The Language, Externalising and Internalising Outcomes of 9.5 Year Old Children Born to Mothers in the Methadone Maintenance Treatment

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of Master of Science in Psychology

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ABSTRACT

Opioid dependence is an increasing global health concern, particularly among pregnant women. The Methadone Maintenance Treatment (MMT) is considered a first-class standard treatment for pregnant opioid dependent women, as it can reduce foetal and birth complications, relapse, and social adversity. There is a limited number of studies examining the developmental outcomes of school-aged children born to mothers in MMT. Children born to methadone maintained mothers are identified as a dual hazard population, due to prenatal opioid exposure, social adversity and caregiver psychological factors. The degree to which of these factors contribute to language, externalising behaviours and internalising behaviours is unknown.

This thesis has three aims: *i.* To describe the extent and nature of language, externalising problems, and internalising problems of children born to mothers maintained on methadone at age 9.5 years. *ii*. To examine the associations between prenatal methadone exposure, social adversity, caregiver psychological factors and language outcomes at age 9.5 years. *iii.* To examine the associations between prenatal methadone exposure, social adversity, caregiver psychological factors and externalising and internalising problems at age 9.5 years.

This cross-sectional study draws on data from a prospective Methadone in Pregnancy longitudinal study. At the 9.5 year wave, 80 methadone exposed children and their caregivers, and 98 comparison children and their caregivers were assessed. The Clinical Evaluation of Language Fundamentals - Fourth Edition Semel et al. (2006), was used to measure children's language. The teacher rating scale for the Behaviour Assessment System for Children, Second Edition (Reynolds & Kamphaus, 2004) was used to measure externalising and internalising problems. Factors related to social adversity and caregiver

psychological factors were obtained during comprehensive caregiver interviews and used to predict child developmental outcomes at 9.5 years.

Study findings show at age 9.5 years methadone exposed children have poorer language and their teachers' reports indicate higher rates of externalising problems relative to the comparison children. No differences were found in teachers' ratings for internalising problems between methadone exposed children and the comparison children. A greater proportion of methadone exposed children displayed comorbid low language, externalising problems and internalising problems relative to the comparison group. Methadone group status did not predict low language at 9.5 years. Gender was the only factor that predicted low language at 9.5 years. Predictors of externalising problems included methadone group status, gender, and social adversity such as low SES, being from a minority group and being parented by a single caregiver. Methadone group status, social adversity and caregiver's psychological factors failed to predict internalising problems.

Overall, findings from the present study indicate that methadone exposed children have low language and higher levels of externalising problems relative to the comparison children. Different predictor factors are associated with different developmental domains. Findings suggest multidisciplinary interventions are necessary to support this group of children and their families to guide positive developmental trajectories.

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LIST OF ABBREVIATIONS

BACS 2: Behaviour Assessment Systems for Children Second Edition

BE: Buprenorphine Exposed

CBCL: Child Behaviour Checklist

CELF 4: Clinical Evaluation Fundamentals Fourth Edition

CLI: Core Language Index

DASS: Depression, Stress, Anxiety Scale

EMT: Enhanced Milieu Teaching

EPC: Externalising Language Composite

HE: Heroin Exposed

HIV: Human Immunodeficiency Virus

IPC: Internalising Language Composite

ITPA: Illinois Test of Psycholinguistic Abilities

IAS: Intrauterine Abstinence Syndrome

MSCA: McCarthy Scale of Children's Abilities

ME: Methadone Exposed

MIP: Methadone in Pregnancy

MMT: Methadone Maintenance Treatment

OE: Opioid Exposed

OR: Odds ratio

SDQ: Strengths and Difficulties Questionnaire

NAS: Neonatal Abstinence Syndrome

SES: Socio-Economic Status

TD: Typically Developing

TRS: Teacher Rating Scale

WISC-R: Wechsler Intelligence Scale for Children Revised

WPPSI-R: Wechsler Preschool and Primary Intelligence Scales Revised

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CHAPTER 1

INTRODUCTION

The first section of the introduction will provide a brief overview of opioids. Opioids are a class of narcotics known for their powerful analgesic properties (Dayer et al., 2019). Traditionally opioids were sourced from the opium poppy. Heroin, morphine and codeine are natural forms of opioids. Today there is a wide range of synthetic forms of opioids, this includes methadone, buprenorphine and oxycodone (Dayer et al., 2019). The history of opioids can be briefly summarised in three waves. The first wave occurred in the early 1800s. Pain relief medication was non-existent, with no regulation on opioids (Jones, 2013). The second wave occurred towards the end of World War II, which was characterised by the rapid emergence of street heroin abuse. In the United States heroin abuse amplified from 7.2 per 10,000 to 35.8 per 10,000 within a decade (Joseph et al., 2000). Subsequently, an increase in the human immunodeficiency virus (HIV) occurred (Joseph et al., 2000). This triggered a worldwide "opiophobia" view (Jones, 2013). The third wave occurred in the late 1900s, and was shaped by an increase in government acts and the pharmaceutical industry attempting to diffuse the stigma associated with opioids and to reduce the use of street heroin (Jones, 2013). Synthetic opioids such as methadone, buprenorphine and oxycodone were introduced to reduce the use of heroin. However, throughout the 2000s, overall opioid use in the USA continued to increase (Jones, 2013).

Opioids are clinically categorised as sedative remedies. They are palliative and are commonly used to depress the central nervous system (Chevalier et al., 2014). They generate euphoric illusions through an upsurge of dopamine in the opioid receptors of the brain (Chevalier et al., 2014). This mechanism promotes endorphins, driving sensations of pleasure and reducing the ambience of pain; consequently, opioids can be extremely addictive.

1.1 Opioid Dependence in New Zealand

Opioid dependence is a global health burden. In 2018, approximately 58 million people worldwide suffered from an opioid addiction (World Health Organisation, 2020). Moreover, the Australasian region is one of the districts with the highest opioid dependency compared to the global pooled prevalence (Degenhardt et al., 2014). Canterbury, in the South Island region of New Zealand, has a higher prevalence of opioid-dependent adults compared to other regions of New Zealand with three times the number of deaths in the South Island compared to the North Island as a result of opioid overdose (Adamson et al., 2012).

Illicit opioid dependence is associated with major physical, biological, psychological, and social consequences. Opioid dependence is associated with an increased risk of incurable blood borne pathogens such as HIV, Hepatitis B, and Hepatitis C. Further, opioid dependence is correlated with polysubstance misuse, fatal and non-fatal overdose, lower quality of life as well as poor absorption of nutrients (Cleary et al., 2012; Johnson et al., 2003; Vucinovic et al., 2008). There is also evidence that shows opioid dependence is comorbid with increased risk of mood disorders particularly depression and anxiety (Khazaal et al., 2013) and externalising behaviours such as impulsivity, irritability, aggressiveness, violence, antisocial behaviour and lack of control ((Deering et al., 2011; Khazaal et al., 2013). Opioid dependence has also been associated with increased risk of unemployment, incarceration, crime, violence, poverty, poorer public health outcomes and poorer maternal-infant care (Deering et al., 2011; Kenworthy et al., 2017). Further a systematic review comprised of 16 articles reported opioid addiction is costing taxpayers approximately 33k to 66k annually in Australia, Canada, Europe, and New Zealand (Deering et al., 2011; Kenworthy et al., 2017).

1.2 Illicit Opioid Use During Pregnancy

Illicit opioids are one of the most abused substances among pregnant women. Approximately 43% of regular opioid users in New Zealand are female, and this prevalence

increases during procreative years 25 - 35 years (Vucinovic et al., 2008). This promulgates risk to the embryo as opioids are readily absorbed across the placenta and into the foetus's system (Minozzi et al., 2008). Prenatal exposure to opioids can increase the risk of premature birth, congenital abnormalities, low birth weight and smaller head circumference, as well as Neonatal Abstinence Syndrome (NAS). NAS is a condition used to describe a group of withdrawal symptoms that a foetus experiences after being exposed to opioids. NAS is characterised by high pitched crying, irritability, seizures, vomiting, poor feeding and gastrointestinal problems (Bandstra et al., 2010).

1.3 The Methadone Maintenance Treatment Programme in Pregnancy

Methadone Maintenance Treatment (MMT) was introduced in New Zealand to prevent the serious risks associated with illicit opioids on the foetus and the mother (Laslo et al., 2017). In Christchurch, the MMT programme combines the care of general practitioners and specialists to address both psychological and neurophysiological symptoms associated with opioid dependence as well as providing antenatal care and supplementary check-ups. This holistic initiative was implemented in order to monitor the mother’s methadone dose and prevent relapse and/or transmission of blood borne viruses (Johnson et al., 2003; Joseph et al., 2000).

MMT is considered a first-class standard of care for pregnant women with a heroin addiction. Synthetic opioids such as methadone have two functional mechanisms of action. Firstly, methadone is an agonist and adheres to the μ-opioid receptor stabilising positive emotions. Secondly, methadone has a slow-release feature, which acts to suppress cravings and withdrawal symptoms, reducing narcotic behaviour (Kreek, 1992, 2000). These actions promote homeostasis in the reproductive system, increase the uptake of nutrients, and reduce the risk of miscarriages and complications during childbirth such as foetal stress, premature birth and low birth weight (Cleary et al., 2012; Farid et al., 2008; Finnegan, 1978). Further,

studies report that methadone decreases the possibility of relapse in the mother (Johnson et al., 2003), lowers the probability of transmitting infectious diseases (Joseph et al., 2000) and Intrauterine Abstinence Syndrome (IAS). Fatal consequences associated with opioid withdrawal are associated with a decrease in placental blood flow and oxygen supply to the foetus; (McCarthy et al., 2017). MMT is also associated with a decrease in obsessive narcotic behaviour, criminal acts and arrests, reduced risk of death from overdose and an increase in paternal support and overall social support (Goehl et al., 1993; Joseph et al., 2000; Mattick et al., 2009; Sheerin et al., 2004).

1.4 Biological Risks and Developmental Outcomes Associated with Prenatal Methadone Exposure

While there is strong evidence to support the benefits of the MMT programme, neurodevelopmental risks associated with prenatal exposure to methadone also need to be considered. The following sections briefly describe the critical developmental stages and the risks associated with prenatal exposure to opioids in age-related phases. The Foetal Origins Framework (Lester & Lagasse, 2010) suggests that opioids can impact foetal programming, brain biochemistry, and the neuroendocrine system, which can translate into repercussions later on in life.

1.4.1 Embryonic and Foetal stage. The embryonic and foetal stage are critical periods of brain development (Lester & Lagasse, 2010; Monnelly et al., 2018; Yanai et al., 2003). Research indicates that prenatal methadone exposure (ME) acts as an intrauterine stressor which interrupts the neuroendocrine system, and can also alter dopaminergic and serotonergic systems and myelination (Farid et al., 2008; Monnelly et al., 2018). Findings from animal and human studies report that these structural and biochemical modifications are linked to later physiological problems (Jansson et al., 2012; Lester & Lagasse, 2010; Wouldes & Woodward, 2013), such as emotional reactivity, activity and irritability (Levy-Shiff et al., 1998), behavioural consequences such as low mood, anxiety, difficulties learning

and memory problems (Chen et al., 2015; Maes et al., 1995; Meador-Woodruff et al., 1990; Nemeroff et al., 1984; Robinson et al., 1996; Vestal-Laborde et al., 2014; Wong et al., 2014).

1.4.2 Infancy and Toddlerhood (Birth - 2 years). Infants prenatally exposed to methadone are at a greater risk of premature birth, lower birth weight and smaller head circumference compared to non-exposed neonates (Hunt et al., 2008; Johnson et al., 2003; Monnelly et al., 2018; Wouldes & Woodward, 2013). Moreover, ME infants are at a greater risk of lowered white and grey matter tract volumes compared to non-exposed neonates (Monnelly et al., 2018). Further, a large percentage (50% - 90%) of ME infants will display symptoms of IAS and NAS (E. S. Bandstra et al., 2010; Joseph et al., 2000; Maguire et al., 2016; Monnelly et al., 2018; Wouldes & Woodward, 2013). The intense fluctuation of stress hormones in new-born infants with NAS (Beckwith & Burke, 2015; Lester & Lagasse, 2010) is linked to neurodevelopmental problems, poorer vision (Counsell et al., 2014; Monnelly et al., 2018); difficulties self-soothing (Bakhireva et al., 2019); atypical psychomotor movements and poorer cognitive abilities compared to non-exposed infants (Beckwith & Burke, 2015; Bunikowski et al., 1998).

1.4.3 Toddlerhood and School Age (2 to 12 years). Drawing on the wider opioid literature, neuroimaging studies indicate that opioid exposed (OE) children have smaller intracranial and brain volumes such as cerebral cortex, amygdala and white matter compared to comparison children at age 9 to 11 years (Walhovd et al., 2007). These areas have been associated with cognitive ability, neuropsychological functioning and self-regulation (Lester & Lagasse, 2010; Nagy et al., 2004; Walhovd et al., 2007).

A recent meta-analysis (Lee et al., 2020), examined the literature within the last 25 years (since 1993) on OE children from birth to 12 years of age, and their developmental trajectories. Overall, OE preschool and school-aged children performed poorly than comparison children on cognitive measures (Hunt et al., 2008; Konijnenberg et al., 2016;

Vanbaar & Degraaff, 1994), expressive and receptive language abilities (Hunt et al., 2008; Vanbaar & Degraaff, 1994), displayed greater levels of externalising and internalising behaviour problems (Levine & Woodward, 2018; Sarfi et al., 2013), and greater attention problems (Levine & Woodward, 2018; Melinder et al., 2013), with medium to large effect sizes. Similar trends were observed among heroin exposed preschool and school-aged children (Nygaard et al., 2016; Ornoy et al., 2016). Language and externalising, and internalising outcomes will be reviewed in greater detail in Chapters 3 and 4.

The overall quality of the included studies within this meta-analysis (Lee et al., 2020) was a medium to low risk of bias. However, the authors noted the following limitations: environmental factors were not taken into account, the composition of the comparison children varied across the different studies, and there was a high attrition rate in the OE children (Lee et al., 2020).

1.5 Social Adversity and Psychological Factors of Opioid Dependent Mothers

It is well documented that maternal caregivers with an opioid dependency typically come from disadvantaged backgrounds. The following section discusses social adversity and caregiver psychological factors associated with opioid dependent mothers.

1.5.1 Social Adversity. Opioid dependent mothers are more likely to have experienced social disadvantages related to low socioeconomic status (SES), be from a minority group, be parented by a single caregiver, and experienced frequent caregiver changes as children, and generally remain experiencing environmental disadvantages as caregivers (Sieger & Haswell, 2020; Suchman & Luthar, 2001). Research has found that opioid dependent mothers are also more likely to come from a low SES background, are less likely to be in employment (Davie-Gray et al., 2013; Konijnenberg et al., 2016; Suchman & Luthar, 2001), have more frequent contact with child services (Dubowitz et al., 2011;

Hjerkinn et al., 2013; Lean, 2012), and are more likely to be single parents and lack familial support (Davie-Gray et al., 2013; Lean, 2012).

Māori and Pacific Islanders tend to be over represented in substance dependent groups (Davie-Gray et al., 2013). Minority groups are more likely to be living in impoverished neighbourhoods, which is likely to be associated with a greater proportion of minority groups with an opioid dependency (Browning & Cagney, 2003; Karriker-Jaffe, 2013; Wen et al., 2003). However, SES does not account for opioid dependence wholly. Drawing on the Meihana Model (Pitama et al., 2007), the impact of colonisation, marginalisation, racism and migration poses significant consequences that place minority groups at a greater risk for developing substance dependence, as it erodes culture and a sense of identity (Fosados et al., 2007; Kulis et al., 2007). While neighbourhood affluence is robustly associated with substance dependence (Browning & Cagney, 2003; Karriker-Jaffe, 2013; Wen et al., 2003), it seems that, despite living in impoverished urban neighbourhoods, similar ethnic groups living within the same community can confer a greater sense of collective identity and efficacy which can mitigate the negative consequences of poverty such as substance use (Kulis et al., 2007).

1.5.2 Caregiver Psychological Factors. There is an increasing body of literature that indicates opioid dependent mothers have elevated levels of mental health difficulties relative to the general population (Davie-Gray et al., 2013; Lean, 2012; Lester & Tronick, 1994; Sarfi et al., 2013; Wouldes & Woodward, 2010). Approximately, 30-45% of opioid dependent mothers reported clinically significant levels of depression (Davie-Gray et al., 2013; Lean, 2012; Sarfi et al., 2013; Wouldes & Woodward, 2010). Similarly, an Australian study reported that 75% of drug dependent women met diagnostic criteria for depression during their pregnancy (Oei et al., 2009). Equally, co-occurring rates of anxiety and depression in opioid dependent mothers are reported to range from 65% to 73%

(Benningfield et al., 2010; Fitzsimons et al., 2007) compared to 20% of non-opioid dependent mothers (Kessler et al., 1994).

1.5.3 Stress Associated with Opioid Dependent Mothers. Similarly, opioid dependent mothers reported higher levels of parental stress (Powis et al., 2000; Suchman & Luthar, 2001); financial stressors related to transport, affordability, substance use (Moreland et al., 2020); and general stress about physical and mental wellbeing (Moreland et al., 2020) relative to non-opioid dependent mothers.

Social adversity and caregiver psychological factors, coupled with the stressful transition of being pregnant and becoming a parent, perhaps function as motivators for substance use (Chan & Moriarty, 2010; Sieger & Haswell, 2020).

