Parenting Stress and Depression in Asthmatic Mothers: Relationships to Infant Development

Helen Armstrong BPsych(Hons)

Submitted in partial fulfilment of the requirements for the degree of Master of Clinical Psychology

University of Newcastle

May 2017

Declarations

Statement of Originality

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to this copy of my thesis, when deposited in the University Library, being made available for loan and photocopying subject to the provision of the Copyright Act 1968.

Statement of Authorship

I hereby certify that the work embodied in this thesis contains a manuscript of which I am a joint author.

Signed:

Date: 17 October 2017

Name: Helen Armstrong

Signed:

Date: 25 October 2017

Supervisor: Dr Linda E. Campbell

Signed:

Date: 24 October 2017

Supervisor: Associate Professor Frini Karayanidis

Acknowledgements

Thank you to my supervisors Dr Linda Campbell and A/Prof. Frini Karayanidis for their continuing support and encouragement throughout this process. Additionally, thank you to the rest of the BLT-ID team, especially A/Prof Alison Lane, Olivia, Carly, Olivia S, Alix and Josh for their dedication in the running of this research project. I would also like to thank the mothers and babies who took part in this study; this would not have been possible without you.

I would also like to say thank you to my masters peers, for their support, camaraderie and true understanding over the past 2.5 years, and to my family and friends for your unconditional love and care.

Finalement, un grand merci à mon mari, Pierre, d'avoir été marrant, gentil et compassionnant quand j'en avais le plus besoin.

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Structured Abstract

Scope

Maternal psychological distress and asthma have been demonstrated as significant pathways through which infant development may be affected. Previous research has demonstrated that asthma in pregnancy is associated with significantly higher rates of prematurity, low infant birth weight, congenital malformations and pre-eclampsia (Murphy et al., 2011; 2013). Not only this, children of mothers with asthma may be more likely to live with Autism Spectrum Disorders (ASD) (Croen, Grether, Yoshida, Odouli, & Van de Water, 2005) and to develop asthma themselves (Murphy & Gibson, 2011). Likewise, maternal psychological distress in pregnancy and in the postnatal period has also been associated with the poorer cognitive and social-emotional development of infants (e.g. Bergman, Sarkar, O'Connor, Modi, & Glover, 2007; Wadhwa, 2005). This thesis will begin with a critical review of the asthma and maternal psychological distress literature, including how and why this relates to infant development. Following this, an original research article will be presented, a summary of which is outlined below.

Purpose

The longer-term effects of maternal asthma on infant development are not well known. This study aimed to elucidate the mental health status of asthmatic mothers. Additionally, the study aimed to better understand how mental health in asthmatic mothers is linked to infant cognitive, language, motor, social and emotional development in the first six months of life.

Methodology

Mother-infant dyads were recruited as part of the Breathing for Life: Infant Development Trial. Thirty-one asthmatic mothers and their infant were recruited at six weeks after birth, when parenting stress and postnatal depression were measured using the Parenting Stress Index (Short Form) and the Edinburgh Postnatal Depression Scale (Cox, Holden, & Sagovsky, 1987). At six months, mother-infant dyads were tested again, using the Bayley Scales of Infant Development-III and measured on their cognitive, language, motor, social and emotional development.

Results

A series of multiple linear regressions revealed that more symptoms of postnatal depression (PND) at six weeks postpartum significantly predicted poorer expressive language and adaptive behaviour skills of infants at 6 months. Additionally, higher levels of parenting stress at six weeks significantly predicted poorer social emotional skills at six months. One-sample t-tests also showed that asthmatic mothers also had significantly more symptoms of PND, but significantly lower levels of parenting stress, compared to norms.

Conclusions

These results shed interesting light on the particular mental health status of asthmatic mothers, and how this may impact on subsequent infant developmental prospects. They suggest that for asthmatic mothers, both parenting stress and postnatal depression may be contributing to poorer infant outcomes in the first six months of life across a range of domains; particularly, social-emotional, adaptive behaviour and expressive language development. These findings highlight the importance of early assessment and treatment of women at high risk of psychopathology, such as mothers with asthma, given the negative effects this may have on the development of their children. Future studies are encouraged to

further explore the mechanisms through which asthma and maternal psychological distress affect infant development.

Keywords: asthma, infant development, maternal depression, parenting stress

Critical Literature Review

The following literature review aims to explore and critically analyse the current research and understanding of maternal psychological distress and asthma, including how and why this can impact on infant development. Firstly, the review will define parenting stress and depression, and the negative child outcomes associated with these phenomena. Following this, the review will elucidate the experience of asthma in pregnancy and throughout the lifespan, including how this represents a chronic source of physical and psychological stress for mothers. This will also include a discussion of the mechanisms through which asthma affects foetal and infant development. The review will then conclude with an introduction to, and justification of the current study.

Parenting Stress

Becoming a parent is one of life's most impactful events and comes with many diverse costs and benefits. Men and women alike report significant increases in levels of both personal and marital stress (Miller & Sollie, 1980), and decreases in life happiness as a result of pregnancy and parenthood (Umberson & Gove, 1989). However, parents also report an elevated sense of meaning and satisfaction in life, compared to non-parents (Umberson & Gove, 1989). The relationship between parenthood and increased levels of psychological distress is more marked for mothers with younger children (Evenson & Simon, 2005), those who make an early transition to motherhood (Mirowsky & Ross, 2002) and for those with chronic physical illness (Lewis, Woods, Hough, & Southwick, 1989), such as asthma.

Defining parenting stress. Psychological stress has been described by Folkman, Lazarus, Dunkel-Schetter, DeLongis and Gruen (1986) as the relationship between a person's perceived resources and the demands placed upon them. In a parenting context,

Deater-Deckard (1998) describes stress as "...parents' perceptions of not having access to available resources for meeting the demands of parenthood... relative to the perceived demands of the parenting role" (p. 315). These resources may include emotional and physical support from others, knowledge about parenting, healthy beliefs about their child's behaviour and a sense of perceived competence (Mash & Johnson, 1990). 'Demands' may be conceptualised as any life event that elicits a stress response, such as physical illness, relationship conflict or financial difficulty. However, what constitutes a demand differs between individuals (Mulder et al., 2002). When a parent is no longer able to manage the resources-demands relationship, they may become physically or psychologically unwell.

Crnic, Gaze and Hoffman (2014) maintain that parenting stress is better defined as the cumulative result of daily life hassles and minor irritations associated with child rearing. They argue that this process can build to negatively affect a family. Using this definition of stress, they were able to demonstrate that cumulative parenting stress across the preschool period predicted poorer quality parent-child interactions when the child was five years old (Crnic et al., 2014). However, despite these differences in definition, most agree that stress differs between individuals and is dependent on a range of factors, such as temperament, genetics, social support, past experience and coping styles (Mulder et al., 2002).

Postnatal Depression

Around 16% of Australian women experience postnatal depression (Beyond Blue, 2016). Postnatal depression is defined as a depressive episode that begins in pregnancy or in the first four weeks following birth. Symptoms of postnatal depression are present for at least two weeks and must include anhedonia and/or pervasive low mood. Other symptoms may include feelings of guilt or worthlessness, changes in appetite and sleep, loss of energy, diminished ability to concentrate and recurrent thoughts of death (American Psychiatric

Association, 2013). An Australian study of 161 women found that the strongest predictor of postnatal depression was antenatal depression, suggesting that those with a history of depression are at highest risk of experiencing it in the postnatal period (Leigh & Milgrom, 2008).

Postnatal depression is thought of as a related, but distinct phenomenon from parenting stress. Whilst postnatal depression is classified as a pathological mental health issue, parenting stress is often regarded as a normal reaction to the demands of parenting, but nevertheless can range from the "normal" to "extreme" ends of the spectrum (Deater-Deckard, 1998). Parenting stress and anxiety are relatively common. A Melbourne-based study found that, from a sample of 1,431 Australian women, 15.7% reported that they had experienced intense anxiety or panic in the 3 months following birth (Woolhouse, Brown, Krastev, Perlen, & Gunn, 2009). Importantly, all variations of maternal psychological distress (including depression, parenting stress, anxiety or psychiatric diagnoses) are connected to poor infant development (Kingston, Tough, & Whitfield, 2012). For the purposes of this critical literature review, depression and parenting stress will be encompassed under the term 'psychological distress'.

Maternal Psychological Distress and Infant Development

Prenatal psychological distress. Psychological distress in mothers has been shown to have an enduring influence on infant development, even when children are in the foetal (or 'antenatal') stages of development. Bergman, Sarkar, O'Connor, Modi, and Glover (2007) conducted a longitudinal study on the effects of prenatal stress on infant cognitive ability amongst 123 mother-infant dyads. They found that levels of maternal stress and the presence of stressful life events in pregnancy were significantly and negatively correlated with infant cognitive ability at 14-19 months. With a large sample size of 7448 British women, O'Connor et al.

(2002) also found significant associations between anxiety in pregnancy and inattention/hyperactivity problems in boys and emotional/behavioural problems for both genders when they reached four years of age. Similar findings have been demonstrated elsewhere (Brouwers, van Baar, & Pop, 2001; Huizink, Robles De Medina, Mulder, Visser, & Buitelaar, 2002). Additionally, psychological distress in pregnancy is linked to prematurity and low infant birth weight (Dunkel Schetter & Tanner, 2012), characteristics associated with poorer social development and cognitive outcomes (Wadhwa, 2005). These findings point to pregnancy as a central point of influence in infant development.

The argument that foetal exposure to maternal stress significantly and negatively affects infant outcomes is strengthened by the findings that even after controlling for post-natal depression, anxiety and stressful life events, prenatal maternal stress is still significantly associated with poorer infant developmental outcomes (Bergman et al., 2007; O'Connor et al., 2002). However, as O'Donnell, O'Connor and Glover (2009) note, not all children are affected in the same way by maternal prenatal distress, suggesting that other genetic and environmental factors play an important role in the development of infants.

Postnatal psychological distress. This leads to the proposition that maternal psychological distress after birth may also be an important determinant of later infant development. For example, higher levels of parenting stress have been linked to delayed social capabilities in the preschool context (Gutermuth Anthony et al., 2005). A large cohort study of 1,507 Australian mothers demonstrated that maternal depressive symptoms were associated with significantly increased odds of their children experiencing emotional and/or behavioural issues (Woolhouse, Gartland, Mensah, Giallo, & Brown, 2016). Likewise, a Dutch study by van der Pol et al. (2016) demonstrated that greater symptoms of parental psychopathology in a sample of 241 two-parent families when infants were three years old

significantly predicted poorer infant social emotional development one year later. A detailed systematic review of 18 studies investigating the effects of both pre natal and postnatal psychological distress on several aspects of infant development concluded that infant social-emotional and cognitive domains were areas particularly adversely affected by postnatal maternal distress (Kingston et al., 2012). However, this systematic review did not include studies in languages other than English or studies from non-developed nations, reducing the generalizability of these results.

A meta-analysis by Connell and Goodman (2002) demonstrated that across studies, parental psychopathology, and particularly maternal depression, was significantly associated with internalising problems (such as depression and anxiety) in young children. Connell and Goodman (2002) were able to systematically analyse the results of 134 studies published since 1974, however they did not account for possible comorbidity in children and parents, perhaps making these results less realistic. A longitudinal study by Conroy et al. (2012) demonstrated that higher levels of maternal depression two months after birth were associated with higher levels of infant emotional dysregulation, poorer cognitive development and higher rates of internalising behaviour at 18 months. Similarly, a study of 130 American infants found that maternal depression when the infant was nine months old, alongside low levels of reported social support, was also associated with poorer cognitive function of infants at 16 months of age (McManus & Poehlmann, 2013).

Psychological Distress and Infant Development: Mechanisms of Effect

Prenatal explanations. There are several theories as to why maternal psychological distress negatively affects infant development. Physiological explanations emphasise the

possibility that maternal prenatal distress during pregnancy is experienced by the foetus and subsequently influences later development and maturation (Mulder et al., 2002). Stress and maternal mood disorders are linked to changes in the maternal hypothalamic pituitary adrenal (HPA) axis, and subsequent programming of the foetal HPA axis (Dunkel Schetter & Tanner, 2012). Activation of the HPA axis during times of psychological distress increases levels of the stress hormone cortisol in all people (McEwen, 1998), including pregnant women (Kane, Dunkel Schetter, Glynn, Hobel, & Sandman, 2014). Elevated maternal cortisol during pregnancy has been shown to significantly predict rates of spontaneous abortion, prematurity and low birth weight, and has been linked to poorer postnatal development (Buitelaar, Huisink, Mulder, de Medina, & Visser, 2003; Kramer et al., 2009). During times of psychological distress, maternal cortisol passes through the placenta, resulting in increased levels of foetal cortisol (Field & Diego, 2008). This, in turn, negatively affects foetal organ growth and development, and therefore foetal outcomes (Huizink et al., 2002).

