Of note, the association between PND and breastfeeding self-efficacy is rarely the primary research question, and therefore, the reporting of findings in this area is somewhat scarce and studies often use cross-sectional designs limiting the possibility of examining causal

relationships between the factors. Poor reporting of important confounding variables such as parity, obstetric health and depression history also make interpretation of results difficult.

The current review aims to look at the longitudinal impact of early breastfeeding self-efficacy on PND later in the postpartum period. To allow for a relatively greater interpretation of causality, only prospective studies were included. Where cross-sectional associations between breastfeeding self-efficacy and PND are included in the prospective studies, they are also reported in this review. This review endeavourendeavorslight on the directionality of the association between breastfeeding self-efficacy and PND and help to delineate the potential risk factors /consequences of PND more clearly. As breastfeeding self-efficacy is a modifiable variable, the current review may offer direction to future intervention studies. To the authors' knowledge, there is no published systematic review addressing the direction of the relationship between PND and breastfeeding self-efficacy.

3.3 Methods

The review was conducted by Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines for the reporting of systematic reviews (Liberati, Altman, Telzaff, Mulrow, Gotzche, Loannidis, …& Moher (2009).

3.3.1 Inclusion Criteria

Studies considered for the review were published longitudinal prospective studies in English. Studies were included if they reported outcomes for healthy primiparous (good physical health/ no serious obstetric complications) or multiparous women, who gave birth to a term or near-term singleton and healthy baby. History of depression/depression during pregnancy was not an exclusion criterion as studies did not typically control for this variable. Only studies that included standardized validated outcome measures of breastfeeding self-efficacy and PND were included. Studies that examined the relationship between breastfeeding self-efficacy with later PND were included. Where such studies also included cross-sectional associations between breastfeeding self-efficacy and PND, these associations were also examined. However, the primary focus was on the prospective relationships. Studies were included if they measured breastfeeding self-efficacy within the first two months postnatal and PND within the first year postnatal.

3.3.2 Search Strategy

A scoping review was conducted to inform the final inclusion criteria and relevant search terms to be used in the final review. To also help generate the search terms, similar systematic reviews were consulted. In addition, common terms used in the research area were identified by searching keywords in Google Scholar. Preliminary search terms were further developed in consultation with a University College Cork's subject librarian.

When the search terms were identified, a systematic review was conducted by entering the search terms into the following databases: PsycINFO, MEDLINE, PsychArticles, and CINAHL on the 1st of October 2020, no date restriction was applied. This search was repeated in October before submission, the date was restricted to the prior two years for this second search.

The following search terms were used ("postpartum depress*" OR "postnatal depress*") AND (breastfeeding OR "breastfeeding") AND ("breastfeeding self-efficacy" OR "breastfeeding self-efficacy" OR self-efficacy). The search was limited to papers' titles and abstracts. Grey literature was included as an attempt to account for publication bias. In October 2020, key terms were entered into Google Scholar and the first 200 items were reviewed. In addition, the reference list of the final review papers was hand-searched for studies that met the inclusion criteria.

Retrieved articles were exported from each database to a data manager *Covidence*, where duplicates were removed. Studies were excluded in a stepwise manner of screening titles, abstracts, and full texts The two authors (MW and CM) independently reviewed the studies. The studies were first reviewed at the title and abstract level and then the remaining studies at full-text level were read in depth. Agreement on articles for inclusion was 100% between the two authors. Studies were excluded if they did not meet the inclusion criteria set out by the author. Studies were excluded for the following reasons: the study was cross-sectional in nature and did not include a longitudinal PND outcome variable, measures of breastfeeding self-efficacy or PND were either not standardized or were not completed within the timescales set out in the inclusion criteria, and one study was excluded because participants (mothers) in the study were younger than 18 years old.

3.3.3 Study quality

The *National Heart, Lung, and Blood Institute-Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies* was used to assess study quality (Appendix D). The scale consists of 14 quality assessment statements evaluating a range of quality criteria. Statements related to the specification of the research question and population sample, justification of sample size, level of attrition, reliability of measures used, and inclusion and adjustment for confounding variables. All included papers were assessed by the first author (MW) and a subset (43%) was cross-checked by the second author (CM). Discrepancies between authors' scores that arose were addressed through discussion until consensus was reached. A score ≥12 was deemed 'good' quality, studies receiving scores between ten and twelve were deemed 'fair' quality and papers ≤10 were deemed 'poor' quality. This categorisation was reached through author discussion and review of The *National Heart, Lung and Blood Institute-Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies* guidelines.

Figure 2: Prisma Flow Chart Demonstrating Systematic Search Process

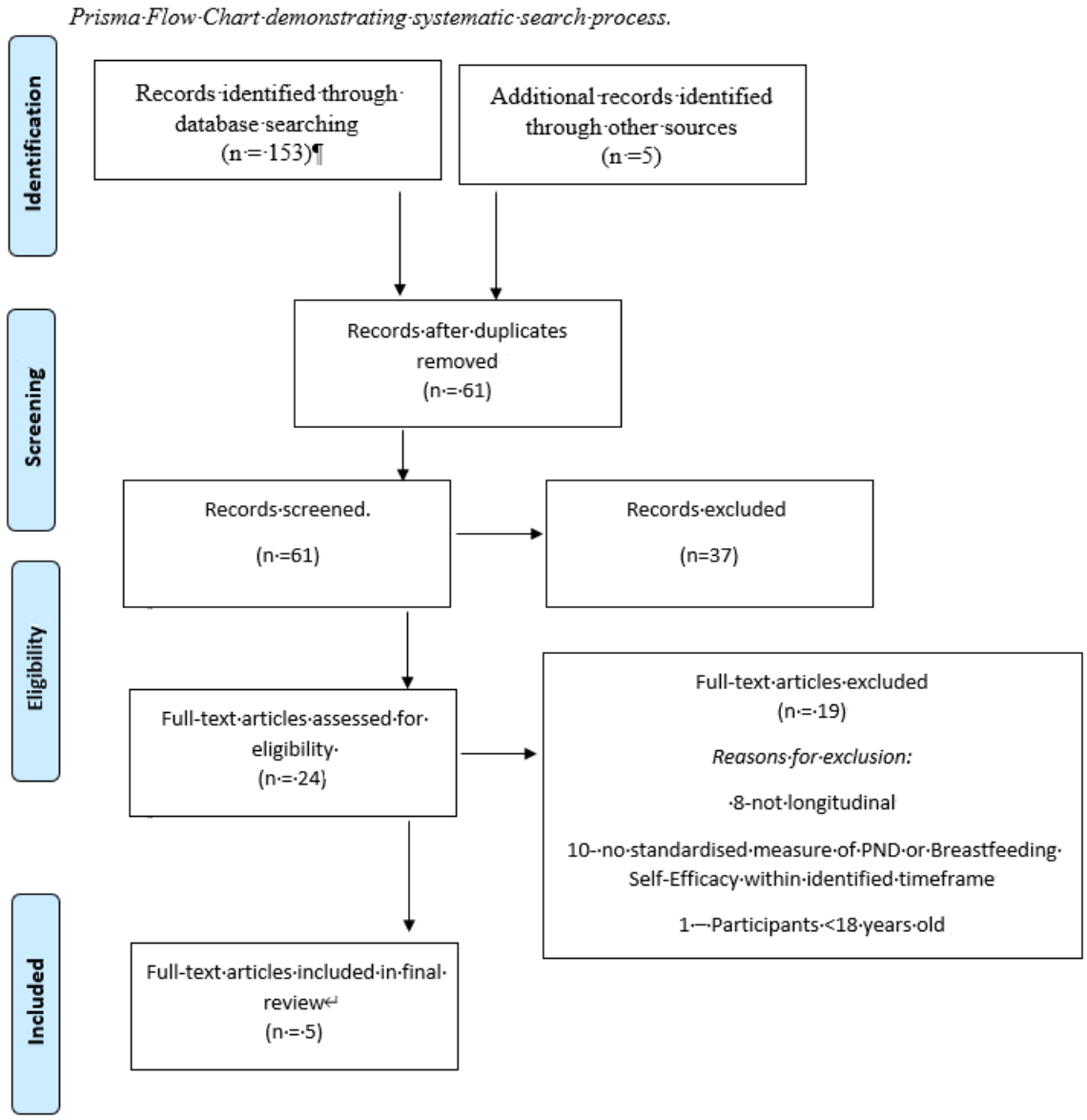


Table 1: Quality assessment of included studies- National Heart, Lung, and Blood Institute; Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.

Study, Year	The research question clearly stated	The study popularly specified and defined	Participant rate of the eligible person's at least 50%	Participants recruited from the same or similar population	Sample size justified	Exposures of interest measured before outcomes of interest	Examination of different levels of exposure as related to outcome	Exposure measures are clearly defined, valid, reliable, and implemented across all participants	Exposure (s) measured more than once over time	Outcome measures are clearly defined, valid, reliable, and implemented across all participants	Outcome assessors blinded to the exposure status of participants	Loss to follow-up after baseline 20% or less	Key confounding variables were measured and adjusted statistically for their impact between exposure(s) and outcome(s)
Dennis 2003**	✓	✓	✓	✓	×	✓	✓	✓	✓	✓	✓	✓	✓
Haga 2012*	✓	✓	✓	✓	×	✓	✓	✓	✓	✓	✓	×	✓
Henshaw 2015*	✓	×	✓	✓	×	✓	✓	✓	✓	✓	✓	×	✓
Minamida 2020**	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	×	✓
Dennis 2007**	✓	✓	×	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Note: ✓ indicates criterion was met, X indicates criterion was absent, NR indicates not reported ** indicates 'Good' quality * indicates 'Fair' quali

3.4 Results

The study screening and selection process is illustrated in the PRISMA flow chart in Figure 1. Of the initial 158 articles identified by the search, five papers were suitable for inclusion in the review (Dennis, 2003; Dennis et al., 2007; Haga et al., 2012, Henshaw et al., 2015; Minamida et al., 2020). All papers were longitudinal, prospective designs that collected data at least three times within the first six months postpartum. It appears that both Dennis's papers shared a pool of participants, although this is not made explicit within the respective papers. There were 1,299 participants across all included studies, the participants in both Dennis studies were only counted once fof this review. Moreover, the overall average maternal age was 29 years. The studies were conducted in both western and eWesterncountEastern.e., Japan, Canada, USA, and Norway), representing varying cultural influences and health and social care infrastructures. In two of the studies, all mothers were primiparous (Henshaw et al. 2015; Minamida et al. 2020), while the other studies included a combination of primiparous and multiparous mothers (Dennis, 2003; Dennis et al. 2007; Haga et al. 2012). Most participants had post-secondary qualifications and were in a relationship.

The quality of each study, according to *National Heart, Lung and Blood Institute-Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies* is outlined in Table 1. All studies were rated ‘good’ or ‘fair’, none of the studies received a ‘poor’ rating. The main limitation of the included studies was the attrition rates were high, potentially introducing bias into the sample. This is a common criticism of longitudinal studies. Participant characteristics and the study's main findings are summarised in Table 2. Due to the differing research designs, analyses, and measures used, conducting a meta-analysis was not possible. Instead, bivariat, and multivariate associates are described, effect sizes were calculated and are presented in Figures 2 and 3 and a narrative synthesis of the findings is outlined.

Table 2: Summary of participant characteristics and key findings of reviewed studies.

Study	N	Mean age (SD)	Parity	Sample characteristics	Measures	Key findings
Dennis 2003 (Canada)	491	29 (5.0)	45% primiparous, 55% multiparous	40% had completed a college or technical school diploma and 24% had completea d university degree or higher. Relationship status: not reported	BSES-SF, EPDS, RSES, PSS	The cross-sectional analysis found a significant negative correlation between breastfeeding self-efficacy and EPDS scores at one week postnatal (r =-.38). The longitudinal analysis found a significant negative correlation between breastfeeding self-efficacy at one week postnatal and EPDS scores at four weeks (r = -.35) and 8 (r = -.25) weeks postpartum.
Haga 2012 (Norway)	344	32 (4.32)	64.6% primiparous, 28.2% were mother to two children,7% were mother to 2+ children	42% completed a bachelor and 41.7% completea d master's degree or higher. 45.2% were married, 53.2% were in common law marriages and 15% were single	EPDS, CERQ, BSES-SF, BSSS	Breastfeeding self-efficacy was a significant predictor of EPDS score at 1.5 months postpartum (B = -.1) and the change in EPDS score over time (B = -.01) The best model for predicting EPDS included BSES, the Berlin Social Support Scale, and Cognitive Emotion Regulation Scales (R^2 = 37.7).
Henshaw 2015 (USA)	142	30 (5.12)	All participants were primiparous	Not reported. 73.53% were married, 18.63% were in common law marriages and 7.84% were single	EPDS, PDPI-R, BaM-13, BSES-SF (Single item rating on the following: breastfeeding ease, partner support, use of breastfeeding education resources).	BSES-SF at two days postnatal was a significant predictor of depressive symptoms at 6 weeks (B = -.32) and 6 months (B = -.11) postpartum. The best model for predicting depressive symptoms included ethnicity, education, income, EDPI-R, EPDS, work status, breastfeeding status, breastfeeding ease, breastfeeding class, lactation support and consultation, and breastfeeding self-efficacy (R^2 = .4 at 6 weeks; R^2 = .16 at 6 months).
Minamida 2020 (Japan)	185	28 (4.9)	All participants were primiparous	43.14% completed college and 29.90% completed a master's degree or higher. Relationship status: not reported	EPDS, BSES-SF, PBQ, and STAI	When the BSES-SF scores from baseline (1 day postnatal) were compared with depressed and non-depressed mothers at 1 month follow-up, a significant difference was evident (p <.05, r=.27) Both the depressed group and non-depressed group showed significant increases in BSES-SF over time (1 day, 3 days, and 1 month postnatally).

Dennis 2007 (Canada)	594	28 (5.0)	44% primiparous, 56% were multiparous	38% completed college and 21% completed university with a bachelor's degree or higher. 90% were married or in common-law marriages.	EPDS & BSES	When the BSES-SF scores from baseline (one-week postnatal) were compared for depressed and non-depressed mothers, a significant difference was evident at four weeks ($p < .001$, $r = 39$). At 8 weeks, the depressed group had significantly lower BSES-EF scores ($p = .004$, $r = .11$)

Edinburgh Postnatal Depression Scale. PDPI-R, Postpartum Depression Predictors Inventory-Revised, BaM13 a mother scale. BSES-SF, Breastfeeding Self-efficacy Scale-Short form. CES-D, PBQ, Postnatal Bonding Questionnaire. STAI, State-Trait Anxiety Inventory. RSES, Rosenberg Self-Esteem Scale. PSS, The Perceived Stress Scale. CERQ, Cognitive Emotional Regulation Questionnaire. BSSS, Berlin Social Scal

Figure 3: Effect size (r) for the effect of self-efficacy on depression at baseline.

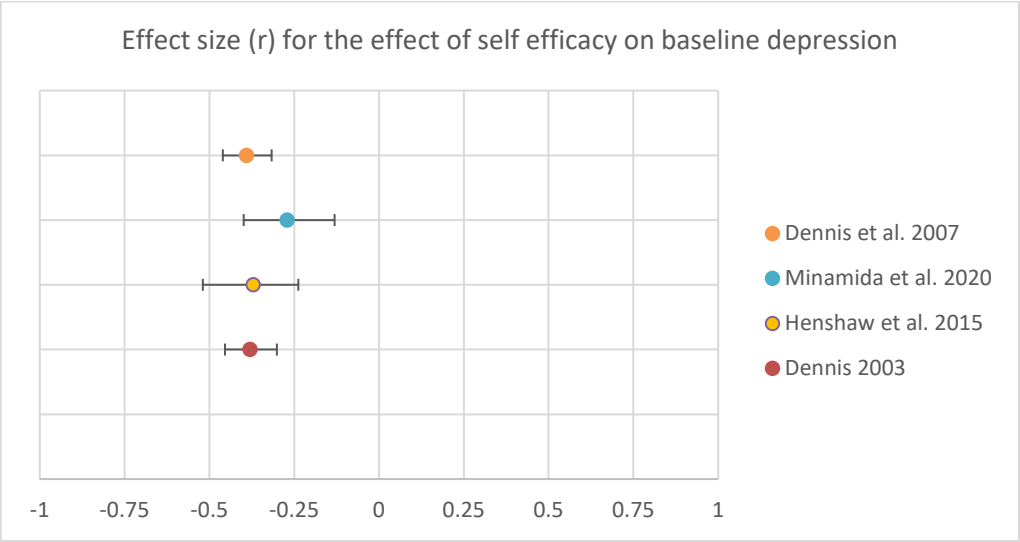
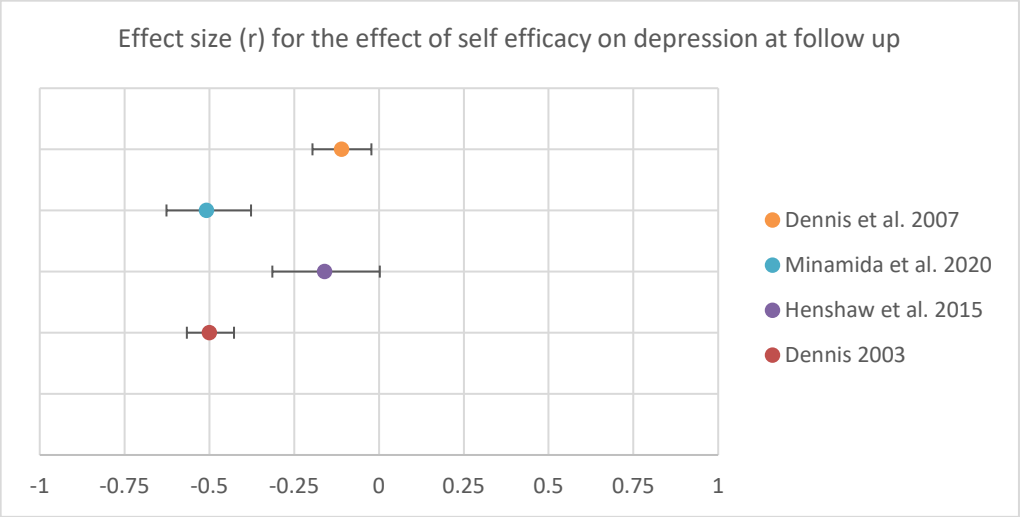


Figure 4: Effect size (r) for the effect of self-efficacy on depression at follow-up



3.4.1 Study Findings

Table 2 presents a summary of the included studies. The *Edinburgh Postnatal Scales* (EPDS) was used as the measure of PND in all studies (Cox, Holden & Sagovsky, 1987). Three of the studies used the breastfeeding self-efficacy scale while four of the studies used the shortened version of the breastfeeding self-efficacy scale (Dennis, 2003; Dennis et al., 1999).

The statistical analysis varied considerably between studies. One of the studies (Henshaw, 2015), carried out a hierarchical linear regression, examining the unique variance of breastfeeding self-efficacy after controlling for multiple factors: race/ethnicity, education, income, postnatal depression, postpartum depression, work status, breastfeeding ease, breastfeeding, breastfeeding class, breastfeeding support, and lactation consulting. One study used a multilevel longitudinal model (Haga et al. 2012) and one used correlation analysis (Dennis, 2003). All the studies found a cross-sectional association, demonstrating that breastfeeding self-efficacy at baseline (ranging between one day to six weeks postnatal) was predictive of depressive symptoms at baseline (effect sizes ranging from medium to large, r = -.35 to r = -.55), and all studies also found breastfeeding self-efficacy at baseline predictive of depression at a later stage (ranging from four weeks to six months postpartum) in the postpartum period (effect sizes ranging from small to large, r = -.16 to r = -.5).

In addition, Dennis (2007) and Minamida (2020) utilised between-group statistical analyses, such as t-tests and ANOVAs. These studies collected breastfeeding self-efficacy at baseline (ranging between one-day to one-week postnatal) and depression scores at baseline and at follow-up (follow-up ranging between one month and two months postnatal). Participants were categorised into groups at follow-up (depressed v not depressed) and compared across baseline breastfeeding self-efficacy scores. Minamida et al., (2020) utilised a two-way repeated measures ANOVA to examine the relationship between PND and breastfeeding self-efficacy, while Dennis et al. (2007) used T-tests. Both studies found that the breastfeeding self-efficacy scores at baseline were significantly lower for women in the depressed group than the non-depressed group (r = 0.27- -0.39). More specifically, Dennis et al. (2007) found that although mothers with breastfeeding self-efficacy scores at baseline had a significantly greater risk of postnatal

depression at four weeks postnatal follow-up, this effect weakened over time, and lower breastfeeding self-efficacy was not associated with a greater risk of postnatal depression at the eight- week postnatal follow up. The results of Minamida's (2020) study indicated a similar effect of time, finding that breastfeeding self-efficacy scores of both depressed and non-depressed groups significantly increased over-time and that there was no significant difference in this change between these groups over time.

3.4 Discussion

Findings suggest that breastfeeding self-efficacy is not just associated with PND contiguously in time but predicts the extent of PND across time. This has been ambiguous in the literature to date. However, all five prospective studies that fit the inclusion criteria of the current review indicated a significant negative association between breastfeeding self-efficacy at baseline and PND at a later time point in the first postpartum year; indicating that mothers who experience lower breastfeeding self-efficacy in the first weeks postnatal are more likely to experience PND at a later stage in the postnatal period. However, the review also indicated that this association weakens over time, and baseline measures of breastfeeding self-efficacy are less predictive of PND as the postnatal year progresses.

However, some inconsistencies across studies existed about the impact of time on relationsthe hip between breastfeeding self-efficacy and PND. For example, Dennis (2003) reported a significant negative relationship between breastfeeding self-efficacy and PND at all three time points (i.e., one week, four weeks and eight weeks postnatal) yet this was not the case in a later study by Dennis et al. (2007). In the later study, the author compared depressed and non-depressed groups at four and eight weeks on breastfeeding self-efficacy taken at baseline (one week postpartum), and he found a significant difference between the groups at four weeks but not at eight weeks. This later

outcome was supported by Henshaw et al. (2016) who indicated that breastfeeding self-efficacy was a stronger predictor of PND at six weeks than it was at six months.

The weaker and more varied relationship between baseline breastfeeding self-efficacy and PND at later time points may be understood in the context of self-efficacy theory where performance accomplishment through actual mastery of the task (e.g., actual breastfeeding) is the most powerful source of self-efficacy information (Dennis, 2003). This theory may also help to explain why previous research has found that women with previous breastfeeding experience had significantly higher breastfeeding self-efficacy than women without those previous experiences (Dennis et al.1999) We can hypothesis that the findings, for the current review, may suggest that as mothers gain more experience of breastfeeding, their breastfeeding self-efficacy scores increase regardless of their depression status, therefore weakening the association between breastfeeding self-efficacy and PND as time progresses.

However, other factors are also likely to impact more on the association between self-efficacy and PND as time goes on, such as social support and infant temperament, possibly weakening the relative weighting of the original relationship between breastfeeding self-efficacy and PND. While all included studies found an association between breastfeeding self-efficacy and later PND, the strength of the association varied across studies. For example, Henshaw et al. (2015) found that breastfeeding self-efficacy accounted for a larger proportion of the variance than in the Haga et al. (2012) study. This difference may be due to the variance accounted for by an additional factor such as social support that was included in the Haga et al. (2012) study. Bandura (1977) identified several key sources of information needed when making self-efficacy judgments, these included vicarious experience and verbal persuasion such as encouragement from influential others. Considering the importance of social influence in the definition of self-

efficacy, it is likely that social support is highly related to breastfeeding self-efficacy. While breastfeeding self-efficacy still shows unique significance in the association, this effect appears to be attenuated by social support in the Haga et al. (2012) study. Future studies should consider whether the effect of breastfeeding self-efficacy is direct or indirect by considering possible mediating variables and interactional effects.