1.6 A Dual Hazard Model of Methadone Childhood Development

Children's development is influenced by the interaction of biological and social adversity and caregiver's psychology (Hans & Jeremy, 2001). Ecological models of development propose that children's developmental outcomes are influenced by a combination of distal (e.g., gender, prenatal drug exposure, minority group status) and proximal (e.g., family SES, caregiver circumstances) factors (Belsky & MacKinnon, 1994; Bronfenbrenner & Morris, 1998; Ryan & Adams, 1995).

Children born to pregnant mothers in the MMT programme, are commonly identified as a 'dual hazard' population (Lester & Tronick, 1994). The Systems Approach to Study Cocaine Model (*see* **Figure 1.1**), proposed by Lester and Tronick (1994) considers the interaction of the prenatal environment, the caregiver's personality, substance use and lifestyle, as well as environmental regulators, and how these interacting variables influence a child's development.

Prenatal environment associated with ME, may drive difficult behaviours (e.g., irritability as a result of NAS) in the child. Further, males tend to be more sensitive to ME

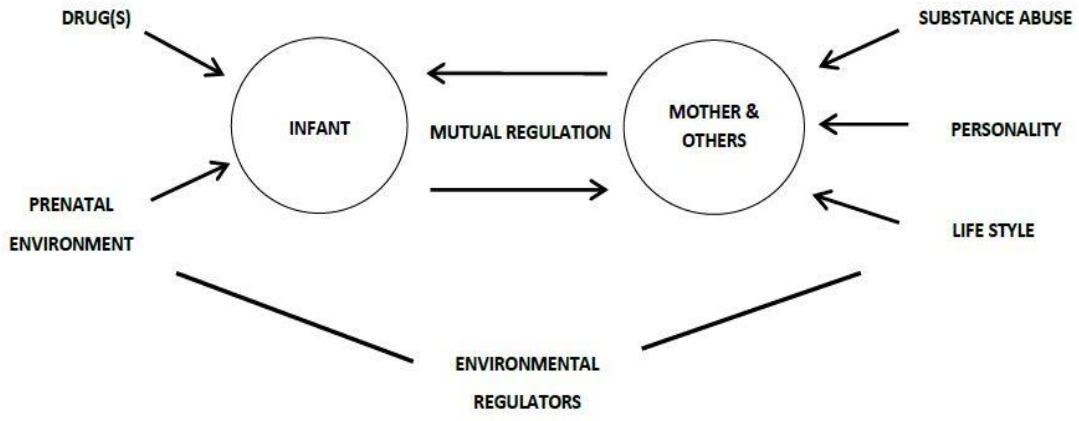
relative to females, and therefore may experience greater consequences such as cognitive difficulties and externalising problems (Cicero et al., 1996; Moe, 2002).

The second component is caregiver's personality, substance use and lifestyle (*see Chapter 1.5*). Opioid dependent mothers will often use several substances (e.g., alcohol and cigarettes), are likely to be depressed, anxious and highly stressed, and tend to have challenging personalities (Belsky & MacKinnon, 1994; Kochanska et al., 2007; Konijnenberg et al., 2016; Lester & Tronick, 1994; Wu et al., 2011). These mechanisms, along with an irritable infant, compromise childrearing practices, as caregivers will often be preoccupied with their own difficulties overlooking their child's requirements or they may not have the skills to soothe a difficult child (Suchman & Luthar, 2001). This interrupts the transactional relationship between the child and the caregiver (Lester & Tronick, 1994), exacerbating negative developmental outcomes for the child (Beeghly & Tronick, 1994; Belsky & MacKinnon, 1994; Goodman et al., 2005; Sameroff, 1975).

Finally, broader chaotic environmental regulators (e.g., poverty, lack of support) in which these interactions take place have the capacity to further disrupt child-caregiver interactions and the mutual regulatory process. Environmental factors directly and indirectly influence the caregiver's substance use behaviours, mental health and personality, further compromising their ability to engage in positive childrearing behaviours (Lester & Tronick, 1994).

Figure 1. 1

Systems Approach to the Study of Cocaine



(Lester & Tronick, 1994).

CHAPTER 2

Language Development

The following section will discuss language trajectories and define language and detail language components, their developmental process and how difficulties in different language domains may present.

2.1 Language Trajectories

Language is an essential component of overall optimal development, failure to address language difficulties after preschool years may have long lasting developmental consequences. It is well documented that language difficulties can negatively impact other developmental areas. For example, language is associated with self-regulation, therefore reducing externalising and internalising problems (Brownlie et al., 2004; Fagan & Iglesias, 2000; Morse & Cangelosi, 2017; Newport, 2016). Language trajectories display variability in preschool years but tend to stabilise by the age of 6 years. Language difficulties which persist until the age of 5 to 6 years are likely to be ongoing (Church, 2015; Hart & Risley, 1995; St Clair et al., 2011; Stothard et al., 1998).

2.2 Language Terminology

The nosology of language is complex, as it is multifactorial, comprising of the expression of voicing thoughts and feelings clearly (expressive) and comprehension of language (receptive; Bishop et al., 2017; Bloom & Lahey, 1978; Dockrell et al., 2011). There has also been a longstanding debate within the literature and in clinical practice, regarding whether language ability is a continuum or if children at the low end of language ability are a separate group, which poses another challenge (Bishop et al., 2017). According to the DSM-5, language disorders can be diagnosed when language abilities are substantially and quantifiably below age matched peers, resulting in functional limitations, without an identifiable biomedical cause (American Psychiatric Association, 2013). However, a variety

of cut-offs have been used, although cut-offs are typically 1-1.5 standard deviations below the mean of a standardised test for research purposes (Beitchman et al., 2008; Johnson et al., 2010; Law et al., 2009; McKean et al., 2017; Norbury et al., 2008; Schoon et al., 2010a, 2010b; Young et al., 2002).

The terminology that has been widely used in the literature to identify this group includes specific language impairment, language disorder / impairment, language learning disorder / impairment, language delay and more recently developmental language disorder (Bishop et al., 2017). For the purpose of this study the term "low language" will be alluded to for individuals with a score of 1 standard deviation (SD) or more below the mean on a standardised psychometric language test. This cut-off was selected as several studies have indicated 1 SD is associated with poorer long term behavioural, educational and psychosocial outcomes (Beitchman et al., 2008; Johnson et al., 2010; Law et al., 2009; Schoon et al., 2010a, 2010b; Young et al., 2002). The aim of this cut-off is to capture individuals on the borderline as well as those with moderate to profound low language.

2.3 Language Components and Language Development

Expressive and receptive language comprise structure (sentence structure and word level grammar) and content (semantics, vocabulary; Semel et al., 2006).

2.3.1 Structure. In the current study, two components of structure that will be analysed are syntax (the rules that state how words and phrases must be used in language; Bloom & Lahey, 1978) and morphology (the internal structure of words; Bloom & Lahey, 1978). Bishop et al. (2014) described the acquisition of syntax and morphology by referring to a three-phase model: *i.* The child encounters utterances on several occasions; *ii.* The child begins to recognise word order patterns; *iii.* The child gradually starts to use sequential rules to form novel sentences following the patterns learned, for example the verb follows the subject.

School-aged children in structuring language may omit the main verb or overgeneralise a verb ending (Bishop, 2014). Further, difficulties with syntax and morphology may result in functional difficulties with understanding and following instructions in the classroom, socialising with peers, verbalising narratives using complex language and comprehending written material (Paul et al., 2018).

2.3.2 Content. Content refers to learning new words, using a variety of vocabulary, humour, figurative language, metaphors and similes (Bloom & Lahey, 1978). Typically, content and general language components are learnt through interactive conversations, repetition and corrective responses (Bloom & Lahey, 1978; Camarata & Yoder, 2002; Kiernan & Gray, 1998). The first three years of life is the most critical time for the development of content (Morgan et al., 2015; Norbury et al., 2017; Rodriguez et al., 2009; Rowe et al., 2012), however, children continue to learn vocabulary throughout their lives (Dickinson & Porche, 2011; Hoff, 2006). The interactionist account of language acquisition (Camarata & Yoder, 2002) is fundamentally about the back and forth conversations as a learning experience for language. This model highlights the importance of caregivers responding with grammatical corrections to inform the child on any linguistics errors as well as adjusting the complexity of their language to the child's developmental level (Camarata & Yoder, 2002).

School years are significant for learning new content through educational experiences (Dickinson & Porche, 2011; Hoff, 2006; Owens, 2016). Therefore around this time, there is a rapid development in content and vocabulary becomes more creative, richer and broader (Owens, 2016). Children with difficulties in content at the age of 9 years may find it difficult to understand different meanings of the same word and have a limited pool of words to select from when trying to express themselves (Gray, 2005; Kan & Windsor, 2010; Owens, 2016) and struggle to understand instructions in the classroom or the connotations of words. They

may also find it a challenge to defend themselves and understand the opposing view in discussions with peers or an adult (Dockrell & Lindsay, 1998; Nippold, 2010).

Children who have a primary difficulty with structure and content tend to have poor pragmatics (social use of language) secondary to an immature linguistic system. These children may experience difficulties starting and upholding conversations with others, requesting and providing clarification, turn-taking in a conversation and matching communication style to the social context (Norris, 1995).

In the general literature, it is common for children to have comorbid low expressive and low receptive language, however there is evidence that indicates children can have difficulties in one language domain as well (Selassie et al., 2005; Westerlund & Sundelin, 2000). Perhaps variations in findings are the result of multiple interacting factors (Clark et al., 2007; Law et al., 1998; Letts et al., 2013; Rapin, 1996; Tomblin et al., 1997).

2.4 Language Development and Prenatal Exposure to Opioids: A Review of the Literature

2.4.1 Search Criteria. To date there is a limited number of reviews that examine the relationship between prenatal opioid exposure and language development at the age of 9 years. To identify the literature on prenatal opioid exposure and language development among school-aged children, a comprehensive database search was conducted. Appropriate studies were selected through a systematic search of PsycINFO and Pubmed. A combination of the following search terms was used to retrieve articles: *School-aged children, elementary students, children, primary school students, opioid, opioid substitution, opium, buprenorphine, heroin, methadone, morphine, language, language development, language outcomes, specific language impairment, developmental language delay, language impairment, language disorder.*

2.4.2 Inclusion and Exclusion Criteria. The selected papers met the following criteria: presented with empirical research, participants were prenatally exposed to opioids,

participants were school aged at outcome (5-12 years), language is explicitly measured as the outcome variable, studies were reported in English and were peer reviewed, research design included a cohort, case control or cross-sectional study, non-original publications were excluded. **Table 1.1** presents findings from published research examining the effects of prenatal exposure to opioids on language outcomes of school-aged children.

2.4.3 Summary of Methods Used in Studies That Met the Inclusion Criteria. In this review, seven studies met the inclusion criteria. As shown in **Table 1.1**, six studies used a cross-sectional design and one study used a longitudinal study designs. Five studies assessed language using verbal IQ measures, one used an achievement measure and two used comprehensive language measures. However, only one study reported on expressive and receptive language. In four studies mothers were maintained on methadone or buprenorphine, however, mothers also reported taking other substances. In the remaining three studies mothers reported using heroin during their pregnancy or an opioid that was not specified. Three studies explicitly examined factors associated with social adversity and caregiver psychological factors.

2.4.4 Study Findings. As shown in **Table 1.1**, one longitudinal study reported significant differences between ME children and the comparison children on language measures (Vanbaar & Degraaff, 1994). More specifically, Vanbaar and Degraaff (1994), explored word meanings and found a significant difference between the two groups with a large effect size. Similarly, Pulsifer et al., (2008) used a cross sectional study design and reported a significant difference on expressive and total language with a medium effect size difference, however failed to find a significant difference in receptive language between ME and comparison children. Drawing on the wider drug literature, it is possible that prenatal substance exposure has a greater impact on expressive language relative to receptive language (Bandstra et al., 2002; Morrow et al., 2004).

Wahlsten and Sarman (2013), assessed language using the MSCA (McCarthy, 1970) and the WPPSI-R (Wechsler, 1989). Researchers found that buprenorphine-exposed (BE) children performed significantly below published population norms on the MSCA verbal scale, but not on the WPPSI-R verbal scale. One possible explanation for this incongruence in results, is that the MSCA has only been standardised in the USA and not on a Swedish population sample, whereas the WPPSI-R has been.

De Cubas and Field (1993) compared ME children and comparison children: groups were matched on age, gender, socio economic status (SES), maternal education, prenatal alcohol and cigarette use and perinatal complications. The authors only found a significant difference on one of the Kaufman Achievement Subscales (Kaufman & Lichtenberger, 1998): faces and places. Further, there were no differences between the two groups on reading, decoding and comprehension.

The remaining three cross-sectional studies attempted to minimise risk factors associated with social adversity, and caregiver psychological difficulties, by examining children's living situation. Davis and Templer (1988) compared ME children living in maternal care and non-ME children who were in the care of a substance-dependent father. Researchers used the WISC-R to assess verbal abilities and found no significant difference between the two groups, with a small effect size (Davis & Templer, 1988).

Ornoy et al., (2001) examined five groups: *i*. Prenatal heroin exposed children in maternal care; *ii.* Prenatal heroin exposed children who were adopted; *iii.* Non-heroin exposed comparison children; *iv*. Non-heroin exposed children in the care of a substance dependent father; *v*. Non-heroin exposed children living in low SES. The WISC-R was also used in this study to examine language abilities. Results showed that, heroin exposed children who remained in maternal care and non-heroin exposed children living in low SES environments performed significantly lower on the verbal scales relative to heroin exposed

children who were adopted and the non-heroin exposed comparison children, showing a medium effect size difference across the groups (Ornoy et al., 2001).

As shown in **Table 1.1**, similar findings were reported in (Wilson et al., 1979). The authors, compared four groups: *i.* Heroin exposed children in maternal care; *ii*. Non-heroin exposed children living with a substance dependent caregiver; *iii.* A high risk group (characterised by medical complications e.g., dysmaturity, intrauterine growth, retardation, foetal stress); *iv*. Non-heroin exposed comparison children. No difference was found between the groups on the doll play task. However, on the ITPA (Hammill et al., 2001), the comparison children performed significantly better on this task, relative to the other groups, with a small to medium effect sizes.

Taken all together, it seems that no differences emerged between ME/heroin exposed children living in maternal care and non-exposed children living with a substance-dependent father, across the three studies (Davis & Templer, 1988; Ornoy et al., 2001; Wilson et al., 1979). Drawing on Ornoy et al., (2001) and Wilson et al., (1979), comparison children without biological or environmental risks are preforming significantly better on language tasks, relative to the other groups with at least one risk. Nevertheless, it seems that living with adopted caregivers can mitigate the biological risk of heroin exposure (Ornoy et al., 2001). In support of this, Vanbaar and Degraaff (1994) conducted a sub-analysis, only using adopted ME children and the comparison children.

All together these studies illustrate that significant differences in language measures emerged between OE children and the comparison children, however OE children still performed within the average range of published population norms, (Davis & Templer, 1988; de Cubas & Field, 1993; Ornoy et al., 2001; Vanbaar & Degraaff, 1994; Wahlsten & Sarman, 2013; Wilson et al., 1979). In contrast, one study (Pulsifer et al., 2008) found that ME children performed in the low average range (mean range = 81.4 - 83.8). It is possible that the

discrepancy in findings is due to the variability of the cohorts across the different studies. For example, comparison children in Pulsifer et al. (2008) performed relatively poorer (mean range = 87.7 - 89.3), than average range classification. Alternatively, opioid dependent caregivers also reported taking cocaine, which may have exacerbated language difficulties.

2.4.5 Methodological Limitations. The first limitation is the small sample sizes due to low participation of families with ME children, which can affect statistical power (Davis & Templer, 1988; de Cubas & Field, 1993; Vanbaar & Degraaff, 1994; Wahlsten & Sarman, 2013; Wilson et al., 1979). For example, de Cubas and Field (1993) did not find a significant difference between 20 heroin exposed children and 20 control children on most of their language subscales. In the study conducted by Ornoy et al., (2001) a slightly larger sample size group (e.g., ranging from 30 to 32 participants), resulted in significant differences across the groups.

The second limitation identified is maternal polysubstance use. Polysubstance use is generally self-reported, therefore, other substances used are possibly underreported due to feelings of guilt, humiliation or poor recall. An additional concern associated with this is the inability to isolate the sole effect of opioids from an amalgamation of substances. Both these factors reduce the robustness of research in this area. In this review (see **Table 1**), participants reported using heroin, cigarettes, alcohol, marijuana, cocaine and amphetamines alongside their methadone. Studies have found that after minimising the effects of covariates, these substances remained to have an impact on children's language (for example, see Bandstra et al., 2010; Hunt et al., 2008; Lester & Lagasse, 2010; Lewis et al., 2012).

The third limitation identified is controlling for all covariates. Prenatally ME children typically come from lower SES backgrounds. Low SES and the other difficulties alongside this have negative consequences on language development (Hoff, 2006; Hoff & Tian, 2005; Hughes et al., 2016; J. Haabrekke et al., 2015). This compromises the validity of the research

in this area. For example, the studies that factored out environmental disadvantages weakened the association between ME and low language (Davis & Templer, 1988; de Cubas & Field, 1993; Ornoy et al., 2001; Pulsifer et al., 2008; Vanbaar & Degraaff, 1994; Wilson et al., 1979). In addition, there is an absence of longitudinal studies in this field of research.