Postnatal explanations. Postnatal explanations of poorer infant development highlight maladaptive parenting as the mechanism through which stress and depression affect infant outcomes. In accordance with this hypothesis, maladaptive parenting strategies have been associated with higher levels of maternal psychological distress. For example, Murray, Fiori-Cowley and Hooper (1996) found that when comparing control mothers (n=42) to depressed mothers (n=56), depressed mothers were significantly less sensitively attuned and provided fewer affirmations to their infants than control mothers. Crnic et al. (2014) were also able to demonstrate that parenting stress assessed longitudinally across the preschool period in a sample of 125 mother-child dyads was strongly and significantly associated with parent-infant conflict in naturalistic observations.

In turn, more negative parenting profiles have been associated with poorer infant development, including lower scores on scales of cognitive development (Murray et al., 1996) and higher levels of infant distress and disturbance (Cohn & Tronick, 1989). Conversely, children exposed to a parenting style that emphasises consistent, predictable rules whilst encouraging independence, display resilience and competence in multiple domains (Masten & Coatsworth, 1998).

Given that psychological disturbances often reflect issues with emotional regulation (Kring & Bachoroswki, 1999), it is perhaps unsurprising that parental psychopathology is associated with poorer social emotional skills in infants (Kingston et al., 2012; Murray et al., 1999). van der Pol et al., (2016) postulate that poorer social-emotional development predicted by maternal psychopathology could be a result of a type of 'emotional contagion', where children's internalising issues are modelled on that of their mothers'.

These findings assert that poor parenting mediates the relationship between parental psychological distress and poorer infant outcomes. However, Gutermuth Anthony et al. (2005) tested this hypothesis and found that poor parenting behaviours did *not* mediate the relationship between parenting stress and child behaviour (e.g. internalising and externalising behaviours, social competence) in preschool classrooms. Only parenting stress itself accounted for a significant amount of variance in infant behaviour (Gutermuth Anthony et al., 2005). However, given the correlational nature of this study, it is difficult to infer the direction of causality of this effect.

There is extensive literature investigating the effects of parental, and in particular maternal, distress on infant development. Both the prenatal and postnatal periods appear to represent an important window of influence on infant development. Whilst the mechanisms of these effects are largely not agreed upon or well-established, there is a consensus that…

"maternal psychological distress represents a prevalent, enduring, and modifiable influence that may significantly impact foetal and child development" (Kingston et al., 2012, p. 684). The following section of this literature review will clarify the role that maternal asthma plays as a significant source of stress in pregnancy and after childbirth, and how this affects infant development.

Asthma As a Source of Stress

Introduction to asthma in pregnancy. Asthma represents a significant source of stress for women during pregnancy, childbirth and child rearing. Up to 12% of Australian women display asthma symptoms while pregnant (Clifton et al., 2009), making asthma one of the most common medical conditions to affect women during pregnancy (Sawicki et al., 2011). An estimated 100-150 million people are currently affected by asthma (WHO, 2017). Asthma is a chronic inflammatory disease of the lungs that leads to airway obstruction characterised by periodic chest tightness, wheezing, shortness of breath and coughing (Rocklin, 2011). These symptomatic episodes can be precipitated by triggers such as irritants (e.g., allergens, cold, dry air or smoke) or physical exertion and are interspersed with symptom-free episodes (WHO, 2017).

The treatment of asthma may itself represent a significant source of stress to mothers. Asthma is usually treated using inhaled controller and reliever medications. Controller medications are commonly inhaled corticosteroids and reliever medications are synthetic analogues of adrenaline such as salbutamol. More severe asthmatics may have to use oral steroids such as prednisone to control their symptoms (Nelson-Piercy, 2001). Reliever medications are often associated with side- effects such as increased heart rate and anxiety because of their pharmacological similarity to adrenaline (Schatz et al., 1988).

Perinatal effects of asthma. Asthma affects pregnant women at several stages. In pregnancy, asthma can cause critical episodes (exacerbations or 'asthma attacks') and recurring symptoms for the mother (Schatz et al., 2003). Exacerbations of asthma most often occur between 25 and 32 weeks gestation (Schatz et al., 1988). Asthma in pregnancy also increases the likelihood of adverse perinatal outcomes (Bracken et al., 2003). A comprehensive meta-analysis of 134 studies concluded that pregnant women with asthma are at increased risk of experiencing pre-eclampsia, pre-term birth, low infant birth weight and the child being small for gestational age, compared to non-asthmatic females (Murphy et al., 2011). A more recent review reported that children born to asthmatic mothers are also at increased risk of congenital malformations, such as cleft lip, with or without cleft palate (Murphy et al., 2013).

Additional to these risks, pregnant women with asthma, especially those with poorly controlled asthma, are at risk of experiencing maternal hypoxia (low levels of oxygen in the blood). Hypoxia represents a major stressor for the foetus, as it affects their oxygenation and potential for growth (Murphy et al., 2011). In addition, as oxygen decreases, stress hormones in the mother increase and cross the placental barrier, which then impacts on the foetus. Negative perinatal outcomes following asthma in pregnancy (e.g., reduced foetal growth, prematurity) are thought to be a result of foetal hypoxia, amongst other causes (Murphy, Gibson, Smith, & Clifton, 2005). The more severe forms of asthma, as defined by objective analysis of lung function, seem to be directly associated with a higher incidence of adverse foetal outcomes (Murphy & Schatz, 2014). However, these outcomes may be associated with features of asthma other than hypoxia, such as the presence of chronic inflammation (Bowden, Barrett, Fallow, & Silman, 2001).

Mental Health and Asthma

Asthma and stress in pregnancy. Asthma represents a significant source of stress for the mother throughout pregnancy, both psychologically and physiologically. 'Pregnancy anxiety' is a term describing the concerns of mothers within the specific context of pregnancy; including upcoming labour and delivery, the baby's health and their own health (Dunkel Schetter & Tanner, 2012). There are strong associations between increased pregnancy anxiety and poor perinatal outcomes, such as low birth weight, prematurity and restricted infant development (Kane et al., 2014). Two qualitative studies (Anderson Beckmann, 2002; Lim, Stewart, Abramson, Ryan, & George, 2012) demonstrated that asthmatic women going through pregnancy display similar anxiety about the possible negative health implications of asthma, especially how this may affect their unborn child. Women in these studies were also anxious about the potential negative effects of using asthma medication whilst pregnant, and many ceased their medication without consulting their doctor (Lim et al., 2012). This is despite reviews suggesting that the decision not to use of preventative asthma medication in pregnancy should always be carefully weighed against risks of poorly controlled asthma whilst pregnant (Lim, Stewart, König, & George, 2011).

Asthma and stress throughout life. Asthma acts as a source of stress and ill-health not only during pregnancy and childbirth, but throughout the lifespan of the mother. In general, chronic diseases, such as asthma, are known to have harmful effects on the psychology of affected individuals (Verhaak, Heijmans, Peters, & Rijken, 2005). Asthma is principally associated with the psychiatric disorders of depression and anxiety (Kullowatz, Kanniess, Dahme, Magnussen, & Ritz, 2007). The prevalence rates of mood and anxiety disorders in asthmatic patients vary greatly between studies (e.g. Feldman et al., 2005; Lavoie et al., 2005). However, a large, population-based, cross-national study has

demonstrated that the odds of people with asthma suffering co-occurring depression and anxiety are significantly elevated compared to the general population (odds ratio of 1.7) (Scott et al., 2007). Compounding this, the presence of any psychiatric disorder is also associated with poorer asthma-related quality of life and disease control amongst patients (Lavoie et al., 2005).

Maternal asthma and developmental outcomes. Beyond the psychological implications for mothers with asthma (and the potential consequences of this for subsequent infant development), asthma has also been linked to several negative developmental outcomes for their children. Leonard, de Klerk, Bourke and Bower (2006) sought to better understand the corollaries of physical health issues during pregnancy. This Australian study found that mothers with asthma during pregnancy were at the highest risk of having children with intellectual disabilities. A case-control study by Croen, Grether, Yoshida, Odouli and Van de Water (2005) compared 420 children with a diagnosis of autism spectrum disorder (ASD) to 2100 controls, according to the presence of maternal asthma, autoimmune and allergic diseases over a 4-year period. Croen et al., (2005) found that mothers of children with autism were significantly more likely to have asthma. Additionally, children whose parents have asthma were also at an increased risk of developing asthma themselves (Murphy & Gibson, 2011). Interestingly, this predisposition is significantly heightened for maternal versus paternal asthma (Lim, Kobzik, & Dahl, 2010) and for children whose mothers experienced higher levels of anxiety in the prenatal period (Cookson, Granell, Joinson, Ben-Shlomo, & Henderson, 2009).

The adverse perinatal outcomes associated with maternal perinatal asthma, such as low birth weight and prematurity, are also associated with poorer developmental outcomes. Premature, low birth weight infants are at a significant risk of developmental delays and

neurologic abnormalities (Barrera, Rosenbaum, & Cunningham, 1987; Vohr et al., 2000). A systematic review and meta-analysis of 17 studies by Huang, Zhu, Qu and Mu (2016) also demonstrated that low infant birth weight and prematurity were both significant risk factors for intellectual disability (ID). However, Huang et al., (2016) recognise that several of these studies reviewed used different diagnostic criteria for ID. Schatz, Harden, Kagnoff, Zeiger and Chilingar (2001) also found that infants who were classified as low birth weight (less than 2,500g) demonstrated poorer psychomotor abilities at 15 month follow-up. So far, research has focused on the short term, perinatal outcomes of maternal asthma, but little information has been gathered on the longer-term effects of maternal asthma and stress on infant development.

To our knowledge, only one study has completed a follow-up investigation of the longer-term effects of maternal asthma on infant development (Schatz, Harden, Kagnoff, Zeiger, & Chilingar, 2001). This study found no significant difference between the mental and physical development of 379 infants of asthmatic and non-asthmatic mothers at 15 months of age. However, it is significant to note that asthmatic mothers had well controlled asthma and the study used a now out-dated second edition of the Bayley Developmental Scales (Bayley, 1993), which has been shown to produce significantly different results compared to the more recent Bayley-III (Anderson & Burnett, 2016).

Childhood asthma and developmental outcomes. The hereditary nature of asthma is an additional risk factor for poorer developmental outcomes, as a number of issues have been associated with childhood asthma. A meta-analysis of 26 studies by McQuaid, Kopel and Nassau (2001) found that children with asthma were significantly more likely to have difficulties with global adjustment (behavioural issues) and internalizing and externalizing problems compared to controls. Likewise, asthmatic children have been shown to have a

significantly increased risk of developing neurological problems (Arif, 2010), and have increased odds of developing emotional, developmental and behavioural issues (Blackman & Gurka, 2007). There is also some evidence to suggest that children with asthma show distinctive personality and temperament profiles in comparison to otherwise healthy children. Kim, Ferrara, and Chess (1980) demonstrated that asthmatic children displayed lower rhythmicity levels and poorer persistence and adaptability compared to controls. However, a more recent study by Lilljeqvist, Smørvik, and Faleide (2002) found no differences across these domains for asthmatic versus non-asthmatic children. The contradictory findings and the small number of participants in both of these studies means that these findings must be interpreted with caution.

Children with asthma have also been shown to demonstrate poorer cognitive function; demonstrating difficulties in shifting attention and self-regulation (Fryt, Pilecka, & Smolen, 2013). Blackman and Gurka (2007) reported that children with asthma also have an increased risk of a comorbid diagnosis of Attention Deficit Hyperactivity Disorder (ADHD). Conversely, Biederman, Milberger, Faraone, Guite, and Warburton (1994) compared 6-17 year old boys with and without ADHD and found no significant difference in risk of asthma between the groups, concluding that asthma and ADHD are unlikely to share an etiological relationship. However, cross-sectional studies such as these make it difficult to determine whether asthma predates other associated problems, or vice versa.

Conclusion

In conclusion, there is some evidence that both asthma and maternal psychological distress may have significant negative impact on infant development. Despite this, the combined effects of maternal psychological distress and asthma on infant development are not well studied or understood. There is still debate regarding the potential mechanisms and

directions of impact, be they through maladaptive parenting strategies or foetal programming in utero. However, what remains to be understood is how these effects interact to impact the development of infants of mothers with asthma.