Many of the studies within the literature base that examined the association between breastfeeding self-efficacy and PND are cross-sectional, providing no information regarding the direction of the relationship between self-efficacy and PND. One of the major strengths of this review is its inclusion of prospective studies only, enhancing our interpretation of causality. The prospective nature of the studies also addresses the potential for recall bias, a common criticism in breastfeeding research. The review only included studies that used standardised measures of breastfeeding self-efficacy and PND to enhance the reliability and validity of the findings and allow for a comparison of results. As most studies reported the association between breastfeeding self-efficacy and PND as secondary data analysis, and due to the inconsistencies in data analysis across studies, interpretations of the data in this field of study were difficult. Therefore, this review provided an important synthesis of the findings to date. In addition, a comparison of effect sizes across included studies demonstrated the varied strength of the affect of breastfeeding self-efficacy on PND across time, an important finding that up to this point has not been emphasised or well-articulated.

Current findings provide some clarity that breastfeeding self-efficacy may indeed influence the development of PND, rather than being a consequence of it. Women often perceive breastfeeding as one of the most important tasks of early motherhood, how a woman feels about her apparent success or failure at this task, it seems, may shape her early postnatal emotional response. The first postnatal year is a period of huge

vulnerability for women. Women are more likely to develop depression in this period than in any other period in their lives (Figueiredo et al. 2012). The ongoing research into the protective role of breastfeeding against postnatal depression, however, relatively few have focused on the link between PND and breastfeeding self-efficacy, with even fewer fitting the inclusion criteria for this study. However, the findings of this review suggest that social-cognitive factors connected to breastfeeding such as breastfeeding self-efficacy may play an important protective role and warrant further investigation.

The social-cognitive theory holds that human behaviour is determined by the dynamic interplay between personal, behavioural, and environmental influences, more specifically these factors include goals/intentions, self-efficacy, outcome expectancy and social structural factors (e.g., living conditions, health, etc) (Locke, 2011; McAlister et al. 2008). Various studies have indicated that social-cognitive factors, in particular breastfeeding self-efficacy, as well as breastfeeding intentions and outcome expectancy, are the mechanisms by which breastfeeding is affected by or effects PND. (Borra et al. 2015; Davey et al. 2011, Dennis & McQueen, 2007, & Galler et al. 2006) A greater understanding of the complex interplay between these social-cognitive factors relating to breastfeeding is necessary. While the current review has only examined the relationship between breastfeeding self-efficacy and PND, the wider social-cognitive research base is suggestive that the mothers' negative perceptions of their breastfeeding experiences are associated with PND (Pope & Mazmanian, 2016). Future studies should take into consideration other important social-cognitive factors such as outcome expectancy when examining the relationship between breastfeeding self-efficacy and PND. A study looking at predictors of exclusive breastfeeding indicated that breastfeeding self-efficacy and outcome expectancy when combined were a stronger predictor of exclusive breastfeeding

than either of the factors individually, this may also be the case in predicting PND (Minas & Ganga-Limando, 2016).

There are some limitations to this review that should be considered. Firstly, the number of studies that fitted the inclusion criteria was very limited. The review highlighted a real need for more prospective studies, as the majority of studies in this area used a cross-sectional design. Moreover, two of the included studies appeared to draw from the same pool of participants. Furthermore, the variables of interest to this review were mainly secondary data outcomes, and as such, the reporting of these findings was often sparse, limiting the conclusions that could be drawn. Statistical tests such as t-tests and ANOVA were less well suited to the question of interest in comparison to correlation and regression as they introduced a retrospective data analysis aspect despite the overall studies being prospective in nature. Three studies included a mix of multiparous and primiparous mothers. As multiparous mothers have been found to have higher breastfeeding self-efficacy than primiparous mothers, likely because of previous experience of breastfeeding bolstering their confidence, the inclusion of a mixed sample makes findings more ambiguous. Future studies should endeavour to recruit homogeneous samples in terms of parity. None of the studies controlled for a history of depression or prenatal depression, as both these factors are considered strong predictors of PND, this is a limitation of these studies. Future research should address the dearth of studies controlling for a history of depression. The EPDS cut-off across studies ranged between 8 and 12, higher EPDS cut-offs can increase the possibility of PND false positives introducing bias into the sample and increasing the possibility of type one error. Overall, the included studies were of good quality, but several studies had a greater than 20% loss to follow-up. If the reason for this attrition rate was related to the exposure or

dependent variables, bias could be introduced into the sample and impact on the studies internal validity (Ferreira & Patino, 2019).

PND poses a significant public health risk that can have long-lasting consequences for both mother and child. The current review indicates that there is an association between breastfeeding self-efficacy and PND and that low levels of breastfeeding self-efficacy, in the early postnatal period, is predictive of depressive symptomology up to six months postpartum. However, the strength of this predictive effect weakens over-time. If how a woman perceives her skill in breastfeeding is related to her early emotional experience of motherhood, then it is important that we consider how to improve a women's breastfeeding self-efficacy because it may reduce the risk of early emotional disturbance, including PND.

Research investigating the development of breastfeeding self-efficacy is relatively recent. Much of this existing research has focused on individual-level interventions (Brockway et al., 2017). However, it has been suggested that for individual-level interventions to be successful in improving self-efficacy the correct structural conditions for creating breastfeeding success also needed to be present, such as the participation of the hospital in the Baby-Friendly Hospital Initiative (Otsuka et al., 2014).

All 19 maternity units in Ireland participate in the Baby Friendly Health Initiative, as part of this it states that new-born infants should receive no food or drink other than breastmilk, unless medically indicated (Quigley et al., 2016). However, research shows that hospital births have been associated with formula supplementation (Bookhart et al., 2022). This maybe clinically indicated but may also be encouraged by hospital staff due to inadequate staffing and shortage of time, with formula providing a more convenient alternative to working through breastfeeding issues (Quigley et al., 2016). Nursing and support staff may also lack training to adequately support mothers with breastfeeding

difficulties. Self-efficacy theory suggests that self-efficacy plays a part in determining how much effort an individual will expend and how long they will persist when faced with a challenge. Moreover, the degree to how self-efficacious someone is, is related to their own previous experience of the task, their vicarious experience of the task, and importantly the encouragement they receive from influential others (social supports) (Dennis, 2003; Dennis & Faux, 1999). If professionals are not encouraging breastfeeding women to persist when faced with challenges and not providing adequate emotional and practical assistance in continuing to breastfeed, considering self-efficacy theory it is likely this would have a negative impact on a mother's breastfeeding self-efficacy.

In a recent Irish study results indicated that Home birthed infants were overall twice as likely to be breast fed (Quigley et al., 2016). Previous published findings from similar studies in other counties were also consistent with these findings (Al-Sahab et al., 2010, Brocklehurst et al., 2011; Cheyney et al., 2014; Norris et al., 2013). These finding are interesting as it provides opportunity to consider what aspects of care may improve breastfeeding outcomes, including breastfeeding self-efficacy. While it is currently unclear what underlies the association between sustained breastfeeding and home birth, some possible factors have been suggested. For example, in Ireland, for mothers choosing a home birth a mid-wife is the primary carer for the mother-infant dyad until the infant is 14 days old (HSE. National Home Birth Services). Consequently, the mother receives consistent advice and support from a single midwife, often with specialist lactation training. In contract, multiple health professionals are involved in care following hospital birth, including the obstetrician, general practitioner, and the public health nurses (PHN) (HSE. Maternity and Infant Care Scheme). Research has also shown that the PHN service often fails to meet postnatal breast-feeding support needs (Leahy-Warren, 2009). It is possible that the consistent input from one well-trained professional, with the time to

trouble short breastfeeding problems with new mothers may help to provide the necessary scaffolding to improve breastfeeding outcomes. However, this study did not examine the impact of location of birth on breastfeeding self-efficacy. Other important psychosocial factors such as breastfeeding expectations, faith in breast milk and dispositional optimism were also not examined and would make for interesting future research (O'Brien et al., 2008; O'Brien et al., 2008).

While the impact of influential others such as health care professionals is likely to have a significant impact on breastfeeding self-efficacy, public health initiatives and how breastfeeding is portrayed in the media may also be of relevance. Breastfeeding is often depicted as a natural feeding option, arguably inherent in this depiction is the suggestion that the act is therefore something that is without effort on the mother's behalf. Many public health initiatives highlight the benefits of breastfeeding without outlining or trouble shooting the common challenges. Talking exclusively about benefits of breastfeeding may create low breastfeeding self-efficacy because mothers feel like they are failing at something they consider to be very important. A public health initiative where normalising of breastfeeding challenges and failures may be beneficial in improving breastfeeding self-efficacy.

Developing improved ways to identify women most at risk may be especially relevant in the current environment where shorter hospital stays are more common, perhaps preventing mothers availing of sufficient breastfeeding support prior to discharge and reducing the chance of mothers who are struggling emotionally coming to the attention of health professionals.

The current findings point towards how breastfeeding women perceive their own ability in breastfeeding impacts her emotional experience in early motherhood.

may also help to inform interventions. Considering the current finding's interventions should place more emphasis on a woman's confidence and perceptions of themselves as effective breast-feeders. More research is required to determine if intervening to improve breastfeeding self-efficacy alters risk of PND, but as breastfeeding self-efficacy is a modifiable variable, it could potentially provide a timely and affective intervention with dual benefits of increasing breastfeeding duration as well as reducing the risk of PND. At the very least, healthcare workers should be aware of the association between these factors and be mindful of the increased risk of PND when mothers present with low breastfeeding confidence, and the role breastfeeding self-efficacy may have within the spectrum of normative adjustment postnatally. This suggests that there might be a role for breastfeeding self-efficacy in emotional adjustment, either at a clinical level (PND) or within the spectrum of normative adjustment.

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4. Main Research Study

Postnatal predictors of child developmental outcomes in the first two years of life: a longitudinal study.

Prepared in accordance with submission guidelines for *Journal of Experimental Child Psychology*

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4.1 Abstract

The postnatal period is a critical time for long-term infant development. The current research sought to investigate the differential associations between PND, maternal-infant attachment and breastfeeding on long-term child developmental outcomes (i.e., cognitive, language, neuromotor and social-emotional development) at 12- and 24-months postnatal follow-up. While a significant amount of research has been conducted in several of these research areas, there remains many gaps and no consensus has been reached. The lack of consensus has in part been due to methodological limitations. Furthermore, there is little research taking a multifactorial approach, investigating the impact of these three important postnatal variables simultaneously. The current study looked to address the methodological limitations within the existing literature base by using a prospective design with multiple follow-ups, clear breastfeeding definitions and inclusion of important sample characteristics. The current study also investigated the effect of multiple independent variables on a wide range of developmental domains, providing a fuller and clearer picture of the impact these interwoven postnatal independent variables have on long-term child development.

The study was a secondary data analysis of an Irish prospective longitudinal birth cohort, it recruited 456 nulliparious women and their infants. In the current study 336 maternal-infant dyads were included in the 12-month follow-up analysis and 120 dyads were included in the 24-month follow-up analysis. The dyads were healthy and of high socio-economic status. Postnatal depression was measured using *the Edinburgh Scale of Postnatal Depression*, attachment was measured using the *Maternal Postnatal Attachment Scale* and infant's developmental outcomes were measured using the *Bayley Scale of Infant Development*-3rd edition and the Child Behaviour Checklist.

Results showed significant associations between PND and attachment with social-emotional development but no associations with cognitive, language or neuromotor outcomes. However, significant associations were found between exclusive/predominant breastfeeding at two months with language and cognitive development. Moreover, there was evidence that attachment mediated the relationship between PND and the likelihood of predominately breastfeeding. The current findings contribute to the literature examining the impact of PND, maternal attachment and breastfeeding on early developmental outcomes.

Keywords: Postnatal depression, Maternal attachment, Breastfeeding, Socio-emotional outcomes, Neurodevelopmental outcomes.

4.2 Introduction

The first 1000 days of an infant's life have been identified as a critical time for brain development (Zeanah, 2019). Babies are born social and ready to learn, and their developmental skills build on each other in a stepwise, sequential process (Simpson et al. 2016). Early disturbances in these developmental processes can cause a knock-on, cascading impact on long-term development (Masten et al. 2005). Infant Mental Health proponents suggest that all infant development takes place in the context of the infant's relationships and that infancy is a key stage of human development that provides the foundation for life-long growth and development (Clinton et al. 2016). For many infants their mother is their primary relationship. Therefore, factors such as postnatal depression (PND), difficulties within the maternal-infant attachment relationship and difficulties with breastfeeding may not only compromise maternal health and well-being but also impact long-term infant neurodevelopment (Aoyagi & Tsuchiya, 2019; Burger et al. 2020; Koutra et al., 2013; Slomian et al. 2019).

While PND, maternal-infant attachment and breastfeeding may each have a direct impact on neurodevelopment, research has also indicated that the effects of PND and breastfeeding on neurodevelopment may be mediated through the maternal-infant attachment relationship. For example, Goodman and Gotlib (1999) suggest that there are three mediating and transactional pathways between postnatal mental health and child outcomes. The first focuses on the impact of biological and bio-developmental theories of child development, arguing that genetics, prenatal vulnerabilities, and early experiences of adversity causes the overactivation of the stress response system leading to less optimal outcomes (Shonkoff 2010). Secondly, they suggest a psychosocial pathway, referring to the impact of the infant's environment, in particular the parent-

infant relationship and parenting behaviours on the infants' developmental outcomes. For example, parental warmth, attunement, and responsiveness to infants' cues have been shown to promote social-emotional and neuro development. However, when mother's suffer symptoms of PND there is an increased risk of maternal disengagement and poor responsiveness to baby's cues, negatively influencing the infants social learning potential (Murray & Cooper, 1997; Rees, 2007; Smith-Nielsen et al. 2016). The third mechanism proposed focuses on structural and contextual variables, for example psychosocial disadvantage may lead to increased levels of parental stress, poorer parental psychological functioning, and less access for families to resources that promote child well-being. In the current study our focus is on the second pathway, specifically the relationship between PND on child developmental outcomes via the potential mediating pathway of maternal-infant attachment. Moreover, the effect of breastfeeding on neurodevelopment may also be indirectly mediated by an enhanced psychosocial experience through maternal-infant interactions, in particular by improving maternal sensitivity and responsiveness to the infant's needs (Anisfeld et al. 1990; Krol & Grossmann, 2018; Lavelli & Poli, 1998; Linde et al. 2020, Schore, 2000). This may potentially result in more secure infant attachment relationships that in turn support neurodevelopment.

As the first three years of life are a critical period for development, understanding the complex web of variables that make up the postnatal experience is a high research priority. Much of the research to date have looked at the individual effects of PND, breastfeeding, and maternal-infant attachment on neurodevelopment, few studies have taken a multifactorial approach. Due to the highly inter-related nature of these variables, examining their effects on neurodevelopment simultaneously seems prudent, in addition to examining the potential mediating pathways. It may provide a more comprehensive

understanding of the impact of these modifiable variables, which could offer routes to intervention to reduce the risk of long-term developmental delay/deficit.

PND is recognised as a serious public health concern due to its high prevalence rate and potential to cause adverse health outcomes for mothers and infants (Slomian et al. 2019). Previously published estimates indicate prevalence to be between 13%-19% (Crotty & Sheehan, 2004; Gavin NI et al. 2005; O'Hara et al. 1982). There are multiple theories proposed to explain the etiology of PND, arguably the most preferred explanation is the rapid change in reproductive hormones (Schiller et al. 2015). However, other psychological theories such as attachment theory hold that individuals have a need for affection, if this need is not fulfilled within the parents' relationship with their infants, uncertainties may arise about the relationship leading to disappointment and bring about depression and anxieties (Abdollahi et al. 2016).

There remains no consensus regarding the effect of PND on neurodevelopment in general this may be due to the inconsistencies between the existing studies, as well as certain neurodevelopmental domains receiving little research attention. The effect of PND on socio-emotional development and cognitive development have been relatively well studies. For example, the majority of research that has looked at the association between PND and measures of children's emotional, social, and behavioural development have found a positive relationship; meaning that mothers with higher scores on PND measures are more likely to have children with increased rates of social, emotional and behavioural difficulties. For example, PND has been found to be associated with increasing risks for hyperactivity, internalizing problems including anxiety and depression, and lower social engagement (Bagner et al. 2010; Feldman et al. 2009; Galéra et al. 2012; Murray et al. 2011; Verbeek et al. 2012).

While research appears to indicate a significant negative relationship between PND and social-emotional outcomes, the findings for the impact of PND on cognitive development have been more mixed (Aoyagi & Tsuchiya, 2019; Grace et al. 2003; Liu et al. 2017; Slomian et al. 2019). Several studies have found a significant negative relationship between PND and child cognitive functioning, meaning that children of mothers scoring higher on measures of PND were at risk of poorer performance on cognitive outcomes than children whose mothers' scored lower on PND measure. (Ali et al. 2013; Azak, 2012; Conroy et al. 2012; Koutra et al. 2013; Sutter-Dallay et al. 2011). For example, Koutra et al., (2013) and Conroy et al., (2012) both reported significant associations between higher maternal PND scores measured at two months postpartum and a lower cognitive composite score on the *Bayley Scale of Infant Development (3rd edition)* at 18 months.

In contrast, other studies did not find a significant association between maternal PND and child cognitive functioning. For example, Kaspers et al (2009) and Smith-Nielsen et al. (2016) both measured PND at three months and infant's cognitive development at 12 and 13 months respectively, using the cognitive composite score of the *Bayley Scale of Infant Development (3rd edition)* and did not find an association (Kaspers et al. 2009; Smith-Nielsen et al. 2016). While the majority of studies show a significant association, there is still a lack of consensus in the research base and in those studies that have found significant results, the effects tend to be small. Moreover, long-term effects tend to be limited to high-risk groups suggesting that there is a complex interaction of different factors at play, rather than a simple and direct relationship (Graignic-Philippe et al. 2014).

There has been less research conducted investigating the impact of PND on neuromotor and language development. Nevertheless, studies that have examined the

relationship between PND and neuromotor development that have used standardised composite motor scores to assess outcome have largely found no association (Cornish et al. 2005; Nasreen et al. 2013; Patel et al. 2003). However, considering that gross motor skills develop earlier and quicker that fine motor skills it may be judicious to examine these competencies individually (Dubois et al. 2014). When studies have looked at gross and fine motor development as separate domains, they have found conflicting results (Keim et al. 2011; Koutra et al. 2013). For example, in the Keim et al. (2011) study no association was found between PND assessed at four months postnatal with either gross or fine motor development assessed at 12 months. However, Koutra et al. (2013) who conducted a similar study but assessed PND at two months postnatal and gross and fine motor development at 24 months postnatal, found a significant association between PND and fine motor, but no association with gross motor development. The lack of consensus between these findings may be in part due the difference in their timing of both predictor and outcome measurements.

Research examining the relationship between PND, and language development has been limited. However, Quevedo et al. (2012) and Ali et al. (2013) respectively conducted two longitudinal, prospective studies, with relatively large sample sizes and found significant negative associations (Ali et al. 2013; Quevedo et al. 2012). The results showed that higher PND scores were associated with poorer language outcomes. As these studies used the language composite scores, it is not possible to determine if PND influences both expressive and receptive language development, or if the association between PND and the language composite score reflects the effect of PND on expressive language only.

A recent systematic review indicated that there has been little evidence to support an association between PND and receptive language development, but some evidence to

support PND's impact on expressive language development (Aoyagi & Tsuchiya, 2019). For example, Aoyagi et al (2019) found that PND measured between one and three months postnatal had a negative impact on expressive language skills at 18, 24 and 32 months but not at 10 or 14 months (Aoyagi et al. 2019). The Aoyagi et al (2019) study's multiple follow-ups provide an interesting insight as it shows the affects of PND may not be present or detectable until later in development (Aoyagi et al. 2019). Future studies should look to include multiple follow-ups and follow-up participants into their second year of life. To the author's knowledge no research to date supports a significant association between PND and receptive language development. However, research with follow-up beyond one year has been limited (Aoyagi & Tsuchiya, 2019).

Breastfeeding is seen as a high-impact intervention, providing multiple benefits for both mother and infant (Chee et al. 2008; Orhon et al. 2007). It may also support neurodevelopment (Dee et al. 2007; Herba et al. 2013; McCrory & Murray, 2013). However, it's impact on neurodevelopment is of yet, unclear. (Horta et al. 2018; McCrory & Layte, 2011; Sacker et al. 2006). Some researchers have suggested that the positive advantages of breastfeeding on neurodevelopment simply reflects a more advantaged childhood environment, and it is these factors that are correlated with enhanced developmental outcomes (Der et al., 2006; Walfisch et al. 2013). For example, mothers who initiate and continue to breastfeed their children tend to be older, have a higher level of education and higher socio-economic status than mothers who never breastfed their children or breastfed for a limited time (Persad & Mensinger, 2008; Thulier & Mercer, 2009). Some studies have shown that the association between breastfeeding and neurodevelopmental outcomes are not statistically significant after adjusting for these confounders (Der et al. 2006; Gibson-Davis & Brooks-Gunn, 2006).

Many studies that have investigated the affect of breastfeeding on cognitive development have indicated that there is a significant positive relationship (Horta et al. 2015). However, what is less clear in many of these studies is whether these results are as a direct result of breastfeeding or an artefact of the above mentioned socioeconomic or environmental factors that may influence both breastfeeding behaviour as well as children's cognitive performance (Guzzardi et al. 2020; Walfisch et al. 2013). In a meta-analysis by Anderson et al. (2019) that reviewed 14 studies, they found that breastfed children scored 3.2 points higher on IQ tests than children who were never breastfed. This finding was after several socio-economic and environmental factors were controlled for. The results showed that differences between the groups were present from 6 months old and persisted into late teenage years. This review also reported a dose-response effect, with children receiving higher quantities of breastmilk benefiting the most. In a separate review by Jain et al (2002) the findings were less persuasive with four studies concluding that breastfeeding promotes intelligence and five studies not supporting this association (Jain et al. 2002).

Angelsen et al (2001) conducted a study to investigate the affect of duration of breastfeeding on both cognitive and motor development in one- and five-year-old children (Anderson et al. 1999). Of note, all infants were being exclusively fed so groups were homogenous. Objective, reliable measures were used to test development and the 345 participants were largely from favourable environmental backgrounds (i.e., low levels of poverty, high levels of maternal education, low levels of maternal smoking and good access to public health system). There findings indicated an affect of duration of breastfeeding on cognition, but no affect of duration on motor development. Other studies also lend support to this finding as they also indicated there was no association between breastfeeding duration and motor development (Florey et al. 1995; Paine et al. 1999)

Conversely, Sacker et al. (2006) found that breastfeeding was protective against gross motor but not fine motor delay, after controlling for biological, socio-economic, and psychosocial factors.

Moreover, a recent study by Guzzardi et al. (2020) compared a group of infants who were exclusively breastfed with a group that received any combination of breastmilk and formula milk. The study found that exclusive breastfeeding was associated with higher hearing-language development, measured by the *Griffiths Mental Development Scales* in five-year-old girls, while controlling for maternal IQ, maternal age, and BMI of the infant. Furthermore, exclusive breastfeeding for the first three months postnatal seemed enough to establish this significant positive relationship. Vestergard et al. (1999) also found a positive association between exclusive breastfeeding and early language development (babble in polysyllables) in infants at eight months. Sociodemographic factors such as maternal education and social class were controlled for in this study.

The aim of the current study is to investigate the associations between PND, breastfeeding and maternal-infant attachment with socio-emotional and neurodevelopmental outcomes over the first two years of life. The author hypothesised that these three predictor variables measured within the postnatal period would significantly impact long term infant neurodevelopment and that taking a multi-factorial approach would help gain a clearer understanding of how they relate to one another as well as on the dependent variables.