The final limitation is lack of robust measures to assess expressive and receptive language. Many of the studies conducted among this age group used IQ assessments to measure verbal components but were not sufficient for assessing the different language components (de Cubas & Field, 1993; Ornoy et al., 2001; Vanbaar & Degraaff, 1994; Wahlsten & Sarman, 2013; Wilson et al., 1979).

2.5 Methadone Exposure, Social Adversity and Caregiver Psychological Factors and Child Language Development

Social adversity and caregiver psychological factors are foundational to optimal language development. Extensive research in this area emphasises that children raised in low SES environments are at a disadvantage for acquiring language (Hoff, 2006; Hughes et al., 2016; Huttenlocher et al., 2002; Jordan et al., 1992; Lloyd et al., 1998). Ornoy et al. (2001) explained that the differences in language outcomes across their groups (see **Table 1.1**) is probably a result of low SES. Wilson et al. (1979) indicated that in their study, differences between groups (see **Table 1.1**) could not be due to gender, ethnic group or SES as these were controlled for. The authors proposed that perhaps the difference was due to lack of contact between the child and the caregiver. Salo et al. (2009) explained that opioid dependent mothers displayed high levels of caregiver insensitivity, intrusiveness and hostility which was associated with poorer language outcomes (Salo et al., 2009).

It have been evidenced that the relationship between low SES and low language is facilitated by numerous factors such as the quality and quantity of utterances within the family, caregiver responsiveness and stimulating activities within the household (Lugo-Gil & Tamis-LeMonda, 2008; Smith et al., 2018).

2.5.1 Quality and Quantity of Linguistic Input Within the Family.

Research suggests that caregivers from high SES families speak more frequently to their children, use richer vocabulary, incorporate a variety of words, ask more questions and use less directive vocabulary compared to caregivers from a low SES family (Hart & Risley, 1995; Hoff-Ginsberg, 1991; Hoff & Tian, 2005; Huttenlocher et al., 2002; Snow et al., 1976). In addition children raised in high SES households are more likely than children raised in low SES households to generate lengthier utterances, perform better on syntax measures and produce more complex speech as toddlers and in the first year of school (Arriaga et al., 1998). Hart and Risley (1995), found that at age 3 years there was a 30 million-word gap difference between children from welfare families and children from white collar families. Not only had the word gap remained at the age of 9 years but the language accumulation gap had continued to widen between the groups as children got older (Hart & Risley, 1995). This seemed to be facilitated by caregiver responsiveness and quantity and quality of vocabulary.

2.5.2 Caregiver Responsiveness. Caregiver responsiveness is the positive child-caregiver communications in which the caregiver offers the appropriate feedback such as positive affect and positive verbal statements (Landry et al., 2012). A hallmark study reported that children with responsive caregivers began utterances at younger ages and reached a 50-word vocabulary milestone at an earlier age (Tamis-LeMonda et al., 2001). Studies have found a robust relationship between SES, caregiver responsiveness and language development (Haabrekke et al., 2015; Konijnenberg et al., 2016; Salo et al., 2009; Smith et al., 2018).

2.5.3 Stimulating Activities. Families from a higher SES background read more, frequently shared reading time with their children, and read books that are lexically and syntactically richer than the books read in families from a low SES background (Berkule et al., 2007; Cooper et al., 2014; Dowdall et al., 2020; Fletcher & Reese, 2005). Perhaps this is a

result of finances, competing demands and high stress (Aikens & Barbarin, 2008; Gershoff et al., 2007; Suchman & Luthar, 2001).

Overall, these findings support the interactionist account of language acquisition, in that early enriched environments and verbal input enable the child to practice emergent language skills (Camarata & Yoder, 2002; Farah et al., 2008; Mol & Bus, 2011; Zimmerman et al., 2009).

Table 1. 1

Summary of Studies Describing Language Outcomes of Children Born to Opioid Dependent Mothers

Author, design Location	Sample (Retention)	Age (years)	Drug	Measures	Findings	Limitations
Davis & Templer (1988) Cross Sectional Norway	28 ME (14 males) 28 C: Non-ME living with substance dependent father: (14 males)	ME : *m* 8.5 C :*m* 11.21	Methadone & Heroin	WISC-R Verbal IQ scale: *i.* Information *ii.* Similarities *iii.* Vocabulary *iv.* Comprehension	No significant difference between ME and C on any subtests Cohen's d = .3	Small sample size No covariate control Examiners weren't blinded child status ME children were significantly younger No inclusion of non-ME, average SES comparison group
de Cubas & Field (1993) Cross Sectional United States	20 ME (11 males) 20 C (11 males)	ME: *m* 7.8 C: *m* 8.5 Range: 6-13 years	Methadone	Kaufman achievement scale (Faces/ places, riddles, reading decoding, reading and understanding)	Significant difference on face & places No significant difference on riddles, reading decoding, and reading understanding ME group performed in average range across subtests	Small sample size Large age variance No covariate control Maternal self-report of drug use Methadone dose not reported Control group not randomly selected
Ornoy et al., (2001) Cross Sectional Israel	31 HEM 33 non-HE substance dependent fathers 32 non-HE low SES 34 HE adopted 33 C (84 males)	5 – 12	Heroin	WISC–R: consists of two subtests: *i.* Vocabulary *ii.* Word similarities	HEM children scored lower on verbal subtests compared to HE adopted and C Cohen's d = .45, 0.50, respectively Non-HE substance dependent fathers, non-HE low SES scored lower on verbal subtests relative to the C No significant difference between HE adopted & C Cohen's d = .11	No covariate control Retrospective maternal self-report of drug use. Methadone dose not reported Unequal gender ratio Examiner was not blinded child status

					All groups scored within average range.	
Pulsifer et al., (2008) Cross Sectional United States	113 ME 31 C (53% males) (Retention) 57%	5	Unspecified Opioids only or Unspecified Opioids and cocaine	PLS-3	No significant difference was found on receptive language between ME and C. Small to medium effect size, Cohen's d = 0.4 Significant difference was found on expressive language and total language skills between ME and C Cohen's d = 0.5	No covariate control Type of opioids not stated Large sample size discrepancy between ME and C Failed to examine gender differences
Vanbaar & Degraaff, (1994) Longitudinal Netherlands	23 ME (11 males) 32 C (15 males) (Retention) ME 78% C 91%	5.5	Methadone Heroin Cocaine	RAKIT IQ Consists of one subtest i. Word meanings	ME scored significantly lower on word meanings, relative to C Cohen's d = 0.7	Small sample size No covariate control Failed to examine gender differences. 9 of ME children were born pre-term
Wahlsten & Sarman (2012) Cross Sectional Sweden	25 BE (15 males)	BE: *m* 5.2 Range: 5-6 years	Buprenorphine	MSCA Consists of *i*. Verbal Scale WPPSI-R Consists of *i*. Verbal Scale	BE children scored significantly below the norms on the MSCA but not on the WPPSI-R BE females performed significantly better on overall MSCA relative to males. Cohen's d = 1.1	No covariate control No examination of social environment impact. No matched control group Small sample size Bias in Published norms
Wilson et al., (1979) Cross Sectional United States	22 HE 20 Drug environment 15 High Risk 20 C (40 males)	Range: 3.1 - 6.4	Heroin	Speech during doll playing task ITPA	No significant difference between groups on doll play task. C performed significantly better on the ITPA than other groups No difference on the ITPA between experimental groups Experimental groups scored in average range	The quantity and types of substances was not verified No covariate control Small sample size

Note. BE, Buprenorphine Exposed. C, Comparison Children. HE, Heroin Exposed. HEM, Heroin Exposed Children in Maternal Care. ITPA, Illinois Test of Psycholinguistic Abilities; Low SES, Low Socioeconomic Status. *m*, Mean. ME, Methadone Exposed. MSCA, McCarthy Scale of Children's Abilities. Non-HE living with substance dependent father, Non-Heroin Exposed living with substance dependent father. Non-HE low SES, Non-Heroin exposed from a low socioeconomic status. OE, Opioid exposed. PLS-3, Preschool Language Scale Third Ed. RAKIT IQ, Revision of the Amsterdam Children's Intelligence Test. WISC-R, Wechsler Intelligence Scale for Children. WPPSI-R, Wechsler Preschool and Primary Scale of Intelligence

CHAPTER 3

Externalising and Internalising Problems in Methadone Exposed Children

Externalising and internalising problems are important developmental constructs as they can influence other developmental domains. For example, a child with externalising or internalising problems is more likely to experience difficulties both academically and socially with their peers (Fujiki et al., 2004; Lee et al., 2019; Roben et al., 2013; St Clair et al., 2011).

Externalising and internalising problems have a high degree of comorbidity, (Beyers & Loeber, 2003; Hannigan et al., 2018; Wiesner & Kim, 2006; Willner et al., 2016; Wolff & Ollendick, 2006), which is the occurrence of two or more conditions (Valderas et al., 2009). It has been well documented that externalising and internalising problems are precursors to poorer life outcomes such as substance dependence (Liu et al., 2011; Loeber et al., 2000; Selinus et al., 2016), criminality (Dodge et al., 2006; Liu et al., 2011), being on welfare (Liu et al., 2011), learning and school difficulties (Arguedas et al., 2016; Howard & Williams, 2018; Hughes et al., 2008; Liu et al., 2011; McCoy et al., 2019; Pedersen et al., 2019), unemployment (Liu et al., 2011), poorer familial interactions (Hughes et al., 2008), peer victimization (Reijntjes et al., 2010), psychological difficulties (Howard & Williams, 2018; Liu et al., 2011), physical health problems, and sleep difficulties (Bub et al., 2016; Howard & Williams, 2018).

It is particularly important to examine externalising and internalising problems, in BE and heroin exposed children as they are at a greater risk of developing externalising and internalising problems (Nygaard et al., 2016; Wahlsten & Sarman, 2013). Specifically, during school years, as there is additional demand on self-regulation, which is strongly associated with externalising and internalising problems (Bakopoulou & Dockrell, 2016; Clegg et al., 2015; Joffe & Black, 2012; Nygaard et al., 2016; Yew & O'Kearney, 2013).

3.1 Externalising Problems in Methadone Exposed Children

Children who experience externalising problems generally present with persistent patterns of hyperactivity, conduct problems and aggression. Externalising problems are prominent among prenatally ME school-aged children and have been well documented in two recent meta-analyses (Andersen et al., 2020; Lee et al., 2020).

Studies employing a mixture of caregiver and teacher ratings reported higher levels of hyperactivity, aggression, conduct behaviours and total externalising problems in OE children relative to the comparison children (de Cubas & Field, 1993; Hjerkinn et al., 2013; Levine & Woodward, 2018; Nygaard et al., 2016; Sarfi et al., 2013).

While some studies reported no difference in specifically externalising problems on the CBCL, a difference was found in total CBCL scores between heroin exposed children and non-exposed children (Soepatmi, 1994; Walhovd et al., 2007). Wahlsten and Sarman (2013) found that teachers rated BE children highly on hyperactivity, however parent ratings did not show this pattern of results.

3.2 Internalising Problems in Methadone Exposed Children

The concept of internalising problems refers to a child's emotional state, which typically reflects difficulties with mood (depression), worry (anxiety) and uncomfortable physical sensations (somatization; Liu et al., 2011; Reynolds & Kamphaus, 2004). An extensive body of evidence has reported that ME and heroin exposed children have higher levels of overall internalising problems relative to comparison children (Bada et al., 2012; de Cubas & Field, 1993; Hjerkinn et al., 2013; Nygaard et al., 2016; Sarfi et al., 2013). A longitudinal study reported that both caregivers and teachers rated heroin exposed children higher on overall internalising symptoms (depression, anxiety, social withdrawal) compared to their peers as measured by the CBCL (Achenbach, 1999; Nygaard et al., 2016). One study reported that biological mothers of ME school-aged children reported that their children

exhibited greater levels of anxiety relative to caregivers of comparison children. However, there was no difference found between the two groups on the depression scale (de Cubas & Field, 1993). Further, maternal caregivers rated their children highly on symptoms of depression, somatization and total internalising problems (de Cubas & Field, 1993).

Gender has been shown to be a significant predictor of externalising and internalising in heroin exposed children (Bada et al., 2012; Ornoy et al., 2001). Further Bada et al. (2012) reported that, relative to females, males had significantly lower slopes over time for externalising and internalising problems.

3.3 Social Adversity and Caregiver Psychological Factors, and Externalising/ Internalising Problems

Social adversity and caregiver psychological factors play a fundamental role in predicting externalising and internalising problems. Research shows that child-parent attachment that is a bond or tie between parent figure and infant based on security and protection (Bowlby, 1982) may become disrupted (Romanowicz et al., 2019) as substance dependent caregivers tend to have chaotic lives.

Ornoy et al. (2001; *see* **Table 1.1**) reported that heroin exposed children living in maternal care and non-heroin exposed children living with a substance-dependent father or living in low SES families displayed higher levels of externalising and internalising problems relative to heroin exposed children in adoption and the comparison children. Similarly, another study reported that the maternal risk model (maternal depression, anxiety, stress, drug use and physical problems) accounted for a significant amount of the overall variance in parent reported externalising and internalising problems (Konijnenberg et al., 2016). However, the teratogenic risk model (dose of methadone or buprenorphine and exposure to other drugs e.g., cigarettes) failed to account for a significant proportion of the variance (Konijnenberg et al., 2016). Sarfi et al. (2013) found that caregiver distress and gender predicted total CBCL scores in children prenatally exposed to methadone or buprenorphine.

The Maternal Lifestyle longitudinal study reported that prenatal poly drug exposure predicted externalising and internalising problems after controlling for covariates (Bada et al., 2012). This study reported that children living with their biological caregivers displayed higher levels of externalising problems compared to substance exposed children in adoption. Moreover, the authors reported that an increase in the number of risk factors by 1 was associated with a 2.14-point increase in externalizing scores (Bada et al., 2012). The authors found that protective factors such as SES and maternal support were associated with decreasing trajectories of internalising problems over time, independent of drug exposure (Bada et al., 2012). Further, an increase in caregiver depression, change in caregivers, and involvement in child protective services increased both externalising and internalising problems (Bada et al., 2012).

In a further study, substance dependent mothers who had comorbid anxiety and depression were twice as likely to report child internalising problems than mothers with a drug dependency without comorbid mental health difficulties (Hser et al., 2015). This trend was not seen with externalising adjustment problems.

A Norwegian study reported that substance exposed children who remained in the care of their biological mothers displayed higher levels of aggression, conduct behaviours, anxiety, depression, and somatization relative to non-substance exposed children. Moreover, this study also reported that, relative to comparison children, substance exposed children who were adopted displayed greater externalising problems but not internalising problems (Hjerkinn et al., 2013).

CHAPTER 4
The Inter-relationships Between Language, Externalising Problems, and Internalising Problems in School Aged Children

In recent years studies have explored the interrelationships between language, externalising, and internalising problems for school-aged children (Fujiki et al., 2004; Roben et al., 2013; St Clair et al., 2011). While these developmental constructs are distinct, their development is interrelated. The demands placed on children in formal education settings increase throughout primary school, as the complexity of academic work increases, along with expectations of independent learning through reading and collaborative learning with peers, which are all reliant on language abilities (Durkin & Conti-Ramsden, 2010; Harrison & McLeod, 2010; McKean et al., 2017).

4.1 Language and Externalising Problems

The relationships between language, externalising problems and internalising problems are well documented in the general literature (Davis et al., 1991; Giddan et al., 1996; St Clair et al., 2011; Yew & O'Kearney, 2013; Yew & O'Kearney, 2015). Early clinical studies reported that a majority of school-aged children diagnosed with behaviour disorders had low language (Davis et al., 1991; Dery et al., 1999; Giddan et al., 1996; Warr-Leeper et al., 1994). A recent meta-analysis consisting of 19 longitudinal studies found that children with low language are at double the risk of displaying externalising problems (Yew & O'Kearney, 2013). A longitudinal study found that conduct problems at age 4 to 6 years follows a curvilinear decreasing trend (Yew & O'Kearney, 2013). Children with low language displayed higher levels of conduct problems compared to their peers over time (Hooper et al., 2003; Levickis et al., 2018; St Clair et al., 2011; Yew & O'Kearney, 2013; Yew & O'Kearney, 2015). Several longitudinal studies have also found that language competence during the preschool years is predictive of overall externalising behaviours

(Petersen et al., 2013), conduct problems (Hooper et al., 2003; Yew & O'Kearney, 2015), hyperactivity (Gooch et al., 2019; Levickis et al., 2018; Petersen et al., 2013), and aggression (Brownlie et al., 2004), over and above covariates during school years.

4.2 Language and Internalising Problems

Children with low language exhibit greater levels of internalising behaviours, specifically anxiety and depressive symptoms, compared to typically developing peers (Beitchman et al., 1996; Conti-Ramsden & Botting, 2008). Some studies have failed to find this (Levickis et al., 2018; Redmond & Rice, 2002; Snowling et al., 2006). The discrepancies in the findings may be a result of different methodologies e.g., teacher reports but not parental reports (Redmond & Rice, 1998, 2002). Perhaps this is because teachers have a much greater foundation for comparing children's functioning as they have a normative referent group of children. In addition, they tend to detect difficulties earlier than caregivers (Nygaard et al., 2016). Moreover, it is evidenced that highly stressed caregivers are more likely to over-report their children's behaviour difficulties (Berg-Nielsen & Wichstrøm, 2012). There is evidence that suggests children's behaviours will change across different contexts such as at home and at school (Redmond & Rice, 1998, 2002).