Current study

This study forms part of the "Breathing For Life- Infant Development" (BLT-ID) trial, a larger investigation into asthma interventions during pregnancy conducted at the Hunter Medical Research Institute (HMRI). The project aims to investigate infant developmental outcomes as a function of levels of psychological distress amongst mothers with asthma. Infants and their parents will be tested at six weeks and six months. Before and during sessions, parents and children will undertake a number of questionnaires and tests. The Bayley Scales of Infant and Toddler Development-III (Bayley, 2006) will be used to assess infants' cognitive, emotional, adaptive, language and psychomotor skills. Similarly, the Parenting Stress Index-Short Form (PSI-SF) (Abidin, 1995) and the Edinburgh Postnatal Depression Scale (EDPS) (Cox et al., 1987) will be used to measure stress and depression, respectively, amongst asthmatic mothers.

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Manuscript Title Page

Parenting stress and depression in asthmatic mothers: relationships to infant development

Helen M Armstrong[a], Frini Karayanidis[a], & Linda E Campbell[a]

[a] School of Psychology, Faculty of Science, University of Newcastle, Australia

Corresponding Author:

Dr Linda Campbell

School of Psychology

University of Newcastle

10 Chittaway Rd, Ourimbah NSW 2258

Email: linda.e.campbell@newcastle.edu.au

Abstract

Background: Large, separate bodies of literature demonstrate that both maternal psychological distress and asthma represent significant pathways through which infant development may be adversely affected. However, the combined, longer term effects of these phenomena on infant development are not well understood.

Method: Mother-infant dyads were recruited as part of the Breathing for Life: Infant Development Trial. 31 asthmatic mothers and their infant were recruited at 6 weeks postpartum, when parenting stress and postnatal depression were measured using the Parenting Stress Index (Short Form) and the Edinburgh Postnatal Depression Scale. At six months, mother-infant dyads were tested again, using the Bayley Scales of Infant Development-III.

Results: Higher scores of maternal depression at six weeks postpartum predicted poorer expressive language and adaptive behaviour skills of infants at six months. Additionally, higher levels of parenting stress at 6 weeks predicted poorer social emotional skills at 6 months. Asthmatic mothers also had significantly higher levels of postnatal depression, but significantly lower levels of parenting stress, compared to norms.

Conclusion: These results help to describe the particular mental health status of asthmatic mothers, and how this is associated with infant developmental prospects. They suggest that both maternal stress and depression may be contributing to poorer infant outcomes across a range of domains; specifically, social-emotional, adaptive behaviour and expressive language development. Limitations and implications of these results are discussed. Future studies are encouraged to further explore the mechanisms through which asthma and maternal psychological distress affect infant development.

There is evidence that both maternal psychological distress and asthma represent significant pathways through which infant development may be adversely affected. For example, higher levels of parent psychological distress has been linked to poorer infant social-emotional and cognitive development (Murray et al., 1996; van der Pol et al., 2016) Similarly, asthmatic mothers are more likely to have children with intellectual disabilities and Autism Spectrum Disorders (Croen et al., 2005; Leonard et al., 2006). However, the combined effects of these phenomena on infant development are not well studied.

Asthma is a chronic, inflammatory lung disease that effects an estimated 100-150 million people worldwide (WHO, 2017). Symptoms of asthma include shortness of breath, coughing, chest tightness and wheezing (Rocklin, 2011). It is estimated that 12% of pregnant women suffer from asthma (Clifton et al., 2009). Asthma in pregnancy has been associated with higher rates of adverse perinatal outcomes, such as pre-eclampsia, congenital malformations, low infant birth weight, pre-term birth and the child being small for gestational age, when compared to non-asthmatic pregnancies (V. E. Murphy et al., 2011, 2013). More severe forms of asthma are also significantly associated with higher rates of adverse foetal outcomes, such as reduced foetal growth (V. E. Murphy & Schatz, 2014). Some have suggested that these effects may be due to maternal hypoxia, as this represents a major stressor for the foetus as it can affect oxygenation and potential for growth (Murphy et al., 2011).

Chronic diseases including asthma are linked with higher rates of mental health issues, especially depression and anxiety (Kullowatz et al., 2007). Throughout pregnancy, asthma also represents a source of anxiety, with many mothers reporting that they feel under-resourced and ill-informed about the potential impacts of asthma on their unborn child (Anderson Beckmann, 2002; Lim et al., 2012). In turn, this ‘pregnancy anxiety’ has been

linked to poorer perinatal and infant outcomes, such as prematurity, low birth weight and delayed development (Kane et al., 2014).

In addition to the negative perinatal outcomes connected with asthma in pregnancy, several studies have demonstrated that children of women with asthma also exhibit poorer developmental prospects later in life. An Australian study by Leonard et al. (2006) found that of all physical health issues present in pregnancy in a sample of 1101 mother-infant pairs, mothers with asthma were at the highest risk of having children with intellectual disabilities. A Californian study which compared children with Autism Spectrum Disorders (ASD) (n=420) to controls (n=2100) found that children with ASD were significantly more likely to have mothers with asthma (Croen et al., 2005). Additionally, adverse perinatal outcomes associated with asthma in pregnancy, such as low birth weight and prematurity, have been consistently and substantially linked to developmental delays and neurological abnormalities in children (Barrera et al., 1987; Vohr et al., 2000).

Children of mothers with asthma are also at an increased risk of developing asthma themselves (Murphy & Gibson, 2011). This genetic risk is significantly elevated for maternal compared to paternal asthma (Lim et al., 2010), and for children whose mothers experienced elevated levels of anxiety throughout their pregnancy (Cookson et al., 2009). The hereditary risk of asthma is worrying because a set of negative developmental outcomes has been associated with childhood asthma. For example, childhood asthma is a condition significantly linked with increased behavioural problems (McQuaid et al., 2001) and difficulties with shifting attention and self-regulation, compared to typically developing populations (Fryt et al., 2013). Thus, maternal asthma in pregnancy and throughout life represents a significant source of stress and a potential risk factor for infant development.

Maternal psychological distress in pregnancy and especially in the first years of life, also has the capacity to have a considerable impact on foetal and infant development (Kingston et al., 2012). Maternal psychological distress includes phenomena such as parenting stress and postnatal depression. "Parenting stress" has been defined as an unequal relationship between the perceived demands and resources associated with parenting (Deater-Deckard, 1998). However, this concept also relates to the cumulative, everyday stressors that accompany the experience of raising a child (Crnic et al., 2014). Maternal depression affects around 16% of women (Beyond Blue, 2016) and is defined as a depressive episode that occurs in the context of pregnancy or the postnatal period (American Psychiatric Association, 2013). Henceforth, both parenting stress and postnatal depression will be encompassed under the term "maternal psychological distress".

Maternal psychological distress can affect infant maturation both in the prenatal and postnatal stages of development. Prenatal maternal stress has been shown to significantly predict later cognitive ability in infancy (Bergman et al., 2007) and has been associated with inattention/hyperactivity and emotional problems at preschool age (O'Connor et al., 2002). Explanations of the effects of prenatal maternal psychological distress identify changes in the maternal hypothalamic pituitary axis (HPA axis) (Dunkel Schetter & Tanner, 2012), and elevated levels of cortisol during times of stress in pregnancy, as mechanisms through which infant development may be adversely impacted (Field & Diego, 2008; Kane et al., 2014). Exposure to elevated cortisol in utero has been shown to negatively affect foetal organ growth and development (Huizink et al., 2002).

However, maternal distress *after* birth has also been suggested as an important determinate of infant outcomes. A systematic review by Kingston et al. (2012) concluded that overall, social-emotional and cognitive domains were particularly negatively affected

by maternal psychological distress after birth. Postnatal explanations of these findings implicate poorer parenting associated with parental psychopathology in changes in infant development. For example, Murray, Fiori-Cowley and Hooper (1996) conducted a longitudinal study and found that depressed mothers were significantly less sensitively attuned and provided fewer affirmations to their infants than control mothers. These children then demonstrated significantly poorer scores on scales of cognitive development 16 months later (Murray et al., 1996). Conversely, children exposed to healthy parenting styles that emphasise consistent, predictable rules whilst encouraging independence, display resilience and competence in multiple domains (Masten & Coatsworth, 1998).

Therefore, both maternal distress and asthma have been demonstrated as significant pathways through which infant development may be affected. However, there is currently very little research investigating the combined effects of maternal psychopathology and asthma on infant development. The current study aimed to investigate infant developmental outcomes as a function of levels of psychological distress amongst mothers with asthma. Infants and their parents were tested at six weeks and six months. Before and during sessions, parents and children completed a number of questionnaires and tests. It was hypothesised that infants of asthmatic women with higher scores of postnatal depression and parenting stress would demonstrate poorer scores across a range of domains of infant development, including cognitive, motor, language, social-emotional and adaptive development.

Methodology

Study Design

This study was longitudinal in design. The primary outcome variables in this study were infant scores in the language, motor, cognitive, social-emotional and adaptive

behaviour domains of the Bayley Scales of Infant Development-III at six months of age. Parenting stress and maternal depression, as measured by the PSI-SF and the EDPS, respectively, were used as a predictor variable when infants were six weeks of age. Other possible confounding variables were also included as predictor variables at six weeks of age; family socio-economic status (SES), mother age, infant gender and infant prematurity-adjusted age.

Mother-infant dyads were recruited from the Breathing for Life Trial (BLT), a double-blind, randomised controlled trial investigating the effects of different asthma treatments during pregnancy at the Hunter Medical Research Institute (HMRI). Women were recruited through antenatal clinics at John Hunter Hospital, Newcastle. Women were included in the BLT based on whether they were between 12-22 weeks gestation (supported by ultrasound dating or obstetric assessment), were 18 years or older, had doctor-diagnosed asthma and had used asthma medication or experienced asthma symptoms in the past 12 months (Powell et al., 2011). Women were excluded if they could not commit to the asthma treatment protocol during pregnancy, had drug or alcohol dependence, had another chronic lung infection or disease which affected participation or had used oral corticosteroids for 14 consecutive days in the past three months. Eligible mothers were randomly assigned to either a control group or active intervention group before 22 weeks gestation. The current study drew data from mothers who were part of both the intervention and control groups.

Participants

Ninety-nine mother-infant dyads consented to participate at 6 weeks. Of these, 34 returned at six months to complete some part of the Bayley Scales of Infant Development-III. However, only 31 mother-infant dyads were able to complete either the PSI-SF or EDPS at six weeks *and* some part of the Bayley subscales at six months. Thirteen declined the subsequent appointment, 17 withdrew and 35 were lost to follow-up (see figure 1). Independent samples t-tests demonstrated that there were no significant differences in maternal age, socioeconomic status, gender, level of depression or parenting stress (all $p>.05$) between those mother-infant dyads who did and did not return at six months. Socio-demographic data can be seen in Table 1.

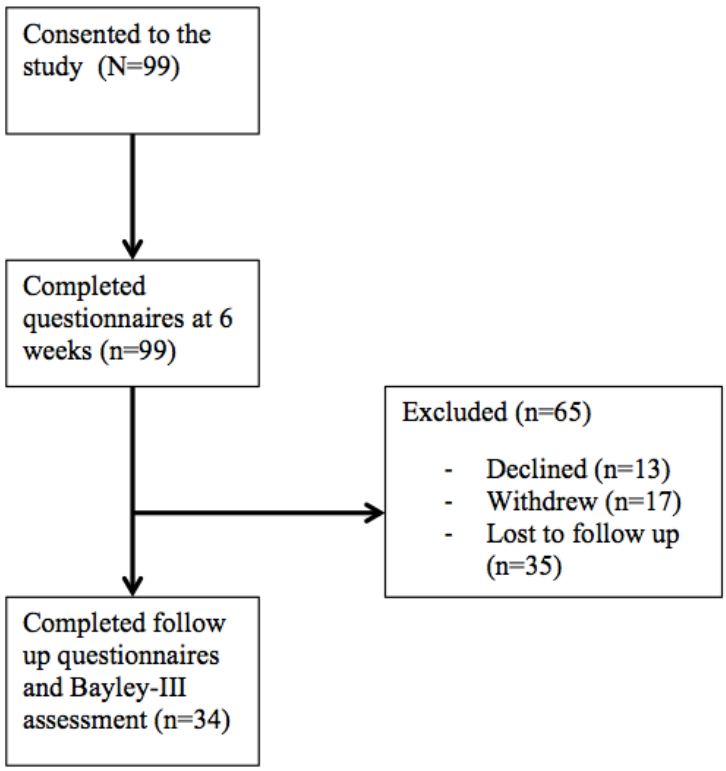

Figure 1. Study consort diagram

Table 1

Summary of Socio-Demographic Data

Socio-demographic Variable	Mean	Standard Deviation	Range
Infant prematurity-adjusted age (year fraction)	.53	0.04	0.38 - 0.65
Mother's age	32.52	13.67	20.22 – 44.02
Yearly Income (median)	$37,001-80,000		$0 - 180,000+
Infant gender:	Male: 52.5%		
	Female: 47.5%		
Marital status:	Married/defacto: 79%		
	Single (never married): 12%		
	Divorced/separated: 8%		
Mother's employment status	Unemployed/stay at home: 35%		
	Maternity leave: 51%		
	Casual: 4%		
	Part time: 4%		
	Full time: 6%		
	Student: 3%		
Mother's years of education	≤11 years (SC): 19%		
	12 years (SC +): 22%		
	13 years (HSC): 23%		
	14 years (HSC + diploma): 10%		
	16 years (Bachelor's degree): 16%		
	17 years Bachelor with honours: 3%		

	18+ years (Postgraduate): 3%
Number of siblings	Zero: 64%
	One: 11%
	Two: 20%
	Three: 6%
Ethnicity	Caucasian: 92%
	Other: 8%

SC, School Certificate; HSC, Higher School Certificate

Recruitment

After birth, participants were recruited for the Breathing for Life Trial: Infant Development (BLT-ID) study, a follow-up investigation of infant developmental outcomes following asthma in pregnancy. Mothers who presented for their infant's six-week medical follow-up also received an information package about the BLT-ID study (see Appendix D). If mothers displayed interest in the study, BLT-ID researchers then obtained their written consent after the nature of the study was fully described to them (see Appendix C). The BLT-ID study was approved by the Hunter New England Health and University of Newcastle Human Research Ethics Committees (see Appendices A and B).