Studies have indicated that PND and breastfeeding may not have a direct relationship with neurodevelopment (Walfisch et al. 2013). It is argued for example that the positive advantages of breastfeeding on neurodevelopment simply reflect a more advantaged childhood environment (Der et al. 2006). Conducting research with a largely homogenous, high socio-economic group, such as the current sample of participants

provides an opportunity to limit residual confounding (e.g., such as poverty variables that would also interact with neurodevelopment) to better illuminate the relationships of interest.

The current study also wished to address some of the methodological issues that may have contributed to the inconsistencies across previous research, for example by including clear breastfeeding definitions that took into consideration the exclusivity of breastfeeding as well as the duration. The study also controlled for important sample characteristics, such as low levels of maternal education, maternal age, a history of maternal depression and low infant birth weight. The prospective design of the current study limited recall bias and its multiple follow-ups addressed gaps in the research-base. In addition, fewer studies to date have looked at the subscales of the motor and language domains separately, previous research has suggested that a more nuanced investigation of the impact of PND on these areas of development may help to widen our understanding (Aoyagi & Tsuchiya, 2019). Bringing all of this to bare, the current study's primary and secondary research questions were, firstly to investigate if PND at two months was associated with socio-emotional and neurodevelopmental (cognitive, language, neuromotor and development) outcomes at one year and two- year follow-ups and secondly, if breastfeeding or attachment are associated with socio-emotional and neurodevelopmental (cognitive, language and neuromotor development) outcomes at one year and two- year follow-ups.

4.3 Method

4.3.1 Design

This study is a secondary analysis of an Irish birth cohort utilizing a longitudinal, observational, quantitative research design. Assessment of predictor variable were

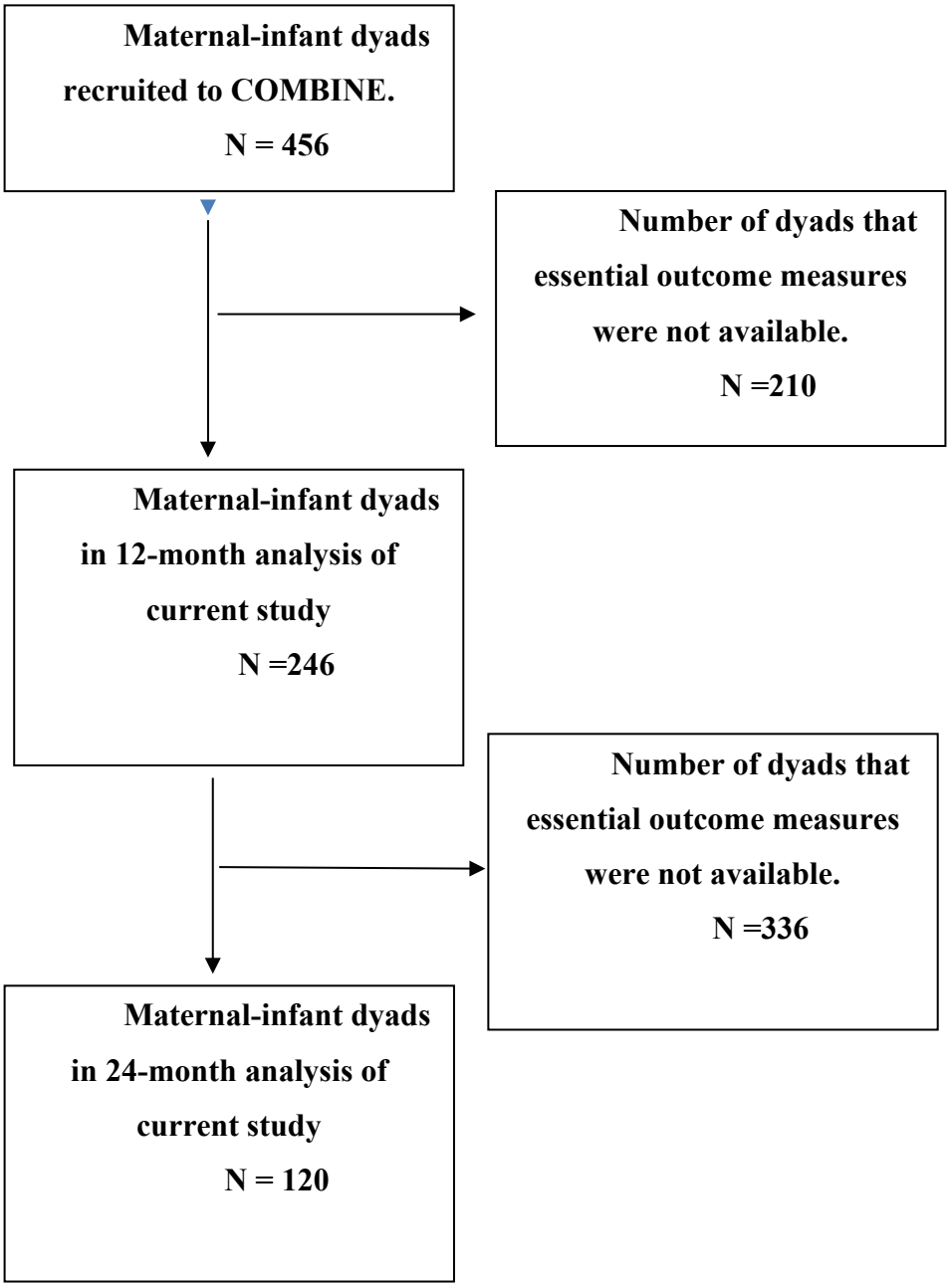
collected prior to one-month postnatal for participant demographic variables, at two-months postnatal for measures of postnatal depression and maternal-infant attachment and at two month and six months postnatal for breastfeeding data. Outcome measures, including measures of cognitive, language, motor and social-emotional development were collected at follow up visits at 12 and 24 months postnatal.

4.3.2 Participants

Participants were recruited between late 2015 and 2017 in Cork University Maternity Hospital, directly after birth. Mothers were health, low-risk first-time mothers and infants were excluded if they spent >2 weeks in the neonatal intensive care unit or had a severe metabolic or genomic anomaly requiring ongoing specialist care in the neonatal period. Four hundred and fifty- six mother-infant dyad were recruited to the original birth cohort. In the current study participants were classified as non-responders if they were missing scores on primary predictor and/or outcomes measures, see figure 4 for flow chart of participant attrition. As illustrated on figure 4, 246 participant dyads were included in the 12- month follow-up and 120 participant dyads were included in the 24-month follow-up.

Across both 12- and 24-month follow-ups, non-responder mothers were significantly younger and breastfeed for a shorter duration (see appendix J). In the 12-month follow-up non-responders also tended to smoke more during pregnancy. Being a younger mother and smoking during pregnancy are associated with an increased risk of maladaptive outcomes that are relative to the research questions (e.g., greater risk of maternal mental health difficulties, offspring behavioural disorders and poorer academic attainment in offspring) (Muraca & Joseph, 2014). In the current sample the non-responders tended to be a more at-risk group than the responders therefore study effects may be underestimated.

Figure 5: Flow chart of participant attrition



4.3.3 Predictor Variables

Edinburgh Postnatal Depression Scale (EPDS) (Cox et al. 1987)

The *EPDS* is the most widely used screening tool for PND (see appendix E). It was developed to help primary health care workers to identify mothers who were suffering from PND. It is a 10-item self-report measure in which respondents are asked to rate how they have been feeling over the previous seven days, selecting one of four

possible responses (0-3) to each of the ten statements. The ten statements assess depressed mood, anhedonia, guilt, anxiety, and suicidal ideation over the previous seven days. Possible scores range from 0-30, with higher scores signifying greater severity. While the most used cut-off score is 13, an evidence synthesis by Hewitt et al (2009) reported that the optimal cut-off for major depression was 12 for major depression and 10 minor depressions. In a recent review, the sensitivity and specificity of the *EPDS* ranged between 80-90% based on the most common cut-offs (Myers et al. 2013). The positive predictive ability of the English language version of the *EPDS* in the general population has been estimated to be 50%-60% (Gibson et al. 2009). However, the *EPDS* has been shown to perform well against other measures of *PND* and the UK National Screening Committee has judged it to be a 'simple, safe, precise and validated screening test' (Gibson et al. 2009).

Maternal Postnatal Attachment Scale (MPAS) (Condon & Corkindale, 1998).

The Maternal Postnatal Attachment Scale- (MPAS) was developed as a self-report measure to assess the affective aspect of mother-infant attachment in the first year postnatal (see appendix F). According to the authors, parent-to-infant attachment refers to the emotional bond or tie of affection experienced by the parent towards the infant.(Condon & Corkindale, 1998)

The scale consists of 19 items, and the responses are based on the mother's frequency of experiences over the previous two weeks. Responses are provided on a 2-, 4- or 5-point scales. To ensure equal weighting of questions, all response options are recoded to represent a score of 1 (low bonding) to 5 (high bonding). (Gibson et al. 2009) Condon and Corkindale (1998) identified four factors, including (1) pleasure in proximity and enjoyment during interactions with the infant (2) lack of resentment towards the impact motherhood has on lifestyle of the mother (3) absence of angry or hostile feeling

towards the baby (4) feelings of competence and confidence as a mother. Each of the four factors are subscales which can be summed together to equal the total *MPAS* score, with the highest scores indicating the most adaptive maternal-infant attachment. Only the total score was used for the purposes of the current study. In a non-clinical Belgian sample, with demographic characteristics similar to the current sample the Cronbach's alpha on the *MPAS* total score was 0.75 at eight to twelve weeks postpartum, indicating good internal reliability.

Breastfeeding data.

Data was collected on infant feeding method and practices at each follow-up appointment. The information was collected through midwife-led interviews using questionnaires that were custom designed. Key questions related to whether the infant was being breast, infant formula, or combination fed. If the infant was being breast-fed, additional questions were asked regarding what other fluids the infant received other than breastmilk (e.g., water, juice, vitamins, and minerals). If the participants' ceased breastfeeding between appointments, the age of breastfeeding cessation was recorded. Based on feeding data infants were retrospectively categorized into feeding groups that were in line with the WHO definitions of breastfeeding (see appendix C). According to these definitions the predominant breastfeeding category does not preclude the use of medicines, vitamins, minerals, water, juice, or water-based drinks. The exclusive breastfeeding category differs in that it precludes water, juice, and water-based drinks. Both these categories preclude infant formula entirely. The current study looked at participants that were exclusively and predominantly breastfeeding at two and six months postnatal. Breastfeeding was operationalised as a dichotomous variable (breastfeeding exclusively or predominantly versus not breastfeeding). The *not breastfeeding* group included those that were exclusively formula feeding.

Demographic information

Background information was collected by midwife-lead interviews across a wide range of demographic and environmental variables. Based on literature review, variables of most relevance and significance to the current research questions were selected for analyses. These included, maternal age, nationality, educational level, employment status, relationship status and smoking status as well as gestational age and infant birthweight.

4.3.4 Outcome Variables

Bayley Scales of Infant Development- 3rd Edition (BSID-3rd edition) (Bayley, 2006).

The *BSID-3rd edition* is a well-known individually administered instrument designed to measure the developmental functioning of infants and toddlers aged 1- to- 42 months (Albers & Grieve, 2007). The *BSID-3rd edition* differs from its predecessor in that it includes five distinct scales (*Cognitive, Language, Motor, Social-emotional & Adaptive Behaviour Scales*) in comparison to the *BSID-2nd edition* that included three distant scales (*Mental, Motor and Behaviour scales*). The *cognitive* scale includes 91 items. The *language scale* also includes 97 items and is divided into *receptive* and *expressive language subtests*. The *motor scale* includes 138 items and consists of *fine motor* and *gross motor subscales*. Scaled scores and composite scores were derived from participants raw scores to a range of 40-160 (M =100, SD =15). The *BSID-3rd edition* is a psychometrically sound instrument. The standardised sample for the *cognitive*, *language* and *motor* subscales included 1,700 American infants aged 1 month to 42 months and was representative of the 2000 U.S. census survey data. 10% of the sample included infants that were premature or who had an identified disability (Bayley, 2006).The Bayley-III has acceptable reliability, with internal consistency of >0.86 and test-retest reliability >0.67 (Bayley, 2006).

BSID-3rd edition Greenspan Social-Emotional Scale (Greenspan et al., 2008)

The Greenspan Social Emotional Scale is a 35-item caregiver response questionnaire for infants and young children from birth to 42 months, screening social and emotional milestones (see appendix G). The questionnaire consists of six major functional emotional milestones (e.g., 1. exhibits growing self-regulation and interest in the world, 2. engages in relationships and 3. uses emotions in an interactive, purposeful manner). Parents, or caregivers, indicate their response by choosing one of the six rating responses on a Likert scale. Scale and composite scores were derived from participant raw scores to a range of 40-160 (M =100, SD =15). As for the psychometric properties, internal consistency was excellent, with a Cronbach's alpha = 0.90 for the social–emotional items and 0.83 for the sensory processing items (Albers & Grieve, 2007).

The Child Behaviour Checklist for Ages 1½–5 (CBCL/1½–5) (Achenbach & Rescorla, 2000)

The *CBCL 1½-5* is a parent-report measure designed to detect behavioural and emotional problems in children (see appendix H). It has 100 items, and each item describes a particular behaviour, and the responder (parent) is asked to rate its frequency over the last two months on a three-point Likert scale. The preschool version of the CBCL, used in the current study, has seven syndrome scales. There is also a total problem score as well as composites for internalising and externalising problems. For the current study, the total problem score is the focus of the analysis. For the total problem score, the cut- off point for normal range is a T-value < 60, borderline is from 60-63 and the clinical range is ≥ 64. Norms are based on a national sample of 700 children. The *CBCL `1½-5* has been shown to have high sensitivity and specificity (>90%) in identifying behavioural and emotional problems in preschool children in comparison to psychiatric diagnosis.

4.3.5 Ethics

The original birth cohort known as the COMBINE study received ethical approval from the University College Cork Clinical Research Ethics Committee *(ECM4(hh)06/01/2015 and ECM3(bbb)10/04/18)* and it is registered at http://www.birthcohorts.net/. Amendments to the COMBINE ethics approval were made in April 2020 and approval was given to the current author and her research supervisor Dr. Christopher McCusker to gain access to the COMBINE data (see appendix I).

4.3.6 Data Analysis Plan

G*power was used to calculate the minimum required sample size for this study. An alpha level of 0.05 and a desired power of 0.8 were specified. A small to medium effect size was expected for predictors of childhood development based on the literature. Allowing up to 4 predictors in a regression model, a minimum sample size of 176 was required. Data analysis was carried out using IBM SPSS. Responders and non-responders were compared on demographic information using independent samples students t-tests (for continuous data) and chi square tests (for categorical data). Non-responders were excluded from the regression analyses. Data were graphed using histograms and boxplots to identify potential outliers and assess the assumption of normality. Following exploratory analysis, a series of simple and multiple linear regressions were carried out to test the primary hypotheses. A simple linear regression was carried out to examine if *MPAS* at two months could predict *BSID, 3rd Edition Social and Emotional Scale* scores at 12 months. A simple linear regression was also carried out to examine if gender could predict the *BSID, 3RD Edition* language composite score at 12 months. Moreover, a multiple linear regression was carried out to examine if mother's age at delivery and the infant gestational age at birth could predict infant motor scores at 12- months follow-up. A hierarchical multiple regression was carried out to examine if a mother's age, infant

gender, *EPDS* and *MPAS* scores predicted infant *CBCL 1½-5* score at 24 months follow-up. Mother's age and infant gender were entered as block one, and *EPDS* and *MPAS* were entered as block two. A simple linear regression was also carried out to examine if a mother predominately breastfeeding at two months could predict language composite score at 24 months. A simple linear regression was conducted to examine if mother's predominately breastfeeding at two months could predict infant cognitive score at 24 months. Finally, a mediation model was carried out to explore the association between depression and social and emotional problems, using the Andrew Hayes SPSS plug-in PROCESS and how this relationship may be mediated by attachment. The assumptions underlying these regressions were also evaluated, e.g., lack of multicollinearity, normality of residuals.

4.4 Results

4.4.1 Sample characteristics on demographics

Maternal age, nationality, relationship status, education attainment and employment status as well as infant gender, gestational age and birth weight were all examined at baseline. The following outlines demographic information for both 12- and 24- month follow-up groups and describes the cohort characteristics in comparison to Irish census norms.

In the overall sample maternal age ranged from 18 to 41 years. The mean maternal age at delivery at the 12- month follow-up was 32 (M = 32, SD =4.64) (see Table 1), while the average age was slightly older at the 24- month follow-up (M =33, SD =3.79) (see Table 2). The Central Statistics Office (2017) reported that 32 years is the average maternal age in Ireland. At the 12-month follow-up, 79% of mothers were of Irish nationality (see Table 1), while 80% of mothers at the 24-month follow-up were of Irish

nationality (see Table 2). This is a larger percentage than the national average (77%) (Central Statistics Office, 2017). In the current study, a stable relationship was classified as being married or in a civil partnership in addition to cohabiting. A high rate of the mothers at both follow-ups were in a relationship, 94% were in a relationship at the 12-month follow-up (see Table 1), while 96% were in a relationship at the 24-month follow-up (see Table 2). In the 2016 Irish census, 18% of families were lone parent households, therefore the current sample has a lower percentage of single mothers than the average Irish population (Central Statistics Office, 2017).

In 2016, 55% of 18–34-year-old females in Ireland had third level qualifications (Central Statistics Office, 2017). The mothers, in the current sample, had a very high level of educational attainment, with 76% at the 12-month follow-up and 82% at the 24-month follow-up having obtained third level qualifications (see Tables 1 and 2). Ninety three percent of mothers at the 12- and 24-month follow-up timepoints were employed (see Tables 1 and 2), this was higher than the national average of 77% (Central Statistics Office, 2017). Ten percent of mothers at the 12-month follow-up and 11% at the 24-month follow-up smoked to some extent during their pregnancy (see Tables 1 and 2). This is on a par with the current national incident rate of smoking during pregnancy of 11% (McDonnell et al. 2019). The average gestational age of infants in the current study was 40 weeks across both follow-up time-points and the mean birthweight was three kilograms across both time-points (see Tables 1 and 2). These were consistent with the national averages, with most infants nationally having a gestational age of 40 weeks or over, and babies between 3,500kg and 3,900kg account for the largest percentage of births nationally (Central Statistics Office, 2017).

Over-all, the participants at both 12 and 24 follow-up timepoints represent a well-resourced community cohort, with a significantly greater percentage of the mothers

obtaining third level qualifications than the average Irish female population. A greater number of mothers were also employed and were in a stable relationship in comparison to national averages. In terms of average age, smoking during pregnancy, infant gestational age, and birth weight, the sample was representative of the general Irish population.

Table 1 Participant demographic information at 12 months follow-up

Characteristics (n=246)	n (%)	Mean (SD)
Maternal		
Age at delivery (years)		3 2(3.8)
Nationality (Irish)	79%	
Partner (Married/*de facto* relationship)	96%	
Education (tertiary)	76%	
Employed (two years post- delivery)	93%	
Smoked to some degree during pregnancy	10%	
Infant		
Sex (female)	44%	
Gestation age (weeks)		40 (1.38)
Birth weight (kilograms)		3 (5.75)

Table 2 Participant demographic information at 24 months follow-up

Characteristics (n=120)	n (%)	Mean (SD)
Maternal		
Age at delivery (years)		33(3.79)
Nationality (Irish)	80%	
Partner (Married/*de facto* relationship)	94%	
Education (tertiary)	82%	
Employed (two years post- delivery)	93%	
Smoked to some degree during pregnancy	11 %	
Infant		
Sex (female)	42%	

Gestation age (weeks)	40 (1.40)
Birth weight (kilograms)	3 (5.51)

4.4.2 Sample characteristics on predictor and outcome measures

Participant profiles on the *EPDS, MPAS, BSID and CBCL* at 12 and 24 months are outlined in Table 3 and 4, including the proportion of participants above / below clinically relevant cut-offs. The percentage of women reaching or exceeding the clinical cut-off of 13 on the *EPDS* and considered at risk of PND is 22% in the 12-month sample and 20% in the 24- month sample. This is higher than recent estimated prevalence rates of 17% taken from a meta-analysis that looked at the global prevalence rate of PND amongst healthy mothers (no previous history of PND or other mental illness) who gave birth to healthy infants (Shorey et al. 2018).The mean scores on the *language* and *neuromotor domains* on the *BSID* are within the average range at both 12 and 24 months and are comparable to population norms. However, the mean scores on the cognitive domain at the 12 and 24 month follow ups are above what would be expected based on population norms.

A greater percentage (15%) of infants fell below the clinical cut- off of 85 indicating mild impairment on the motor domains at the 12-month follow-up in comparison to the 24-month follow-up, where just 3% did not meet the cut-off (Burakevych, 2017). The number of participants falling below the clinical cut off in the cognitive and language domains were relatively stable across time-points (see table 3 and 4). The mean score on the *BSID* social and emotional scale was representative of population norms at the 12-month follow-up. 12% exceeded the clinical cut-off on the *BSID* social and emotional scale, while 4% exceeded the clinical cut off on the CBCL at 24-months, both indicating poor social and emotional outcomes. Descriptive statistics on

participants EPDS, MPAS, BSID and CBCL at 12 and 24 months are provided in table 3 and 4, including the proportion of participants above/below clinically relevant cut-offs.

Table 3. Descriptive statistics for participant of the 12-month follow-up on EPDS, MPAS BSID and CBCL

	Mean	Std. D	Above/below clinical cut-off (%)
EPDS total at 2 months	6.3	4.54	55 (22)
MPAS total at 2 months	83.05	7.79	-
BSID motor at 12 months	99.02	12.79	36 (15)
BSID language at 12 months	102.06	12.95	19 (8)
BSID cognition at 12 months	112.24	10.37	2 (0.8)
BSID social and emotional at 12 months	102.84	15.04	12 (4.9)

EPDS cut-off = >13; BSID sub-score cut-offs = <85

Table 4. Descriptive statistics for participant of the 24-month follow-up on EPDS, MPAS BSID and CBCL

	Mean	Std. D	Above clinical cut-off (%)
EPDS total at 2 months	6.21	4.04	25 (21)
MPAS total at 2 months	82.44	7.53	-
BSID motor at 24 months	100.67	12.22	3 (2.5)
BSID language at 24 months	103.21	12.29	14 (12)
BSID cognition at 24 months	114.06	10.19	4 (3)
CBCL at 24 months	44.92	9.20	4 (3)

EPDS cut-off = >13; BSID sub-score cut-offs = <85; CBCL cut-off = 64

4.4.3 Predictors of child outcomes

Exploratory Data Analysis

Predictor and outcome variables were examined through correlations and univariate t-tests to identify possible associations; these analyses were conducted for both 12-month and 24-month follow-up data (see Table 5). In running exploratory analysis, the Pearson's correlations assumption of linearity was assessed using scatterplots. In all cases, this assumption was upheld. There were no significant associations between the *Edinburgh Postnatal Depression Scale (EPDS)* and the *cognitive, language* or *motor scales* of the *Bayley Scale of Infant Development-Third Edition (BSID-3rd edition*), for both 12-month and 24-month follow-ups. The association between the EPDS and the both the motor and language subscales were also examined, and results indicated no significant effects (see appendix K). However, higher scores on the *EPDS* were significantly associated with higher scores on the *Child Behaviour Checklist 1½-5* in the 24-month follow-up. There was no significant association between the *EPDS -3rd edition* and the *BSID Social and Emotional* in the 12-month follow-up.