CHAPTER 5

Aims and Hypotheses

The preceding review suggests that ME children are at more risk of low language, externalising problems and internalising problems than non-exposed comparison children. There are major gaps in the literature. Firstly, there is limited data examining the biological effects, social adversity, and caregiver psychological factors on language outcomes, externalising problems and internalising problems of ME children at age 9.5 years. Secondly, data examining the language components, expressive and receptive, structure and content, remain scarce. Thirdly, there is limited data on teacher rated externalising and internalising problems, which can be more reliable than caregiver ratings (Nygaard et al., 2016). Finally, the associations between these factors for this population have yet to be explored.

The current research draws on the 9.5 year wave of the Christchurch Methadone in Pregnancy study. Empirical findings with this cohort have been previously published and have demonstrated poorer outcomes for the ME group in multiple developmental domains from birth through to age 9.5 years (Davie-Gray et al., 2013; Lean, 2012; Lee et al., 2019). However, language and teacher rated externalising and internalising problems at age 9.5 years have yet to be assessed for in this unique group of children.

Therefore, the specific research aims are as follows:

i. To describe the extent and nature of language, externalising problems, and internalising problems of children born to mothers maintained on methadone at age 9.5 years. *Hypothesis 1* (Extent): At age 9.5 years, children prenatally exposed to methadone will have poorer outcomes in language domains and display higher levels of externalising problems and internalising problems compared with the comparison children. *Hypothesis 2* (Nature): a greater proportion of ME children will have comorbid low expressive and low receptive language, comorbid

externalising problems, and internalising problems, and comorbid low core language, externalising problems and internalising problems relative to the comparison children.

ii. To examine the associations between prenatal methadone exposure, social adversity, caregiver psychological factors, and child language outcomes at age 9.5 years.

Hypothesis: It is expected that statistical adjustment for social adversity and caregiver psychological difficulties will attenuate the between group difference in children's low language. However, it is expected that methadone group status will remain independently associated with poorer developmental outcomes at 9.5 years of age, following adjustment for social adversity and caregiver psychological factors.

iii. To examine the associations between prenatal methadone exposure, social adversity and caregiver psychological factors, and externalising problems/ internalising problems at age 9.5 years. *Hypothesis:* It is expected that statistical adjustment for social adversity and caregiver psychological factors will attenuate the between group difference in children's externalising problems and internalising problems. However, it is expected that methadone group status will remain independently associated with poorer developmental outcomes at 9.5 years of age, following adjustment for social adversity and caregiver psychological factors.

CHAPTER 6

METHODS

6.1 Research Design

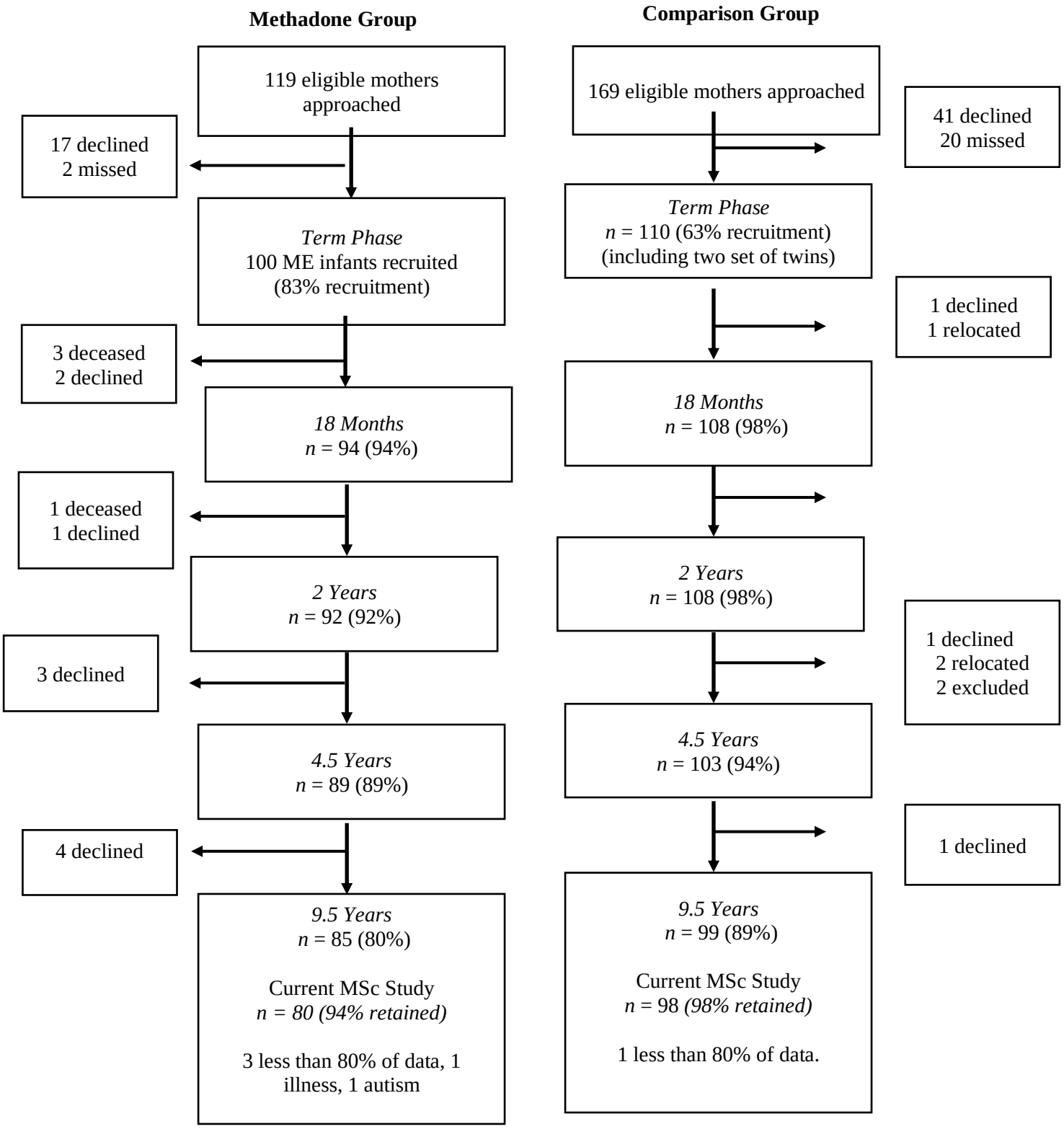
The current research is a cross-sectional study that draws on 9.5-year follow-up data from the Canterbury Methadone in Pregnancy (MIP) study. The larger MIP study is a prospective longitudinal study investigating the developmental outcomes of children who were born to mothers maintained on methadone. This study was conducted by the Canterbury Child Development Research Group in the Department of Psychology. In order to provide context for the current cross-sectional study, the following chapter summarises the larger longitudinal MIPS study participants, alongside the current study procedures, measures used, detailed description of the cohort at 9.5 years and data analysis procedures.

6.2 Methadone in Pregnancy Study Participants

The study participants comprised of two groups of children and their caregivers: the first group was methadone exposed children and the second group was non-ME comparison children (hereafter referred to as the comparison children). Both groups of children were born at the Christchurch Women's Hospital between the years 2003 and 2008. Study exclusion criteria from the study: preterm babies (<32 weeks gestation); diagnosed with Foetal Alcohol Syndrome; congenital abnormality; HIV; born to families who did not speak English; families couldn't consent due to psychological and/or perceptive difficulties. To provide a context for the current study, **Figure 2.1** illustrates a flow diagram of participant retention in the study from term through to age 9.5 years.

Figure 2. 1

Recruitment and Retention Rates of Participants in the Canterbury Methadone in Pregnancy Study



6.2.1 Methadone Participants

Term. Pregnant women enrolled in the MMT were recruited during their second or third trimesters of pregnancy. Follow-ups were at 18 months, 2, 4.5 and 9.5 years of the child's age. 119 mother-infant dyads qualified for the study and of these 100 (83%) mother-infant dyads were successfully recruited. Reasons for non-recruitment included refusals *(n* = 17) and missed recruitment (*n* = 2). The mothers' methadone dosage was regularly monitored, and mothers took the required dose via hospital and drug service records.

18 Months. At 18 months, 94 (94%) participants were retained from term. In this wave, data was collected from home observations, parent-child interactions, and caregiver interviews.

2 Year Wave. At 2 years, 92 (92%) participants agreed to participate, 97% was retained from 18 months. In this wave cognitive, psychomotor, language, executive function and social emotional adjustment data were collected from the children as well as a caregiver interview.

4.5 Year Wave. At 4.5 years, 89 (89%) participants agreed to participate, 96% was retained from the 2 year. Data on child's cognitive, psychomotor, language, executive function and social emotional adjustment were collected and a caregiver interview.

Current Study - 9.5 Year Wave. At 9.5 years, 85 (80% recruitment), of participants agreed to participate, 95% was retained from the 4.5-year wave. Participants were briefed about the study aims and provided consent to complete a range of assessments. Reasons for non-recruitment include declined (*n* = 4).

6.3 Comparison Children Participants

Term: The second group of participants comprised of children born to mothers who reported no illicit opioid use during their pregnancy and were not enrolled in the MMT. The mothers were randomly (using a random number generator), selected from a cohort of

pregnant women that were scheduled to give birth from 2003 to 2008 at Christchurch Women's Hospital. Of the 169 mother-infant dyads who met the inclusion criteria, 110 (63%) participated in the study, including two sets of twins. Reasons for non-participation were declined to participate (n = 41) and non-traceable (n = 20). To ensure that the comparison sample was representative of the general population of the region (Canterbury), the regional census was examined as an indicator of social strata.

Current Study - 9.5 Year Wave: At 9.5 years, 99 caregivers and their children agreed to participate, 96% was retained from the 4.5-year wave. Caregivers were briefed on the study aims and consent was obtained from the caregivers to complete a range of assessments. Reasons for non- recruitment included declined (n = 1) and relocated (n = 1).

6.4 Characteristics of Methadone Children Participants and Comparison Children Participants at Age 9.5 Years

The following section provides a description detailing group characteristics at the 9.5-year wave. At the 9.5-year wave, participants' characteristics were compared between the ME group and the comparison group, as shown in **Table 2.1.**

Children Characteristics. The ME children were more likely to be older (p = .02) and have a lower IQ score relative to the comparison children (p <.001). However, these scores were still within average range (Wechsler, 2011). A larger proportion of ME children were males relative to the comparison group, however there was not a significant difference (57.5% vs 46.9%, p = .16).

Social Adversity. Caregivers with ME children were older (p <.001). A greater proportion of caregivers with ME children were single caregivers (83.3% vs 21.3%, p <.001) and from a low SES (77.4% vs 19.4%, p <.001) relative to the comparison caregivers. Minority groups made up 17.5% of caregivers with ME children and 21.4% of the comparison caregivers.

Caregiver Arrangement. Approximately, 52.5% of ME children remained in the care of their biological mothers compared to 99% of the comparison children. ME children who no longer lived with their biological mothers were living with their fathers/ grandparents (32.5%) or were adopted (15%). From the comparison children, one participant was in paternal care. (1%).

Caregiver Psychological Factors. Caregivers of ME children displayed significantly higher levels of anxiety, depression, and stress relative to the comparison caregivers ($p < .001$).

Table 2. 1

Characteristics of Methadone Exposed and Comparison Children at 9.5 Years

	Methadone Participants (*n* = 80)	Comparison Participants (*n* = 98)	*t/χ2*	*p*
Child Characteristics at 9.5-year assessment				
M (SD) Child Age (years)	9.63 (.40)	9.50 (.34)	2.31	.02
M (SD) IQ score at age 9.5 years.	93.86 (14.02)	108.61 (13.67)	7.07	<.001
% (n) Gender male	57.5 (46)	46.9 (46)	1.97	.16
Social Adversity				
M (SD) Primary Caregiver Age (years)	45.71 (10.45)	41.40 (5.43)	3.34	<.001
% (n) Single Caregiver	83.3 (48)	21.3 (13)	42.71	<.001
% (n) Low Family SES	77.4 (65)	19.4 (19)	71.19	<.001
% *(n)* New Zealand European	82.5 (66)	78.6 (77)		
% *(n)* Minority Group	17.5 (14)	21.4 (21)	1.03	.51
Caregiver Arrangement				
% (*n*) Biological Mother	52.5 (42)	99.0 (97)		
% (n) Father/ Relatives	32.5 (26)	1.0 (1)		
% (n) Foster	15.0 (12)	-	55.66	<.001
Caregiver Psychological Factors				
M (SD) Anxious symptoms	5.42 (7.98)	1.76 (3.04)	3.52	<.001
M (SD) Depressive Symptoms	6.32 (9.00)	2.17 (3.76)	3.52	<.001
M (SD) Stress Symptoms	9.05 (8.67)	5.43 (5.61)	3.22	<.001

Note. M (SD), Mean (Standard Deviation). *n*, number of participants.

6.5 Assessment Procedure at the 9.5-Year Follow-up

6.5.1 Ethical Approval. Ethical consent for the study at the 9.5-year wave was obtained from the Southern Health and Disability Ethics Committee (Reference: urb/07/10/042, see appendix A). At 9.5 years primary caregivers of children were contacted using information from the preceding waves. Medical records were reviewed with assistance from the CCDRG Senior Research Nurse Specialist, for families with invalid contact details. In the initial contact with the primary caregivers a briefing about the study was made, followed by an invitation to participate in the study. Families who agreed to participate were sent information confirming their details and detailing the aims of the study.

6.5.2 Consent. At 9.5 years of age, children participated in extensive developmental assessments that were conducted at the Child Development Research House at the University of Canterbury. Prior to administering the assessments, caregivers were informed of the study aims, as well as the different assessments their child would complete. In addition, caregivers understood that participation was voluntary and that they could withdraw at any stage, anonymity was discussed with the caregivers. Subsequently three consent forms were discussed with the caregiver's: *i.* participation of themselves and their children; *ii.* consent to be video recorded; *iii.* consent to contact the child's teacher and request them to complete an interview booklet (see Appendix B).

6.5.3 Assessment Administration. A registered clinical psychologist administered the assessments along with trained academics. As with previous waves of the study, the researchers were blind to the child's group status. The child and caregiver completed their assessments simultaneously in different rooms. Prior to administering any assessments, the child was informed about the task at hand and oral approval was obtained. Breaks were offered to children at regular intervals to avoid fatigue. Assessments were discontinued if the child no longer wanted to participate. Concurrently, a trained CCDRG researcher interviewed

the caregiver, using a structured interview. Home and school interviews were organised in cases where caregivers and children could not access the interview site. After the child assessments and caregiver interviews were completed, caregivers were gifted a voucher of their choice, and the children were given a small gift as an appreciation for participating in the study.

6.5.4 Teacher Data. Following the assessment, the child's teacher was contacted via mail. This included information that the child was participating in a child development study, however teachers remained blind to the child's group status. The mailed parcel also included The Behaviour Assessment System for Children, Second Edition - BASC 2, (Reynolds & Kamphaus, 2004) questionnaire, and a self-addressed and prepaid return envelope.

6.6 Current Study Measures

6.6.1 Language Measures. The Clinical Evaluation of Language Fundamentals - Fourth Edition - CELF-4 (Semel et al., 2006) was employed to measure language components. The CELF-4 comprises of three composites: The Core Language Composite, the Expressive Language Composite, and the Receptive Language Composite. The Core Language Composite is the total of all the subtests (*see below for description*). The Expressive Language Composite comprises of Recalling Sentences, Formulating Sentences and Word Class Expressive subtests. The Receptive Language Composite comprises of Concepts and Following Directions, and Word Class Receptive subtests. Items on each scale increase in difficulty as the child progresses through the assessment. Subtests are discontinued when the child makes 5 to 7 consecutive errors, depending on the subtest. To attain a score for the different language composites, raw scores from the appropriate subtests are added and then converted into standardised scores (mean 100; standard deviation 15), which are obtained from the CELF 4 manual. Higher standard scores indicate better language

abilities. CELF 4 data was collated from June 2013 to December 2017 by clinical psychologists.

i. *Concepts and Following Directions:* evaluates the individual's ability to comprehend verbal instructions (including concepts, such as, first, above, but not); remember the serial order of instructions and identify pictured objects amongst several choices.

ii. *Recalling Sentences:* evaluates the individual's ability to listen to spoken sentences and repeat them back verbatim.

iii. *Formulating Sentences:* evaluates the individual's ability to produce a semantically and grammatically correct sentence from a given word.

iv. *Word Classes Expressive:* evaluates the individual's ability to explain how the two words from.

v. *Word Classes Receptive:* evaluates the individual's ability to understand a semantic relationship between two given words.

In the current study, the CELF-4 standard scores (mean = 100, SD = 15) will be interpreted using three cut-off scores (≤ 71 = Very Low; 71-85 = Low; ≥ 86 = Typically Developing (TD)). These cut off points are an adapted version of those used in the CELF-4 manual (Semel, Wiig & Secord, 2003). The CELF-4 language composites are recoded to 0 = TD; 1 = low; 2 = very low. When a dichotomous split is required, the lower two categories will be collapsed into one (also called "low language") with a cut off 1 SD below the published mean norms (standard scores ≥85). The CELF-4 language subtests for the dichotomous split will be recoded to 0 = TD; 1 = low. The test- retest reliability for the CELF-4 subtests ranged from .88 to .92, with a split half reliability of .87-.95 (Semel et al., 2003).