Procedures

At the six-week infant appointment, mothers who had consented to participate were given a Parenting Stress Index-Short Form (PSI-SF), the Edinburgh Postnatal Depression Scale (EDPS) and a socio-demographic questionnaire to complete (see Appendix E). Following this, participants were contacted when their child was almost six-months of age to individually arrange appointments for the developmental assessment. Two weeks prior to

this appointment, the parent-report section of the Bayley-III was sent to mothers, with instructions to complete these prior to their scheduled testing session.

When the infant was six months old, face-to-face testing involved the administration of the Bayley Scales of Infant Development-III (screener) by a trained researcher, with both the infant and the mother present. Testing took approximately 45-60 minutes to complete and participants were reimbursed for their time. Following this, parents received a developmental report with information about the Bayley, an overview of their child's performance and recommendations to encourage future development (see Appendix F). If the trained researcher found any cause for concern regarding an infant's development, the mother was called and asked to return for a more comprehensive assessment with a paediatric occupational therapist.

Measures

Bayley Scales of Infant and Toddler Development (Third Edition) (screener). The Bayley-III (screener) was used to assess infant development at six months. The Bayley-III screener is a norm-referenced scale investigating infant development across five domains, including language, cognition, social-emotional, motor and adaptive behaviour (Bayley, 2006). The Bayley-III includes items investigating problem solving (e.g. finding toys, completing puzzles), developing play, response to language, manipulating objects and mobility (walking, using stairs). The Bayley-III screener is a shortened version of the full Bayley-III, adapted for infants under the age of 12 months. The screener gives raw scores across all of the above-mentioned domains, and comparing these to norms, then defines scores into the categories "at risk", "emergent" and "competent". These results can help to identify which infants are at risk of developmental delay.

Internal consistency for the Bayley-III has been shown to be good, with reliability coefficients ranging from .76 to .98 and subtest coefficients ranging from .86 to .91. Test-retest reliability across all ages was .80 or larger for each domain (Albers & Grieve, 2007). The Bayley-III language and cognitive subscales have relatively high correlations with the Wechsler Preschool and Primary Scale of Intelligence-Third Edition in the verbal, performance and full-scale scores (.72-.79). The Bayley-III motor ability subscale also shows moderate correlations (.49-.71) with the Peabody Developmental Motor Skills scale (Albers & Grieve, 2007). Cronbach's alpha across domains in this study ranged from .68 to .86.

Parenting Stress Index- Short Form. Maternal parenting stress was measured at six weeks using the Parenting Stress Index-Short Form (PSI-SF). The PSI-SF is a parent-reported, 36-item questionnaire investigating stress in the context of the parent-child relationship and identifies those families in need of follow-up (Abidin, 1995). The PSI-SF is a summarised version of the original 120-item PSI (Abidin, 1983) and consists of three main subscales; Difficult Child, Parent Distress and Parent-Child Dysfunctional Interaction, giving a Total Stress score. Each subscale is made up of 12 questions, such as "My child seems to cry or fuss more than most children". These are rated from one (*strongly disagree*) to three (*strongly agree*). Higher scores across these subscales indicate higher levels of parenting stress. Several studies have investigated the reliability and validity of the PSI-SF.

The PSI-SF has been demonstrated to be highly internally consistent in a population of parents with infants (Díaz-Herrero, Á., López-Pina, J. A., Pérez-López, J., de la Nuez, A. G. B., & Martínez-Fuentes, 2011). Similarly, Reitman, Currier, and Stickle (2002) demonstrated that Cronbach's alpha for subscales and for total stress ranged between .88 and

.94 in a low socio-demographic population. High test-retest reliability for the PSI-SF has also been demonstrated by Haskett, Ahern, Ward and Allaire (2006). Cronbach's alpha in the current study ranged from .57 to .88 across domains.

The construct validity of the three factor model of the PSI-SF has been confirmed several times (Abidin, 1995; Reitman et al., 2002) and externally validated in a variety of populations (Abidin, 1995; Lee, Gopalan, & Harrington, 2016) and languages (Barroso, Hungerford, Garcia, Graziano, & Bagner, 2015; Touchèque, Etienne, Stassart, & Catale, 2016). The PSI-SF has also been shown to have moderate to large positive correlations with similar constructs, such as maternal depression and child inattention/overactivity (Lee et al., 2016).

Edinburgh Postnatal Depression Scale. The Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987) is the most commonly used screening tool for post-partum depression (Eberhard-Gran, Eskild, Tambs, Opjordsmoen, & Samuelsen, 2001). The EPDS is a self-report questionnaire investigating mothers' mood and functioning over the past seven days, including questions such as "I have felt sad or miserable". Each of the 10 questions is rated between zero and three (*most of the time* to *not at all*), giving women a score ranging from 0-30. Women are considered to have 'probable depression' if their score is equal to or greater than 12 (Cox et al., 1987). A systematic review of studies using the EPDS demonstrated that sensitivity for distinguishing postnatal depression varied from 59 to 100% and specificity varied from 44 to 97% (Gibson, McKenzie-McHarg, Shakespeare, Price, & Gray, 2009). Despite resulting in both some false positives and false negatives, the EDPS is described "as a useful tool in the field of perinatal mental health." (Gibson et al., 2009, p. 331). Cronbach's alpha for the EPDS in this study was .69.

Results from the EDPS in the current study were compared to those of a large, representative sample of Australian women (Milgrom, Ericksen, Negri & Gemmill (2005). Milgrom et al., (2005) screened 4148 Australian mothers in Melbourne and eastern Victoria over three years at 4 months post partum using the EPDS. Average data from this normative sample was used as a comparison group for the current study.

Statistical Methods

Several multiple linear regressions were used to analyse the relationship between predictor variables and each outcome variable. One-sample t-tests were also used to compare mean participant responses on the PSI-SF and EDPS to that of norms. A *p*-value of less than 0.05 was considered significant. Statistical analyses were undertaken using IBM SPSS Statistics (version 23) software. All variables were tested for assumptions, including normality of distribution, collinearity and homoscedescacity.

Results

Descriptive Statistics

Means, ranges and standard deviations for socio-demographic data can be seen in Table 1. A summary of the averages, standard deviations and ranges for both predictor and outcome data used in the analyses can be seen in Table 2.

Table 2

Summary of Variable Data

Variable	Mean	Standard Deviation	Range
PSI-SF Total Stress at 6 weeks	63.52	15.51	38 – 108
EPDS Total at 6 weeks	8.08	3.48	3 – 19
Bayley Cognitive 6 months	10.46	2.56	3 – 15
Bayley Receptive Language 6 months	8.00	1.99	3 - 12
Bayley Expressive Language 6 months	6.80	1.77	3 - 10
Bayley Fine Motor 6 months	8.64	1.81	2 - 12
Bayley Gross Motor 6 months	8.81	2.16	4 – 13
Bayley Social Emotional 6 months	11.24	2.78	7 – 19
Bayley GAC 6 months	76.08	11.06	45 – 97

PSI-SF, Parenting Stress Index- Short Form (Abidin, 1983); EPDS, Edinburgh Postnatal Depression Scale (Cox et al., 1987); GAC, General Adaptive Composite.

Using the previously established cut-off of a total score of ≥ 12, 19.4% of women who completed the EDPS were classified as having "probable depression" (Cox et al., 1987), this is compared to 12.8% in a similar, representative sample of Australian women (Milgrom et al., 2005). In contrast, only one woman (1.8%) was classified as being in the "clinical range" according to the PSI-SF (Abidin, 1995). One sample t-tests were used to compare the current sample responses to normative data. Table 3 demonstrates that the current sample of mothers, in comparison to norms, had significantly more symptoms of postnatal depression, according to the EPDS, but significantly lower levels of parenting stress, according to the PSI-SF. Levels of postnatal depression and parenting stress at six weeks postpartum, as measured by the EPDS and PSI-SF respectively, were positively correlated with each other (r=.23), however this did not reach significance (p=.10). Correlations for all study variables can be seen in Table 4. Results from the Bayley-III (screener) suggested that 1% of infants were classified as "at risk" for their cognitive and receptive language skills, 0% were "at risk" for expressive language skills and 2% were "at risk" for gross and fine motor skills.

Table 3

Sample Data Compared to Normative Data for EPDS and PSI-SF

Scale	Sample data mean	Normative data mean	*t*-statistic
Edinburgh Postnatal Depression Scale	8.08 (3.48)	5.43 (4.59)	6.01***
Parenting Stress Index-Short Form			
Total	63.52 (15.51)	71.0 (15.4)	-3.61**
Defensive Responding	13.98 (4.23)	13.9 (5.2)	.14
Parental Distress	23.80 (6.37)	26.4 (7.2)	-3.05**
Parent-Child Dysfunctional Interaction	18.27 (5.79)	18.7 (4.8)	-.56
Difficult Child	21.45 (6.78)	26.0 (6.7)	-5.03***

Note. Numbers in parentheses are standard deviations
**significant at $p<.01$ level
*** significant at $p<.001$ level

Table 4

Correlation Matrix of all Variables

Variable	Correlations											
	1	2	3	4	5	6	7	8	9	10	11	12
1. PSI-SF Total Stress at 6 weeks												
2. EPDS at 6 weeks	.23											
3. Bayley Cognitive 6 months	-.09	-.28										
4. Bayley Receptive Language 6 months	-.09	-.25	.34**									
5. Bayley Expressive Language 6 months	-.04	-.40*	.43**	.52**								
6. Bayley Fine Motor 6 months	-.09	-.13	.69**	.49**	.46**							
7. Bayley Gross Motor 6 months	.19	-.22	.58**	.46**	.31*	.49**						
8. Bayley Social Emotional 6 months	-.61**	-.09	.03	.00	.15	-.12	-.16					
9. GAC 6 months	-.14	-.52*	.41*	.25	.37*	.24	.21	.39*				
10. Prematurity adjusted age	-.17	-.23	-.50**	.27*	.39**	-.58**	-.39**	-.05	.12			
11. Mother's age	.02	-.05	.12	.12	.21	.15	.27*	-.01	-.01	.45**		
12. Income (median)	-.06	-.51**	.14	.14	-.01	.12	.15	-.11	.26	.06	.15	
Gender: Female: 0 Male: 1	.07	-.02	-.03	-.08	.10	.00	-.11	-.12	-.02	-.04	-.06	-.03

PSI-SF, Parenting Stress Index- Short Form (Abidin, 1983); EPDS, Edinburgh Postnatal Depression Scale ; GAC, General Adaptive Composite.
*significant at $p<.05$ level; **significant at $p<.01$ level; *** significant at $p<.001$ level

Multiple Regression Analysis

A series of simultaneous linear regressions were undertaken in order to understand the relationship between maternal stress/depression of asthmatic mothers at six weeks and infant development at six months. Every regression included the predictor variables of postnatal depression and parenting stress scores, whilst controlling for the variables of; prematurity-adjusted infant age, mother age, gender and socio-economic status. These variables were then regressed on each subscale of the Bayley Scales of Infant Development. Full results from these regressions can be seen in Table 5.

Linear regression analyses found significant relationships between both maternal depression and stress at 6 weeks post birth and infant development at six months of age (see Table 5). More specifically, more symptoms of postnatal depression at six weeks significantly predicted poorer infant expressive language ability at six months (β=-.58, p=.01), explaining 26.01% of variance (see Figure 2), and poorer infant adaptive behaviour skills at 6 months (β=-.61, p=.04) (see Figure 3), explaining 27.77% of variance, after controlling for all other predictor variables. Similarly, higher levels of parenting stress at 6 weeks significantly predicted poorer social emotional skills at 6 months (β=-.58, p=.03), explaining 27.35% of variance in social emotional skills, controlling for all other predictors (see Figure 4).