Moreover, *The Maternal Postnatal Attachment Scale (MPAS)* was not significantly associated with *cognitive, language or motor* scales on the *BSID-3rd edition* in either the 12-month follow-up or the 24-month follow-up. There was also no significant association between MPAS and language and motor subscales (see appendix K). However, there was a significant association between the *MPAS* and the *Bayley Social and Emotional Scale (Greenspan)* in the 12- month follow-up and between the *MPAS* and the *CBCL* in the 24-month follow-up, with higher rates of attachment associated negatively with *the Bayley Social and Emotional Scale* and positively associated with the *CBCL*, both indicating poorer social-emotional outcomes for infants of mothers at risk of PND.

Exclusive/ predominant breastfeeding at two months was significantly associated with higher scores on the *language* and *cognitive domains* of the *BSID* 3rd *edition* in the 24-month follow-up but not in the 12-month follow-up. In addition, exclusive/predominant breastfeeding at two months was significantly associated with higher scores on expressive language development at 24-month follow-up. In addition, there were no significant associations between exclusive/predominant breastfeeding at six months with neurodevelopmental outcomes (*cognitive, language and motor subscales* of the *BSID 3rd edition*) in either the 12-month or 24-month follow-ups.

Table 5: Significant associations between predictor and outcome variables at 12- and 24-month follow-up

	Motor composite	Language composite	Cognitive composite	Social and emotional	CBCL Total
12 Month Analysis					
EPDS at two months					
MPAS at two months				r= **.180***	
Predominant breastfeeding at two months					
Predominant breastfeeding at six months					
Gender		t = **-3.13****			
Gestational age	r =**.122***				
Mother's age at delivery	r= **-.181****				
Maternal relationship status					
Maternal education level					
Maternal employment					
24 Month Analysis					
EPDS at two months					**r =.242****
MPAS at two months					**r = -.218**
Predominant breastfeeding at two months		**t =-2.056***	**t = -2.273***		
Predominant breastfeeding at six months					
Gender	**t = -1.973****				**t = -2.237***
Gestational age					
Mother's age at delivery					**r = -.216****
Maternal relationship status					
Maternal education level					
Maternal employment					

EPDS- Edinburgh Postnatal Depression Scale; MPAS- Maternal Postnatal Attachment Scale; CBCL -Child Behaviour Checklist

Apart from the main predictor factors (i.e., PND, attachment and breastfeeding), other relevant factors were also examined to determine possible associations with outcome variables. Older gestational age was found to be significantly associated with higher scores on the *motor domain* on the *BSID 3rd edition* at 12-months follow-up

analysis. Female infants were found to have significantly higher scores than male infants on *language domain* at 12 and 24-months follow ups and on *motor domain* at 12-months follow-up in comparison to male infants. Gender was also associated with the *CBCL 1½-5* at the 24-month follow-up, with female infants scoring lower on the *CBCL 1½-5,* indicating more optimal social-emotional outcomes than male infants. Note these factors will also be considered in regression models.

Regression analyses

The factors that showed associations within the exploratory analyses were taken forward into the regression analyses which (1) examined whether significance held up when combined with other relevant factors and (2) quantified the variance explained by each factor. Where exploratory analyses indicated a lack of significance in a relationship between a predictor and outcome variable in the exploratory data analysis, these associations were not explored further by regression analyses, unless central to the research question. In carrying out the regression analyses, the assumption of normality of residuals was assessed using QQ plots. The residuals were normally distributed for all models. Heteroscedasticity was assessed by examining fitted vs residuals plots. Multicollinearity was assessed by examining Variance Inflation Factor (VIF) values. In all cases, VIF was below 10.

Social-emotional developmental outcomes

A linear regression was carried out to examine if *MPAS* at two months could predict *BSID, 3rd Edition Social and Emotional Scale* scores at 12 months. A significant model was observed, $F(1,163) = 5.45$, $p<.05$. The model accounted for 3.2% of the variance in social and emotional composite scores. *MPAS* was a significant contributor to the model, (standardised $\beta = .18$, $p<.05$). A hierarchical multiple regression was also carried out to examine if a mother's age, infant gender, *EPDS* and *MPAS* scores predicted

infant *CBCL 1½-5* score at 24 months. All four of these predictor factors were found to be associated with social-emotional outcome at 24 months in the exploratory analyses. Mother's age and infant gender were entered as block one, and *EPDS* and *MPAS* were entered as block two. Block two was a significant predictor of *CBCL 1½-5* score, F (4, 200) = 6.68, p<.05, accounting for 11.8% of the variance. Block 2 significantly added to the variance explained by the model (R^2 change = .056, p<.05). When examining individual predictors in the model, mothers age was the only significant contributor to the model (β = -.22, p<.05). i.e., When adding EPDS and MPAS to the model they added a significant amount of variance explained to the model. However, when looking at individual predictors, neither EPDS nor MPAS significantly contributed to the model while holding the other constant. i.e., you need to consider both depression and attachment together when predicting CBCL scores, rather than looking at them individually.

Language outcomes

A linear regression was carried out to examine if gender could predict language scores at 12 months. A significant model was observed, F (1,323) = 10.97 p<.01. The model accounted for 3.3% of the variance in language scores. Gender was a significant contributor to the model, (β = .18, p<.05), i.e., having a female infant is associated with an increase in language scores. A linear regression was also carried out to examine if a mother predominately breastfeeding at two months could predict language score at 24 months. A significant model was observed, F (1,259) = 4.23, p<.05; the model accounted for 1.6% of the variance in language scores. Breastfeeding was a significant contributor to the model, (β = .13, p<.05), i.e. women who predominately breastfed at two months were associated with an increase in their infant's language scores.

Motor outcomes

A linear multiple regression was carried out to examine if mother's age at delivery and the infant gestational age at birth could predict motor score at 12 months. A significant model was observed, F (2,319) = 7.485, p<.01, accounting for 4.5% of the variance in motor score. Mother's age was a significant contributor to the model, (β = -.17, p<.05). Gestational age was also a significant contributor to the model, (β = .11, p<.05). A linear regression was also carried out to examine if gender could predict motor scores at 24 months. A significant model was observed, F (1,271) = 3.89, p<.05. The model accounted for 1.4% of the variance in motor scores. Gender was a significant contributor to the model, (β = .12, p<.05), i.e., having a female child is associated with an increase in motor score

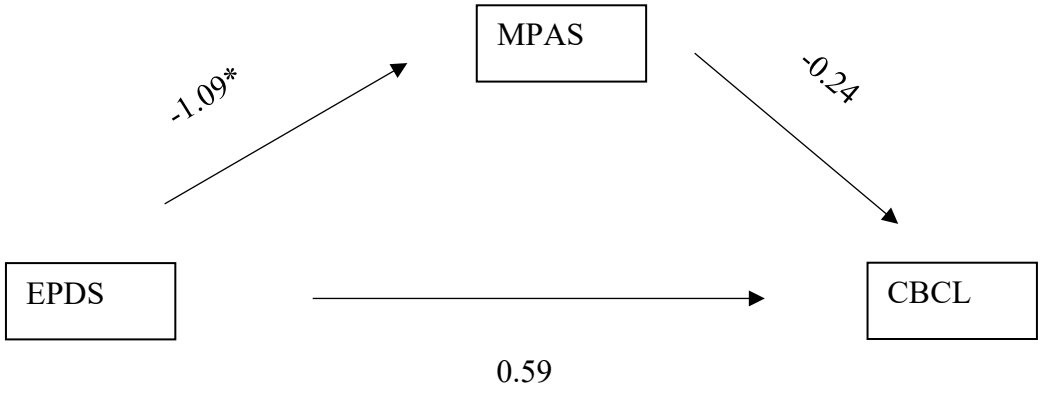
Cognitive outcome

A linear regression was carried out to examine if mother's predominately breastfeeding at two months could predict infant cognitive score at 24 months. A significant model was observed, F (1,283) = 5.17, p<.05, accounting for 1.8% of the variance in cognitive score. Breastfeeding was a significant contributor to the model, (β = .13, p<.05), i.e., mothers who predominately breastfed at two months were associated with an increase in their infant's cognitive score.

4.4.4 Mediation analyses

In the hierarchical regression analysis above, PND and attachment together explained a significant proportion of the variance in the socio-emotional outcome at 24 months but independently it was surprising that neither PND nor attachment reached statistical significance. A finding such as this is suggestive of mediation occurring. A mediation model was carried out to explore the effect of depression on social and emotional problems, and how it may be mediated by attachment. Model 1 in the mediation

model examined if EPDS predicted MPAS score. This model was significant, $F(1,203)=139.33$, $p<.001$, accounting for 41% of the variance. A 1 unit increase in EPDS is associated with a 1.097 decrease in MPAS score (unstandardised B = -1.097, $p<.05$). Model 2 in the mediation model examined if EPDA and MPAS predicted CBCL score. This model was significant, $F(2,202) = 6.65$, accounting for 6.18% of the variance. However, when examining the individual predictors, no factor was a significant contributor to the model. Direct effects illustrated below. In order to determine if mediation occurred, the indirect effects of MPAS on CBCL were examined. The indirect effect of MPAS on CBCL was not significant (95% CI: -.1272, .7420), thus mediation did not occur (see Appendix L for full regression model summary tables).

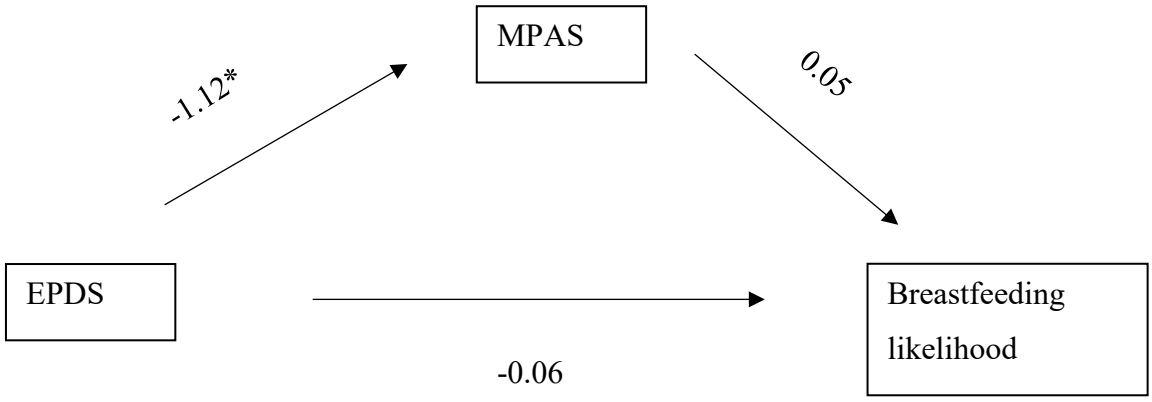


This mediation analysis suggests that PND has a significant effect on attachment. However, there was no evidence that attachment had a significant effect on social and emotional problems (controlling for PND), nor was there any evidence that attachment mediated the relationship between PND and behavioural and emotional problems.

The results indicated that PND and maternal-infant attachment were not associated with neurodevelopmental outcomes. However, these factors were associated

with exclusive/predominantly breastfeeding. As a follow-up, unplanned, supplementary analyses, the author conducted a binomial logistic regression to determine if EPDS and MPAS scores could predict if a mother predominately breastfed at 6 months. A significant model was observed, $\chi^2 = 11.92$, $p<.05$, accounting for 7.5% of the variance. However, neither EDPS nor MPAS were individually significant predictors in the model ($p>.05$). This may be due to the intercorrelation between individual predictors, obscuring their individual significance.

A mediation model was carried out to explore if PND and maternal-infant attachment might be impacting on outcomes of neurodevelopment by indirectly impacting breastfeeding. Model 1 in the mediation model examined if EPDS predicted MPAS score. This model was significant, $F(1,233) =166.93$, $p<.001$, accounting for 42% of the variance. A 1 unit increase in EPDS is associated with a 1.12 decrease in MPAS score ($B = -1.12$, $p<.05$). Model 2 in the mediation model examined if EPDs and MPAS predicted breastfeeding likelihood. This model was significant: Model log-likelihood = 11.92, accounting for 7.5% of the variance. However, when examining the individual predictors, no factor was a significant contributor to the model. Direct effects illustrated below.



In order to determine if mediation occurred, the indirect effects of MPAS on breastfeeding likelihood at 6 months was examined. As attachment score increases, the effect of depression on breastfeeding likelihood decreases. This mediation analysis suggests that PND has a significant effect on attachment. However, there was no evidence that attachment had a significant effect on the likelihood of predominately breastfeeding (controlling for PND). There was evidence that attachment mediated the relationship between PND and the likelihood of predominately breastfeeding (see appendix L for full regression model summary tables).

4.5 Discussion

The current research sought to investigate the associations between PND, maternal-infant attachment and breastfeeding on child developmental outcomes. The study addressed several methodological challenges considered to contribute to inconsistencies within the literature-base. For example, the study used a prospective, longitudinal design with multiple follow-up assessments, in contract to cross-sectional studies the current design allows for the temporal sequence of exposure and outcome to be known. This rigorous design also reduced the likelihood of recall bias, as data was collected on a regular basis. Detailed breastfeeding data was collected so that participants could be retrospectively fitted into WHO defined breastfeeding categories. A common critique of earlier breastfeeding studies is their failure to properly define breastfeeding groups. For example, by failing to account for the number of 'top-up' formula feeds given to breastfed babies, leading to heterogeneity in breastfeeding group. The design of the current study addressed this limitation. Other strengths include its use of a wide range of validated, standardised measures and controlling for multiple variables of importance. Moreover, the study included a healthy sample of primiparous mothers and their infants. The sample were a high socio-economic group.

Initial exploratory data analysis showed significant associations between PND and social-emotional development at 24-month but not at 12-month follow-up, indicating that mothers who were at greater risk of depression at two months postnatal were more likely to have children demonstrating poorer social-emotional development at two-years old. Furthermore, a significant association between attachment and social-emotional development at 24-month but not at 12-month follow-up was found, suggesting that mothers who showed more optimum maternal-infant attachment at two months were more likely to have children demonstrating fewer social-emotional difficulties at two years. Gender was also associated with social-emotional development. Results suggested that female infants were more likely than male infants to score more optimally on measures of socio-emotional development at 24-month follow-up.

Moreover, when a regression analysis was conducted, PND and attachment taken together explained a significant proportion of the variance in social-emotional outcomes at 24-month follow-up. However, neither of these variables independently predicted social-emotional development in the regression analysis. A mediation analysis was conducted to assess if the impact of PND on social-emotional development was mediated through attachment, however this hypothesis did not hold up.

Contrary to the study's predictions, there was no association between PND or attachment with neurodevelopmental outcome. Other demographic variables that emerged as predictors of interest included gestational age, and gender. Infants with an older gestational age did better on measures of motor outcome at 12-month follow-up and female infants scored higher than male infants on language outcomes at 12-and 24-month follow-ups and on motor outcomes at 12-months.

The current study conducted just one assessment of PND symptomology at eight weeks postnatal. Studies have highlighted the importance of the chronicity of PND when

looking at its association with neuro-and-socioemotional development. Chronicity has been seen to moderate the effect of PND on development. For example, Cornish (2005) found that chronic PND assessed at 4,12 and 15 months postnatal was associated with poorer infant cognitive and psychomotor development at 15 months, however, they found a brief period of depressive symptoms did not significantly affect neurodevelopment (Cornish et al. 2005). Studies have also shown that children of mothers with higher scores on PND measures had children with significantly more behavioural problems than children of mothers who had lower scores on PND measures (Cents et al. 2013).

It is possible that mothers who had PND symptoms at eight weeks did not continue to be depressed for much more of the postnatal year. Therefore, if the symptoms were not chronic any negative effects on infant development could be minimal and perhaps ameliorated by other factors by the time of neurodevelopmental testing at follow-up. Moreover, this cohort is of high socio-economic status, giving them financial and social advantages, perhaps making accessing resources and supports easier. It is worth noting the majority of the mothers were in a relationship, and it is possible that other caregivers may also play an important buffering role in the infant's learning environment. For example, previous research has identified sensitive fathering as a key mitigator for the adverse effects of maternal depression (Vakrat et al. 2018). Additionally, non-clinical children's language research has provided support for the idea that fathers may uniquely contribute to young children's linguistic development (Pancsofar & Vernon-Feagans, 2006). Further research should incorporate information from both parents to better understand the potential factors moderating associations between PND and children's neurodevelopment. It should also test PND symptoms at numerous points in the child's development.

In line with the study's hypotheses, breastfeeding was found to be associated with neurodevelopmental outcomes, namely cognitive and language outcomes at the 24-month follow-up (McCrory & Murray, 2013) Infants being exclusively/predominantly breastfed up to two months did better on cognitive and language outcomes at 24-months follow-up that formula fed infants. The supplementary data analysis indicated that the association with language outcomes was mainly accounted for by expressive language development (see appendix J). Interestingly, no association was found between infants being exclusively/predominantly breastfed up to six months and neurodevelopmental outcomes. Similar findings were reported by McCrory and Murray (2013) who indicated that breastfeeding for one week or less conferred a greater advantage than breastfeeding for longer durations, or indeed breastfeeding exclusively for six months or more (McCrory & Murray, 2013). In contrast, previous findings have found favourable effects of both dose and exclusivity (Paine et al. 1999; Thorsdottir et al. 2005) . In both the current McCrory and Murray (2013) studies an advantage of breastfeeding on infant neurodevelopment was found. However, the lack of a dose-response effect may indicate confounding by unobserved variables, or there may be a threshold during which time the effect of breast milk may be especially salient for strengthening neurodevelopment.

A supplementary regression analysis was conducted to determine if PND and attachment could predict if a mother predominately breastfed at six months. PND and attachment were found together to predict predominant breastfeeding at six months. However, neither of these variables independently reached statistical significance. To investigate if PND and maternal-infant attachment might be impacting on outcomes of neurodevelopment by indirectly impacting breastfeeding, a mediation model was conducted. There was evidence that attachment mediated the relationship between PND and the likelihood of predominately breastfeeding at six months, suggesting that. mothers

who were at risk of PND were more likely to breastfeed at six months if they had higher (i.e., more optimum) maternal attachment at two months postnatal. Previous research has indicated that exclusive breastfeeding is related to mother-infant attachment measured in the first days postnatal. Mothers with better attachments to their infants in the days after birth were found to have a significantly higher frequency of breastfeeding at 6 weeks (Brandt et al, 1998; Cernadas et al. 2003). The current finding extends these findings by suggesting that mothers at risk of PND are also more likely to breastfeed for longer if they have more optimal maternal-infant attachments. More replications are required.

In terms of limitations, the study used parental report measures to assess social-emotional development. Research has highlighted the difficulties in using parental ratings to access child psychopathology, especially in depressed mothers, as it increases the risk of biased maternal reporting (Müller & Furniss, 2013). Future studies should endeavour to triangulate findings by also including independent informant data (e.g., from preschool teacher). The majority of mothers in this study had a high level of education, were employed and were either married or cohabiting, which limits the generalisability of the findings. Furthermore, attrition did occur, and mothers who did not respond shared common variables (i.e., shorter breastfeeding duration, younger age and more likely to smoke), reducing the likelihood of group differences.

However, exploring the associations of interest in a homogenous high-socio-economic cohort also has benefits. Continuing debate exists regarding the direct impact of breastfeeding on neurodevelopment, as studies have shown that the effect may be indirectly related to parental advantage factors such as maternal education. One of the key difficulties for breastfeeding studies is controlling for confounders, as randomised controlled trials are largely not possible due to ethical implications. Historically, many studies have failed to account for sociodemographic confounders (Jain et al. 2002).

However, more recent studies with tighter controls on confounders have shown a greater disappearance of the breastfeeding effect (Der et al. 2006).Therefore, in a largely homogenous, high-socio-economic group such as the current cohort, not only are important confounding factors directly controlled for, but other residual, uncontrolled bias is also likely to be reduced as the groups are socio-economically similar across groups. This makes the associations found between breastfeeding and neurodevelopment more reliable, strengthening the findings of the current study.

Some of the findings of this study support our study hypotheses, for example the significant associations between PND and socio-emotional development and the association between attachment and socio-emotional development. However, the lack of associations between PND and attachment with neurodevelopmental outcomes was by in large, not expected. While an association between breastfeeding and neurodevelopment was anticipated, it was surprising that a dose-response effect of breastfeeding on neurodevelopment was not found, further replications are needed in relation to this finding. Attachment was not seen to have a direct impact on neurodevelopment, and it did not mediate the effect of PND on socio-emotional development. However, attachment did mediate the effect of PND on the likelihood of breastfeeding at six months. Due to the highly interconnected nature of these variables, interventions targeting either PND or breastfeeding need to be multifaceted, as intervening to improve PND in conjunction with attachment may result in better outcomes. The findings also suggest that strengthening maternal attachment in cases where PND is present may increase likelihood of breastfeeding, which in turn may improve expressive language and cognitive outcomes.

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5. Extended Methods

The purpose of this chapter is to provide a detailed account of the methodology followed in both the major research project (MRP) and the systematic review (SR); it provides more detail than was possible to include in the individual research articles. Topics common to both the MRP and SR will be discussed first before individual sections for each piece of research.

5.1 Quantitative framework and rationale for study design

Both the empirical research project (ERP) and systematic review (SR) aimed to examine the relationship between the respective independent and dependent variables, more specifically the ERP aimed to determine the impact of early maternal-infant relational-based variables (i.e., PND, breastfeeding exclusivity and maternal-infant attachment) on infant development. The SR aimed to examine the longitudinal impact of breastfeeding self-efficacy on postnatal depression. Both the ERP and the SR were located within a quantitative paradigm, and the methodological designs were also consistent with the quantitative approach. The goal of all quantitative studies is to measure and analyse causal relationships between variables within an objective framework, without the investigator influencing, or being influenced by, the phenomenon of interest (Nelson et al., 2017). Using a quantitative approach was deemed most appropriate for both the ERP and SR as the current literature-base in these research areas largely consists of quantitative studies. Therefore, choosing a quantitative design allowed the researcher to address identified inconsistencies and gaps in the existing literature base.

5.2 Major Research

5.2.1 Secondary Data Analysis

Secondary data analysis refers to the use of existing data to explore research questions that are different to the original. The use of secondary data has several benefits including avoiding unnecessary repetition of research and wastage of resources, it also ensures that sensitive subjects or hard to reach populations are not over researched (Johnston, 2017).When working with secondary data it is essential that data confidentiality and security is attended to. The amount of identifying information available in a dataset determines the need for additional ethical approval in addition to participant agreement to secondary data analysis in the original consent form (Johnston, 2017). Moreover, the methodology of the original data collected should be taken into consideration as well as its accuracy and its content. It is the responsibility of original researchers to ensure proper data stewardship, to allow for it to be re-used for downstream investigations. The FAIR data principles were set out to guide researchers in good data stewardship, these four principles are Findability, Accessibility, Interoperability, and Reusability (Wilkinson et al. 2016).

COMBINE Research Project

The COMBINE study- The Cork Nutrition and Microbiome Maternal-Infant Cohort Study (COMBINE) is funded through a grant from Science Foundation, Ireland to Professor Mairead Kiely (Principal Investigator) (grant no. INFANT/B3067), which is co-funded by the European Regional Development Fund under Ireland's European Structural and Investment Funds programmes 2014-2020. The COMBINE study was designed by Professor Kiely to investigate how nutrition and environmental factors over the first two years of life impact the gut bacteria, and the infants' physical and neurodevelopment.

5.2.2 Recruitment procedure

Cork University Maternity Hospital (CUMH) was the recruitment site and recruitment took place between late 2015 and 2017. The IMPROvED pregnancy study acted as a feeder study for COMBINE; mothers were recruited to COMBINE at their IMPROvED appointments antenatally or after delivery by the IMPROvED and COMBINE research midwifes.