6.6.2 Externalising and Internalising Problem Composite. The BASC 2 (Reynolds & Kamphaus, 2004) was employed to measure externalising and internalising problems. The BASC-2 is an extensive multi-factorial assessment designed to assess adaptive

and maladaptive behaviours across a variety of settings, between the ages of 2 to 25 years. The current study used the Teacher Rating Scale (TRS), which was completed by the child's current teacher. Teachers rated the child's externalising and internalising behaviours on a 4-point Likert scale (Never, Sometimes, Often, Always). The TRS comprises of 15 primary scales constituting five composites including Adaptive Skills, Behavioural Symptoms, Externalising Problems, Internalising Problems, and School Problems, as well as seven content scales for additional data if required. The reliability and validity for the BASC 2 is well validated across various races, ethnic and cultural groups, SES, geographic locations and special needs groups (Reynolds & Kamphaus, 2004). The reliability for the BASC 2 composites for a general norm sample are in the mid .90s for the Teacher Rating, Externalising Problems Composite and range from .80s to .90s for the Teacher Rating, Internalising Problems Composite. Individual Teacher Rating scale's reliability ranges from .85 to .89 (Reynolds & Kamphaus, 2004).

The Externalising Problems Composite was employed to assess disruptive and under controlled behaviour. It consists of a Hyperactivity scale, an Aggression scale, and a Conduct Problems scale. A higher score indicates greater presence of externalising behaviour.

The Internalising Problems Composite was employed to assess non- disruptive behaviours and over controlled behaviours. It consists of an Anxiety scale, a Depression scale, and a Somatisation scale. This composite assesses over-controlled behaviours. Higher scores indicate greater levels of internalising behaviours.

The BASC-2 data was interpreted by creating three groups and using two cut off points. The cut off points and labels were derived from the BASC-2 manual and were adhered to in this research: *t* scores = 41-59 Typically Developing; 60-69 At Risk; ≥70 Clinically Significant. The BASC-2 data was also interpreted dichotomously: Individuals who fell into the "At Risk" and "Clinically Significant" categories (a score of ≥60), were

combined into one group and referred to as having externalising or internalising problems. Participants who experienced externalising and/or internalising problems within these severity brackets were coded to 1; participants who fell within the Typically Developing were recoded to 0.

6.7 Covariate Measures

Caregivers completed a comprehensive maternal lifestyle interview and questionnaire given by a CCDRG Senior Nurse Specialist. Seven factors were derived from the interview and included in this study. The Biological variables employed included methadone group status and gender. The Social Adversity variables that were employed included SES, minority group, single caregiver, and primary caregiver changes. The Caregiver Psychological factors that were measured included the depression, anxiety, and stress scale (DASS) scores. All scales were dichotomised, apart from primary caregiver changes and employed to predict low language, externalising problems, and internalising problems. Factors were selected on a theoretical basis (e.g., Dual Hazard Model; Lester & Tronick, 1994), current literature or methadone participants significantly differed on these factors relative to the comparison participants.

6.7.1 Biological Factors

Methadone Group Status: Children whose caregivers were not enrolled in the MMT programme during their pregnancy, and did not report taking illicit substances, were coded 0 for comparison children. Children whose mothers were enrolled in the MMT programme during their pregnancy were coded 1 for Methadone exposed.

Gender: In the caregivers structured interview participants were asked about their child's gender. Females were coded 0, and males were coded 1.

6.7.2 Social Adversity Factors

Socioeconomic Status (SES): The Elley-Irving Socio- Economic Index (Elley & Irving, 2003) was used based on the highest rated occupation of the caregiver or their partner. The Elley- Irving Index (Elley & Irving, 2003) has six levels; 1 indicates a highest ranking (professional/ managerial technical employment) and 8 indicates the lowest ranking (unskilled/unemployed). SES was dichotomised, if participants were employed in professional, managerial or technical jobs they were coded 0; if participants were unemployed, in an unskilled or semi-skilled profession they were coded 1.

Minority Group: Participants were assigned 0 if they reported being of New Zealand European descent or any other European descent. Caregivers were assigned 1 if they reported being of an ethnic minority (NZ Māori, Pacific Islander, Asian, African, Middle Eastern, South American, individuals that identified with more than one ethnicity).

Single Parent: Participants who reported being a primary caregiver living with a partner, engaged, or married were coded 0. Participants who reported being a primary caregiver without a partner or in a relationship were coded 1.

Number of Caregiver changes: Children's primary caregivers reported who the child's maternal and paternal figures were for each six-month period preceding the child's developmental assessments at 18 months, 2 years, 4.5 years, and 9 years. The present study classed the child's primary caregiver as the person who was currently looking after the child for most of the time. Children's total number of primary caregiver changes was calculated through the summation of the total number of primary caregivers from birth to age 9 years.

6.7.3 Caregiver Psychological Factors. The Depression, Anxiety, Stress Scale (DASS; Lovibond & Lovibond, 1995) was used to measure caregiver's symptoms of anxiety, depression and stress. Each of the three scales contains seven items. Participants are asked to use a 4-point scale to rate the extent to which they had experienced symptoms of anxiety, depression and somatization over the past week.

The Depression Scale assesses hopelessness, anhedonia, lack of interest/involvement. Scores are divided into categories of severity: 0 - 9 = normal; 10 - 13 = Mild; 14 - 20 = Moderate; 21 - 27 = Severe; ≥28 = Extremely Severe. The Anxiety Scale assesses autonomic arousal, situational; anxiety, subjective experience of anxious affect. Scores are divided into categories of severity: 0 - 7 = normal; 8 - 9 = Mild; 10 - 14 = Moderate; 15 - 19 = Severe; ≥20 = Extremely Severe. The Stress Scale assess for difficulties relieving, nervous arousal and being easily agitated and upset. Scores are divided into categories of severity: 0 - 14 = normal; 15 - 18 = Mild; 19 - 25 = Moderate; 26 - 33 = Severe; ≥34 = Extremely Severe.

The scales on this measure were dichotomised: caregivers who scored in the mild range were coded 0 and caregivers who scored in the moderate, severe and extremely severe ranges were coded 1. The reason for this is that data indicates that clinical populations scored in the moderate range and above on the different scales (Lovibond & Lovibond, 1995). The total scale score had a Cronbach internal consistency of 0.89. The test retest and split half reliability coefficient score were 0.99 and 0.96, respectively (Akin & Cetin, 2007).

6.8 Statistical Analyses

Data analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 25. Statistical significance was set at $p < .05$. Bonferroni's correction for chance significant results was not carried out. Note this increases the chance of a type I error. Three analyses were conducted:

i. Independent sample *t* tests and chi square analyses were conducted to compare language outcomes, externalising problems and internalising problems between ME children and the comparison children at 9.5 years. Cohen's *d* effects sizes were calculated to provide the standardised difference between the two sample means.

ii. Chi square analyses and odds ratios were calculated to examine between group differences and comorbidities on language outcomes and internalising/externalising problems between ME children and the comparison children. Comorbidities were represented using Venn diagrams to allow visual inspection, chi square and *p* values were calculated to see if there was a significant difference between the two groups.

iii. Hierarchical logistic regression analyses were conducted to examine the predictive ability of biological, social adversity and caregiver psychological factors for language outcomes, externalising problems and internalising problems among the whole cohort at age 9.5 years.

CHAPTER 7

RESULTS

7.1 Language, Externalising Problems, and Internalising Problems of Methadone Exposed Children and Comparison Children at Age 9.5 Years

The performance of ME children and the comparison children across language domains measured by the CELF 4, and externalising problems and internalising problems as measured by teacher report BASC 2 are presented below.

7.1.1 Language Indices. **Table 7.1** presents the descriptive data illustrating the differences on the Core, Expressive and Receptive Language Indices between the ME children and the comparison children at 9.5 years of age. As shown, ME children achieved significantly lower mean scores on the Core Language Index (CLI) (m = 88.95 vs m = 105.69, p <.001), Expressive Language Index (m = 91.23 vs m = 109.69, p <.001), and Receptive Language Index (m = 90.49 vs m = 102.10, p <.001) relative to the comparison children, respectively. The ME children performed poorly relative to the comparison children across all expressive language subscales, including: Sentence Recall, that is the ability to recall and verbalise a sentence verbatim (m = 6.90 vs m = 9.55 p < .001); Formulating Sentences, that is the ability to formulate grammatically and semantically correct sentences (m = 8.48 vs m = 12.28 p <.001); and Word Class Expressive, in which the children verbally explain the semantic relationship between two words (m = 10.15 vs m = 12.90; p <.001).

As shown in **Table 7.1** the ME children performed poorly relative to the comparison children across all receptive language subscales including: Concepts and Following Direction, which is the ability to recall and follow increasingly complex verbal instructions (m = 7.89 vs m = 9.68; p <.001); Word Class Receptive, which involves understanding and distinguishing the semantic relationship between two words (m = 8.81 vs m = 10.95; p <.001). Word Class Total is a total score of Word Class Expressive and Word Class

Receptive. ME children performed poorly on this subscale relative to the comparison children (*m* = 9.50 vs *m* = 12.08; *p* <.001).

It must be noted that whilst there were statistically significant differences between the ME children and the comparison children across all the language indices, the mean scores for the scales in the ME children ranged from 88.95 to 91.23, and thus are within average range relative to the published normative population sample. **Table 7.1** also shows that there were large effect sizes between the ME children and the comparison children, across the CELF-4 indices, as indicated by Cohen's *d*. The effect sizes were larger for Expressive Index (*d* = 1.10) than for the Receptive Index (*d* = .85).

7.1.2 Externalising Problems Composite. As shown in **Table 7.1** teacher ratings indicated that ME children displayed higher levels of externalising problems relative to the comparison children (*m* = 59.94 vs *m* = 47.64; *p* <.001). ME children relative to the comparison group children displayed greater levels of Aggression (*m* = 61.34 vs *m* = 48.04 *p* <.001), Conduct problems (*m* = 58.24 vs *m* = 46.11 *p* <.001), and Hyperactivity (*m* = 59.25 vs *m* = 48.99; *p* <.001). Within the Externalising Problems Composite (EPC), large effect sizes between ME children and the comparison children were seen across the subscales.

7.1.3 Internalising Problems Composite. As shown in **Table 7.1** teacher ratings indicated that ME children displayed greater levels of internalising problems relative to the comparison children (*m* = 56.79 vs *m* = 51.92; *p* <.001). ME children relative to the comparison children displayed significantly greater levels Depression (*m* = 60.81 vs *m* = 50.70, *p* <.001). However, no difference was found on Anxiety (*m* = 54.49 vs *m* =52.20; *p* <.001) and Somatization (*m* = 51.36 vs *m* = 51.36; *p* <.001) between ME children and the comparison children.

Table 7. 1

Language, Externalising Problems, and Internalising Problems in Methadone Exposed and Comparison Children at Age 9.5 Years

Measures	Methadone Exposed (n = 80)	Comparison Group (n = 98)	t	p	d	(95% CI)
M (SD) Core Language	88.95 (18.26)	105.69 (14.0)	-6.92	<.001	-1.03	(11.97 - 21.51)
Range	41 - 123	68 - 131				
Word Class Total	9.50 (2.98)	12.08 (2.53)	6.26	<.001	-0.93	(1.77 - 3.40)
M (SD) Expressive Language	91.23 (18.46)	109.62 (14.77)	-7.38	<.001	-1.10	(13.48 - 23.31)
Range	49 - 128	70 - 134				
Recalling sentences	6.90 (3.10)	9.55 (2.85)	-5.93	<.001	-0.89	(1.77 - 3.53)
Formulating Sentences	8.48 (4.02)	12.28 (3.53)	-6.71	<.001	-1.0	(2.68 - 4.92)
Word Class Expressive	10.15 (3.10)	12.90 (2.48)	-6.58	<.001	-1.0	(1.92 - 3.57)
M (SD) Receptive Language	90.49 (14.84)	102.10 (12.31)	-5.71	<.001	-0.85	(7.60 - 15.63)
Range	50 - 118	67 - 130				
Concepts, Following Directions	7.89 (3.03)	9.68 (2.69)	-4.18	<.001	-0.62	(0.95 - 2.64)
Word Class Receptive	8.81 (2.65)	10.95 (2.40)	-5.64	<.001	-0.85	(1.39 - 2.88)
M (SD) Externalising Problems	59.94 (13.86)	47.64 (8.95)	-6.81	<.001	1.05	(-15.88 - -8.88)
Range	41 - 59	41 - 47				
Aggression	61.34 (16.25)	48.04 (8.96)	-6.51	<.001	1.01	(-17.35 - -9.25)
Conduct	58.24 (14.50)	46.11 (9.70)	-6.35	<.001	0.98	(-15.90 - -8.35)
Hyperactivity	59.25 (11.53)	48.99 (8.86)	-6.49	<.001	1.0	(-13.39 - -7.14)
M (SD) Internalising Problems	56.79 (11.31)	51.92 (11.94)	-2.73	.01	0.42	(-8.38 - -1.36)
Range	39 - 60	39 - 48				
Anxiety	54.49 (11.16)	52.20 (11.73)	-1.32	.19	0.20	(-5.74 - 1.14)
Depression	60.81 (14.60)	50.70 (11.0)	-5.08	<.001	0.78	(-13.93 - -6.29)
Somatization	51.36 (10.87)	51.36 (13.28)	.003	.10	-	(-3.68 - 3.69)

Note: *M (SD)*, Mean (Standard Deviation). *n*, number of children participants

7.2 Low Language, Externalising Problems, and Internalising Problems in Methadone Exposed Children and Comparison Children at Age 9.5 Years

Table 7.2 displays the extent of low language, externalising problems and internalising problems in ME and comparison children. The following cut off categories were used for this analysis: 1 SD below the mean to define low language on CELF-4 subtests and *t* scores of over 60 on teacher reported externalising and internalising problems on the BASC-2. Overall, the results showed that a greater proportion of ME children were experiencing difficulties across the Language Indices and in the EPC compared to the comparison children ($p < .001$). However, no difference was found between the ME children and the comparison children on the Internalising Problems Composite (IPC) ($p = .65$).

7.2.1 Core Language Index. As shown in **Table 7.2**, over half (54 %) of ME children and the majority (86%) of comparison children achieved scores in the Typically Developing Range on the CLI. ME children's risk for performing in the Low Range on the CLI was almost 3.52 times greater than the comparison children (22.5% vs 10.2%, OR = 3.52 [1.49 - 8.28], $p = .003$). Nearly a quarter (24%) of ME children and 4% of the comparison children achieved a core language score in the Very Low Range. The risk for ME children performing in the Very Low Range on the CLI was 9.26 times greater than the comparison children (OR = 9.26 [2.97 - 29.41], $p <.001$).

7.2.2 Expressive Language Index. As shown in **Table 7.2**, two-thirds (67%) of ME children and the majority of (94%) of the comparison children achieved an expressive language score in the Typically Developing Range. The risk for ME children performing in the Low Range on the Expressive Language Index was 7.35 times greater (21.3% vs 4.1%, OR = 7.35 [2.36 - 23.26], $p < .001$), and 8.70 times greater for performing in the Very Low Range (12.5% vs 2.0%, OR = 8.70 [1.83 - 41.67], $p <.001$) relative to the comparison children.

7.2.3 Receptive Language Index. As shown in **Table 7.2**, two thirds of ME children (68%) and the majority (84%) of the comparison children performed in the Typically Developing Range on the Receptive Language Index. The risk of ME children achieving a receptive language score in the Low Range was 1.62 times greater than the comparison children, however this was not a statistically significant difference (20% vs 15.3%, OR = 1.62 [0.74 - 3.55], $p = 0.23$). The risk for ME children achieving a receptive language score in the Very Low Range was 15.15 times greater than the comparison children (12.5% vs 1.0%, OR = 15.15 [1.89 - 125.0], $p < .001$). Only one comparison child scored in the Very Low Range on the Receptive Language Index, which explains the large confidence interval.

7.2.4 Externalising Problems Composite. As shown in **Table 7.2**, just over half (55%) of the ME children and most of the comparison children (91%) displayed no externalising problems (scoring within the average range). Teacher ratings indicated that ME children were 6.47 times more likely to display At Risk externalising problems relative to the comparison children (20.3 % vs 5.2 %, OR = 6.47 [2.22 - 18.85], $p < .001$) and had 10.12 times the risk of displaying Clinically Significant externalising problems relative to the comparison children (25.3% vs 4.2%, OR = 10.12 [3.26 - 31.44], $p < .001$).

7.2.5 Internalizing Problems Composite. As shown in **Table 7.2**, 62% of ME children and 55% of the comparison children displayed no internalising problems (scoring within the average range), according to their teachers. Teacher ratings indicated that ME children were 1.48 times more likely to display At Risk internalising problems, relative to the comparison children. However, this was not a significant difference (21.8% vs 13.5%, OR = 1.48 [0.65 - 3.36], $p = 0.36$). Teacher ratings showed no group difference in the likelihood of ME children or the comparison children to have Clinically Significant internalising problems (14.1% vs 10.4%, OR = 1.24 [0.48 - 3.18], $p = 0.65$).