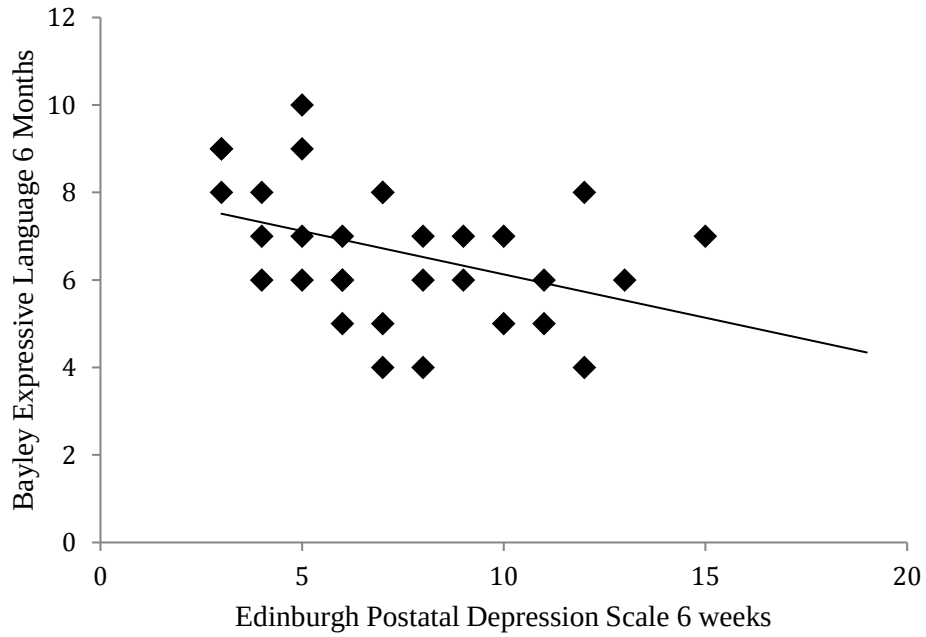

Figure 2. Relationship between maternal depression at six weeks and infant expressive language at six months

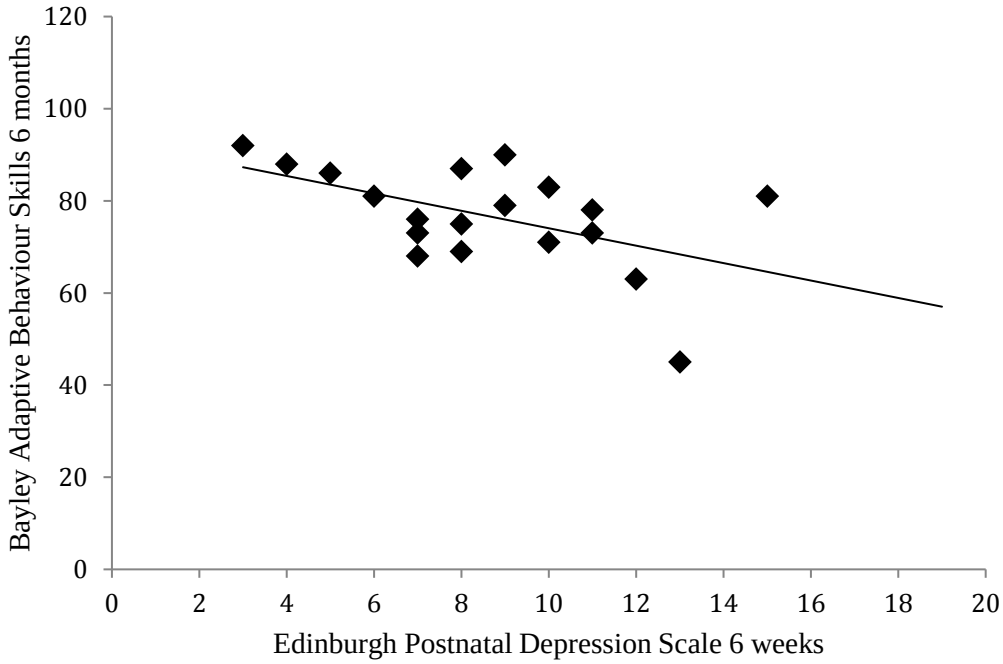

Figure 3. Relationship between maternal depression at six weeks and infant adaptive behaviour at six months

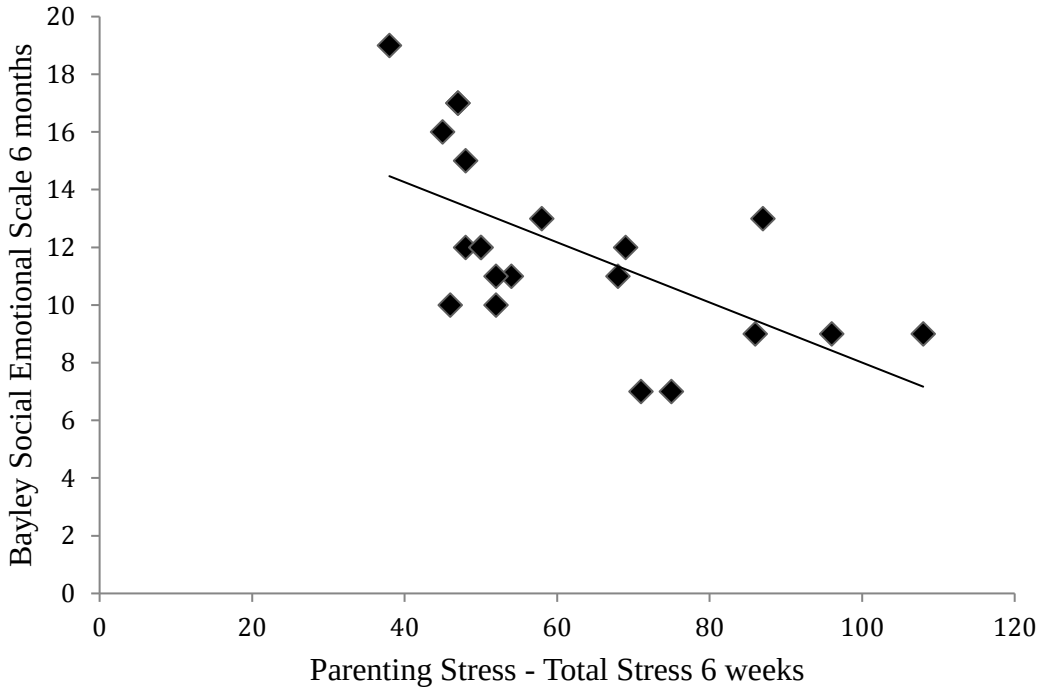

Figure 4. Relationship between parenting stress at six weeks and infant social emotional development at six months

Table 5

Summary of Multiple Linear Regression Analyses (N=31)

	Bayley Scales of Infant Development: Subscales																			
	Cognitive			Receptive Language			Expressive language			Fine Motor			Gross Motor			Social-Emotional			Adaptive Behaviour		
Predictor Variable	*B*	*SE*	*β*	*B*	*SE*	*β*	*B*	*SE*	*β*	*B*	*SE*	*β*	*B*	*SE*	*β*	*B*	*SE*	*β*	*B*	*SE*	*β*
EDPS at 6 weeks	-.33	.16	-.33	-.20	.11	-.34	-.31	.11	-.58*	-.04	.10	-.07	-.11	.13	-.21	.61	.39	.38	-1.72	.73	-.61*
PSI-SF 6 weeks	-.03	.03	-.20	-.01	.02	-.08	-.01	.02	-.06	-.01	.02	-.17	.01	.02	.09	-.14	.05	-.58*	-.14	.10	-.34
Adjusted infant age	3.37	14.37	.06	-5.20	9.86	-.12	-5.42	10.19	-.13	20.01	9.14	.54*	-7.94	11.68	-.19	-9.77	31.53	-.08	-70.14	59.43	-.33
Mother age	.07	.10	.15	-.13	.07	-.41	.05	.07	.17	-.03	.06	-.11	-.13	.08	-.11	.29	.21	.32	-.08	.40	-.05
Socio-Economic Status	-1.15	.63	-.38	-.63	.43	-.27	-1.01	.45	-.47*	-.45	.41	-.232	-.27	.52	-.13	-1.21	1.43	-.21	-5.83	2.67	-.57
Gender	-1.48	.91	-.33	-1.89	.62	-.55**	.07	.64	.02	.12	.60	.04	-1.39	.76	-.43	-3.18	2.18	-.34	-3.78	4.11	-.23
R^2		.37			.48			.36			.39			.19			.57			.20	
F		1.83			2.91			1.75			1.93			.71			2.18			1.65	

Regression is significant at *p<.05. **p<.01. EDPS, Edinburgh Postnatal Depression Scale. PSI-SF, Parenting Stress Index-Short Form

As expected, a number of covariates in the regression model also significantly predicted certain infant developmental outcomes (see Table 5). Older (prematurity-adjusted) infants scored significantly higher in fine motor skills (β= .54, p<.05) and infants living in lower socio-economic status families had significantly lower levels of expressive language skills (β=-.47, p<.05). Additionally, male infants displayed significantly poorer receptive language skills compared to females (β=-.55, p<.01).

Discussion

This study aimed to gain a better understanding of the particular mental health status of asthmatic mothers, especially in relation to depression and parenting stress, and how this may be linked to their children's development over the first six months of life. Levels of parenting stress and depression in asthmatic mothers were scored at 6 weeks postpartum, followed by an assessment of infant development at 6 months. Regression analyses were then used to determine whether parenting stress and/or depression significantly predicted various aspects of infant development at 6 months. Indeed, both maternal depression and parenting stress were shown to significantly predict poorer outcomes in certain domains of infant development; namely social-emotional, expressive language and adaptive behaviour skills.

Additionally, these mothers' scores on the EPDS and PSI-SF were compared to norms using one sample t-tests. This demonstrated that levels of postnatal depression at six weeks postpartum were significantly higher than that of a comparable, representative sample of Australian mothers at the same period postpartum (Ross, Evans, Sellers, & Romach, 2003). However, parenting stress was significantly lower at six weeks postpartum, across a range of domains (parental distress, difficult child and total stress) compared to normative data (Abidin, 1995).

The social emotional subscale of the Bayley-III is a parent-reported measure of a range of skills relating to interpersonal connectivity, emotional expression and related behaviours (Bayley, 2006). In the current study, higher levels of parenting stress in asthmatic mothers at six weeks were found to significantly predict poorer social-emotional development in their infants four and a half months later. Previous research has also demonstrated that parental psychopathology can negatively impact on the social emotional development of infants (e.g. Gutermuth Anthony et al., 2005; van der Pol et al., 2016). Given that women with asthma are at higher risk of experiencing psychopathology (Kullowatz et al., 2007; Verhaak et al., 2005), it is perhaps unsurprising that their children may be a higher risk of delayed social and emotional development. It is hypothesised that children learn social and emotional regulation through reciprocal interactions with their caregivers (Conroy et al., 2012). Goodman and Gotlib (2002) suggest that children of mothers with depression are exposed to more negative affect, behaviour and cognitions, and through social modelling and learning, they may exhibit poorer social-emotional development. This provides a compelling explanation of the poorer social emotional scores of infants seen in this study; that asthmatic mothers suffering higher levels of parenting stress have difficulty modelling positive behaviour and affect in reciprocal interactions, which then impacts their child's development.

It is interesting to note that while social-emotional development was significantly and negatively associated with higher levels of maternal parenting stress in this study, only one mother reached the PSI-SF cut-off for clinical levels of parenting stress. Indeed, overall, asthmatic mothers in this study had significantly *lower* levels of self-reported parenting stress compared to norms. This apparent contradiction may suggest that asthmatic mothers and their infants are more sensitive to the effects of parenting stress, so that even significantly lower levels of parenting stress can impact significantly and negatively on infant social-emotional

development. It may also suggest that stress associated with other aspects of their life, which was not picked up by the PSI-SF, such as their chronic asthmatic status, could be influencing their functioning and interactions with their children. Lower levels of parenting stress in this sample could also be a result of the fact that mothers in this study possessed advantages that may protect them against the presence of parenting stress. This may have included more regular medical follow up, increased social support and greater familiarity with medical practices needed for both themselves and their baby. Studies have demonstrated that regular medical follow up for mothers with depression is associated with significant improvements in mental health status (Weissman et al., 2006).