5.2.3 Data collection

The maternal-infant dyads attended nine study appointments throughout the infants first two years of life, these were scheduled at two days postpartum and at 1, 2, 4, 6, 9, 12, 18 and 24 months. The day two appointment collected basic feeding data, at each consecutive appointment more in-dept feeding data was collected. Parental demographic information was recorded and data relating to the infant's living environment and general health was also collected using interviewer-led questionnaires throughout the study. These questionnaires were designed based on experience and literature review.

The Edinburgh Postnatal Depression Scale and *The Maternal-postnatal attachment scale* were emailed to the participants via *SurveyMonkey* at two months. The participants were given a two- week timeline to complete the measures. The neurodevelopmental assessments included the *Bayley Scale of Infant and Toddler Development 3rd edition* (Wilkinson et al., 2016)*(BSID-3rd edition)* at 12, 18 and 24 months and the child behaviour checklist at 24 months. All maternal mental health and neurodevelopmental assessments were administered by research psychologists.

Apart from the day two appointment that occurred in the hospital all other appointments took place in the Brookfield Health Sciences Complex in UCC in a purpose-built baby lab. Each appointment followed the same schedule of assessments to ensure consistency. The length of the appointments varied and typically increased in length as

the infant got older and engaged more with the *BSID-3rd edition* material. All information was recorded on specifically designed questionnaires or on standardised assessment recording sheets. Participant's scores were calculated when relevant and all data was immediately transferred to the case-report form (CRF) database. Continuous data monitoring was undertaken to ensure consistency in data collection and entry. Research psychologists completed accredited training in the *BSID 3rd edition* assessment and completed inter-rater reliability checks regularly to ensure consistency, they were also supervised by a Senior Clinical Psychologist.

5.2.4 Ethics approval

COMBINE received ethical approval from the Clinical Research Ethics Committee (ECM4(hh)06/01/15 and EMC3(bbb)20/04/18), the current author was named on an amendment to this ethical approval. As the database shared with the author was completely ammonised it was not necessary to seek additional ethical approval. However, the author did submit an ethics application to the School of Psychology's Ethics Committee in the interest of meeting the requirements of the course. Participants were made aware of their right to withdraw without impacting the healthcare services normally available to them (see patient information sheet- appendix M). Written informed consent was obtained from all participants (see appendix N)

As part of the COMBINE consent form, participants gave permission for their information to be used for future unrelated studies without further consent being required. Data protection and security guidelines were adhered to by the COMBINE research staff and the current author. The current author stored the ammonised COMBINE dataset on a password protected computer, and it was shared only with her supervisor (also named on the COMBINE ethics approval). Participants were asked to consent to referrals being made to their GP in the event of any concerns regarding their health or that of their infants.

Other referral pathways were also set up including access to a Paediatrician in the event of developmental concerns. All referrals were made in consultation with the participant.

5.2.5 Data Preparative Work

Data cleaning or data preparation work is an essential part of statistical analysis. Birth cohorts tend to produce a huge volume of data. The process of data preparation in the current study began with the author having an initial meeting with her supervisor and the Principal Investigator of the COMBINE study to discuss the author's proposed research questions. Once a direction was agreed upon, the author spent a considerable amount of time getting familiar with the dataset. Missing data was coded in the dataset as 999, and then excluded from the final analysis.

Decisions were necessary on which variables were appropriate. For example, the COMBINE database had multiple breastfeeding variables across several timepoints and categorised in various ways. After consulting the research and engaging in discussions with supervisors the author chose to include two month and six months exclusive and predominate breastfeeding (i.e., breastmilk as main milk source, not receiving formula top-ups). The rationale for this choice related to wanting to avoid the inherent bias associated with looking at duration of *any* breastfeeding (i.e., does not provide information on breastfeeding 'dose') and this issue is commonly identified as a limitation of previous studies (Dias & Figueiredo, 2015). The two and six-month timepoints were chosen because the two-month timepoint coincided with the other predictor variables and six months marks a time where many infants are weaned onto solid food and the picture becomes complicated by same. Decisions were also needed regarding inclusion of which demographic variables, these decisions were again guided by relevant research, discussions with supervisors and exploratory data analysis to look at associations between variables.

A response analysis was then conducted. Only participants who had completed all predictor and outcome variables were included in the analysis (see appendix K). The study looked at outcomes at both 12 and 24-months follow-up. Tests of normality were preformed, and Collinearity was also examined.

5.3 Systematic review:

The current review conducted a narrative synthesis, while it was not possible to conduct a meta-analysis due to the variation in analysis between studies and incomplete reporting, effect sizes were calculated to assist in comparing and interpreting findings. One of the aims of this study was to better understand the direction of the effect between breastfeeding self-efficacy and PND. A greater understanding of the impact of this association could help in the development of clinical interventions and recommendations for mothers at risk of PND and early breastfeeding cessation. The purpose of this section is to give a more comprehensive account and appraisal of the method used in conducting the current systematic review.

5.3.1 Stages in the current systematic review

Performing scoping searches, identifying the review question.

The current systematic review was conducted based on the PRISMA-P checklist, a predefined protocol outlining the important steps of a systematic review (Moher et al., 2015). The methodological steps in the PRISMA-P checklist include developing eligibility criteria, describing information sources, search strategies, study selection processes, assessment of individual study bias, and data synthesis (Moher et al. 2015). The first step in the current systematic review process was developing the research question, this is a critical step as it not only outlines the need for the review, but a well-

developed research question also increases the efficiency of the review by limiting the time spent identifying relevant research.

In the current study the SPIDER approach was used in developing the research question (Booth, 2006). Once the research question was broadly identified, a scooping review was conducted to help identify background literature to help refine the review question, identify if enough papers were available to address the question and identify relevant search terms to be used in the final review.

Inclusion and exclusion criteria

The next step after the author had established the research question was to establish the inclusion and exclusion criteria. The concept of inclusion and exclusion criteria in a systematic review provides a base on which the reviewer draws valid and reliable conclusions regarding the effect of the phenomenon under study (Strech & Sofaer, 2012). The criteria are set prior to the literature search to minimise the possibility of bias (Strech & Sofaer, 2012). The scooping review provided the author with a certain knowledge of the research area that allowed her to set the criteria so that it wasn't too broad or to narrow leading to an ineffective screening process. An outline of the inclusion and exclusion criteria for the current study are outlined in the systematic review.

Research protocol

A research protocol was developed that included a detailed search strategy which named the electronic databases to be searched. The decision about which databases were to be searched in the current study was informed by consulting previous similar reviews, discussions with the author's supervisor and a UCC subject librarian. In addition to searching the electronic databases, the reference lists of included studies were checked for relevant studies. The author attended a lecture on the development of search terms and

consulted a UCC subject librarian for more specific advice in the development of the specific search terms relevant to the current study.

Screening titles and abstracts and selecting full text papers

The first step in the screening process was de-duplicating the references, this was done electronically by the Covidence data management software. A screening tool was developed in *Microsoft Excel* with the inclusion and exclusion criteria for the current study outlined. This was used to screen papers at both the title and abstract stage and the full-text review stage. The Covidence software also provided a step-by-step process where studies could be selected from the title and abstract stage to be included in the full-text review stage and then selected to be included in the final review. When studies were excluded at the full-text review stage, a dialogue box was provided to allow recording of the reason for exclusion. When studies were unavailable from the usual library sources the author was contacted directly to obtain the full-text articles so it could be reviewed. The second author screened a percentage of papers at both the title and abstract stage and the full-text review stage, and any disagreements were resolved through discussion.

Data extraction

Once the final review papers had been identified the next stage was to extract relevant information from the individual studies. This information was input into a data extraction table. The data extraction table included both descriptive and analytical data. In terms of the type of data that was extracted the author was guided by both similar reviews and her research supervisor. The author created a pilot data extraction form and extracted data from a percentage of the final papers to determine if it was fit-for-purpose. After some amendments data extraction was carried out across all papers included in the final review. The results of data extraction are presented in table and narrative form in the systematic review paper.

Quality assessment

The next step in the review was to examine the quality of each of the included studies. When referring to the quality of a study in a systematic review it is referring to the degree to which the study measures and minimises bias and error, in other words the scientific rigour in its design, and in the way the study was conducted, and analysis carried out (Khan et al., 2011). If the study is of good quality, it is reasonable to be confident that the results are trustworthy and generalisable. A quality assessment tool asks a series of questions looking to assess different forms of bias. There are many different quality assessment tools and choosing a tool should be based on the design(s) of your included studies. As the studies included in the current review were observational *the National Heart, Lung and Blood Institute Quality Assessment Tool for Observational Cohorts and Cross-Sectional Studies* was chosen as the quality measure for the current study(National Institutes of Health, 2014).This decision was informed by discussions with the authors supervisor. A summary of the quality assessment was included in the empirical article and the results of the quality assessment were considered and highlighted in the interpretation of the overall findings.

Analysis and synthesis, write up

For all studies included in the systematic review, the effect size of the relationship between breastfeeding self-efficacy and PND was calculated. Effect sizes were calculated at baseline, and at a follow up time-point. In some studies, this relationship was expressed in Pearson's r if variables were continuous, or as Cohen's D, if PND was dichotomized. In studies where no effect size was reported, Cohen's D was calculated using the means, standard deviations and samples sizes reported. Effect sizes expressed as Pearson's r were converted to Cohens D to enable comparison between studies, this conversion was carried out using an online effect size converter (https://www.escal.site/"

https://www.escal.site/). The 95% confidence interval around each effect size was also calculated for each study. Once all effect sizes and confidence intervals were established, they were then graphed on a forest plot.

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6. Conclusions

The postnatal period is a very significant developmental phase in the lives of both mothers and their infants. It is a time in which mothers must cope with physical demands such as sleep deprivation and breastfeeding as well as recovering from birth, she must also adapt to parenthood, and develop secure emotional ties/attachment with her infant. With such considerable tasks to be undertaken within this early period it makes sense that we ask questions regarding the impact of this time on both maternal and infant health and development. As outlined in the introductory chapters the current thesis is underpinned by infant mental health theory (IMH). Proponents of this theory view infant development as occurring within the context of their early relationships. This understanding has shaped the design of this thesis and the conclusions that have been drawn. The overarching aim of this research thesis was to investigate how several relational variables that make up part of the postnatal experience impact long-term developmental outcomes in children up to two-years. It also considered how these postnatal variables were related to one another.

The main research study took a multifactorial approach and investigated the impact of three important postnatal variables, namely PND, maternal-infant attachment and exclusive/predominant breastfeeding on social-emotion and neurodevelopmental outcomes within the infant's first two years of life. The results indicated that PND and maternal-infant attachment does not influence neurodevelopment at either 12- or 24-month postnatal outcomes, but they do influence social-emotional outcomes at 24 months. Thus, mothers with lower levels of PND and more optimal levels of maternal-infant attachment had children with better social-emotional outcomes. While depression and attachment together were found to predict social-emotional outcome at 24 months, individually they did not predict social-emotional outcomes. Therefore, mediation was

considered as a possible explanation for these results. Given the theoretical understanding on which the thesis is based (i.e., that the attachment relationship is the context for all infant development), in addition to research suggesting that maternal-infant attachment serves as the trans-generational mechanism of transmission of vulnerabilities in infants (Tsivos et al. 2015) it was conceptualised that depression had an indirect effect on social-emotional outcomes, through the maternal-infant attachment relationship. However, attachment was not found to mediate the relationship between depression and social-emotional development at 24 months postnatal.

Also of interest is that attachment had an impact on social-emotional development at 12 months follow-up, but depression didn't show an effect till 24 months follow-up. It is possible that depression has a longer latency. However, the direct effects of maternal-infant attachment appear to be evident earlier in the postnatal period. Studies with multiple follow-ups are needed to better understand the effects of these variables over time within the same cohort. In addition, it would also be important for future research to consider the role of fathers (or the infant's other parent). The Goodman and Gotlib model suggest that fathers may moderate the transmission of risk between maternal PND and adverse child development outcomes. Research should consider the dyadic relationship between both parents and the developing infant (Goodman et al. 1999). As the majority of participants in the current study were in a relationship, positive parental interactions may have moderated any possible effects of PND on developmental outcomes.

Furthermore, a limitation of the current study is that PND was measured at only one time point and a self-report screener was used rather than a clinical interview to identify mothers at risk of PND. Research has shown a greater disadvantage in terms of neurodevelopment in children of mothers who have persistent levels of depression symptomology in comparison to mothers who were depressed for shorter durations. As

the current study only measured PND at two months postnatal, the importance of chronicity of PND is not accounted for. (Campbell et al. 1997; Kurstjens et al. 2001). Moreover, the use of a parent-report instrument to measure PND introduced a possible reporting bias, where depressed mothers perceived their infants' behaviour on the measure of social-emotional development more negatively, over-inflating any possible effect.

An association was found between predominant/ exclusive breastfeeding at two months postnatal with neurodevelopment, specifically with cognitive and language development (in particular, expressive language development) at the 24 months outcome. When breastfeeding at six months was examined, no associations were found with neurodevelopmental outcomes. Based on the former result a mediation analysis was conducted to investigate if depression and maternal-infant attachment indirectly influenced neurodevelopment by directly influencing predominant/ exclusive breastfeeding. Maternal-infant attachment did mediate the relationship between depression and predominant/ exclusive breastfeeding at six months. This suggested that mothers with a more optimum attachment relationship to their infants, even in the presence of depression are more likely to breastfeed for longer, and breastfeeding up to two months was associated with neurodevelopmental advantages.

The postnatal period is made up of a complex web of variables. Many studies to date have examined the effect of the independent variables of interest in this study on neuro/ social-emotional development independently. However, considering the current results that point towards numerous interactions between the dependent variables and indirect pathways of influence a multifactorial approach provides a more comprehensive and representative picture of the complex nature of this research area. Future research should consider using this approach.

As mentioned, the main research study found that infants that were exclusively or predominantly breastfed up to the age of two months were more likely to score more optimally on both cognitive and language outcomes, in particular expressive language development. However, no association was found when the association was studied using data from infants that were breastfed till six months. The fact that a dose response effect was not found is of particular interest and warrants further research. Breastfeeding guidelines are centred on the understanding that babies who receive the most breastmilk for the longest time benefit the most. Research suggests this is true of certain health outcomes, however, it may not be the case for neurodevelopment (Su et al., 2021). There may exist certain windows of development in which breast milk has its greatest effects. In other words, breastfeeding may have a threshold rather than dose response effect.

A longstanding debate exists within the breastfeeding literature, researchers have argued whether there are real breastfeeding effects on neurodevelopment or if the effects shown are related to parental advantage, as mothers who breastfeed tend to be from higher social-economic backgrounds, a variable that is also associated with improved neurodevelopmental outcomes. However, the current study sample is highly homogenous across demographic variables in both breastfeeding and non-breastfeeding groups. Therefore, the current study not only controls for important confounder variables but also other residual bias is likely reduced, strengthening the study findings. Therefore, the current research contributes to this long-standing debate in favour of a breastfeeding effect on neurodevelopmental outcomes. In addition, the study addressed important criticism within the breastfeeding literature by providing precise definitions of the breastfeeding variables, this methodological rigor allows for sound interpretations to be drawn and issues of replicability in the research base to be addressed.

While the main research study considered the consequences of important postnatal variables on long-term infant development, the systematic review considered breastfeeding self-efficacy as a possible predictor/ risk factor of PND. The review examined available prospective, longitudinal research. The results indicated that there is an association between breastfeeding self-efficacy and PND. More specifically, low levels of breastfeeding self-efficacy, in the early postnatal period is predictive of depressive symptomology up to six months postnatal. However, the strength of this predictive effect weakens over-time. The direction of this relationship between these variables was ambiguous within the research before the current review. PND poses significant public health risks and is typically under diagnosed (O'Hara & Swain, 1996). However, if breastfeeding self-efficacy is predictive of PND, as the current systematic review suggests than assessing breastfeeding self-efficacy early in the postnatal period may help to identify women most at risk of developing PND and those most in need of supports.

More research is warranted in this area, as the review highlighted the dearth of well-controlled prospective studies in this area, future studies should look to control for maternal history of depression and look separately at first-time mothers and mothers with multiple children, as mothers with and without experience of breastfeeding are heterogenous groups in terms of breastfeeding self-efficacy. Moreover, when multiple socio-cognitive factors such as breastfeeding self-efficacy and outcome expectancy were combined, together their predictive ability of later PND was stronger than when looked at individually. Future research should investigate other possible social-cognitive factors such as breastfeeding intensions/ goals. Future intervention research should examine whether increasing a mother's breastfeeding self-efficacy reduces their risk of PND.

The current thesis highlighted the complex and integrated nature of the postnatal period. While it is often a time of great challenges for mothers, infants, and their families it is also a time of great opportunity. To ensure that women and their infants not only survive this period but thrive and flourish, it is important to understand the impact of postnatal variables and what supports enable the most optimal start in life. However, the postnatal period is often a neglected phase of maternity care with more emphasis and resources focused on antenatal and intrapartum care (Sacks, 2016). The variables of interest in this study are modifiable in nature, therefore there exists opportunities to intervene and improve infant outcomes.

For example, the current findings suggested that low breastfeeding self-efficacy is predictive of PND, therefore identifying ways of improving breastfeeding self-efficacy may indeed reduce the public health burden associated with PND and reduce the risk of later adverse child development outcomes. Maternal-infant attachment was shown to mediate the relationship between depression and breastfeeding, this suggested that mothers with more optimum attachment relationships with their infants, even if they were at risk of depression were more likely to breastfeeding their infants to six months. This finding suggests that interventions focused on improving PND symptomology may not be sufficient in increasing breastfeeding duration. Future research should consider if interventions for PND exert a protective effect on the mother-infant attachment relationship and if in turn this increases breastfeeding duration.

The current research also showed that exclusive/predominant breastfeeding supported neurodevelopment. It is important that clinicians are aware that a positive maternal-infant attachment relationship may improve breastfeeding outcomes, even in the presence of PND and that in turn breastfeeding may support neurodevelopment. These variables should not be considered clinically in isolation and instead intervention research

should look to address the attachment relationship as well as depressive symptoms to improve infant outcomes.

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7. Appendices

Appendix A

Manuscript Submission Guidelines: International Breastfeeding Journal

Research articles should report on original primary research.

International Breastfeeding Journal strongly encourages that all datasets on which the conclusions of the paper rely should be available to readers. We encourage authors to ensure that their datasets are either deposited in publicly available repositories (where available and appropriate) or presented in the main manuscript or additional supporting files whenever possible. Please see Springer Nature's information on recommended repositories. Where a widely established research community expectation for data archiving in public repositories exists, submission to a community-endorsed, public repository is mandatory. A list of data where deposition is required, with the appropriate repositories, can be found on the Editorial Policies Page.

International Breastfeeding Journal does not except for publication any manuscript that has received funding, sponsorship or any other means of support from infant formula manufacturers.

- **Preparing your manuscript**

The information below details the section headings that you should include in your manuscript and what information should be within each section.

Please note that your manuscript must include a 'Declarations' section including all of the subheadings (please see below for more information).

- **Title page**

The title page should:

- present a title that includes, if appropriate, the study design e.g.:
    - "A versus B in the treatment of C: a randomized controlled trial", "X is a risk factor for Y: a case control study", "What is the impact of factor X on subject Y: A systematic review"
    - or for non-clinical or non-research studies a description of what the article reports
- list the full names and institutional addresses for all authors
    - if a collaboration group should be listed as an author, please list the Group name as an author. If you would like the names of the individual members of the Group to be searchable through their individual PubMed

records, please include this information in the “Acknowledgements” section in accordance with the instructions below

- indicate the corresponding author

- **Abstract**

The Abstract should not exceed 350 words. Please minimize the use of abbreviations and do not cite references in the abstract. Reports of randomized controlled trials should follow the CONSORT extension for abstracts. The abstract must include the following separate sections:

- **Background:** the context and purpose of the study
- **Methods:** how the study was performed and statistical tests used
- **Results:** the main findings
- **Conclusions:** brief summary and potential implications
- **Trial registration:** If your article reports the results of a health care intervention on human participants, it must be registered in an appropriate registry and the registration number and date of registration should be in stated in this section. If it was not registered prospectively (before enrollment of the first participant), you should include the words 'retrospectively registered'. See our editorial policies for more information on trial registration

- **Keywords**

Three to ten keywords representing the main content of the article.

- **Background**

The Background section should explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.

- **Methods**

The methods section should include:

- the aim, design and setting of the study
- the characteristics of participants or description of materials
- a clear description of all processes, interventions and comparisons. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses
- the type of statistical analysis used, including a power calculation if appropriate

- **Results**

This should include the findings of the study including, if appropriate, results of statistical analysis, which must be included either in the text or as tables and figures.

- **Discussion**

This section should discuss the implications of the findings in context of existing research and highlight limitations of the study.

- **Conclusions**

This should state clearly the main conclusions and provide an explanation of the importance and relevance of the study reported.

- **List of abbreviations**

If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations should be provided.

- **Declarations**

All manuscripts must contain the following sections under the heading 'Declarations':

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and materials
- Competing interests
- Funding
- Authors' contributions
- Acknowledgements
- Authors' information (optional)

Please see below for details on the information to be included in these sections.

If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

- **Ethics approval and consent to participate**

Manuscripts reporting studies involving human participants, human data or human tissue must:

- include a statement on ethics approval and consent (even where the need for approval was waived)
- include the name of the ethics committee that approved the study and the committee’s reference number if appropriate

Studies involving animals must include a statement on ethics approval and for experimental studies involving client-owned animals, authors must also include a statement on informed consent from the client or owner.

See our editorial policies for more information.

If your manuscript does not report on or involve the use of any animal or human data or tissue, please state "Not applicable" in this section.

- **Consent for publication**

If your manuscript contains any person's data in any form (including any individual details, images, or videos), consent for publication must be obtained from that person, or in the case of children, their parent or legal guardian. All presentations of case reports must have consent for publication.

You can use your institutional consent form or our consent form if you prefer. You should not send the form to us on submission, but we may request to see a copy at any stage (including after publication).

See our editorial policies for more information on consent for publication.

If your manuscript does not contain data from any person, please state "Not applicable" in this section.

- **Availability of data and materials**

All manuscripts must include an 'Availability of data and materials' statement. Data availability statements should include information on where data supporting the results reported in the article can be found including, where applicable, hyperlinks to publicly archived datasets analysed or generated during the study. By data, we mean the minimal dataset that would be necessary to interpret, replicate and build upon the findings reported in the article. We recognise it is not always possible to share research data publicly, for instance when individual privacy could be compromised, and in such instances data availability should still be stated in the manuscript along with any conditions for access.

Authors are also encouraged to preserve search strings on searchRxiv https://searchrxiv.org/, an archive to support researchers to report, store and share their searches consistently and to enable them to review and re-use existing searches. searchRxiv enables researchers to obtain a digital object identifier (DOI) for their search, allowing it to be cited.

Data availability statements can take one of the following forms (or a combination of more than one if required for multiple datasets):

- The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]

- The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
- All data generated or analysed during this study are included in this published article [and its supplementary information files].
- The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
- Data sharing does not apply to this article as no datasets were generated or analysed during the current study.
- The data that support the findings of this study are available from [third party name] but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available from the authors upon reasonable request and with permission of [third party name].
- Not applicable. If your manuscript does not contain any data, please state 'Not applicable' in this section.

More examples of template data availability statements, which include examples of openly available and restricted access datasets, are available here.