Table 7. 2

Low Language, Teacher Rated Externalising Problems, and Internalising Problems in Methadone Exposed and Comparison Children at Age 9.5 Years

	Methadone (*n* = 80)	Comparison (*n* = 98)	*p*	$\chi 2$	Odds Ratio (95% CI)
Core Language					
Very low range % *(n)*	23.8 (19)	4.1(4)	<.001	19.09	9.26 (2.97 - 29.41)
Low range % *(n)*	22.5 (18)	10.2 (10)	.003	8.90	3.52 (1.49 - 8.28)
TD Range % *(n)*	53.8 (43)	85.7(84)			
Expressive					
Very low range % *(n)*	12.5 (10)	2.0 (2)	<.001	10.10	8.70 (1.83 - 41.67)
Low range % *(n)*	21.3 (17)	4.1 (4)	<.001	14.83	7.35 (2.36 - 23.26)
TD Range % *(n)*	66.3 (53)	93.9 (92)			
Receptive					
Very low range % *(n)*	12.5 (10)	1.0 (1)	<.001	10.85	15.15 (1.89 - 125.0)
Low range % (*n*)	20.0 (16)	15.3 (15)	.23	1.47	1.62 (0.74 - 3.55)
TD Range % *(n)*	67.5 (54)	83.7 (82)			
Externalising					
Clinically Significant % *(n)*	25.3 (20)	4.2 (4)	<.001	21.17	10.12 (3.26 - 31.44)
At Risk % *(n)*	20.3 (16)	5.2 (5)	<.001	14.12	6.47 (2.22 - 18.85)
Average % *(n)*	54.3 (43)	90.6 (87)			
Internalising					
Clinically Significant % *(n)*	14.10 (11)	10.4 (10)	.65	0.20	1.24 (0.48 - 3.18)
At Risk % *(n)*	21.8 (17)	13.5 (13)	.35	0.86	1.48 (0.65 - 3.36)
Average % *(n)*	61.5 (48)	55.2 (53)			

Note. BASC Composites: Average 41-59; At Risk 60-69; Clinically Significant >70. Language Indices: Typically developing (TD) >86; Low Language 85-71; Very low <70. *n*, number of children participants.

7.3 Comorbidities in Low Language, Externalising Problems, and Internalising Problems in Methadone Exposed Children and Comparison Children

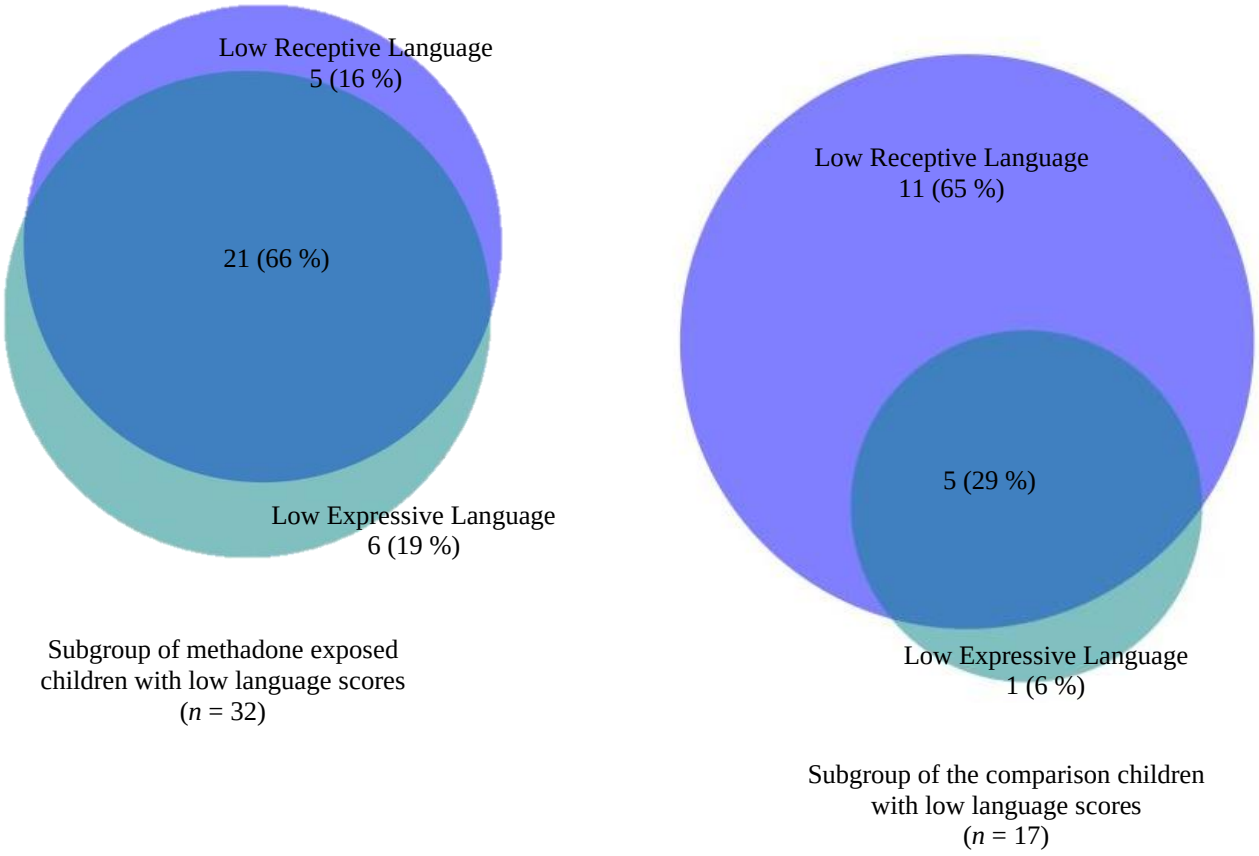
The following set of analyses was conducted to describe the nature of comorbidities in low language, externalising problems and internalising problems in ME children and comparison children at 9.5 years of age. Throughout this section, note that subgroups of the ME and comparison children are used: those children who scored in the Low or Very Low Range on the language indices and/or displayed At Risk or Clinically Significant externalising problems or internalising problems.

7.3.1 Low Expressive and Receptive Language Comorbidity. The patterns of comorbid low expressive and low receptive language ('low' score <1 SD below the mean) among the subgroups of ME children and comparison children are examined next. As shown in **Figure 7.1**, two thirds (66%) of the ME children subgroup with a low score in either domain of language had comorbid low expressive language and low receptive language. In contrast, almost a third (29%) of the comparison children had comorbid low expressive language and low receptive language and this was statistically significant (χ^2 = 22.52, p <.001).

7.3.2 Externalising Problems and Internalising Problems Comorbidities. The patterns of comorbid externalising problems and internalising problems ('At Risk' score of ≥60) among ME children and the comparison children are examined next. As shown **Figure 7.2**, of the subgroups of children who scored 'At Risk' in either the EPC or IPC, just under half of ME children (44%) displayed comorbid externalising and internalising problems compared with under one fifth of the comparison children (17%), and this was a statistically significant difference (χ^2 = 30.0, p < .001). As shown, a greater proportion of the ME children displayed externalising problems only (37%) relative to the comparison children (14%). However, a greater proportion of the comparison children displayed internalising problems only (69%) relative to the ME children (19%).

Figure 7. 1

Patterns of Low Expressive and Receptive Language Comorbidity Amongst Methadone Exposed and Comparison Children on the Clinical Evaluation of Language Fundamentals Fourth Edition- (CELF-4)

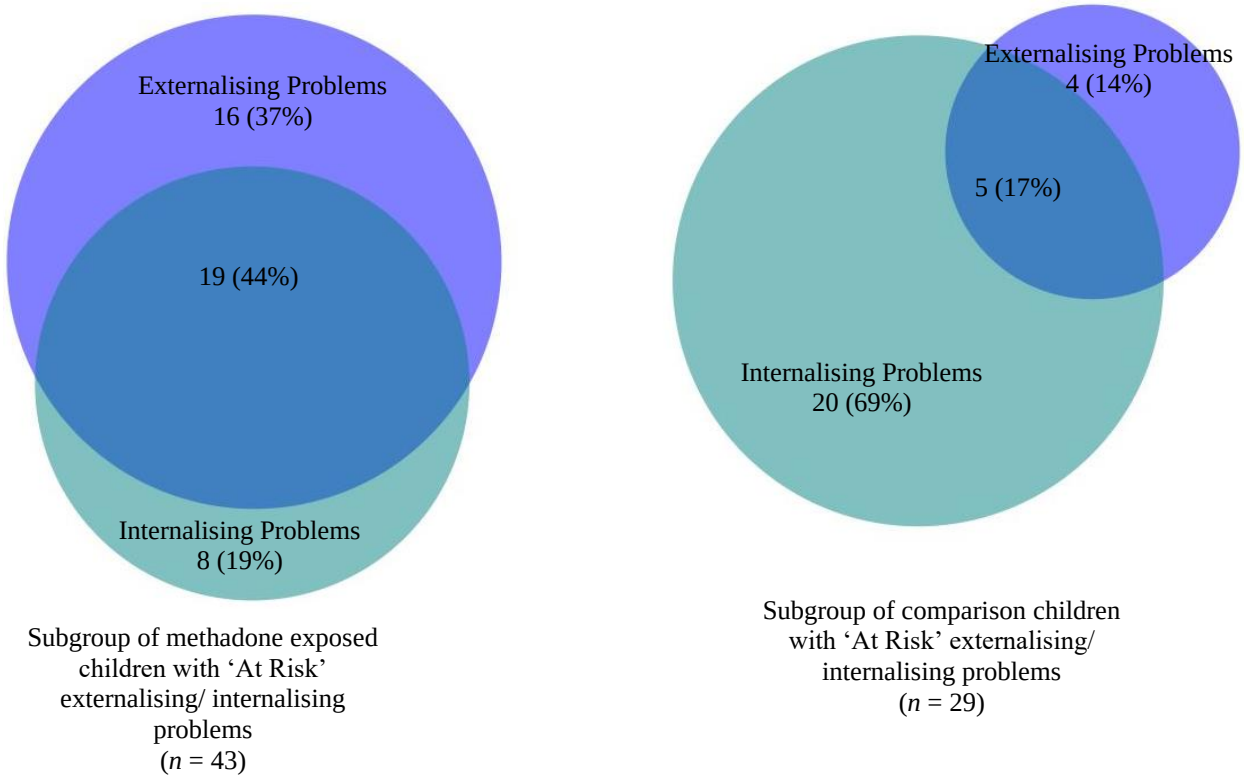


Subgroup of methadone exposed children with low language scores (n = 32)

Subgroup of the comparison children with low language scores (n = 17)

Figure 7. 2

Patterns of Comorbid Externalising Problems and Internalising Problems Amongst Methadone Exposed and Comparison Children on the Behaviour Assessment Systems for Children Second Edition (BASC-2)



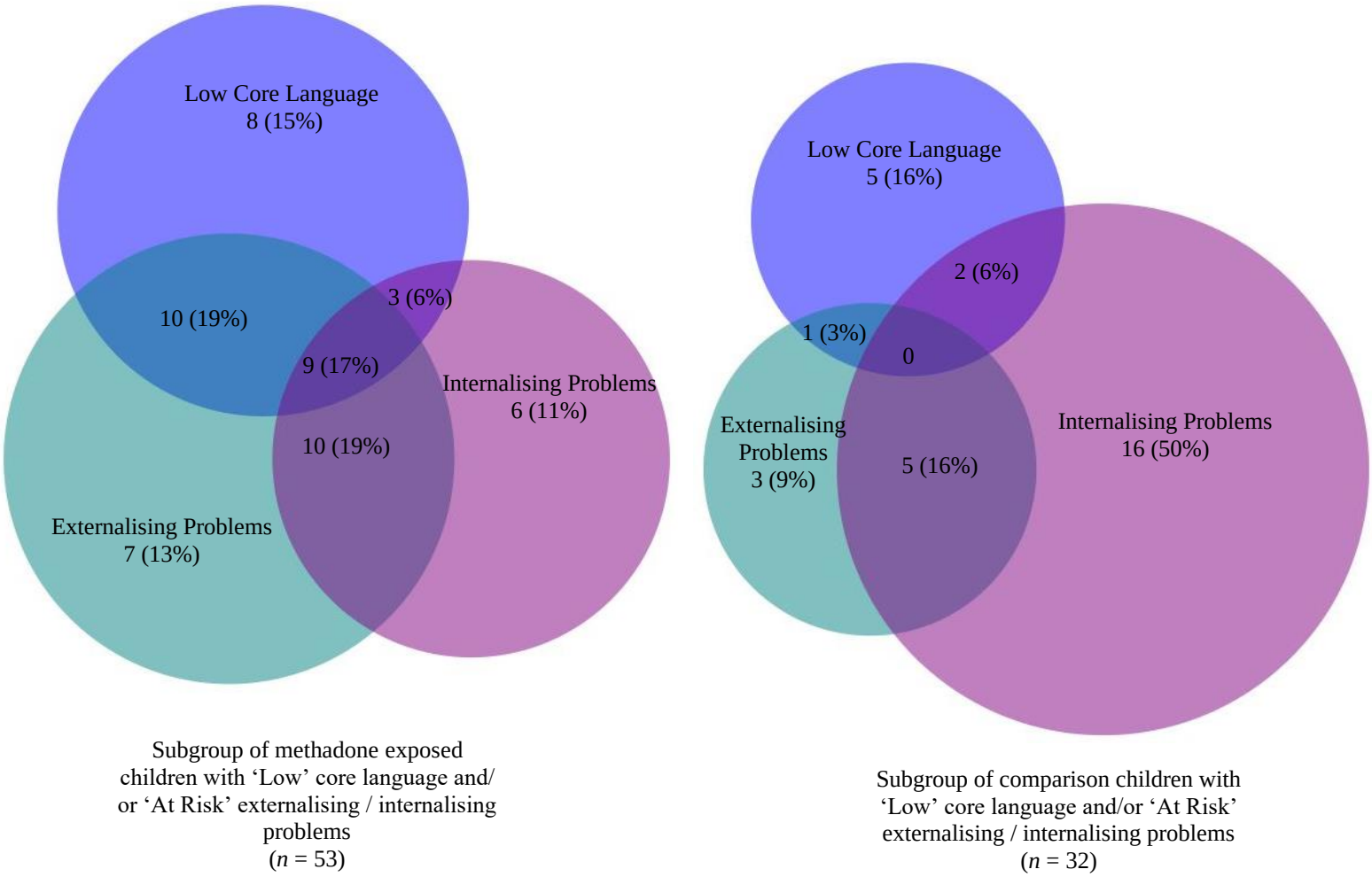
7.3.3 Low Core Language, Externalising Problems, and Internalising Problems

Comorbidities. The patterns of comorbid low core language, externalising problems, and internalising problems among ME children and the comparison children subgroups are examined in **Figure 7.3**. The most common single area of difficulty for the comparison subgroup was internalising problems (50%) whereas the ME subgroup showed more variation (low language only 15%; externalising problems only 13%; internalising problems only 11%). The ME subgroup was also more likely to show comorbidities, for example, 17% displayed difficulties in all three areas (low core language, externalising problems, and internalising problems) compared to none of the comparison children ($\chi^2 = 38.98$, $p < .001$), this was a statistically significant difference. A greater proportion of ME children displayed comorbid

patterns of low core language and externalising problems (19% vs 3%) than the comparison children.

Figure 7. 3

Patterns of Comorbid Low Core Language, Externalising Problems, and Internalising Problems Amongst Methadone Exposed and Comparison Children at age 9.5 Years



7.4 Predictors of Low Language, Externalising Problems, and Internalising Problems in Methadone Exposed Children and Comparison Children at Age 9.5

The following section will examine social adversity and caregiver psychological predictors of Low language, externalising problems and internalising problems among ME and comparison children (combined group).

A series of three stage hierarchical logistic regression analyses follows **(Tables 7.3, 7.4, 7.5)** with CLI, EPC and IPC as the independent dichotomous variables. Each analysis was completed in three steps. In the first stage model (Step 1), prenatal methadone group status and child gender were entered as predictors. The second stage model (Step 2), then adds caregiver minority group status, single caregiver status, caregiver SES and the number of caregiver changes. The third stage model (Step 3) then adds the DASS scores: anxiety, depression and stress. The social adversity and caregiver psychological variables were selected based on the differences between ME and comparison children in this cohort from previous research (Jordan, 2018; Bennett, 2018), and the Dual Hazard Model (Lester & Tronick, 1994).

7.4.1 Predictors of Low Core Language. Table 7.3 displays the results of a 3-stage hierarchical logistic regression used to predict dichotomous scores on the CLI. The CLI was selected as a measure of overall language.

In the first stage model (Step 1) of methadone group status and child gender predicting dichotomous CLI score correctly categorized 85.1% of children below the CLI score cut-off and 58.3% of the children above the cut-off, with an overall accuracy of 79.0%, a rate better than random chance ($\chi^2(2) = 35.72$, $p < .001$, $R^2 = .20$). ME children had a significantly higher risk of falling below the CLI score cut-off (OR = 6.70, CI_{OR} = [2.77, 16.19], $p < .001$). Male children were more likely to fall below the CLI score cut-off than female children (OR = 4.79, CI_{OR} = [1.85, 12.41], $p < .001$).