The expressive language subscale of the Bayley-III is a measure of the infant's ability to vocalise mood and communicate with others (Albers & Grieve, 2007; Bayley, 2006). In the current study, more symptoms of depression at six weeks postpartum significantly predicted poorer scores of infant expressive language skills at six months of age. Similar findings that link postnatal depression with poorer infant language ability have been reported elsewhere, even for those mothers with subclinical levels of depression (Paulson, Keefe, & Leiferman, 2008). The ability to contingently respond to their children is negatively affected in mothers suffering from postnatal depression (Murray et al., 1996). Additionally, the negative affect, lower levels of infant-directed speech and flattened vocal tone associated with postnatal depression have been hypothesised to lessen infants' motivation and likelihood to communicate with others (Sohr-Preston & Scaramella, 2006). Given that mothers in this study demonstrated significantly elevated levels of depressive symptoms, as measured by the EPDS, these elements of postnatal depression may have also been present in the mothers in this study, therefore negatively impacting on their infants' ability to effectively communicate.

The adaptive behaviour subscale of the Bayley-III is a parent-report questionnaire composed of items from the Adaptive Behaviour Assessment System (ABAS-II; Harrison & Oakland, 2003) and includes aspects such as infants' skills in health and safety, self-care and communication. As with expressive language abilities, higher levels of postnatal depression at six weeks also predicted poorer infant adaptive behaviour skills at six months. Previous research has suggested that depressed mothers are less likely to provide the external support and "scaffolding" required to help infants develop a sense of themselves, their relationships and encourage participation in extra-curricular activities and autonomous functioning (Goldsmith & Rogoff, 1995; Murray et al., 1996). This also provides an interesting account of the lower scores seen in this study; mothers with greater depressive symptoms are less likely to encourage independent functioning and foster the development of daily living skills, which resulted in lower scores of adaptive functioning.

The overall predictive relationship between maternal psychological distress at six weeks and poorer child development outcomes at six months may be explained by poorer infant-mother dyadic interactions. Crnic et al., (2014) found that higher levels of parenting stress were associated with lower levels of dyadic pleasure and increased conflict observed through naturalistic observations. Others have found that mothers with depression display less sensitive attunement and fewer positive affirmations to their children, in comparison to control mothers (Murray, Fiori-Cowley & Hooper, 1996). This, in turn, has been shown to be associated with poorer cognitive and social-emotional development (Murray et al., 1996; van der Pol et al., 2016). These explanations suggest that it may be the subsequent *interactions* between mother and child that mediated the relationship between maternal distress and infant development in this study.

However, given that asthma represents a significant source of stress both in pregnancy and throughout life (e.g. Lim et al., 2012; Murphy & Schatz, 2014), it is difficult to disregard the role that asthma and related physical and psychological stress could have played in determining infant social emotional, expressive language and adaptive behaviour development measured at six months of age. The negative effects of postnatal maternal stress/depression in combination with the stress a foetus may experience prenatally, could have had a combined, negative effect on their later development. However, given the nature of this study, and the fact that prenatal maternal psychological distress was not measured, it is difficult to fully understand this relationship.

Finally, the Bayley-III estimated that between 0-2% of infants in this study were classified as "at risk" for developmental delay. However, the Bayley-III may be underestimating this number. Other studies using large, representative samples have estimated the prevalence of developmental delay in children to be around 13-17% (Anderson & Burnett, 2016; Rosenberg, Zhang, & Robinson, 2008). A study by Anderson et al. (2010) also found that the Bayley-III estimated rates of developmental delay in a characteristic population to be between 1-4% across developmental domains. This has led some to claim that the Bayley-III significantly and consistently overestimates levels of development and therefore leads to the under-reporting of developmental delay in children (Anderson & Burnett, 2016). Therefore, the percentage rates of infants "at risk" for developmental delay in this study should be interpreted with caution.

Limitations

While this study provided some interesting insights into the mental health of asthmatic mothers and subsequent infant development, it is not without limitations. Given the scope of this study, we were limited by the relatively small sample size and poor retention rate of

participants. A larger sample size would have improved power to detect an effect and increased the sensitivity of the findings. Additionally, several key risk factors known to affect infant development were not collected, including infant birth weight and maternal asthma control and severity during pregnancy. Controlling for factors such as this may have strengthened the current findings.

Also, given that infant scores of social-emotional development and adaptive behaviour skills are both gathered through parent report, as are the PSI-SF and EDPS, it may be that mothers who perceive themselves to be more psychologically distressed also view their children's behaviour and development more negatively, thus introducing bias into these results. Additionally, it is not clear whether it is prenatal stress associated with asthma in pregnancy, or postnatal psychological distress that affects later infant development. In order to clarify this relationship, it would be interesting to measure levels of stress in asthmatic mothers during pregnancy, as well as postpartum, to tease this issue apart.

The lack of a comparison or control group (children of mothers without asthma) was also a limitation of this study, as this could have provided an interesting point of difference from which to compare our results. It is also difficult to confidently infer the direction of causality of these results. While it is possible that poorer mental health in asthmatic mothers at six weeks leads to poorer infant development at six months, it is also possible that this relationship is bidirectional. That is, delayed infant development may have represented a source of strain for mothers, thereby increasing their levels of self-reported psychological distress. Previous studies have reported that parental strain related to childhood developmental and emotional disorders have significant and adverse effect on parents', especially mothers', psychological functioning (Gross, Shaw, Moilanen, Dishion, & Wilson, 2008; Umberson, Pudrovska, & Reczek, 2010). Having said this, delayed infant development can be very

difficult for the layperson to discern, especially at 6 weeks of age. It could have been beneficial to include a longitudinal analysis of infant development over several time periods, as this could strengthen findings and clarify the direction of causality between maternal distress, asthma and infant development.

Finally, this study did not include a measure paternal stress or depression. Other studies have demonstrated that while infant development is significantly influenced by mother-infant interactions, fathers play an important role too (Connell & Goodman, 2002; Gross et al., 2008). Incorporating a measure of paternal distress may have created a more holistic understanding of how parental psychological distress in asthmatic families contribute to infant development.

Implications

These results shed interesting light on the particular mental health status of asthmatic mothers, and how this may impact on subsequent infant developmental prospects. They also strengthen the argument that both maternal stress and depression may be contributing to poorer infant outcomes across a range of domains; namely infant expressive language, adaptive behaviour and social-emotional skills. These findings are significant because they accentuate the importance of early assessment and treatment of women at high risk of psychopathology, such as mothers with asthma, given the negative effects this may have on the development of their children. Future studies could compare the developmental outcomes of children of mothers with asthma and children of mothers without asthma, in relation to maternal psychopathology, in order to determine whether these relationships are different between mothers with and without asthma.

While these findings must be interpreted with caution, they may impact on recommended care for mothers with asthma, and their children, both in pregnancy and after birth. Current best care practices for the management of asthma in pregnancy and after birth focus on the maintenance of healthy airways and the prevention of exacerbations (Murphy, 2015). The results of this study suggest that proactive assessment and monitoring of maternal psychopathology by family doctors, physicians and nurses is also important, in order to aid in the early identification and necessary support of mothers with asthma. Additionally, these results suggest that children of mothers with asthma could benefit from closer monitoring by general practitioners, paediatricians and nurses in order to recognise and treat children at risk of developmental delay as early as possible.

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Appendices

Appendix A: Notice of University of Newcastle Human Research Ethics Committee Approval

HUMAN RESEARCH ETHICS COMMITTEE

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

Notification of Expedited Approval

To Chief Investigator or Project Supervisor:	**Doctor Linda Campbell**
Cc Co-investigators / Research Students:	**Associate Professor Frini Karayanidis** **Miss Olivia Whalen** **Doctor Vanessa Murphy** **Miss Kelsey Philpott-Robinson** **Ms Helen Armstrong** **Miss Carly Mallise** **Associate Professor Alison Lane** **Miss Alix Woolard** **Mr Max Katz-Barber** **Miss Gabrielle Easey** **Doctor Titia Benders**
Re Protocol:	**Breathing for life trial: Infant Development**
Date:	**21-Aug-2015**
HREC Reference No:	**H-2015-0307**
External HREC Reference No:	**15/05/20/4.05**
Date of Initial Approval:	**21-Aug-2015**

Thank you for your **Initial Application** submission to the Human Research Ethics Committee (HREC) seeking approval in relation to the above protocol.

Your submission was considered under **Expedited Review of External Approval** review by the Chair/Deputy Chair.

I am pleased to advise that the decision on your submission is **External HREC Approval Noted** effective **21-Aug-2015**.

In approving this protocol, the Human Research Ethics Committee (HREC) is of the opinion that the project complies with the provisions contained in the *National Statement on Ethical Conduct in Human Research, 2007*, and the requirements within this University relating to human research.

As the approval of an External HREC has been "noted" the approval period is as determined by that HREC.

The full Committee will be asked to note this decision at its next scheduled meeting. A formal *Certificate of Approval* will be available upon request. Your approval number is **H-2015-0307**.

PLEASE NOTE:
As the HREC has "noted" the approval of an External HREC, progress reports and reports of adverse events are to be submitted to the External HREC only. In the case of Variations to the approved protocol, or a Renewal of approval, you will apply to the External HREC for approval in the first instance and then Register that approval with the University's HREC.

Linkage of ethics approval to a new Grant

HREC approvals cannot be assigned to a new grant or award (ie those that were not identified on the application for ethics approval) without confirmation of the approval from the Human Research Ethics Officer on behalf of the HREC.

Best wishes for a successful project.

Professor Allyson Holbrook
Chair, Human Research Ethics Committee

For communications and enquiries:
Human Research Ethics Administration

Research Services
Research Integrity Unit
The Chancellery
The University of Newcastle
Callaghan NSW 2308
T +61 2 492 17894
F +61 2 492 17164
Human-Ethics@newcastle.edu.au

RIMS website - https://RIMS.newcastle.edu.au/login.asp

Appendix B: Notice of Hunter New England Human Research Ethics Committee approval

25 May 2015

Dr Linda Campbell
School of Psychology
University of Newcastle

Dear Dr Campbell,

Re: Breathing for life trial: Infant Development - BLT-ID (15/05/20/4.05)

HNEHREC Reference No: 15/05/20/4.05
NSW HREC Reference No: HREC/15/HNE/164

Thank you for submitting the above application for single ethical review. This project was first considered by the Hunter New England Human Research Ethics Committee at its meeting held on **20 May 2015.** This Human Research Ethics Committee is constituted and operates in accordance with the National Health and Medical Research Council's *National Statement on Ethical Conduct in Human Research (2007)* (National Statement) and the *CPMP/ICH Note for Guidance on Good Clinical Practice*. Further, this Committee has been accredited by the NSW Department of Health as a lead HREC under the model for single ethical and scientific review. The Committee's Terms of Reference are available from the Hunter New England Local Health District website.

I am pleased to advise that following acceptance under delegated authority of the requested clarifications and revised Information Statement and Consent Form by Dr Nicole Gerrand Manager, Research Ethics & Governance, the Hunter New England Human Research Ethics Committee has granted ethical approval of the above project.

The following documentation has been reviewed and approved by the Hunter New England Human Research Ethics Committee:

- For the NEAF [Submission Code: AU/1/B19E16];
- For the Breathing for Life Trials – Infant Development Research Proposal;
- For the Parent Information Pamphlet (Version 2 dated 22 May 2015);
- For the Consent Form (Version 2 dated 22 May 2015);
- For the Consent Form for Videoing (Version 2 dated 22 May 2015);
- For the BLT 6 week Checklist;
- For the BLT 6 month Checklist;
- For the BLT 12 Month checklist;
- For the Bayley Scale of Infant Development (Bayley-III):
  - Bayley Caregiver Report;
  - Bayley Social-Emotional/Adaptive Behavioural Questionnaire;
  - Bayley Record Form;
- For the Test of Sensory Function in Infants (TFSI);
- For the Carey Temperament Scales (CTS):
  - Carey 6 weeks version;

Hunter New England Research Ethics & Governance Unit
Locked Bag 1
New Lambton NSW 2305
Telephone: (02) 49214950 Facsimile: (02) 49214818
Email: HNELHD-HREC@hnehealth.nsw.gov.au
http://www.hnehealth.nsw.gov.au/research_ethics_and_governance_unit

    - Carey 6 months version;
    - Carey 12 months version;
- For the Infant/Toddler Sensory:
    - Infant version;
    - Toddler version;
- For the Temperament Adjective Triad Assessment (TATA):
    - Methodology paper (Seifer et al. 2004);
- For the Parenting Stress Index (PSI-4) short-form;
- For the Edinburgh Postnatal Depression Screening;
- For the Macarthur Communication Development Inventory (CDI);
- For the Achenbach System of Empirically Based Assessment –Adult (ASEBA):
    - Adult self-report;
- For the First Year Inventory;
- For the Behaviour Rating Inventory of Executive Function – adult version (BRIEF):
    - Brief Self-report

For the study: **Breathing for life trial: Infant Development - BLT-ID**

Approval has been granted for this study to take place at the following site:

- **Hunter Medical Research Institute**

Approval from the Hunter New England Human Research Ethics Committee for the above protocol is given for a maximum of **5** years from the date of this letter, after which a renewal application will be required if the protocol has not been completed.