BioMed Central also requires that authors cite any publicly available data on which the conclusions of the paper rely in the manuscript. Data citations should include a persistent identifier (such as a DOI) and should ideally be included in the reference list. Citations of datasets, when they appear in the reference list, should include the minimum information recommended by DataCite and follow journal style. Dataset identifiers including DOIs should be expressed as full URLs. For example:

Hao Z, AghaKouchak A, Nakhjiri N, Farahmand A. Global integrated drought monitoring and prediction system (GIDMaPS) data sets. figshare. 2014. http://dx.doi.org/10.6084/m9.figshare.853801

With the corresponding text in the Availability of data and materials statement:

The datasets generated during and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS].[Reference number]

If you wish to co-submit a data note describing your data to be published in *BMC Research Notes*, you can do so by visiting our submission portal. Data notes support open data and help authors to comply with funder policies on data sharing. Co-published data notes will be linked to the research article the data support (example).

- **Competing interests**

All financial and non-financial competing interests must be declared in this section.

See our editorial policies for a full explanation of competing interests. If you are unsure whether you or any of your co-authors have a competing interest please contact the editorial office.

Please use the author's initials to referauthor's authors' competing interests in this section.

If you do not have any competing interests, please state "The authors declare that they have no competing interests" in this section.

- **Funding**

All sources of funding for the research reported should be declared. The role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript should be declared.

- **Authors' contributions**

The individual contributions of authors to the manuscript should be specified in this section. Guidance and criteria for authorship can be found in our editorial policies.

Please use initials to refer to each author's contribution in this section, for example: "FC analyzed and interpreted the patient data regarding the hematological disease and the transplant. RH performed the histological examination of the kidney and was a major contributor in writing the manuscript. All authors read and approved the final manuscript."

- **Acknowledgements**

Please acknowledge anyone who contributed to the article who does not meet the criteria for authorship including anyone who provided professional writing services or materials.

Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements section.

See our editorial policies for a full explanation of acknowledgments and authorship criteria.

If you do not have anyone to acknowledge, please write "Not applicable" in this section.

Group authorship (for manuscripts involving a collaboration group): if you would like the names of the individual members of a collaboration Group to be searchable through their PubMed records, please ensure that the title of the collaboration Group is included on the title page and in the submission system and also include collaborating author names as the last paragraph of the “Acknowledgements” section. Please add authors in the format First Name, Middle initial(s) (optional), Last Name. You can add institution or country information for each author if you wish, but this should be consistent across all authors.

Please note that individual names may not be present in the PubMed record at the time a published article is initially included in PubMed as it takes PubMed additional time to code this information.

- **Authors' information**

This section is optional.

You may choose to use this section to include any relevant information about the author(s) that may aid the reader's interpretation of the article and understand the standpoint of the author(s). This may include details about the authors' qualifications, current positions they hold at institutions or societies, or any other relevant background information. Please refer to authors using their initials. Note this section should not be used to describe any competing interests.

- **Footnotes**

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

- **References**

Examples of the Vancouver reference style are shown below.

See our editorial policies for author guidance on good citation practice

Web links and URLs: All web links and URLs, including links to the authors' websites, should be given a reference number and included in the reference list rather than within the text of the manuscript. They should be provided in full, including both the title of the site and the URL, as well as the date the site was accessed, in the following format: The Mouse Tumor Biology Database. http://tumor.informatics.jax.org/mtbwi/index.do. Accessed 20 May 2013. If an author or group of authors can be associated with a web link, such as for weblogs, then they should be included in the reference.

Example reference style:

Article within a journal

Smith JJ. The world of science. Am J Sci. 1999;36:234-5.

Article within a journal (no page numbers)

Rohrmann S, Overvad K, Bueno-de-Mesquita HB, Jakobsen MU, Egeberg R, Tjønneland A, et al. Meat consumption and mortality - results from the European Prospective Investigation into Cancer and Nutrition. BMC Medicine. 2013;11:63.

Article within a journal by DOI

Slifka MK, Whitton JL. Clinical implications of dysregulated cytokine production. Dig J Mol Med. 2000; doi:10.1007/s801090000086.

Article within a journal supplement

Frumin AM, Nussbaum J, Esposito M. Functional asplenia: demonstration of splenic activity by bone marrow scan. Blood 1979;59 Suppl 1:26-32.

Book chapter, or an article within a book

Wyllie AH, Kerr JFR, Currie AR. Cell death: the significance of apoptosis. In: Bourne GH, Danielli JF, Jeon KW, editors. International review of cytology. London: Academic; 1980. p. 251-306.

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Dataset with persistent identifier

Zheng L-Y, Guo X-S, He B, Sun L-J, Peng Y, Dong S-S, et al. Genome data from sweet and grain sorghum (Sorghum bicolor). GigaScience Database. 2011. http://dx.doi.org/10.5524/100012.

Appendix B:

Journal of Experimental Child Psychology

GUIDE FOR AUTHORS

INTRODUCTION The Journal of Experimental Child Psychology is a leading source of empirical research on all aspects of children's development from infancy through adolescence, including cognitive, social, and physical development. Types of contributions The Journal of Experimental Child Psychology is devoted primarily to reports of empirical work on behavioral and psychological development. Although the emphasis is on empirical work with infants, children, and adolescents, manuscripts that report research on adults or special populations fall under the purview of JECP if the work expands our understanding of development. Integrative papers that present findings from multiple experiments focused on a problem are encouraged; piecemeal papers that carve up findings from a single project are discouraged.

To facilitate the review process and the communication of research findings, manuscripts should be no longer than necessary. The maximum number of words of text for a regular submission is 10, 500 (text plus references). Single-experiment studies will usually be shorter than those with multiple experiments.

The journal also publishes short communications (Brief Reports), not to exceed 4,000 words. This word count includes the main text and references but excludes the title page, abstract, tables, and figures, (maximum of two tables/figures per report). Despite their short length, shortt communications are expected to make substantial contributions to new knowledge and to be of broad interest to JECP's readership. Manuscripts are evaluated for their methodological adequacy, evidence of replicability of results, contribution to our understanding of developmental process and theory, and clarity of presentation, both verbal and graphic.

All manuscripts must follow the specifications of the Publication Manual of the American Psychological Association (7th ed.), with the following exceptions: (1) Embed tables and figures in text, close to where they are called out; and (2) place footnotes at the bottom of the page, not at the back of the article. Authors will be asked

to provide the names and email addresses of three objective reviewers that they nominate to review their paper, although this is not mandatory. The Editors can choose whether to use these nominations. Authors of revised manuscripts should not provide reviewer nominations when resubmitting papers paper.

Submission checklist

You can use this list to carry out a final check of your submission before you send it to the journal for review. Please check the relevant section in this Guide for Authors for more details. Ensure that the following items are present:

One author has been designated as the corresponding author with contact details: • E-mail address • Full postal address All necessary files have been uploaded:

Manuscript:

• Include keywords

• All figures (include relevant captions)

• All tables (including titles, descriptions, footnotes)

• Ensure all figure and table citations in the text match the files provided

• Indicate clearly if color should be used for any figures in print Graphical Abstracts / Highlights files (where applicable) Supplemental files (where applicable)

• Manuscript has been 'spell checked' and 'grammar checked'

• All references mentioned in the Reference List are cited in the text, and vice versa

• Permission has been obtained for use of copyrighted material from other sources (including the Internet)

• A competing interest statement is provided, even if the authors have no competing interests to declare

• Journal policies detailed in this guide have been reviewed

• Referee suggestions and contact details provided, based on journal requirements

Appendix C

World Health Organisation (WHO) criteria that define selected infant feeding practices

Feeding Practice	Requires that the infant receive	Allows the infant to receive	Does not allow the infant to receive
Exclusive breastfeeding	Breast milk	Vitamins, Minerals, and Medicines	Anything else
Predominant breastfeeding	Breast milk	Vitamins, Minerals, Medicines, water, juice, and water-based drinks.	Anything else

Appendix D:

The National Heart, Lung & Blood Institute- Quality Assessment

Guidance for Assessing the Quality of Observational Cohort and Cross-Sectional Studies

The guidance document below is organized by question number from the tool for quality assessment of observational cohort and cross-sectional studies.

Question 1. Research question

Did the authors describe their goal in conducting this research? Is it easy to understand what they were looking to find? This issue is important for any scientific paper of any type. Higher-quality scientific research explicitly defines a research question.

Questions 2 and 3. Study population

Did the authors describe the group of people from which the study participants were selected or recruited, using demographics, location, and period? If you were to conduct this study again, would you know who to recruit, from where, and fromperiodperiod? Is the cohort population free of the outcomes of interest at the time they were recruited?

An example would be men over 40 years old with type 2 diabetes who began seeking medical care at Phoenix Good Samaritan Hospital between January 1, 1990, and December 31, 1994. In this example, the population is clearly described as: (1) who (men over 40 years old with type 2 diabetes); (2) where (Phoenix Good Samaritan Hospital); and (3) when (between January 1, 199,0 and December 31, 1994). Another example is women ages 34 to 59 years of age in 1980 who were in the nursing profession and had no known coronary disease, stroke, cancer, hypercholesterolemia, or diabete, and were recruited from the 11 most populous States, with contact information obtained from State nursing boards.

In cohort studies, the population at baseline must be free of the outcnursesinterest. For example, the nurses' population above would be an appropriate group in which to study incident coronary disease. This information is usually found either in descriptions of population recruitment, definitions of variables, or inclusion/exclusion criteria.

You may need to look at prior papers on methods tassessor this question. Those papers are usually in the reference list.

If fewer than 50% of eligible persons participated in the study, then there is concern that the study population does not adequately represent the target population. This increases the risk of bias.

Question 4. Groups recruited from the same population and uniform eligibility criteria

Were the inclusion and exclusion criteria developed bthe efore recruitment or selection of the study population? Were the same underlying criteria used for all of the subjects involved? This issue is related to the description of the study population, above, and you may find the information for both of these questions in the same section of the paper.

Most cohort studies begin with the selection of the cohort; participants in this cohort are then measured or evaluated to determine their exposure status. However, some cohort studies may recruit or select exposed participants in a different time or place than unexposed participants, especially retrospective cohort studies–which is when data are obtained from the past (retrospectively), but the analysis examines exposures before outcomes. For example, one research question could be whether diabetic men with clinical depression are at higher risk for cardiovascular disease than those without clinical depression. So, diabetic men with depression might be selected from a mental health clinic, while diabetic men without depression might be selected from an internal medicine or endocrinology clinic. This study recruits groups from different clinic populations, so this example would get a "no."

However, the women nurses described in the question above were selected based on the same inclusion/exclusion criteria, so that example would get a "yes."

Question 5. Sample size justification

Did the authors present their reasons for selecting or recruiting the number of people included or analyzed? Do they note or discuss the statistical power of the study? This question is about whether or not the study had enough participants to detect an association if one truly existed.

A paragraph in the methods section of the article may explain the sample size needed to detect a hypothesized difference in outcomes. You may also find a discussion of power in the discussion section (such as the study had 85 percent power to detect a 20 percent increase in the rate of an outcome of interest, with a 2-sided alpha of 0.05). Sometimes estimates of variance and/or estimates of effect size are given, instead of sample size calculations. In any of these cases, the answer would be "yes."

However, observational cohort studies often do not report anything about power or sample sizes because the analyses are exploratory in nature. In this case, the answer would be "no." This is not a "fatal flaw." It just may indicate that attention was not paid to whether the study was sufficiently sized to answer a prespecified question–i.e., it may have been an exploratory, hypothesis-generating study.

Question 6. Exposure assessed before outcome measurement

This question is important because, to determine whether an exposure causes an outcome, the exposure must come before the outcome.

For some prospective cohort studies, the investigator enrolls the cohort and then determines the exposure status of various members of the cohort (large epidemiological studies like Framingham used this approach). However, for other cohort studies, the cohort is selected based on its exposure status, as in the example above of depressed diabetic men (the exposure being depression). Other examples include a cohort identified by its exposure to fluoridated drinking water and then compared to a cohort living in an area without fluoridated water, or a cohort of military personnel exposed to combat in the Gulf War compared to a cohort of military personnel not deployed in a combat zone.

With either of these types of cohort studies, the cohort is followed forward in time (i.e., prospectively) to assess the outcomes that occurred in the exposed members compared to nonexposed members of the cohort. Therefore, you begin the study in the present by looking at groups that were exposed (or not) to some biological or behavioral factor, intervention, etc., and then you follow them forward in time to examine outcomes. If a cohort study is conducted properly, the answer to this question should be "yes," since the exposure status of members of the cohort was determined at the beginning of the study before the outcomes occurred.

For retrospective cohort studies, the same principle applies. The differene is that, rather than identifying a cohort in the present and following them forward in time, the investigators go back in time (i.e., retrospectively) and select a cohort based on their exposure status in the past and then follow them forward to assess the outcomes that occurred in the exposed and nonexposed cohort members. Because in retrospective cohort studies the exposure and outcomes may have already occurred (it depends on how long they follow the cohort), it is important to make sure that the exposure preceded the outcome.

Sometimes cross-sectional studies are conducted (or cross-sectional analyses of cohort-study data), where the exposures and outcomes are measured during the same timeframe. As a result, cross-sectional analyses provide weaker evidence than regular cohort studies regarding a potential causal relationship between exposures and outcomes. For cross-sectional analyses, the answer to Question 6 should be "no."

Question 7. Sufficient timeframe to see an effect

Did the study allow enough time for a sufficient number of outcomes to occur or be observed or enough time for an exposure to have a biological effect on an outcome? In the examples given above, if clinical depression has a biological effect on increasing the risk for CVD, such an effect may take years. In the other example, if higher dietary sodium increases BP, a short timeframe may be sufficient to assess its association with BP, but a longer timeframe would be needed to examine its association with heart attacks.

The issue of timeframe is important to enable meaningful analysis of the relationships between exposures and outcomes to be conducted. This often requires at least several years, especially when looking at health outcomes, but it depends on the research question and outcomes being examined.

Cross-sectional analyses allow no time to see an effect since the exposures and outcomes are assessed at the same time, so those would get a "no" response.

Question 8. Different levels of exposure to interest

If the exposure can be defined as a range (examples: drug dosage, amount of physical activity, amount of sodium consumed), were multiple categories of that exposure assessed? (for example, for drugs: not on the medication, on a low dose, medium dose, high dose; for dietary sodium, higher than average U.S. consumption, lower than recommended consumption, between the two). Sometimes discrete categories of

exposure are not used, but instead, exposures are measured as continuous variables (for example, mg/day of dietary sodium or BP values).

In any case, studying different levels of exposure (where possible) enables investigators to assess trends or dose-response relationships between exposures and outcomes–e.g., the higher the exposure, the greater the rate of the health outcome. The presence of trends or dose-response relationships lends credibility to the hypothesis of causality between exposure and outcome.

For some exposures, however, this question may not be applicable (e.g., the exposure may be a dichotomous variable like living in a rural setting versus an urban setting or vaccinated/not vaccinated with a one-time vaccine). If there are only two possible exposures (yes/no), then this question should be given an "NA," and it should not count negatively toward the quality rating.

Question 9. Exposure measures and assessment

Were the exposure measures defined in detail? Were the tools or methods used to measure exposure accurate and reliable–for example, have they been validated or are they objective? This issue is important as it influences confidence in the reported exposures. When exposures are measured with less accuracy or validity, it is harder to see an association between exposure and outcome even if one exists. Also, as important is whether the exposures were assessed in the same manner within groups and between groups; if not, bias may result.

For example, a retrospective self-report of dietary salt intake is not as valid and reliable as prospectively using a standardized dietary log plus testing participants' urine for sodium content. Another example is measurement of BP, where there may be quite a difference between usual care, where clinicians measure BP however it is done in their practice setting (which can vary considerably), and use of trained BP assessors using standardized equipment (e.g., the same BP device which has been tested and calibrated) and a standardized protocol (e.g., patient is seated for 5 minutes with feet flat on the floor, BP is taken twice in each arm, and all four measurements are averaged). In each of these cases, the former would get a "no" and the latter a "yes."

Here is a final example that illustrates the point about why it is important to assess exposures consistently across all groups: If people with higher BP (exposed cohort) are seen by their providers more frequently than those without elevated BP (nonexposed group), it also increases the chances of detecting and documenting changes in health outcomes, including CVD-related events. Therefore, it may lead to the conclusion that higher BP leads to more CVD events. This may be true, but it could also be because the subjects with higher BP were seen more often; thus, more CVD-related events were detected and documented simply because they had more encounters wihealthcareth care system. Thus, it could bias the results and lead to an erroneous conclusion.

Question 10. Repeated exposure assessment

Was the exposure for each person measured more than once during the course of the study period? Multiple measurements with the same result increase our confidence that the exposure status was correctly classified. Also, multiple measurements enable investigators to look at changes in exposure over time, for example, people who ate

high dietary sodium throughout the follow-up period, compared to those wharted out high then reduced their intake, compared to those who ate low sodium throughout. Once again, this may not be applicable in all cases. In many older studies, exposure was measured only at baseline. However, multiple exposure measurements do result in a stronger study design.

Question 11. Outcome measures

Were the outcomes defined in detail? Were the tools or methods for measuring outcomes accurate and reliable–for example, have they been validated or are they objective? This issue is important because it influences confidence in the validity of study results. Also important is whether the outcomes were assessed in the same manner within groups and between groups.

An example of an outcome measure that is objective, accurate, and reliable is death–the outcome measured with more accuracy than any other. But even with a measure as objective as death, there can be differences in the accuracy and reliability of how death was assessed by the investigators. Did they base it on an autopsy report, death certificate, death registry, or report from a family member? Another example is a study of whether dietary fat intake is related to blood cholesterol level (cholesterol level being the outcome), and the cholesterol level is measured from fasting blood samples that are all sent to the same laboratory. These examples would get a "yes." An example of a "no" would be a self-report by subjects that they had a heart attak, or a self-report of how much they weigh (if body weight is the outcome of interest).

Similar to the example in Question 9, results may be biased if one group (e.g., people with high BP) is seen more frequently than another group (people with normal BP) because more frequent encounters with the healthcaincrease increases the chances of outcomes being detected and documented.

Question 12. Blinding of outcome assessors

Blinding means that outcome assessors did not know whether the participant was exposed or unexposed. It is also sometimes called "masking." The objective is to look for evidence in the article that the person(s) assessing the outcome(s) for the study (for example, examining medical records to determine the outcomes that occurred in the exposed and comparison groups) is masked to the exposure status of the participant. Sometimes the person measuring the exposure is the same person conducting the outcome assessment. In this case, the outcome assessor would most likely not be blinded to exposure status because they also took measurements of exposures. If so, make a note of that in the comments section.

As you assess this criterion, think about whether the person(s) doing the outcome assessment would likely know (or be able to figure out) the exposure status of the study participants. If the answer is no, then blinding is adequate. An example of adequate blinding of the outcome assessors is to create a separate committee, whose members were not involved in the care of the patient and had no information about the study participants' exposure status. The committee would then be provided with copies of participants' medical records, which had been stripped of any potential exposure information or personally identifiable information. The committee would then review

the records for prespecified outcomes according to the study protocol. If blinding was not possible, which is sometimes the case, mark "NA" and explain the potential for bias.

Question 13. Follow up rate

Higher overall follow-up rates are always better thfollow-upfollow up rates, even though higher rates are expected in shorter studies, wherfollow-up overall follow up rates are often seen in studies of longer duration. Usually, an acceptable overall follow-up rate is considered 80 percent or more of participants whose exposures were measured at baseline. However, this is just a general guideline. For example, a 6-month cohort study examining the relationship between dietary sodium intake and BP level may have over 90follow-upfollow up, but a 20-year cohort study examining effects of sodium intake on stroke may have only a 65follow-upfollow up rate.

Question 14. Statistical analyses

Were key potential confounding variables measured and adjusted for, such as by statistical adjustment for baseline differences? Logistic regression or other regression methods are often used to account for the influence of variables not of interest.

This is a key issue in cohort studies, because statistical analyses need to control for potential confounders, in contrast to an RCT, where the randomization process controls for potential confounders. All key factors that may be associated both with the exposure of interest and the outcome–that are not of interest to the research question–should be controlled for in the analyses.

For example, in a study of the relationship between cardiorespiratory fitness and CVD events (heart attacks and strokes), the study should control for age, BP, blood cholesterol, and body weight, because all of these factors are associated with low fitness and CVD events. Well-done cohort studies control for multiple potential confounders.

Some general guidance for determining the overall quality rating of observational cohort and cross-sectional studies

The questions on the form are designed to help you focus on the key concepts for evaluating the internal validity of a study. They are not intended to create a list that you simply tally up to arrive at a summary judgment of quality.

Internal validity for cohort studies is the extent to which the results reported in the study can truly be attributed to the exposure being evaluated and not to flaws in the design or conduct of the study–in other words, the ability of the study to draw associative conclusions about the effects of the exposures being studied on outcomes. Any such flaws can increase the risk of bias.

Critical appraisal involves considering the risk of potential for selection bias, information bias, measurement bias, or confounding (the mixture of exposures that one cannot tease out from each other). Examples of confounding include co-interventions, differences at baseline in patient characteristics, and other issues throughout the questions above. A high risk of bias translates to a rating of poor quA lowty. Low risk of bias translates to a rating of good quality. (Thus, the greater the risk of bias, the lower the quality rating of the study.)

In addition, the more attention in the study design to issues that can help determine whether there is a causal relationship between the exposure and outcome, the higher quality of the study. These include exposures occurribefore to outcomes, evaluation of a dose-response gradient, accuracy of measurement of both exposure and outcome, sufficient timeframe to see an effect, and appropriate control for confounding–all concepts reflected in the tool.

Generally, when you evaluate a study, you will not see a "fatal flaw," but you will find some risk of bias. By focusing on the concepts underlying the questions in the quality assessment tool, you should ask yourself about the potential for bias in the study you are critically appraising. For any box where you check "no" you should ask, "What is the potential risk of bias resulting from this flaw in study design or execution?" That is, does this factor cause you to doubt the results that are reported in the study or doubt the ability of the study to accurately assess an association between exposure and outcome?

The best approach is to think about the questions in the tool and how each one tells you something about the potential for bias in a study. The more you familiarize yourself with the key concepts, the more comfortable you will be with critical appraisal. Examples of studies rated good, fair, and poor are useful, but each study must be assessed on its own based on the details that are reported and consideration of the concepts for minimizing bias.

Appendix E

Edinburgh Postnatal Scale

Edinburgh Postnatal Depression Scale[1] (EPDS)

Name: _____ Address: _____

Your Date of Birth: _____ _____

Baby's Date of Birth: _____ Phone: _____

As you are pregnant or have recently had a baby, we would like to know how you are feeling. Please check the answer that comes closest to how you have felt **IN THE PAST 7 DAYS**, not just how you feel today.

Here is an example, already completed.

I have felt happy:
- ☐ Yes, all the time
- ☒ Yes, most of the time — This would mean: "I have felt happy most of the time" during the past week.
- ☐ No, not very often — Please complete the other questions in the same way.
- ☐ No, not at all

In the past 7 days:

1. I have been able to laugh and see the funny side of things
   - ☐ As much as I always could
   - ☐ Not quite so much now
   - ☐ Definitely not so much now
   - ☐ Not at all

2. I have looked forward with enjoyment to things
   - ☐ As much as I ever did
   - ☐ Rather less than I used to
   - ☐ Definitely less than I used to
   - ☐ Hardly at all

*3. I have blamed myself unnecessarily when things went wrong
   - ☐ Yes, most of the time
   - ☐ Yes, some of the time
   - ☐ Not very often
   - ☐ No, never

4. I have been anxious or worried for no good reason
   - ☐ No, not at all
   - ☐ Hardly ever
   - ☐ Yes, sometimes
   - ☐ Yes, very often

*5 I have felt scared or panicky for no very good reason
   - ☐ Yes, quite a lot
   - ☐ Yes, sometimes
   - ☐ No, not much
   - ☐ No, not at all

*6. Things have been getting on top of me
   - ☐ Yes, most of the time I haven't been able to cope at all
   - ☐ Yes, sometimes I haven't been coping as well as usual
   - ☐ No, most of the time I have coped quite well
   - ☐ No, I have been coping as well as ever

*7 I have been so unhappy that I have had difficulty sleeping
   - ☐ Yes, most of the time
   - ☐ Yes, sometimes
   - ☐ Not very often
   - ☐ No, not at all

*8 I have felt sad or miserable
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Not very often
   - ☐ No, not at all

*9 I have been so unhappy that I have been crying
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Only occasionally
   - ☐ No, never

*10 The thought of harming myself has occurred to me
   - ☐ Yes, quite often
   - ☐ Sometimes
   - ☐ Hardly ever
   - ☐ Never

Administered/Reviewed by _____ Date _____

[1]Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786 .