Social adversity predictors were added in the second stage model (Step 2), which had a significantly higher categorization accuracy than the stage 1 model ($\Delta\chi^2(4) = 23.92$, $p < .001$). The second stage model correctly categorized 93.4% of children below the CLI score cut-off and 58.3% of the children above the cut-off with an overall accuracy of 85.4% ($\chi^2(6) = 59.64$, $p < .001$, $R^2 = .32$). In this model, methadone group status continued to increase the risk of falling below the CLI cut-off (OR = 3.03, CI_{OR} = [0.99, 9.26], $p = .05$). Male children

continued to be more likely to fall below the CLI cut-off than female children (OR = 3.36, CI_{OR} = [1.14, 9.89], p = .03). There was no evidence that children with a caregiver from a minority group were at a higher risk of falling below the low language cut-off (OR = 2.71, CI_{OR} = [0.78, 9.46], p = .12). Nor was there evidence for a higher risk of falling below the cut-off for children with a single caregiver (OR = 0.95, CI_{OR} = [0.33, 2.73], p = .92), living with a caregiver from a low SES (OR = 5.96, CI_{OR} = [0.79, 45.16], p = .08), or having a higher number of caregiver changes (OR = 1.52, CI_{OR} = [0.49, 4.69], p = .47).

The DASS score was added in the third stage model (Step 3). This addition did not improve the predictive power of the model compared with the second stage model ($\Delta\chi^2(3)$ = 3.52, p_{change} = .32). The third stage model correctly categorized 93.4% of children below the CLI score cut-off and 63.9% of the children above the cut-off with an overall accuracy of 86.6% ($\chi^2(9)$ = 63.17, R^2 = .33, p < .001). In the third stage model there was no longer evidence that ME children were more likely to have low language scores (OR = 2.55, CI_{OR} = [0.80, 8.12], p = .11). Male children remained more likely to have lower CLI scores than females (OR = 3.80, CI_{OR} = [1.22, 11.85], p = .02). There was no evidence of risk differences across minority groups (OR = 3.30, CI_{OR} = [0.91, 11.96], p = .07), single caregiver households (OR = 0.93, CI_{OR} = [0.31, 2.76], p = .90), SES (OR = 6.09, CI_{OR} = [0.76, 48.84], p = .09), or number of caregiver changes (OR = 1.56, CI_{OR} = [0.48, 5.05], p = .46). There was no evidence of a higher risk of children falling below the CLI cut-off when their caregivers scored more highly on the DASS anxiety (OR = 1.24, CI_{OR} = [0.17, 9.04], p = .83), depression (OR = 1.34, CI_{OR} = [0.10, 17.70], p = .82), or stress (OR = 3.62, CI_{OR} = [0.18, 71.98], p = .40) subscales.

Table 7. 3

Summary of Logistic Regression Analysis Predicting Low Core Language for the Methadone Exposed and Comparison Children Combined (0 = Typically Developing Language; 1 = Low Core Language).

Variable	B (SE)	*p*	Odds Ratio (95% CI)
Step 1. Unadjusted			
($\chi^2(2) = 35.72$, $p < .001$, $R^2 = .20$)			
Methadone group status	1.90 (0.45)	<.001	6.70 (2.77 - 16.19)
Gender	1.57 (0.49)	<.001	4.79 (1.85 - 12.41)
Step 2. Adjusted for Social Adversity			
($\chi^2(6) = 59.64$, $p < .001$, $R^2 = .32$; $\Delta\chi^2(4) = 23.92$, $p_{change} < .001$)			
Methadone group status	1.12 (0.57)	.05	3.03 (0.99 - 9.26)
Gender	1.21 (0.55)	.03	3.36 (1.14 - 9.89)
Minority Group	1.00 (0.64)	.12	2.71 (0.78 - 9.46)
Single Caregiver	-0.05 (0.54)	.92	0.95 (0.33 - 2.73)
SES	1.79 (1.03)	.08	5.96 (0.79 - 45.16)
Caregiver Changes	0.42 (0.57)	.47	1.52 (0.49 - 4.69)
Step 3 Adjusted for Caregiver Psychological Factors			
($\chi^2(9) = 63.17$, $p < .001$, $R^2 = .33$; $\Delta\chi^2(3) = 3.52$, $p_{change} = .32$)			
Methadone group status	0.94 (0.59)	.11	2.55 (0.80 - 8.12)
Gender	1.33 (0.58)	.02	3.80 (1.22 - 11.85)
Minority Group	1.20 (0.66)	.07	3.30 (0.91 - 11.96)
Single Caregiver	-0.07 (0.56)	.90	0.93 (0.31 - 2.76)
SES	1.81 (1.06)	.09	6.09 (0.76 - 48.84)
Caregiver Changes	0.44 (0.60)	.46	1.56 (0.48 - 5.05)
Caregiver Anxiety	0.21 (1.01)	.83	1.24 (0.17 - 9.04)
Caregiver Depression	0.30 (1.32)	.82	1.34 (0.10 - 17.70)
Caregiver Stress	1.29 (1.53)	.40	3.62 (0.18 - 71.98)

7.4.2 Predictors of Externalising Problems. Table 7.4 displays the results of a 3-stage hierarchical logistic regression used to predict dichotomous scores on the EPC. The EPC was selected as a measure of overall externalising problems. A *t* score of 60 and above on the EPC indicated that externalising problems were present.

In the first stage model (Step 1) methadone group status and child gender predicting dichotomous EPC score correctly categorized 86.2% of children below the EPC score cut-off and 56.1% of the children above the cut-off, with an overall accuracy of 78.3%, a rate better than random chance ($\chi^2(2) = 42.31$, $p < .001$, $R^2 = .24$). Children with prenatal methadone exposure had a significantly higher risk of falling above the EPC score cut-off (OR = 9.38, CI_{OR} = [3.93, 22.43], $p < .001$). Male children were more likely to fall above the EPC score cut-off than female children (OR = 3.57, CI_{OR} = [1.48, 8.64], $p = .005$).

Social adversity predictors were added in the second stage model (Step 2), which had significantly higher categorization accuracy than the stage 1 model ($\Delta\chi^2(4) = 24.30$, $p < .001$). The second stage model correctly categorized 90.5% of children below the EPC score cut-off and 58.5% of the children above the cut-off with an overall accuracy of 82.2% ($\chi^2(6) = 66.62$ $p < .001$, $R^2 = .35$). In this model, methadone group status continued to increase the risk of falling above the EPC cut-off (OR = 11.88, CI_{OR} = [3.50, 40.38], $p <.001$). Male children continued to increase the risk of falling above the EPC cut-off (OR = 3.18, CI_{OR} = [1.11, 9.12], $p = .03$). Children with a caregiver from a minority group (OR = 4.96, CI_{OR} = [1.40, 17.54], $p = .01$), with a single caregiver (OR = 0.21, CI_{OR} = [0.06, 0.69], $p = .01$) or low SES (OR = 11.38, CI_{OR} = [1.46, 88.59], $p = .02$), had a significantly higher risk of falling above the EPC cut off. There was no evidence of a high risk of children falling above the EPC cut-off if they experienced a higher number of caregiver changes (OR = 0.86, CI_{OR} = [0.28, 2.59], $p = .78$).

DASS scores were added in the third stage model (Step 3). This addition did not improve the predictive power of the model compared with the second stage model ($\Delta\chi^2(3) =$

4.61, p_{change} = .20). The third stage model correctly categorized 93.1% of children below the EPC score cut off and 58.5% of the children above the cut-off with an overall accuracy of 84.1% ($\chi^2(9) = 71.22$, $R^2 = .37$, $p < .001$).

In the third stage model (step 3) methadone group status (OR = 12.16, CI_{OR} = [3.46, 42.77], p <.001), being a male (OR= 3.56 CI_{OR} = [1.16, 10.91], p = .03), having a caregiver from a minority group (OR = 4.70, CI_{OR} = [1.31, 16.92], p = .02), having a single caregiver (OR = 0.22, CI_{OR} = [0.07, 0.76], p = .02), or being from a low SES (OR = 13.96, CI_{OR} = [1.73, 112.73], p = .01) continued to increase the risk of falling above the EPC cut-off. There was still no evidence that experiencing higher caregiver changes increased the risk of falling above the EPC cut-off (OR = 0.73, CI_{OR} = [0.23, 2.34], p = .60).

There was no evidence of a higher risk of children falling above the EPC cut off when their caregivers scored more highly on the DASS anxiety (OR = 9.73, CI_{OR} = [0.50, 190.19], p = .13), depression (OR = 0.23, CI_{OR} = [0.01, 6.47], p = .39) or stress (OR = 0.15, CI_{OR} = [0.03, 7.88], p = .35) subscales.

Table 7. 4

Summary of Logistic Regression Analysis Predicting Externalising Problems for the Methadone Exposed and Comparison Children Combined (0 = No Externalising Problems; 1 = At Risk of Externalising Problems)

Variable	B (SE)	*p*	Odds Ratio (95% CI)
Step 1. Unadjusted			
($\chi^2(2) = 42.31$, $p < .001$, $R^2 = .24$)			
Methadone group status	2.24 (0.45)	<.001	9.38 (3.93 - 22.43)
Gender	1.27 (0.45)	.005	3.57 (1.48 - 8.64)
Step 2. Adjusted for Social Adversity			
($\chi^2(6) = 66.62$, $p < .001$, $R^2 = .35$; $\Delta\chi^2(4) = 24.30$, $p_{change} < .001$)			
Methadone group status	2.48 (0.62)	<.001	11.88 (3.50 - 40.38)
Gender	1.16 (0.54)	.03	3.18 (1.11 - 9.12)
Minority Group	1.60 (0.64)	.01	4.96 (1.40 - 17.54)
Single Caregiver	-1.58 (0.62)	.01	0.21 (0.06 - 0.69)
SES	2.43 (1.05)	.02	11.38 (1.46 - 88.59)
Caregiver Changes	-0.16 (0.57)	.78	0.86 (0.28 - 2.59)
Step 3 Adjusted for Caregiver Psychological Factors			
($\chi^2(9) = 71.22$, $p < .001$, $R^2 = .37$; $\Delta\chi^2(3) = 4.61$, $p_{change} = .20$)			
Methadone group status	2.50 (0.64)	<.001	12.16 (3.46 - 42.77)
Gender	1.27 (0.57)	.03	3.56 (1.16 - 10.91)
Minority Group	1.55 (0.65)	.02	4.70 (1.31 - 16.92)
Single Caregiver	-1.50 (0.63)	.02	0.22 (0.07 - 0.76)
SES	2.64 (1.07)	.01	13.96 (1.73 - 112.73)
Caregiver Changes	-0.31 (0.59)	.60	0.73 (0.23 - 2.34)
Caregiver Anxiety	2.28 (1.52)	.13	9.73 (0.50 - 190.19)
Caregiver Depression	-1.45 (1.70)	.39	0.23 (0.01 - 6.47)
Caregiver Stress	-1.92 (2.03)	.35	0.15 (0.03 - 7.88)

7.4.3 Predictors of Internalising Problems. Table 7.5 displays the results of a 3-stage hierarchical logistic regression used to predict dichotomous scores on IPC. The IPC was selected as a measure of overall internalising problems. A *t* score of 60 and above on the IPC indicated that internalising problems were present.

In the first stage model (Step 1) of methadone group status and child gender predicting dichotomous IPC score correctly categorized 100% of children below the IPC score cut-off and 0% of the children above the cut-off, with an overall accuracy of 70.5%, a rate better than random chance ($\chi^2(2) = 6.24$, $p = .04$, $R^2 = .04$). There was no evidence that methadone group status (OR = 1.94, CI_{OR} = [0.95, 3.93], p =.07) or gender (OR = 1.69, CI_{OR} = [0.83, 3.46], p = .15), significantly increased the risk of having an IPC score above the cut-off.

Social adversity predictors were added in the second stage model (Step 2), which had a significantly higher categorization accuracy than the stage 1 model ($\Delta\chi^2(4) = 13.83$, $p = .008$). The second stage model correctly categorized 83.6% of children below the IPC score cut-off and 45.7% of the children above the cut-off with an overall accuracy of 72.4% ($\chi^2(6) = 20.07$ $p = .003$, $R^2 = .12$).

In this model, there was still no evidence that methadone group status (OR = 0.92, CI_{OR} = [0.36, 2.33], p = .85) or gender (OR = 1.14, CI_{OR} = [0.51, 2.55], p = .75), increased the risk of falling above the IPC cut-off. There was also no evidence that minority group (OR = 0.92, CI_{OR} = [0.35, 2.40], p = .86), single caregiver (OR = .95, CI_{OR} = [0.39, 2.31], p = .92), SES (OR = 3.37, CI_{OR} = [0.69, 16.41], p = .13), or number of caregiver changes (OR = 1.30, CI_{OR} = [0.56, 3.02], p = .55) influenced an IPC score above the cut-off.

DASS scores were added in the third stage model (Step 3). This addition did not improve the predictive power of the model compared with the second stage model ($\Delta\chi^2(3) = 2.21$, p_{change} = .53). The third stage model correctly categorized 85.5% of children below the IPC score cut

off and 43.5% of the children above the cut-off with an overall accuracy of 73.1% ($\chi^2(9) = 22.28$, $R^2 = .13$, $p = .008$).

In the third stage model (Step 3) methadone group status (OR = 0.92, CI_{OR} = [0.35, 2.42], $p = .87$), gender (OR= 1.15 CI_{OR} = [0.50, 2.63], $p = .74$), minority group (OR = 0.87, CI_{OR} = [0.33, 2.32], $p = .79$), single caregiver (OR = 1.0, CI_{OR} = [0.41, 2.45], $p = .99$), SES (OR = 3.77, CI_{OR} = [0.76, 18.75], $p = .11$), or number of caregiver changes (OR = 1.20, CI_{OR} = [0.51, 2.84], $p = .68$) did not increase the risk of obtaining a IPC score above the cut-off.

In addition, there was no evidence of a higher risk of children falling above the IPC cut off when their caregivers scored more highly on the DASS anxiety (OR = 2.42, CI_{OR} = [0.39, 15.14], $p = .35$), depression (OR = 0.47, CI_{OR} = [0.05, 4.59], $p = .51$) or stress (OR = 0.47, CI_{OR} = [0.05, 5.77], $p = .49$) subscales.

Table 7. 5

Summary of Logistic Regression Analysis Predicting Internalising Problems for the Methadone Exposed and Comparison Children Combined (0 = No Internalising Problems; 1 = At Risk of Internalising Problems)

Variable	B (SE)	*p*	Odds Ratio (95% CI)
Step 1. Unadjusted			
($\chi^2(2) = 6.24$, $p = .044$, $R^2 = .04$)			
Methadone group status	0.66 (0.36)	.07	1.94 (0.95 - 3.93)
Gender	0.53 (0.37)	.15	1.69 (0.83 - 3.46)
Step 2. Adjusted for Social Adversity			
($\chi^2(6) = 20.07$, $p = .003$, $R^2 = .12$; $\Delta\chi^2(4) = 13.83$, $p_{change} = .008$)			
Methadone group status	-0.09 (0.48)	.85	0.92 (0.36 - 2.33)
Gender	0.13 (0.41)	.75	1.14 (0.51 - 2.55)
Minority Group	-.09 (0.49)	.86	0.92 (0.35 - 2.40)
Single Caregiver	-0.05 (0.45)	.92	0.95 (0.39 - 2.31)
SES	1.22 (0.81)	.13	3.37 (0.69 - 16.41)
Caregiver Changes	0.26 (0.43)	.55	1.30 (0.56 - 3.02)
Step 3 Adjusted for Caregiver Psychological Factors			
($\chi^2(9) = 22.28$, $p = .008$, $R^2 = .13$; $\Delta\chi^2(3) = 2.20$, $p_{change} = .53$)			
Methadone group status	-0.08 (0.49)	.87	0.92 (0.35 - 2.42)
Gender	0.14 (0.42)	.74	1.15 (0.50 - 2.63)
Minority Group	-0.13 (0.50)	.79	0.87 (0.33 - 2.32)
Single Caregiver	-.003 (0.46)	.99	1.0 (0.41 - 2.45)
SES	1.33 (0.82)	.11	3.77 (0.76 - 18.75)
Caregiver Changes	0.18 (0.44)	.68	1.20 (0.51 - 2.84)
Caregiver Anxiety	0.88 (0.94)	.35	2.42 (0.39 - 15.14)
Caregiver Depression	-0.76 (1.17)	.51	0.47 (0.05 - 4.59)
Caregiver Stress	-0.95 (1.38)	.49	0.47 (0.05 - 5.77)

CHAPTER 8

DISCUSSION

The current study examined the extent and nature of language, externalising problems, and internalising problems of children born to mothers maintained on methadone during pregnancy. In addition, the current study examined social adversity and caregiver psychological factors in relation to language, externalising problems, and internalising problems in ME children at age 9.5 years.

To date, this is the first study to examine language in detail, between ME children and comparison children at age 9.5 years. Secondly, it is one of the studies to date that employs teacher ratings to measure externalising and internalising problems in ME children. Thirdly, it examines the role of social adversity and caregiver psychological factors on language outcomes, externalising problems and internalising problems in ME children at 9.5 years, studies of which remain relatively sparse. Generally, findings from the present study show that ME children have poorer developmental outcomes relative to comparison children and this is due to multiple factors.

As hypothesised, ME children experienced low language difficulties and greater externalising problems relative to the comparison children. Contrary to the hypothesis, teachers did not report ME children to have high rates of internalising problems relative to the comparison children. A greater proportion of ME children experienced comorbid low expressive and receptive language relative to the comparison children. Finally, a greater proportion of ME children experienced comorbid low core language, externalising problems, and internalising problems relative to the comparison children.