The *National Statement on Ethical Conduct in Human Research (2007),* which the Committee is obliged to adhere to, include the requirement that the committee monitors the research protocols it has approved. In order for the Committee to fulfil this function, it requires:

- A report of the progress of the above protocol be submitted at 12 monthly intervals. Your review date is **May 2016.** A proforma for the annual report will be sent two weeks prior to the due date.

- A final report must be submitted at the completion of the above protocol, that is, after data analysis has been completed and a final report compiled. A proforma for the final report will be sent two weeks prior to the due date.

- All variations or amendments to this protocol, including amendments to the Information Sheet and Consent Form, must be forwarded to and approved by the Hunter New England Human Research Ethics Committee prior to their implementation.

- The Principal Investigator will immediately report anything which might warrant review of ethical approval of the project in the specified format, including:

    - any serious or unexpected adverse events

        - Adverse events, however minor, must be recorded as observed by the Investigator or as volunteered by a participant in this protocol. Full details will be documented, whether or not the Investigator or his deputies considers the event to be related to the trial substance or procedure. These do not need to be reported to the Hunter New England Human Research Ethics Committee

Hunter New England Research Ethics & Governance Unit
Locked Bag 1
New Lambton NSW 2305
Telephone: (02) 49214950 Facsimile: (02) 49214818
Email: HNELHD-HREC@hnehealth.nsw.gov.au
http://www.hnehealth.nsw.gov.au/research_ethics_and_governance_unit

- Serious adverse events that occur during the study or within six months of completion of the trial at your site should be reported to the Manager, Research Ethics & Governance, of the Hunter New England Human Research Ethics Committee as soon as possible and at the latest within 72 hours.

- All other safety reporting should be in accordance with the NHMRC's Safety Monitoring Position Statement – May 2009 available at http://www.nhmrc.gov.au/health_ethics/hrecs/reference/_files/090609_nhmrc_position_statement.pdf

- Serious adverse events are defined as:

  - Causing death, life threatening or serious disability.
  - Cause or prolong hospitalisation.
  - Overdoses, cancers, congenital abnormalities whether judged to be caused by the investigational agent or new procedure or not.

- Unforeseen events that might affect continued ethical acceptability of the project.

- If for some reason the above protocol does not commence (for example it does not receive funding); is suspended or discontinued, please inform Dr Nicole Gerrand, as soon as possible.

You are reminded that this letter constitutes ethical approval only. You must not commence this research project at a site until separate authorisation from the Chief Executive or delegate of that site has been obtained.

A copy of this letter must be forwarded to all site investigators for submission to the relevant Research Governance Officer.

Should you have any concerns or questions about your research, please contact Dr Gerrand as per the details at the bottom of the page. The Hunter New England Human Research Ethics Committee wishes you every success in your research.

Please quote **15/05/20/4.05** in all correspondence.

The Hunter New England Human Research Ethics Committee wishes you every success in your research.

Yours faithfully

For: Ms M Hunter
Acting Chair
Hunter New England Human Research Ethics Committee

Hunter New England Research Ethics & Governance Unit
Locked Bag 1
New Lambton NSW 2305
Telephone: (02) 49214950 Facsimile: (02) 49214818
Email: HNELHD-HREC@hnehealth.nsw.gov.au
http://www.hnehealth.nsw.gov.au/research_ethics_and_governance_unit

Appendix C: BLT-ID consent form

Dr Linda Campbell
The University of Newcastle (UoN), Science Office (E1.19)
BLT_ID_Consent_Form
10 Chittaway Road, Ourimbah NSW 2258
T: +61 2 434 94490, F: +61 2 434 94404
E: linda.e.campbell@newcastle.edu.au

version 3, 3/06/2016

Parent/Guardian Consent Form

The Breathing for Life Trial - Infant Development

A follow-up study of infant and childhood development subsequent to maternal asthma intervention.

Investigators: Dr Linda Campbell, Dr Vanessa Murphy, A/Prof Alison Lane, Dr Titia Benders, A/Prof Frini Karayanidis.

I, ... [name of parent/guardian]

of .....[address],

Parent/Guardian of ..... [name of child]

have read and understand that the study will be conducted as described in the Information Statement, a copy of which I have retained.

- I have been made aware of the procedures involved in the study, including any known or expected inconvenience, risk, discomfort or potential side effect and of their implications.
- I understand that I can withdraw myself and/or my child at any time without providing a reason.
- I understand that my own and my child's personal information will remain confidential.
- I have had my questions answered to my satisfaction.
- I understand that information from the BLT and the BLT-follow-up study will be linked to the current study.

In signing this form, I agree to my own and my child's participation in this research study.

In addition (please circle as appropriate)

1. I consent for the information I provide, once de-identified:
   - to be used for future studies by this research team. **YES / NO**
   - to be shared with other researchers for related studies **YES / NO**
2. I consent to be contacted about follow-up studies, in the next five years **YES / NO**

NAME OF PARENT/GUARDIAN: _____

SIGNATURE: _____

DATE: _____

Declaration by person conducting the consent process

I, the undersigned, have fully explained this research to the patient named above.

NAME: _____

SIGNATURE: _____

Appendix D: BLT-ID Information flyer for parents

Information for Parents/Guardians

Breathing for Life Trial

The Breathing for Life Trial - Infant Development:

A follow-up study of infant and childhood development subsequent to maternal asthma intervention.

The Breathing for Life Trial would like to invite you and your baby to participate in our follow-up study on

Infant Development

Contact person: Dr Linda Campbell

Co-Investigators:

Associate Professor Alison Lane

Associate Professor Frini Karayanidis

Dr Vanessa Murphy

Dr Titia Benders

Prof Joerg Mattes

Prof Peter Gibson

Dr Adam Collison

Contact us:

Dr Linda Campbell
The University of Newcastle (UoN), Science Office (E1.19)
10 Chittaway Road, Ourimbah NSW 2258
T: +61 2 434 94490, F: +61 2 434 94404
E: linda.e.campbell@newcastle.edu.au

HMRI Hunter Medical Research Institute

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

In partnership with our community
The University of Newcastle | HUNTER NEW ENGLAND NSW HEALTH

Why is the research being done?

Some studies suggest that children whose mothers suffered from asthma during pregnancy may show a different developmental profile to other babies. However, the evidence is weak. Robust research is needed to establish the developmental profile of children whose mothers had asthma during pregnancy and recommend early interventions, if needed.

In this study, we profile the first year of development of infants whose mothers had asthma during pregnancy and compare them to infants of mothers without asthma. This research will allow us to identify whether there are differences in development and how they can be prevented or remedied. This research will help clinicians plan appropriate clinical services to meet the developmental needs of these infants.

Who can participate?

All mothers who participated in the Breathing for Life Trial (BLT) and their infants.

What does the study involve?

If you agree to participate and sign the Parent/Guardian Consent form, you and your baby will be invited attend testing at 6 weeks, 6 months and 12 months of age.

We will complete a developmental assessment of your baby and assess your wellbeing in your role as a parent. Testing will include:

- A videotaped interaction between you and your infant
- An assessment of your baby's response to sensory stimulation
- A detailed assessment of motor and cognitive development at 6 and 12 months
- A set of questionnaires about
    - your baby's temperament, responses to care etc.
    - your parenting experience and family situation
    - your psychological well-being and coping skills

Some of these questions are quite personal, asking about substance use and negative thoughts. It is known that parental stress and mental health may affect child outcomes. Therefore, we need to take these into account when looking at the relationship between maternal asthma and child development. ***However, you do not have to answer any questions that make you feel uncomfortable.***

Some tests are identical across the three testing sessions. Others differ, as your baby becomes able to achieve more tasks.

Each session can be completed on the same day as your visit for the parent BLT study, or at another time that suits you.

Session1: 4-6 weeks of age

In addition to the requirements of the parent BLT study, this session will include:

- A short videotaped play session with your baby (15min).

- A set of questionnaires about your baby and yourself which you can complete during the visit or at home. The whole set takes 1.5 – 2 hours, but can be done at your own pace.

Session 2: 6 months of age

In addition to the requirements of the parent BLT study, this session will include:

- A short videotaped play session with your baby (15min).
- A set of questionnaires about your baby and yourself which you can complete during the visit or at home. Again, the whole set takes 1.5 – 2 hours, but can be done at your own pace.
- An assessment of your baby's developmental milestones. While your baby sits on your lap or lies on a mat, the experimenter will:
    - examine your baby's response to different objects or sounds.
    - measure your baby's ability to track objects presented on a computer screen with their eyes.

The session takes approximately 1.5 - 2 hours on top of the parent BLT study. The exact time will depend on your baby (if they are tired or need a feed, we will take breaks as appropriate).

Session 3: 12 months of age

This session is almost identical to the 6 month session. However, as your baby is older and can complete more tasks, it may take a bit longer (e.g., we can complete a more thorough assessment of language development). We estimate it will take 1.5-2.5 hours on top of the parent BLT study. As with the other sessions, we can book this on a separate day, to avoid over-tiring you or your baby.

Are there risks and benefits of participating?

All researchers of the BLT Infant Development team have a background in psychology or occupational therapy. The team is headed by a registered Psychologist (Dr Linda Campbell) and registered Occupational Therapist (A/Prof Alison Lane). All persons participating in the assessments are experienced in assessments and have a "Working with Children Check".

The assessments do not carry any risks to you or your child. If your child becomes tired or needs a nap or a feed, we can take a break or complete testing another time.

While this research will help us understand whether there is any relationship between maternal asthma and infant development, there is no direct benefit for your baby.

However, you will be given the results of your infant's developmental tests. If these results suggest any cause for concern (e.g., signs of developmental delay), we will discuss this with you and refer you to an appropriate service provider in your area for follow-up.

Some of the questions about your own wellbeing may cause you distress. If that occurs, we can offer you an initial assessment by a registered Psychologist and referral to your local community mental health service for further support. Alternatively, you can call Lifeline on 13 11 14 for immediate telephone counselling.

Participation in this study will not cost you anything, nor will you or your child be paid.

How will my privacy be protected?

Any information you provide for this study will be de-identified (that is, you and your child will be allocated a study code and your names will be removed) and kept confidential. Only the research team will have access to this information. The link between the study code and you or your child will be removed when the study is complete.

The results of this study will be collated and communicated to the scientific community. They may also be compared to results from other studies. However, individual participants will not be identifiable in any report.

What choice do I have?

It's up to you! Participation is entirely voluntary. If you decide not to participate in the study, this will not affect your health care by the hospital or your participation in the parent BLT project.

If you consent to participate, you can change your mind and withdraw from the study without having to give a reason. In this case, you can withdraw all your data from the study. The only exception involves data related to an adverse event which need to be retained for regulatory reporting.

What do I need to do to participate?

When you attend your 6-week BLT visit, a member of the BLT-ID team will meet you briefly to answer any questions and ask if you would like to participate.

If you want to ask any questions before then, please phone us on 02 4042 0130.

As part of the consent process, we will ask your permission to contact you with information about follow-up studies.

We thank you for taking the time to consider this study.

What if I have a complaint about the study?

This research has been approved by the Hunter New England Human Research Ethics Committee of the Hunter New England Local Health District, Reference number [15/05/20/4.05]

If you want any information about your rights as a research participant, or if you have a complaint about the manner in which the research is conducted, you can contact Dr Linda Campbell. If you prefer to speak to an independent person, please contact Dr Nicole Gerrand, Manager, Research Ethics and Governance Unit, Hunter New England Human Research Ethics Committee, Locked Bag 1, New Lambton NSW 2305, Ph (02) 4921 4950. Email: hnehrec@hnehealth.nsw.gov.au.

Find us on facebook (www.facebook.com/breathingforlifetrial)

Appendix E: Socio-demographic Questionnaire

BLT-ID Number	Visit no.	Date:	Data entry:
		Assessor:	Data checked:

Breathing For Life Trial
Infant Demographics

First name	Middle Name	Surname

Date of Birth: ____/____/_____
(dd/mm/yyyy)

Visit attended by: Mother ☐ Father ☐ Guardian ☐ Other ☐

Contact Details:

Parent / Primary Caregiver: _____

Address: _____

Suburb: _____ Post Code: _____

Phone (HOME): _____ (include area code)

Phone (WORK): _____ (include area code)

Mobile: _____

Email: _____

Remove this page and file in Demographic folder with completed consent forms.