[2]Source: K. L. Wisner, B. L. Parry, C. M. Piontek, Postpartum Depression N Engl J Med vol. 347, No 3, July 18, 2002, 194-199

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Edinburgh Postnatal Depression Scale[1] (EPDS)

Postpartum depression is the most common complication of childbearing.[2] The 10-question Edinburgh Postnatal Depression Scale (EPDS) is a valuable and efficient way of identifying patients at risk for "perinatal" depression. The EPDS is easy to administer and has proven to be an effective screening tool.

Mothers who score above 13 are likely to be suffering from a depressive illness of varying severity. The EPDS score should not override clinical judgment. A careful clinical assessment should be carried out to confirm the diagnosis. The scale indicates how the mother has felt ***during the previous week***. In doubtful cases it may be useful to repeat the tool after 2 weeks. The scale will not detect mothers with anxiety neuroses, phobias or personality disorders.

Women with postpartum depression need not feel alone. They may find useful information on the web sites of the National Women's Health Information Center <www.4women.gov> and from groups such as Postpartum Support International <www.chss.iup.edu/postpartum> and Depression after Delivery <www.depressionafterdelivery.com>.

SCORING

QUESTIONS 1, 2, & 4 (without an *)
Are scored 0, 1, 2 or 3 with top box scored as 0 and the bottom box scored as 3.

QUESTIONS 3, 5-10 (marked with an *)
Are reverse scored, with the top box scored as a 3 and the bottom box scored as 0.

Maximum score: 30
Possible Depression: 10 or greater
Always look at item 10 (suicidal thoughts)

Instructions for using the Edinburgh Postnatal Depression Scale:

1. The mother is asked to check the response that comes closest to how she has been feeling in the previous 7 days.
2. All the items must be completed.
3. Care should be taken to avoid the possibility of the mother discussing her answers with others. (Answers come from the mother or pregnant woman.)
4. The mother should complete the scale herself, unless she has limited English or has difficulty with reading.

[1]Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786.

[2]Source: K. L. Wisner, B. L. Parry, C. M. Piontek, Postpartum Depression N Engl J Med vol. 347, No 3, July 18, 2002, 194-199

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Appendix F

Maternal Postnatal Attachment Scale

The following reference relates to this questionnaire:

Condon, J. & Corkindale, C. (1998). The assessment of parent-to-infant attachment: Development of a self-report questionnaire instrument. Journal of Reproductive and Infant Psychology, 16(1), 57-76. DOI: 10.1080/0264683980840455 8

MATERNAL POSTNATAL ATTACHMENT SCALE

These questions are about your thoughts and feelings about your baby. Please tick one box only in answer to each question.

PM1 When I am caring for the baby, I get feelings of annoyance or irritation:

- ☐ Very frequently
- ☐ Frequently
- ☐ Occasionally
- ☐ Very rarely
- ☐ Never

PM2 When I am caring for the baby I get feelings that the child is deliberately being difficult or trying to upset me:

- ☐ Very frequently
- ☐ Frequently
- ☐ Occasionally
- ☐ Very rarely
- ☐ Never

PM3 Over the last two weeks I would describe my feelings for the baby as:

- ☐ Dislike
- ☐ No strong feelings towards the baby
- ☐ Slight affection
- ☐ Moderate affection
- ☐ Intense affection

PM4 Regarding my overall level of interaction with the baby I:

- ☐ Feel very guilty that I am not more involved
- ☐ Feel moderately guilty that I am not more involved
- ☐ Feel slightly guilty that I am not more involved
- ☐ I don't have any guilty feelings regarding this

PM5 When I interact with the baby I feel:

- ☐ Very incompetent and lacking in confidence
- ☐ Moderately incompetent and lacking in confidence
- ☐ Moderately competent and confident
- ☐ Very competent and confident

PM6 When I am with the baby I feel tense and anxious:

- ☐ Very frequently
- ☐ Frequently
- ☐ Occasionally
- ☐ Almost never

PM7 When I am with the baby and other people are present, I feel proud of the baby:

- ☐ Very frequently
- ☐ Frequently
- ☐ Occasionally
- ☐ Almost never

PM8 I try to involve myself as much as I possibly can PLAYING with the baby:

- ☐ This is true
- ☐ This is untrue

PM9 When I have to leave the baby:

- ☐ I usually feel rather sad (or it's difficult to leave)
- ☐ I often feel rather sad (or it's difficult to leave)
- ☐ I have mixed feelings of both sadness and relief
- ☐ I often feel rather relieved (and it's easy to leave)
- ☐ I usually feel rather relieved (and it's easy to leave)

PM10 When I am with the baby:

- ☐ I always get a lot of enjoyment/satisfaction
- ☐ I frequently get a lot of enjoyment/satisfaction
- ☐ I occasionally get a lot of enjoyment/satisfaction
- ☐ I very rarely get a lot of enjoyment/satisfaction

PM11 When I am not with the baby, I find myself thinking about the baby:

- ☐ Almost all the time
- ☐ Very frequently
- ☐ Frequently
- ☐ Occasionally
- ☐ Not at all

PM16 Over the past three months, I have felt that I do not have enough time for myself or to pursue my own interests:

- ☐ Almost all the time
- ☐ Very frequently
- ☐ Occasionally
- ☐ Not at all

PM17 Taking care of this baby is a heavy burden of responsibility. I believe this is:

- ☐ Very much so
- ☐ Somewhat so
- ☐ Slightly so
- ☐ Not at all

PM18 I trust my own judgement in deciding what the baby needs:

- ☐ Almost never
- ☐ Occasionally
- ☐ Most of the time
- ☐ Almost all the time

PM19 Usually when I am with the baby:

- ☐ I am very impatient
- ☐ I am a bit impatient
- ☐ I am moderately patient
- ☐ I am extremely patient

Preliminary Factor Structure

Items in brackets( ) are reverse scored

Quality of attachment: 3 4 5 6 (7) (10) (14) 18 19

Absence of hostility: 1 2 15 16 17

Pleasure in interaction: all reversed (8 9 11 12 13)

To ensure equal weighting of all questions it is recommended that response options be recoded to represent a score of 1 (low attachment) to 5 (high attachment) for every question. For example:

Question PM4 would be scored as: 1; 2.3; 3.6; 5

Question 8 would be (reverse) scored as: 5; 1

Appendix G

Greenspan Social-Emotional Growth Chart

Questionnaire

Stanley I. Greenspan, M.D.

Child's name: _____ **Age in months:** _____

Sex: ☐ Male ☐ Female

Completed by: _____

Relationship to child: _____

Examiner's name: _____

Date of testing: _____

	Year	Month	Day
Date of Test			
Date of Birth			
Age			
Age in Months and Days	Years x 12 + Months		
Adjustment for Prematurity	Adjust Through 24 Months		
Corrected Age			

Directions

For each question, place a check mark in the column that best describes how often you observe the behavior. Make **only one** check mark for each question. Complete the questionnaire until you reach the stop point for your child's age. If your child has not displayed the behavior, please mark **Can't tell.**

	BEHAVIOR FREQUENCY					
	Can't tell	None of the time	Some of the time	Half of the time	Most of the time	All of the time
1. Does your child take a calm and enjoyable interest in most sounds?	☐	☐	☐	☐	☐	☐
2. Can you easily get your child's attention without having to be very dramatic?	☐	☐	☐	☐	☐	☐
3. Does your child take a calm and enjoyable interest in most sights, including colorful or bright things?	☐	☐	☐	☐	☐	☐
4. Can you easily get your child to look at things without them being very bright or colorful?	☐	☐	☐	☐	☐	☐
5. Does your child calmly enjoy touching or being touched by different things?	☐	☐	☐	☐	☐	☐
6. Can you easily get your child to respond to your touch without having to touch your child firmly to get his or her attention?	☐	☐	☐	☐	☐	☐
7. Does your child like it when you swing him or her around, dance with him or her in your arms, or quickly lift him or her up in the air?	☐	☐	☐	☐	☐	☐
8. Can you easily get your child's attention by approaching him or her, or moving him or her around slowly?	☐	☐	☐	☐	☐	☐
For Sensory Processing Score calculations, total the check marks for each column for Items 1–8.						

continued

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	BEHAVIOR FREQUENCY					
	Can't tell	None of the time	Some of the time	Half of the time	Most of the time	All of the time
9. Can you help your child calm down?	☐	☐	☐	☐	☐	☐
10. Does your child look at interesting sights, such as your face or a toy?	☐	☐	☐	☐	☐	☐
11. Does your child look at or turn toward interesting sounds?	☐	☐	☐	☐	☐	☐
Stop here if your child is 0–3 months old.			**Stage 1**			
12. Does your child seem happy or pleased when he or she sees a favorite person (e.g., look or smile, make sounds, or move arms in a way that expresses joy or delight)?	☐	☐	☐	☐	☐	☐
13. Does your child respond to people talking or playing with him or her by making sounds or faces (e.g., happy sounds or a curious or annoyed look)?	☐	☐	☐	☐	☐	☐
Stop here if your child is 4–5 months old.			**Stage 2**			
14. Does your child reach for or point at things, or make distinct sounds to show you what he or she wants (e.g., reach out to be picked up or point at a toy)?	☐	☐	☐	☐	☐	☐
15. Does your child exchange two or more smiles, other looks, sounds, or actions (e.g., reaching, giving, or taking) with a favorite person?	☐	☐	☐	☐	☐	☐
Stop here if your child is 6–9 months old.			**Stage 3**			
16. Does your child show you that he or she understands your actions or gestures by making an appropriate gesture in return (e.g., make a funny face back at you; look at something you point to; stop doing something when you shake your head and use a firm voice to say "No!"; or smile and do more of something when you nod with a big smile and say "Yes!")?	☐	☐	☐	☐	☐	☐
17. Does your child use many consecutive actions in a back-and-forth way to show you what he or she wants or to have fun with you (e.g., smile, reach out for a hug, and, when you hug, take your hat, put it on his or her head, and smile proudly OR take your hand, lead you to the refrigerator, tug on the handle, and, after you open it, point to something he or she likes, such as food, a bottle of juice, or milk)?	☐	☐	☐	☐	☐	☐
Stop here if your child is 10–14 months old.			**Stage 4a**			
18. Does your child copy or imitate many of your sounds, words, or actions while playing with you (e.g., if you make funny faces and sounds, does she or he copy them)?	☐	☐	☐	☐	☐	☐
19. Does your child search for something he or she wants by looking or getting you to look for it?	☐	☐	☐	☐	☐	☐
20. Does your child show you what he or she wants or needs by using a few actions in a row (e.g., lead you by the hand to open a door and then touch or bang on the door)?	☐	☐	☐	☐	☐	☐
21. Does your child use words or try to use words when people talk with or play with him or her?	☐	☐	☐	☐	☐	☐
Stop here if your child is 15–18 months old.			**Stage 4b**			

GREENSPAN SOCIAL-EMOTIONAL GROWTH CHART

FOR EXAMINER USE ONLY

	BEHAVIOR FREQUENCY					
	Can't tell	None of the time	Some of the time	Half of the time	Most of the time	All of the time
Total check marks for each column (Items 1–35):						
Multiply	x 0	x 1	x 2	x 3	x 4	x 5
Sum						

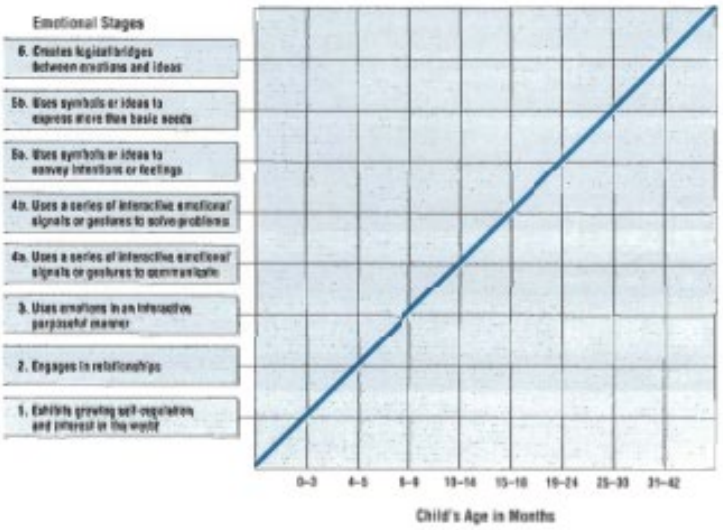
Total Growth Chart Score ☐

	BEHAVIOR FREQUENCY					
	Can't tell	None of the time	Some of the time	Half of the time	Most of the time	All of the time
Total check marks for each column (Items 1–8):						
Multiply	x 0	x 1	x 2	x 3	x 4	x 5
Sum						

Sensory Processing Score ☐

Score Summary	Possible Challenges	Emerging Mastery	Full Mastery	Highest Stage Mastered (Scores of **Most** or **All of the time**):
Total Growth Chart Score: _____	☐	☐	☐	_____
Sensory Processing Score: _____	☐	☐	☐	

Social-Emotional Growth Chart



	BEHAVIOR FREQUENCY					
	Can't tell	None of the time	Some of the time	Half of the time	Most of the time	All of the time
22. Does your child copy or imitate familiar make-believe play (e.g., feed or hug a doll)?						
23. Does your child tell you what he or she wants with one or a few words (e.g., "Juice," "Open," or "Kiss")?						
24. Does your child show you he or she understands your simple verbal wish (e.g., "Please show me your toy.")?						
Stop here if your child is 19–24 months old.	**Stage 5a**					
25. Does your child play make-believe (e.g., feed a doll, play house, or pretend to be a TV or movie character) with you or others?						
26. Does your child use words or pictures to tell you what he or she is interested in (e.g., "See truck!")?						
27. Does your child use words with one or more peers?						
28. Does your child use words or pictures to show what he or she likes or dislikes (e.g., "Want that" or "No want")?						
Stop here if your child is 25–30 months old.	**Stage 5b**					
29. Does your child play make-believe with one or more peers?						
30. Does your child play make-believe with you or others where the story makes sense (e.g., have the bears go visit grandmother and then have a big lunch)?						
31. Does your child use phrases or sentences with you to ask a question about something he or she wants to do (e.g., "Mommy go out?" "What you doing outside?" "Play?")?						
32. Can your child explain why he or she wants something or wants to do something (e.g., "Why do you want the juice?" "Because I'm thirsty.")?						
33. Does your child describe his or her feelings to explain why he or she is doing something or wants something (e.g., "Because I'm happy/sad/excited.")?						
34. Does your child play make-believe with peers as well as adults where the story makes sense and has many parts to it (e.g., the children go to school, do work, have lunch, and meet an elephant on the way home)?						
35. Does your child have conversations with adults and peers that make sense, with four or more back-and-forth exchanges about a variety of topics (e.g., feelings, foods, bedtimes, friends, or school)?						
Stop here if your child is 31–42 months old.	**Stage 6**					
Total check marks in each column (Items 1–35)						

Appendix H

Child Behaviour Checklist

Please print. **CHILD BEHAVIOR CHECKLIST FOR AGES 1½-5**

For office use only ID #

CHILD'S FULL NAME First Middle Last

CHILD'S GENDER ☐ Boy ☐ Girl | CHILD'S AGE | CHILD'S ETHNIC GROUP OR RACE

TODAY'S DATE Mo.____ Day____ Year____ | CHILD'S BIRTHDATE Mo.____ Day____ Year____

Please fill out this form to reflect your view of the child's behavior even if other people might not agree. Feel free to write additional comments beside each item and in the space provided on page 2. **Be sure to answer all items.**

PARENTS' USUAL TYPE OF WORK, even if not working now. Please be specific — for example, auto mechanic, high school teacher, homemaker, laborer, lathe operator, shoe salesman, army sergeant.

PARENT 1 (or MOTHER) TYPE OF WORK _____

PARENT 2 (or FATHER) TYPE OF WORK _____

THIS FORM FILLED OUT BY: (print your full name)

_____

Your relation to child: ☐ Parent 1 (or Mother) ☐ Parent 2 (or Father) ☐ Other (specify):

Below is a list of items that describe children. For each item that describes the child **now or within the past 2 months**, please circle the **2** if the item is **very true or often true** of the child. Circle the **1** if the item is **somewhat or sometimes true** of the child. If the item is **not true** of the child, circle the **0**. Please answer all items as well as you can, even if some do not seem to apply to the child.

0 = Not True (as far as you know) 1 = Somewhat or Sometimes True 2 = Very True or Often True

0 1 2 1. Aches or pains (without medical cause; **do not** include stomach or headaches)
0 1 2 2. Acts too young for age
0 1 2 3. Afraid to try new things
0 1 2 4. Avoids looking others in the eye
0 1 2 5. Can't concentrate, can't pay attention for long
0 1 2 6. Can't sit still, restless, or hyperactive
0 1 2 7. Can't stand having things out of place
0 1 2 8. Can't stand waiting; wants everything now
0 1 2 9. Chews on things that aren't edible
0 1 2 10. Clings to adults or too dependent
0 1 2 11. Constantly seeks help
0 1 2 12. Constipated, doesn't move bowels (when not sick)
0 1 2 13. Cries a lot
0 1 2 14. Cruel to animals
0 1 2 15. Defiant
0 1 2 16. Demands must be met immediately
0 1 2 17. Destroys his/her own things
0 1 2 18. Destroys things belonging to his/her family or other children
0 1 2 19. Diarrhea or loose bowels (when not sick)
0 1 2 20. Disobedient
0 1 2 21. Disturbed by any change in routine
0 1 2 22. Doesn't want to sleep alone
0 1 2 23. Doesn't answer when people talk to him/her
0 1 2 24. Doesn't eat well (describe): _____
0 1 2 25. Doesn't get along with other children
0 1 2 26. Doesn't know how to have fun; acts like a little adult
0 1 2 27. Doesn't seem to feel guilty after misbehaving
0 1 2 28. Doesn't want to go out of home
0 1 2 29. Easily frustrated
0 1 2 30. Easily jealous
0 1 2 31. Eats or drinks things that are not food—**don't** include sweets (describe): _____
0 1 2 32. Fears certain animals, situations, or places (describe): _____
0 1 2 33. Feelings are easily hurt
0 1 2 34. Gets hurt a lot, accident-prone
0 1 2 35. Gets in many fights
0 1 2 36. Gets into everything
0 1 2 37. Gets too upset when separated from parents
0 1 2 38. Has trouble getting to sleep
0 1 2 39. Headaches (without medical cause)
0 1 2 40. Hits others
0 1 2 41. Holds his/her breath
0 1 2 42. Hurts animals or people without meaning to
0 1 2 43. Looks unhappy without good reason
0 1 2 44. Angry moods
0 1 2 45. Nausea, feels sick (without medical cause)
0 1 2 46. Nervous movements or twitching (describe): _____
0 1 2 47. Nervous, highstrung, or tense
0 1 2 48. Nightmares
0 1 2 49. Overeating
0 1 2 50. Overtired
0 1 2 51. Shows panic for no good reason
0 1 2 52. Painful bowel movements (without medical cause)
0 1 2 53. Physically attacks people
0 1 2 54. Picks nose, skin, or other parts of body (describe): _____

Be sure you answered all items. Then see other side.

7-10-14 Edition-601

Please print your answers. Be sure to answer all items.

0 = Not True (as far as you know) 1 = Somewhat or Sometimes True 2 = Very True or Often True

0 1 2 55. Plays with own sex parts too much
0 1 2 56. Poorly coordinated or clumsy
0 1 2 57. Problems with eyes (without medical cause) (describe): _____
0 1 2 58. Punishment doesn't change his/her behavior
0 1 2 59. Quickly shifts from one activity to another
0 1 2 60. Rashes or other skin problems (without medical cause)
0 1 2 61. Refuses to eat
0 1 2 62. Refuses to play active games
0 1 2 63. Repeatedly rocks head or body
0 1 2 64. Resists going to bed at night
0 1 2 65. Resists toilet training (describe): _____
0 1 2 66. Screams a lot
0 1 2 67. Seems unresponsive to affection
0 1 2 68. Self-conscious or easily embarrassed
0 1 2 69. Selfish or won't share
0 1 2 70. Shows little affection toward people
0 1 2 71. Shows little interest in things around him/her
0 1 2 72. Shows too little fear of getting hurt
0 1 2 73. Too shy or timid
0 1 2 74. Sleeps less than most kids during day and/or night (describe): _____
0 1 2 75. Smears or plays with bowel movements
0 1 2 76. Speech problem (describe): _____
0 1 2 77. Stares into space or seems preoccupied
0 1 2 78. Stomachaches or cramps (without medical cause)
0 1 2 79. Rapid shifts between sadness and excitement
0 1 2 80. Strange behavior (describe): _____
0 1 2 81. Stubborn, sullen, or irritable
0 1 2 82. Sudden changes in mood or feelings
0 1 2 83. Sulks a lot
0 1 2 84. Talks or cries out in sleep
0 1 2 85. Temper tantrums or hot temper
0 1 2 86. Too concerned with neatness or cleanliness
0 1 2 87. Too fearful or anxious
0 1 2 88. Uncooperative
0 1 2 89. Underactive, slow moving, or lacks energy
0 1 2 90. Unhappy, sad, or depressed
0 1 2 91. Unusually loud
0 1 2 92. Upset by new people or situations (describe): _____
0 1 2 93. Vomiting, throwing up (without medical cause)
0 1 2 94. Wakes up often at night
0 1 2 95. Wanders away
0 1 2 96. Wants a lot of attention
0 1 2 97. Whining
0 1 2 98. Withdrawn, doesn't get involved with others
0 1 2 99. Worries
0 1 2 100. Please write in any problems the child has that were not listed above.
0 1 2 _____
0 1 2 _____
0 1 2 _____

Please be sure you have answered all items. Underline any you are concerned about.

Does the child have any illness or disability (either physical or mental)? ☐ **No** ☐ **Yes—Please describe:**

What concerns you most about the child?

Please describe the best things about the child:

LANGUAGE DEVELOPMENT SURVEY FOR AGES 18-35 MONTHS

For office use only
ID #

The Language Development Survey assesses children's word combinations and vocabulary. By carefully completing the Language Development Survey, you can help us obtain an accurate picture of the child's developing language. ***Please print your answers. Be sure to answer all items.***

I. Was the child born earlier than the usual 9 months after conception?

☐ No ☐ Yes—how many weeks early? _____weeks early.

II. How much did the child weigh at birth? _____ pounds _____ounces; or _____ grams.

III. How many ear infections did the child have before age 24 months?

☐ 0-2 ☐ 3-5 ☐ 6-8 ☐ 9 or more

IV. Is any language beside English spoken in the child's home?

☐ No ☐ Yes—please list the languages: _____ _____
_____ _____

V. Has anyone in the child's family been slow in learning to talk?

☐ No ☐ Yes—please list their relationships to the child; for example, brother, father:
_____

VI. Are you worried about the child's language development?

☐ No ☐ Yes—why? _____

VII. Does the child spontaneously say words in any language? (not just imitates or understands words)?

☐ No ☐ Yes—if yes, please complete item VIII and page 4.