BLT-ID Number	Visit no.	Date:	Data entry:
		Assessor:	Data checked:

The following is a questionnaire that will ask questions about basic socio-demographics related to you, your partner, and your child. It will also ask questions related to your medical, family, and substance use history. All information in this questionnaire is confidential and will only be used for research purposes.

Personal Details

1. What is *your* date of birth (DD/MM/YYYY): ___/___/_____	2. What is your country of birth? (please state):

Infant Information

Given name(s): _____

3. Infant's gender (please tick): ☐ Male ☐ Female

4. Infant's date of birth (DD/MM/YYYY): ___/___/_____

5. What was your estimated date of delivery (due date)? ____/____/_____

6. Is your current partner the father of your child? (please tick)

☐ No ☐ Yes ☐ I do not have a partner

7. Do any siblings live with your child? (if yes, please state how many):

☐ No ☐ Yes _____

Sibling 1: Age:____ Sex: M/F (please circle)
Sibling 2: Age:____ Sex: M/F
Sibling 3: Age:____ Sex: M/F
Sibling 4: Age:____ Sex: M/F
Sibling 5: Age:____ Sex: M/F

What was your baby's birthweight? _____

8. Is your child:

☐ Breastfed only
☐ Bottle only
☐ Both breastfed and bottle

9. If you have stopped breast feeding:

How old was your child when you stopped breastfeeding? _____

How old was your child when they started solids? _____

BLT-ID Number	Visit no.	Date:	Data entry:
		Assessor:	Data checked:

10. Does any close biological family member of your child suffer from:

- ☐ Parkinson's disease
- ☐ Huntington's disease
- ☐ Multiple sclerosis
- ☐ Epilepsy or seizures
- ☐ Other neurological disease
- ☐ Alzheimer's disease or other dementia
- ☐ Depression
- ☐ Bipolar disorder
- ☐ Schizophrenia
- ☐ Other psychiatric illness
- ☐ Speech or language disorder
- ☐ Learning or behaviour problems
- ☐ Other (please specify): _____

If you marked any boxes, please specify the relation of the person to your child.

_____

_____

_____

Education and Occupation Information

11. What is the highest level of education **you** have **completed**? (E.g. School Certificate, Higher School certificate, TAFE Diploma, Bachelor's degree):

_____

12. What is **your** current occupational status? (please circle all that apply):

Employed: Full-time / Part-time / Casual
Unemployed
Job searching
Stay at home parent
On Maternity leave
Home-maker
Student
Retired

13. What is the highest level of education **your partner** has **completed**? (E.g. School Certificate, Higher School certificate, TAFE Diploma, Bachelor's degree):

_____

14. What is **your partner's** current occupational status? (circle all that apply):

Employed: Full-time / Part-time / Casual
Unemployed
Job searching
Stay at home parent
On parental leave
Home-maker
Student
Retired

BLT-ID Number	Visit no.	Date:	Data entry:
		Assessor:	Data checked:

15. Which of the following best characterises your net annual **household** income? (before tax):

☐ $0-$18,200 ☐ $18,201- $37,000 ☐ $37,001 - $80,000

☐ $80,001 – $180,000 ☐ $180,001 and over

Medical History

16. Do **you** suffer from any chronic illnesses or chronic mental health conditions?

☐ No ☐ Yes (please specify)

_____

_____

_____

17. Are you currently taking any medication?

☐ No ☐ Yes (please specify)

No.	Brand Name	Dosage	Reason	Duration
(1)				
(2)				
(3)				
(4)				
(5)				
(6)				

18. Are you currently taking any supplements?

☐ No ☐ Yes (please specify)

(1)
(2)
(3)
(4)
(5)
(6)

19. Are you currently in counselling or psychiatric care? ☐ No ☐ Yes

20. Have you ever been in counselling or psychiatric care? ☐ No ☐ Yes

Now thinking about the child's biological father,

21. What is the **child's biological father**'s date of birth? ___/___/_____

BLT-ID Number	Visit no.	Date:	Data entry:
		Assessor:	Data checked:

22. Does the **child's biological father** suffer from any chronic illnesses or chronic mental health conditions?

☐ No ☐ Yes (please specify)

_____

_____

_____

23. Does the **child's biological father** take any medication?

☐ No ☐ Yes (please specify)

No.	Brand Name	Dosage	Reason	Duration
(1)				
(2)				
(3)				
(4)				
(5)				
(6)				

24. Does the **child's biological father** currently take any supplements?

☐ No ☐ Yes (please specify)

(1)
(2)
(3)

25. Is the **child's biological father** currently in counselling or psychiatric care?

☐ No ☐ Yes

26. Has the **child's biological father** ever been in counselling or psychiatric care?

☐ No ☐ Yes

Family History

*Please respond about **your biological** mother, father, brothers, and sisters*

27. What is their highest level of education?

Mother:

Father:

28. What is/was their occupation?

Mother:

Father:

29. Do **you** have brothers and/or sisters?

☐ No ☐ Yes

If yes, how many? _____

BLT-ID Number	Visit no.	Date:	Data entry:
		Assessor:	Data checked:

*Please respond about **your child's biological father** - his mother, father, brothers, and sisters* 28. What is their highest level of education? Mother: Father: 29. What is/was their occupation? Mother: Father:	30. Does he have brothers and/or sisters? ☐ No ☐ Yes If yes, how many? _____

Substance use history

Part A

31. Have you ever drunk alcohol? ☐ No ☐ Yes If NO, please move to **Part B** below

32. What age did you start drinking alcohol?

☐ Below 10y ☐ 10-12y ☐ 13-15y ☐ 16-17y ☐ 18-21y ☐ Over 21y

33. How often do you drink alcohol now?

☐ Rarely/never ☐ Once a month ☐ 1-2 days/week ☐ 3-5 days/week ☐ Daily

Part B

34. Have you ever used non-prescription drugs?

If NO, please move to **sleep section**

☐ No ☐ Yes

35. Please tick any drugs that you are now using or have used in the past

	Currently using (Now or in the past month)	Used in the past
Amphetamines (incl. diet pills)	☐	☐
Barbiturates (downers, etc.)	☐	☐
Cocaine or crack	☐	☐
Hallucinogenics (LSD, acid, STP, etc.)	☐	☐
Inhalants (glue, nitrous oxide, etc.)	☐	☐
Party drugs (Ecstasy, etc)	☐	☐
Opiate narcotics (heroin, morphine, etc.)	☐	☐
Sleeping pills	☐	☐

BLT-ID Number	Visit no.	Date:	Data entry:
		Assessor:	Data checked:

Painkillers	☐	☐
Cannabis / marijuana	☐	☐
Other	☐	☐

If other, please specify): _____

Sleep

36. How often in the past week did you:	No days							Every day
1. Have difficulty getting to sleep	0	1	2	3	4	5	6	7
2. Wake up during your sleep period	0	1	2	3	4	5	6	7
3. Wake up too early at the end of a sleep period	0	1	2	3	4	5	6	7
4. Feel rested upon awakening at the end of a sleep period	0	1	2	3	4	5	6	7
5. Sleep poorly	0	1	2	3	4	5	6	7
6. Feel sleepy during the day	0	1	2	3	4	5	6	7
7. Struggle to stay awake during the day	0	1	2	3	4	5	6	7
8. Feel irritable during the day	0	1	2	3	4	5	6	7
9. Feel tired or fatigued during the day	0	1	2	3	4	5	6	7
10. Feel satisfied with the quality of your sleep	0	1	2	3	4	5	6	7
11. Feel alert and energetic during the day	0	1	2	3	4	5	6	7
12. Get too much sleep	0	1	2	3	4	5	6	7
13. Get too little sleep	0	1	2	3	4	5	6	7
14. Take a nap at a scheduled time	0	1	2	3	4	5	6	7
15. Fall asleep at an unscheduled time	0	1	2	3	4	5	6	7
16. Drink an alcoholic beverage to help get you to sleep	0	1	2	3	4	5	6	7
17. Use tobacco to help you get to sleep	0	1	2	3	4	5	6	7
18. Use herbal product to help you get to sleep	0	1	2	3	4	5	6	7
19. Use an over the counter sleeping pill to help you get to sleep	0	1	2	3	4	5	6	7
20. Use a prescription sleeping pill to help you get to sleep	0	1	2	3	4	5	6	7
21. Use aspirin or other pain medication to help you get to sleep	0	1	2	3	4	5	6	7

								Date:	Data entry:
	BLT-ID Number						*Visit no.*	Assessor:	Data checked:

Comments	*If you have any comments, please write them below:*

Appendix F: Sample Bayley-III Caregiver Report

Linda Campbell
Science Office (E1.19)
School of Psychology
University of Newcastle
10 Chittaway Road
Ourimbah, NSW 2258
Telephone: 02 43494490
Email: linda.e.campbell@newcastle.edu.au

INSERT DATE

THE UNIVERSITY OF NEWCASTLE AUSTRALIA

Breathing for Life Trial – Infant Development study
Bayley Scales of Infant and Toddler Development- Third Edition (Bayley-III)

Name: **D.O.B:** **Date Of Assessment:**

Chronological Age: **Venue:** Hunter Medical Research Institute **Assessor:**

Dear (parent/caregiver),

Thank-you for bringing CHILD, who was CHRONOLOGICAL AGE, as part of a research study at the Hunter Medical Research Institute. The following is a brief summary of our findings.

CHILD was assessed using the Bayley-III screener. The Bayley-III screener examines a child's established and emerging skills in cognitive, language (receptive and expressive) and motor (fine and gross) development. The abilities covered by the different scales vary depending on the child's age but include activities that explore problem solving (e.g. finding toys, completing puzzles), developing play, response to language, manipulating objects and mobility (walking, using stairs).

Performance levels are determined according to a standardisation group (a group of children of a similar age to the child being assessed). Results are presented in risk categories:

- *At risk*- child at risk for some delay.
- *Emerging*- age appropriate skills beginning to emerge.
- *Competent*- child shows competence in age appropriate tasks.

At a chronological age of ** months, and a corrected age of ** months the results were:

	Score	*Risk Category*
Cognitive		
Receptive Communication		
Expressive Communication		
Fine Motor		
Gross Motor		

These results are overall within the average range for a child of CHILD's age. CHILD's strengths are his fine motor skills which fell well within the average range for his age.

Cognitive Composite: CHILD was able to respond to novel surroundings, retain two blocks in hand for a few seconds, solve simple puzzles and persistently reach for an object.

Receptive and Expressive Communication: CHILD was able to sustain play with objects of interest, discriminate sounds, vocalise her mood and get another person's attention.

Fine and Gross Motor: CHILD was able to grasp a suspended ring, manipulate blocks, briefly sit with support, and maintain head control.

We thank you for taking the time to participate this research study. If you have any questions please do not hesitate to contact us,

Yours sincerely,

[INSERT ELECTRONIC SIGNATURE]
[name and designation]

Appendix G: Journal of Asthma- Submission Guidelines

Retrieved from: https://www.elsevier.com/journals/respiratory-medicine/0954-6111/guide-for-authors

We now differentiate between the requirements for new and revised submissions. You may choose to submit your manuscript as a single Word or PDF file to be used in the refereeing process. Only when your paper is at the revision stage, will you be requested to put your paper in to a 'correct format' for acceptance and provide the items required for the publication of your article.

The Journal of Asthma is an internationally-renowned, clinically-oriented journal, combining cutting-edge original research with state-of-the-art reviews dealing with all aspects of respiratory diseases and therapeutic interventions, but with a clear clinical relevance. The journal is an established forum for the publication of phased clinical trial work at the forefront of interventive research. As well as full-length original research papers, the journal publishes reviews, correspondence, and short reports. The Journal also publishes regular supplements on areas of special interest.

NEW SUBMISSIONS

Submission to this journal proceeds totally online and you will be guided stepwise through the creation and uploading of your files. The system automatically converts your files to a single PDF file, which is used in the peer-review process.

As part of the Your Paper Your Way service, you may choose to submit your manuscript as a single file to be used in the refereeing process. This can be a PDF file or a Word document, in any format or lay-out that can be used by referees to evaluate your manuscript. It should contain high enough quality figures for refereeing. If you prefer to do so, you may still provide all or some of the source files at the initial submission. Please note that individual figure files larger than 10 MB must be uploaded separately.

References

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct.

Formatting requirements

There are no strict formatting requirements but all manuscripts must contain the essential elements needed to convey your manuscript, for example Abstract, Keywords, Introduction, Materials and Methods, Results, Conclusions, Artwork and Tables with Captions.

If your article includes any Videos and/or other Supplementary material, this should be included in your initial submission for peer review purposes.

Divide the article into clearly defined sections.

Figures and tables embedded in text

Please ensure the figures and the tables included in the single file are placed next to the relevant text in the manuscript, rather than at the bottom or the top of the file. The corresponding caption should be placed directly below the figure or table.