VIII. Does the child combine 2 or more words into phrases? For example: "more cookie," "car bye-bye."

☐ No ☐ Yes—please print 5 of the child's longest and best phrases or sentences.
For each phrase that is not in English, print the name of the language.

1. _____
2. _____
3. _____
4. _____
5. _____

Be sure you answered all items. Then see other side.

Please circle each word that the child says SPONTANEOUSLY (not just imitates or understands). If your child says non-English versions of words on the list, circle the English word and write the first letter of the language (e.g., S for Spanish). Please include words even if they are not pronounced clearly or are in "baby talk" (for example: "baba" for bottle).

FOODS
1. apple
2. banana
3. bread
4. butter
5. cake
6. candy
7. cereal
8. cheese
9. coffee
10. cookie
11. crackers
12. drink
13. egg
14. food
15. grapes
16. gum
17. hamburger
18. hotdog
19. ice cream
20. juice
21. meat
22. milk
23. orange
24. pizza
25. pretzel
26. raisins
27. soda
28. soup
29. spaghetti
30. tea
31. toast
32. water

TOYS
33. ball
34. balloon
35. blocks
36. book
37. crayons
38. doll
39. picture
40. present
41. slide
42. swing
43. teddy bear

OUTDOORS
44. flower
45. house
46. moon
47. rain
48. sidewalk
49. sky
50. snow
51. star
52. street
53. sun
54. tree

ANIMALS
55. bear
56. bee
57. bird
58. bug
59. bunny
60. cat
61. chicken
62. cow
63. dog
64. duck
65. elephant
66. fish
67. frog
68. horse
69. monkey
70. pig
71. puppy
72. snake
73. tiger
74. turkey
75. turtle

BODY PARTS
76. arm
77. belly button
78. bottom
79. chin
80. ear
81. elbow
82. eye
83. face
84. finger
85. foot
86. hair
87. hand
88. knee
89. leg
90. mouth
91. neck
92. nose
93. teeth
94. thumb
95. toe
96. tummy

VEHICLES
97. bike
98. boat
99. bus
100. car
101. motorcycle
102. plane
103. stroller
104. train
105. trolley
106. truck

ACTIONS
107. bath
108. breakfast
109. bring
110. catch
111. clap
112. close
113. come
114. cough
115. cut
116. dance
117. dinner
118. doodoo/poop
119. down
120. eat
121. feed
122. finish
123. fix
124. get
125. give
126. go
127. have
128. help
129. hit
130. hug
131. jump
132. kick
133. kiss
134. knock
135. look
136. love
137. lunch
138. make
139. nap
140. open
141. outside
142. pattycake
143. peekaboo
144. peepee
145. push
146. read
147. ride
148. run
149. see
150. show
151. shut
152. sing
153. sit
154. sleep
155. stop
156. take
157. throw
158. tickle
159. up
160. walk
161. want
162. wash

HOUSEHOLD
163. bathtub
164. bed
165. blanket
166. bottle
167. bowl
168. chair
169. clock
170. crib
171. cup
172. door
173. floor
174. fork
175. glass
176. knife
177. light
178. mirror
179. pillow
180. plate
181. potty
182. radio
183. room
184. sink
185. soap
186. spoon
187. stairs
188. table
189. telephone
190. towel
191. trash
192. T.V.
193. window

PERSONAL
194. brush
195. comb
196. glasses
197. key
198. money
199. paper
200. pen
201. pencil
202. penny
203. pocketbook
204. tissue
205. tooth brush
206. umbrella
207. watch

PLACES
208. church
209. home
210. hospital
211. library
212. park
213. school
214. store
215. zoo

MODIFIERS
216. all gone
217. all right
218. bad
219. big
220. black
221. blue
222. broken
223. clean
224. cold
225. dark
226. dirty
227. dry
228. good
229. happy
230. heavy
231. hot
232. hungry
233. little
234. mine
235. more
236. nice
237. pretty
238. red
239. stinky
240. that
241. this
242. tired
243. wet
244. white
245. yellow
246. yucky

CLOTHES
247. belt
248. boots
249. coat
250. diaper
251. dress
252. gloves
253. hat
254. jacket
255. mittens
256. pajamas
257. pants
258. shirt
259. shoes
260. slippers
261. sneakers
262. socks
263. sweater

OTHER
264. any letter
265. away
266. booboo
267. byebye
268. excuse me
269. here
270. hi, hello
271. in
272. me
273. meow
274. my
275. myself
276. nightnight
277. no
278. off
279. on
280. out
281. please
282. Sesame St.
283. shut up
284. thank you
285. there
286. under
287. welcome
288. what
289. where
290. why
291. woofwoof
292. yes
293. you
294. yumyum
295. any number

PEOPLE
296. aunt
297. baby
298. boy
299. daddy
300. doctor
301. girl
302. grandma
303. grandpa
304. lady
305. man
306. mommy
307. own name
308. pet name
309. uncle
310. name of TV or story character

Other words your child says, including non-English words:

_____
_____
_____
_____

Appendix I

Ethical Approval

COISTE EITICE UM THAIGHDE CLINICIÚIL

Clinical Research Ethics Committee of the Cork Teaching Hospitals

Tel: +353-21-4901901
Email: crec@ucc.ie

University College Cork
Lancaster Hall
6 Little Hanover Street
Cork
Ireland

Our ref: ECM 4 (hh) 06/01/15 & ECM 3 (d) 05/05/2020

15th April 2020

Dr Mairead Kiely
Senior Lecturer
Room 127
Food Science Building
University College Cork

Re: The Cork Nutrition and Microbiome Maternal-Infant Cohort Study (COMBINE).

Dear Dr Kiely

The Chairman approved the following:

- Cover Letter dated 14th April 2020 (E.C.)
- Addition of Professor Eugene Dempsey, Consultant Neonatologist and Meadhbh Wilson, Trainee Clinical Psychologist
- CV's for Professor Dempsey and Ms Wilson.

Yours sincerely

Professor David Kerins
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

Appendix J

Response analysis results table

Characteristics	12-month Responders (total n =245)	12-month Non-responders (total n=246)	T (df) / X^2 (df)	P
Maternal				
Nationality (Irish)	79.18%	72.51%	2.77 (1)	.096
Partner (Married/ *de facto* relationship)	95.90%	94.26%	2.06 (1)	.310
Education (tertiary)	76.32%	83.33%	3.74 (1)	.053
Employed (two years post-delivery)	93.40%	87.20%	3.41 (2)	.181
Cigarettes (during pregnancy)	9.7%	15.91%	4.09 (1)	.043
Infant				
Sex (female)	44.48%	43.67%	.033 (1)	.856
Delivery mode (normal & planned cesarean section)	47.30%	52.45%	.862 (1)	.353
	Responder mean (sd)	**Non-responder mean (sd)**	**T (df) / X^2 (df)**	**P**
Maternal				
Age at delivery (years)	32.44 (3.84)	31.38 (4.75)	-2.70 (467.740)	.007
Infant				
Gestational age (weeks)	40.06 (1.38)	39.78 (2.03)	-1.79 (489)	.074
Birth weight (kilograms)	3.44 (575.535)	3.49 (504.800)	1.15 (489)	.250
Age stopped breastfeeding (weeks)	17.87 (22.69)	8.02 (15.72)	-5.44 (434.854)	.000

Appendix K

Supplementary exploratory data analysis 12-month outcomes

	Motor composite	Fine motor	Gross motor	Language composite	Receptive language	Expressive
EPDS at two months						
MPAS at two months						
Exclusive/predominant breastfeeding at two months						
Exclusive/predominant breastfeeding at six months						
Gender				t = **-3.13****	**t=-2.71****	
Gestational age	r =**.122***		r =**.155***			
Mother's age at delivery	r= **-.181****		r = **-.193****			
Maternal relationship status						
Maternal education level						
Maternal employment						
Smoking during pregnancy						
History of depression					**-2.03***	

	Supplementary exploratory data analysis of 24-month outcomes		
EPDS at two months			
MPAS at two months			
Exclusive/predominant breastfeeding at two months		t = **-2.056***	**t=-2.09***
Exclusive/predominant breastfeeding at six months			
Gender	**t = -1.973****		
Gestational age			
Mother's age at delivery			
Maternal relationship status			
Maternal education level			
Maternal employment			
Smoking during pregnancy			
History of depression			

Appendix L

Full Regression Model Summary Tables

Table A. Regression coefficients for predicting BSID social and emotional composite scores at 12 months

Variable	B	SE (B)	β	t	p
Constant	73.66	12.43		5.93	<.001
MPAS	0.35	0.15	0.18	2.33	.021

Model: $F(1,163) = 5.45$, $p = .021$ $R^2 = .032$

Table B. Hierarchical regression coefficients for predicting CBCL composite scores at 24 months

Variable	B	SE (B)	β	t	p
Step 1					
Constant	56.79	5.82		9.75	<.001
Age	-0.49	0.168	-.198	2.89	.004
Gender	2.31	1.30	.12	1.77	.08
Step 2					
Constant	71.28	12.36		5.77	<.001
Age	-0.48	0.17	-0.20	-2.89	.004
Gender	2.03	1.27	0.11	1.60	.11
EPDS	0.25	0.19	0.11	1.29	.20
MPAS	-0.19	0.11	-0.15	-1.72	.09

Model step 1: $F(2,202) = 5.81$, $p = .004$, $R^2 = .054$

Model step 2: $F(4,200) = 6.29$, $p < .001$, $R^2 = .112$

Table C. Regression coefficients for predicting BSID motor score at 12 months

Variable	B	SE (B)	β	t	p
Constant	76.38	21.86		3.49	<.001
Age	-0.57	0.18	-0.17	-3.16	.002
Gestational age	1.03	0.52	0.11	2	.046

Model: $F(2,319) = 7.49$, $p < .001$ $R^2 = .045$

Table D. Regression coefficients for predicting BSID motor scores at 24 months

Variable	B	SE (B)	β	t	p
Constant	101.45	2.06		49.17	<.001
Gender	2.69	1.36	0.12	1.97	.049

Model: $F(1,271) = 3.89$, $p = .049$, $R^2 = .014$

Table E. Regression coefficients for predicting BSID cognitive score at 24 months

Variable	B	SE (B)	β	t	p
Constant	102.55	1.05		97.72	<.001
Predominant breastfeeding	4.13	1.82	0.13	2.73	.024

Model: $F(1,283) = 5.17$, $p = .024$, $R^2 = .018$

Table F. Mediation regression coefficients for predicting CBCL score at 24 months

Variable	B	SE (B)	t	p
Model 1				
Constant	89.64	0.71	127.09	<.001
EPDS	-1.10	0.09	-11.81	<.001
Model 2				
Constant	54.67	10.03	5.45	<.001
EPDS	0.34	0.19	1.77	.08
MPAS	-0.15	0.11	-1.35	.18
Direct effect	0.34	0.19	1.77	.08
Indirect effect	0.16	0.12		>.05

Model 1 (Predictor: EPDS; Outcome: MPAS): $F(1,203) = 139.44$, $p < .001$, $R^2 = .41$

Model 2 (Predictors: EPDS, MPAS; Outcome: CBCL): $F(2, 202) = 6.75$, $p = .002$, $R^2 = .06$

Table G. Logistic regression coefficients for predicting predominant breastfeeding status at 6 months

Variable	B	SE (B)	Wald	p	Exp(B)
Constant	-.06	0.05	1.4	.24	.94
EPDS	.05	0.03	3.22	.07	1.06
MPAS	-5.43	2.73	3.95	.05	.004

Model: $X^2 (2) = 11.92$, $p = .003$, Nagelkerke $R^2 = .075$

Table H. Mediation logistic regression coefficients for predicting predominant breastfeeding status at 6 months

Variable	B	SE (B)	t/z	p
Model 1				
Constant	90.02	0.67	134.92	<.001
EPDS	-1.12	0.09	-12.92	<.001

Model 2				
Constant	-5.42	2.73	-1.99	.05
EPDS	-0.06	0.05	-1.18	.24
MPAS	0.05	0.03	1.79	.07
Direct effect	0.06	.05	-1.18	.24
Indirect effect	-.06	.04		<.05

Model 1 (Predictor: EPDS; Outcome: MPAS): $F(1,233) = 166.93$, $p < .001$, $R^2 = .42$

Model 2 (Predictors: EPDS, MPAS; Outcome: Breastfeeding status): Model least likelihood = 11.92, $p = .002$, Nagelkerke $R^2 = .07$

Appendix M

Participant Information Sheet

Combine
The Cork Nutrition & Microbiome Maternal-Infant Cohort Study

Participant Information Sheet

Study Title:	The Cork Nutrition and Microbiome Maternal-Infant Cohort Study [COMBINE]
Principal Investigator:	Prof Mairead Kiely
Sites of Investigation:	Cork University Maternity Hospital (CUMH) & University College Cork (UCC)

WHAT IS THE COMBINE STUDY?

While we know that the early months and years of life are very important for infant growth and healthy development, we still have many unanswered questions about optimising health outcomes through early feeding. The COMBINE study is an observational study following 1,200 babies, to investigate how nutrition and environment in the first two years of life affects the development of gut bacteria. Gut bacteria is associated with positive future health outcomes including optimal physical and mental development. This is the first time a study like this has been carried out.

AM I ELIGIBLE TO PARTICIPATE IN THIS STUDY?

As you are a participant in the IMPROvED pregnancy study, your baby is eligible to take part in the COMBINE study.

WHAT WILL THIS STUDY INVOLVE?

If you agree to participate in the study, we will meet you and your baby 9 times over the first 2 years of his/her life. Visits will take place at Cork University Maternity Hospital and Brookfield Health Sciences Complex in UCC. Your first visit will take place in the hospital after your baby is born. The remaining visits will take place at 1, 2, 4, 6, 9, 12, 18 and 24 months. You will be contacted a week in advance to arrange your next study visit. Your visit at 1 month is an optional visit, but we greatly appreciate your attendance at this visit. There are no foreseen risks associated with participation in the COMBINE study

You:

Firstly, we would like to access information about your pregnancy and birth outcome which was collected by the IMPROvED study. From Day 60, we would like to measure your height and weight as well as ask some questions about your lifestyle and the environment in which you live. You will be offered the opportunity to download the Michild mobile phone application. This application will capture daily information on feeding, sleeping and bowel patterns of your baby.

If you are breastfeeding, we would like to collect a breastmilk sample when your baby is 4 weeks old. We will give you instructions on how to collect this sample at home. At two months, you will be asked to complete an online survey about your general postnatal wellbeing. We will contact you should we have any concerns about your answers.

Ireland's European Structural and Investment Funds Programmes 2014-2020
Co-Funded by the Irish Government and the European Union
EUROPEAN UNION
Investing in your future
European Social Fund
Science Foundation Ireland
sfi For what's next
Infant
apc Microbiome Institute
V5: 08/12/2016

Your child:

Visits start at Day two when we will weigh and measure you baby. These measurements will be repeated at every visit. We will ask you questions about your baby's living environment, diet and general health. At your first 4 study visits, we will measure amount of fat and lean tissue in your baby's body using the PEA POD Infant Body Composition System.

We would like to collect samples from your baby throughout the study. We will begin by saving cord blood from the placenta in the birthing suite. The other samples we will collect are as follows:

Type	How?	How much?	When?
Stool	At Home by you	1 teaspoons	All visits
Saliva	At Study Visit by nurse	2 swabs	All visits from 2 months
Urine	At Home by you	2-3 teaspoons	At 2 & 18 months
Blood	At Study Visit by nurse	2 teaspoons	At 12 & 24 months

We will provide you with the appropriate instructions and materials to collect the samples at home. When taking your baby's blood sample, every care will be taken to minimise any discomfort to your baby. The sample will be taken by a highly trained and experienced paediatric nurse, who will use a local anaesthetic cream before taking the sample. All samples are only taken with your consent and verbal consent will be taken again on the day of the visit.

Throughout the study we will also have a number assessments with our research psychology team. These assessments begin at the 4 month study visit. The assessments carried out are:

- The Visual Habituation assessment measures of the infants' visual attention which is reflective of underlying mental processes, for example information processing skills.
- The Free Play Attention assessments also measure the infants' visual attention, however different measures of attention at different points in time reflect different underlying mental processes, for example attention span
- The Mc Arthur Bates Communication Development Inventories are questionnaires that look at the development of the Infants' communication skills; including comprehension, non- verbal gestures, vocabulary and grammar.
- The Bayleys Scales of Infant and Toddler Development is a standardised developmental assessment which looks at the Infants' thinking, language and movement skills.
- The Child Behaviour Checklist is a questionnaire used to looks at the Infants emotional, behavioural and social development

WHAT HAPPENS TO THE INFORMATION AND SAMPLES COLLECTED?

All information collected about you and your baby will be stored in a secure web based database. The information will be anonymised and any information that could identify you will *not be stored* on the database. Blood samples will be stored in the COMBINE biobank in Cork University Maternity Hospital. All other samples will be stored in COMBINE biobank at the APC Microbiome Institute, UCC. All specimens will be anonymous and no information that could identify you will be stored with these samples. Initially samples will be analysed by research staff based in both the INFANT centre and APC. We will publish results from the study in International medical journals. In the future, researchers and commercial companies may apply to the study to access and use the data and samples collected for related research projects.

VOLUNTARY PARTICIPATION

You have volunteered to participate in this study. You and your baby are free to withdraw from the COMBINE study at any stage. This will not affect the medical care of you or your baby and you can continue to be a part of the IMPROvED study during your pregnancy. If you decide to withdraw from the study, you can request to have your samples and any data associated with you and your baby removed from the study. Due to the complexity of ensuring participant confidentiality, it is not possible to return any specimens.

THE RESEARCH TEAM

The COMBINE study will be managed by the staff of the INFANT centre in Cork University Maternity Hospital. Analysis of samples will be conducted by the staff of the INFANT and APC centres

CONFIDENTIALITY

Your identity will remain confidential. Your name will not be published and will not be disclosed to anyone outside the COMBINE team. With your permission we will keep your family doctor up to date with any relevant health issues should they arise for you or your baby during the study.

STATEMENT OF APPROVAL

The COMBINE study has been granted ethical approval from the Cork University Hospitals Research Ethics Committee. We have the necessary insurances as required by law.

WHERE CAN I GET MORE INFORMATION?

The study will be fully explained to you and any questions answered before you decide if you want to take part. If you have any further questions regarding the COMBINE study, please contact the Principal Investigator:
Prof Mairead Kiely; Tel: (021) 4903394; Email: m.kiely@ucc.ie

***To express interest in registering for the study, please contact*:**

COMBINE Team: **Tel:** 087 1175018 **Email:** combine@ucc.ie

Ireland's European Structural and Investment Funds Programmes 2014-2020
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Science Foundation Ireland sfi For what's next
Infant
apc Microbiome Institute

VS: 08/12/2016

Appendix N

Consent form

Combine

The Cork Nutrition & Microbiome Maternal-Infant Cohort Study

PARTICIPANT CONSENT FORM

Mother's Name: _____

Mother's Date of Birth: _____/_____/_____

Participant ID for this study: _____

Chief Investigator: Professor Mairead Kiely

PLEASE TICK THE APPROPRIATE BOXES

1. I have read the Participant Information Sheet about this research project, and have been given a copy to keep. The information has been fully explained to me and I have been able to ask questions. I understand the purpose of the research. **YES** ☐ **NO** ☐
2. All experimental procedures have been identified and no guarantees have been given about the possible results. **YES** ☐ **NO** ☐
3. I am aware that participation is voluntary and I may withdraw consent at any time. I am aware that my decision not to participate or to withdraw at any stage will not restrict my access to health care services normally available to me. **YES** ☐ **NO** ☐
4. I have been assured that all information collected pertaining to me and by baby will be kept confidential. **YES** ☐ **NO** ☐
5. I understand that the investigators have insurances as required by law. **YES** ☐ **NO** ☐
6. I give permission for research personnel to access information collected in the IMPROvED study about my pregnancy and birth outcome. **YES** ☐ **NO** ☐
7. I consent to both mine and my baby's participation in the physical, lifestyle, nutritional and developmental assessments as outlined in the patient information sheet. **YES** ☐ **NO** ☐
8. I give permission to the COMBINE research team to contact me to complete an online survey about my own postnatal health. Based on my responses, I understand that the research team may contact me or need to refer me to my GP. **YES** ☐ **NO** ☐

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9. If I decide to breastfeed, I consent to provide a breastmilk sample to the research team. I understand that giving a sample for this research is voluntary and that I am free to withdraw my approval at any time without my medical treatment being affected. **YES ☐** **NO ☐**

10. On behalf of my baby, I agree to donate samples of his/her blood, DNA, stool, saliva & urine. I understand that giving a sample for this research is voluntary and that I am free to withdraw my approval at any time. **YES ☐** **NO ☐**

11. I give permission for the samples and information collected about me and my baby to be stored for possible future research **unrelated** to this study (including DNA studies), subject to approval by a Research Ethics Committee, **without my further consent** being required. **YES ☐** **NO ☐**

12. I agree that biological samples donated can be used now or in the future for commercial purposes. I understand that I will not benefit financially if this research leads to the development of new treatment of medical test. **YES ☐** **NO ☐**

13. I agree that the research team may contact my GP with any relevant health issues that may arise for me and / or my baby. **YES ☐** **NO ☐**

14. I agree that the study team can keep in contact with me about this study and approach me directly about follow-up and future studies. **YES ☐** **NO ☐**

I understand that if I have any questions concerning this research, I can contact Prof. Mairead Kiely. If I have further queries concerning my rights in connection with the research, I can contact the Clinical Research Ethics Committee of the Cork Teaching Hospitals, Lancaster Hall, 6 Little Hanover Street, Cork.

Signed: _____ **Date:** ____/____/____

Name of research participant parent/guardian

Signed: _____ **Date:** ____/____/____

Name of person taking consent

Appendix 0

Significant associations between predictor and outcome variables at 12- and 24-month follow-up

12 Month Analysis

	Motor composite	Language composite	Cognitive composite	BSID Social and emotional
EPDS at two months	r = .056	r =-.062	r =.057	r =-.138
MPAS at two months	r =-.029	r =.051	r =-.065	r = .180*
Predominant/ Exclusive Breastfeeding at two months	t =.462	t =-.791	t =1.244	t =-635
Predominant/ Exclusive Breastfeeding at six months	t =-.834	t =.435	t =-.356	t =-.043
Gender	t =.269	t =-3.13	t =-1.841	t =-.522
Gestational Age	r = .122*	r =-.042	r =.051	r =.041
Mother's age at delivery	r = -.181**	r =-.045	r=-.038	r =-.068
Mother's relationship Status	t= .533	t = 1.862	t =-.573	t= .485
Maternal education level	t =1.614	t =1.167	t= -.169	t =-.909
Maternal employment	t =.602	t =1.194	t =1.320	t =2.563
24 Month Analysis				

	Motor composite	Language composite	Cognitive composite	CBCL
EPDS at two months	r =-.003	r =.059	r = .013	r = .242**
MPAS at two months	r =.031	r =-.039	r =-.054	r = -.218
Predominant/ Exclusive Breastfeeding at two months	t = -1.814	t = -2.056*	t = -2.273*	t =1.236
Predominant/ Exclusive Breastfeeding at six months	t =.858	t = 1.817	t = 1.754	t =.859
Gender	t = -1.973**	t =-1.151	t = .157	t = -2.237*
Gestational Age	r = .070	r =.034	r = .027	r = .035
Mother's age at delivery	r = -.080	r = -.015	r = .049	r = -.216**
Mother's relationship Status	t = -.818	t = -.285	t =-.894	t =-.527
Maternal education level	t = 1.175	t = .238	t = 1.121	t = .723
Maternal employment	t = -643	t = -329	t = .178	t = -2.991