The predictive utility of biological, social adversity, and caregiver psychology on children's low core language, externalising problems and internalising problems was examined. Gender was the only predictor for low core language. Externalising problems was

predicted by social adversity along with gender and methadone exposure but not caregiver psychological factors. Children's internalising problems were marginally predicted by methadone exposure. However, this was no longer significant when social adversity and caregiver psychological factors were entered. Further, neither social adversity, nor caregiver psychological factors significantly predicted internalising problems.

8.1 Low Language, Externalising Problems and Internalising Problems in ME Children and Comparison Children.

The following section discusses the differences in developmental outcomes (language outcomes, externalising problems and internalising problems), between ME and the comparison children.

8.1.2 Low Language. There is a growing body of evidence reporting that ME children are at risk of having low language. In line with the predicted hypothesis, the current study found ME children performed poorly on all three language indices relative to the comparison children. To date, Pulsifer et al. (2008) is the only study to have examined core, expressive and receptive language in ME school-aged children. Researchers found that ME children performed poorly on core and expressive language, but not receptive language relative to the comparison children. Pulsifer et al. (2008) matched ME children and the comparison children on age and SES. The present study did not control for these covariates in the descriptive analysis, which may explain the difference in findings. In contrast, Davis and Templer (1988) found no difference in language between ME children and comparison children living with a substance dependent father. Perhaps this is due to differences in the composition of the comparison group. Overall, it appears that the present findings are in line with most of the existing literature (Ornoy et al., 2001; Pulsifer et al., 2008; Vanbaar & Degraaff, 1994; Wahlsten & Sarman, 2013; Wilson et al., 1979) despite using different measures (IQ) to assess language. The existing literature has shown that ME children have lower language relative to the comparison children.

8.1.3 Externalising and Internalising Problems. It is well documented that ME children have higher levels of externalising and internalising problems relative to the comparison children, as rated by their caregivers. To date, there appear to be restricted studies reporting on teacher rated externalising problems and internalising problems among ME children at age 9.5 years. The current study employed teacher ratings to assess externalising problems and internalising problems, in order to address this gap. Teacher ratings are shown to be strong predictors of children's later clinical difficulties (Ferdinand et al., 2003; Verhulst et al., 1994). Generally, teachers have a greater foundation for comparing children's functioning as they have a normative referent group of other children (Nygaard et al., 2016). In addition, teachers tend to detect difficulties earlier than caregivers (Nygaard et al., 2016).

There is evidence suggesting that opioid dependent caregivers who are highly stressed are more likely to over-report their children's externalising and internalising problems (Berg-Nielsen & Wichstrøm, 2012). To date, Nygaard et al. (2016) and Wahlsten and Sarman (2013) are the only studies that used teacher ratings to assess externalising and internalising problems in heroin exposed and BE children at age 9.5 years.

8.1.4 Externalising Problems. In line with the predicted hypothesis, the current study found that ME children were rated higher on total externalising problems, aggression, conduct problems, and hyperactivity compared to the comparison children, according to their teachers. The current study supports previous findings, despite using teacher ratings and not caregiver ratings. Nygaard et al. (2016) employed both caregiver and teacher rating measures to assess externalising problems in heroin exposed children. Both caregiver and teacher ratings indicated that heroin exposed children displayed higher levels of total externalising problems than the comparison children. Using caregiver ratings, differences have been found

between ME and comparison children on total externalising problems, aggressive behaviour and rule breaking behaviour as measured by the CBCL (de Cubas & Field, 1993).

One study reported teacher rated hyperactivity was elevated in prenatal BE children when compared to published population norms, but no difference was found on caregiver rated hyperactivity (Wahlsten & Sarman, 2013). No conduct problems were reported by caregiver or teacher ratings in prenatal BE children (Wahlsten & Sarman, 2013). Perhaps the inconsistency in the findings is a result of the different measures used. In contrast to the current study, Walhovd et al. (2007) failed to find a difference between heroin exposed children and comparison children on the caregiver rated externalising problems scale of the CBCL. This could be due to the small sample size and lack of statistical power.

8.1.5 Internalising Problems. The current study findings did not support the hypothesis predicted. Findings from the present study indicated no difference between ME children and the comparison children on total internalising problems, anxiety, and somatization. However, teachers did rate ME children higher on depression relative to the comparison children. Only one study, Nygaard et al. (2016), used teacher ratings to assess internalising problems in heroin exposed children. The authors found teacher's ratings indicated that heroin exposed children showed higher levels of total internalising problems relative to the comparison children. Using caregiver ratings, one study reported that ME children exhibited greater levels of total internalising problems, anxiety, depression, and somatization (de Cubas & Field, 1993). Similarly, significant difference on caregiver rated anxiety, depression, somatization and total internalising scales have been reported (Hjerkinn et al., 2012).

Most previous studies have used the CBCL to assess internalising problems (de Cubas & Field, 1993; Hjerkinn et al., 2013; Nygaard et al., 2016), in contrast to the present study that utilised the BASC-2 to measure children's internalising problems. There is evidence that

the BASC-2 captures internalising symptoms relative to the CBCL, which is a possible explanation for differences in the findings (Bender et al., 2008).

8.2 Comorbid Low Language, Externalising Problems, and Internalising problems in Methadone Exposed Children and Comparison Children at 9.5 Years

8.2.1 Expressive and Receptive Language. In line with the predicted hypothesis, the current study showed that there are higher rates of low expressive and low receptive language among ME children, relative to the comparison children. However, a greater proportion of the comparison children displayed low receptive language only. Previous research in this area is somewhat limited. Only, one study has reported on the proportion of low language between ME and comparison children (Pulsifer et al., 2008), wherein a greater proportion of ME children displayed low expressive language and no difference on receptive language. Drawing on the general literature, two studies reported that in their sample, two-thirds of children had comorbid low expressive and low receptive language and one third had low expressive language (Selassie et al., 2005; Westerlund & Sundelin, 2000). Language is complex, the general literature highlights that low expressive, low receptive language or both are associated with genetic components and social adversity, perhaps explaining the variety of findings in the literature (Clark et al., 2007; Law et al., 1998; Letts et al., 2013; Rapin, 1996; Tomblin et al., 1997).

8.2.2 Externalising and Internalising Problems. In the current study, ME children were more likely to have co morbid externalising and internalising problems, relative to the comparison children. Research on comorbid externalising and internalising problems in ME children is quite limited. One study reported that heroin exposed children scored within the 95th percentile on the overall CBCL measure of externalising and internalising problems relative to the comparison children (Nygaard et al., 2016). Drawing on the general literature, it is common for school-aged children to have comorbid externalising and internalising problems (Beyers & Loeber, 2003; Hannigan et al., 2018; Wiesner & Kim, 2006; Willner et

al., 2016; Wolff & Ollendick, 2006). One proposition put forward is that shared traits are associated with the manifestation of both externalising and internalising problems (Weiss et al., 1998; Willner et al., 2016).

In the current study, comparison children were more likely to have internalising problems only. Internalising problems are relatively prevalent in typically developing children, therefore it is not unusual for children to display some internalising behaviours, particularly during school years with several life transitions taking place (American Psychiatric Association, 2013).

8.2.3 Low Language, Externalising Problems, and Internalising Problems. In line with the predicted hypothesis, ME children were more likely to have comorbid low core language, externalising problems, and internalising problems relative to the comparison children. To date, literature on comorbid low language, externalising problems, and internalising problems is rare in ME children. Drawing on the literature on typically developing children, a robust relationship exists between low language and externalising problems (Davis et al., 1991; Giddan et al., 1996; St Clair et al., 2011; Yew & O'Kearney, 2013; Yew & O'Kearney, 2015) and low language and internalising problems (Beitchman et al., 2001; Conti-Ramsden & Botting, 2008). One explanation put forward is that language in the mode of self-talk guide's behaviour (Vygotskiĭ, 1962) is an effective method for self-regulating, problem solving, and delaying impulses (Rodriguez et al., 1989). Difficulty in these areas increases the risk of developing externalising and internalising problems (Vallotton & Ayoub, 2011).

8.3 Biological, Social Adversity and Caregiver Psychological Factors, and Low Language, Externalising Problems, and Internalising Problems

The second and third aims of the current study were to examine the association between biological, social adversity and caregiver psychological factors and child language outcomes, externalising problems, and internalising problems.

8.3.1 Predictors of Low Language. Inconsistent with the predicted hypothesis, methadone group status, social adversity and caregiver psychological factors were not found to have any predictive role for low language in the combined sample (ME children and comparison children). Gender was the only variable to predict low language at age 9.5 years. While the literature is limited on predictors of low language in ME school-aged children, the current findings are inconsistent within the existing literature. The few studies that have examined the impact of social adversity and caregiver psychological factors on low language, predominately examined heroin exposed children and showed that children who have been adopted perform better on language constructs relative to heroin exposed and BE children living with their biological mothers (Ornoy et al., 1996; Salo et al., 2009). Ornoy et al. (1996) described that adopted families tend to have higher SES. In support, comparison children living in deprived environments or living with a substance dependent father showed similar language outcomes (Davis & Templer, 1988; Wilson et al., 1979). Furthermore, there is a strong evidence base highlighting the association between low SES and low language (Hart & Risley, 1995; Hoff, 2006; Hoff, 2013).

SES and low language outcomes tend to be arbitrated by quality and quantity of speech and verbal responses in the family (Arriaga et al., 1998; Hoff, 2006; Hoff, 2013; Hoff et al., 2002; Hoff & Tian, 2005; Huttenlocher et al., 2002; Snow et al., 1976), and stimulating activities such as reading (Fletcher & Reese, 2005). Firstly, the current study did not examine these mediator variables, which provides one explanation for the differences in the findings. Secondly, the discrepancy between the current study findings and the existing literature may be due to using concurrent predictor variables at an older age. It is extensively noted that language abilities stabilise from the age of 5 to 6 years and that language is predominately determined by very early factors (Hart & Risley, 1995; St Clair et al., 2011; Stothard et al., 1998). The current study supports the main body of the literature, in that early factors such as

linguistic input, caregiver responsiveness, and stimulating activities have a greater predictive capacity, than adversity and caregiver psychological factors at the age of 9.5 years. By school years, there may not be many factors that predict language. Moe (2002) found that verbal abilities at the age of 1 year predicted language outcomes at age 4.5 years, above and beyond SES. However, the author found that this association was in conjunction with prenatal heroin exposure. It appears that perhaps age plays a role in which factors predict language.

In support of the current study findings, Moe et al. (2002) found that boys preformed lower verbal abilities relative to females. Drawing on the broader substance literature, male children experienced greater cognitive deficits relative to female children (Bennett et al., 2008; Carmody et al., 2011). In one proposition to explain this association, animal studies indicate that males are more sensitive to opioids than females. Males prenatally exposed to substances are associated with greater constriction of blood vessels in the brain than females, producing greater cognitive deficits in boys (Bennett et al., 2008; Cicero et al., 1996).

8.3.2 Predictors of Externalising Problems. In line with the predicted hypothesis, the present study found that methadone group status and gender were predictors of externalising problems after adjusting for social adversity and caregiver psychological factors. In addition, social adversity, such as being from a minority group, having a single caregiver, and being of low SES also predicted externalising problems. However, caregiver psychological factors did not predict externalising problems. These findings support the dual hazard model (Lester & Tronick, 1994).

Similar to previous literature, ME and heroin exposed children experience greater levels of externalising problems relative to the comparison children according to caregiver and teacher ratings (Davis & Templer, 1988; de Cubas & Field, 1993; Nygaard et al., 2016; Ornoy et al., 2001; Wahlsten & Sarman, 2013; Wilson et al., 1979). Overall, studies that

utilised teacher ratings were consistent with the current study findings (Nygaard et al., 2016; Wahlsten & Sarman, 2013).

The literature on gender differences in ME children is relatively limited, there is however some evidence that ME and heroin exposed children displayed higher levels of externalising behaviours in males relative to females (Bada et al., 2012; Ornoy et al., 2001; Sarfi et al., 2013). Drawing on the wider drug literature, biologically, male infants tend to be more emotionally reactive than females (Kraemer, 2000). Neuroimaging studies report that male brain areas associated with emotional regulation tend to be impacted more by drugs relative to females (Carmody et al., 2011). This becomes problematic during school years as requirements to self-regulate increase during this stage of life (Nygaard et al., 2016).

In support of the current study findings, ample studies indicate that low SES and being parented by a single caregiver are associated with greater externalising problems in methadone exposed children (Ornoy et al., 2001; Pulsifer et al., 2008). The number of caregiver changes from birth to 9.5 years were not found to predict externalising problems in ME children. Nygaard et al. (2016) compared children who experienced no caregiver changes to children with one caregiver change and found no difference on externalising problems between ME children and the comparison children.

Inconsistent with previous research, the present study did not find any caregiver psychological factors (e.g., caregiver anxiety, depression, stress), that predicted externalising problems in ME children. Konijnenberg et al. (2016) reported that a maternal risk model (e.g., co-occurring psychiatric difficulties, physical health problems, and drug use) explained a large portion of the variance in externalising problems in ME children. Sarfi et al. (2013) found that caregiver distress predicted total behaviour problems (measured by the CBCL), in conjunction with gender among ME and BE children. Consistent with the current study, Hser et al. (2015) also failed to find caregiver psychiatric difficulties as a significant predictor of

child externalising problems. This study used a historical diagnosis (within the last year), as a measure of psychiatric difficulties, relative to the other studies which used psychometrics to evaluate concurrent (within the last 1 or 2 weeks) psychiatric difficulties.

Taken together the present study findings support the dual hazard model, as it is a combination of biological factors and social adversity caregiver psychological factors that in part account for externalising problems in ME children.

8.3.3 Predictors of Internalising Problems. Inconsistent with the predicted hypothesis, the current study, did not find any factors that predict internalising problems. Methadone group status had marginal predictive capacity but after taking social adversity and caregiver psychological factors into account, methadone group status no longer predicted internalising problems. Further, no social adversity or caregiver psychological factors were found to predict internalising problems. In contrast, previous research found that prenatal heroin exposure and polysubstance exposure remained associated with internalising problems after adjusting for gender and SES (Bada et al., 2012; Nygaard et al., 2016).

Ornoy et al. (2001), found that internalising problems were better explained by low SES than the biological effects of prenatal exposure to heroin. Likewise, Hjerkinn et al. (2013) found that internalising problems were no longer present among poly-substance exposed children following adoption. Further, social adversity factors such as SES and family support were found to be negatively correlated with internalising problems in poly-substance exposed children (Bada et al., 2012).

With regards to caregiver psychological factors, a large proportion of caregiver psychiatric difficulties predicted child internalising problems (Bada et al., 2012). Caregiver depression and anxiety predicted internalising problems in substance exposed children, following adjustment for gender, age, minority status, employment and family conflict (Hser et al., 2015). Further, Bada et al. (2012) found that caregiver's psychiatric health, SES and

familial support explained a large proportion of the variance in internalising behaviours, over and above substance exposure. Similarly, Konijnenberg et al. (2016) found co-occurring psychiatric difficulties, physical health problems and drug use accounted for a large portion of the variance in internalising problems, over above prenatal substance exposure.

8.4 Strengths of the Current Study

The existing literature suggests that a number of developmental domains are impacted in children who have been prenatally exposed to methadone and other opioids (Andersen et al., 2020; Lee et al., 2020). The present study adds to the literature by comprehensively measuring language using the CELF-4 as an alternative to intelligence measures commonly used in previous studies. Secondly, it evaluates long term developmental trajectories of prenatal methadone exposed children which is relatively limited. Thirdly, the present study strengthens the current field of research as it examines the biological effects of prenatal methadone exposure in conjunction with social adversity and caregiver psychological factors and their impact on developmental trajectories. Fourthly, the presenting study bolsters this area of research by employing teacher ratings of externalising and internalising problems, which is relatively scarce. Finally, it examines comorbidities across different developmental domains in ME children, which is limited. Taken together, the current study findings provide a more in-depth understanding of target areas for interventions.

8.5 Limitations of the Current Study

While the current study identified differences in developmental domains between ME children and comparison children, there are several limitations that are crucial to consider. Firstly, although there is data that supports the validity and reliability of teacher reporting, there is contrary evidence suggesting that teachers may unwittingly be influenced to appraise their students based on their relationship with the student rather than the behavioural tendencies the child displays (Berg-Nielsen & Wichstrøm, 2012). Comparatively, this is the

dilemma associated with using self-report measures. The inclusion of multiple informant measures to assess child behaviour, such as caregiver report and observational research, would have strengthened the reliability and validity of this study.

A further limitation is participant retention and recruitment. It is plausible that participants that could not be re-recruited, were in fact the families that are the most vulnerable and their children are at an elevated risk of poorer developmental outcomes compared with participants who remained in the study. It is possible that if these participants were successfully re-recruited, a more acute pattern of findings may have been reached. Therefore, a tentative generalisation of the present findings to the wider New Zealand population of children prenatally exposed to methadone is appropriate.

A further limitation concerns the internalising composite on the BASC-2. It is evidenced that this composite has low sensitivity for sufficiently identifying internalising problems in at risk populations (Bender et al., 2008). For example, one study compared the convergent validity of the CBCL and the BASC-2 among at risk patients (epileptic patients). Findings showed that the CBCL identified a larger proportion of patients as displaying internalising problems relative to the BASC-2. By employing an alternative measure such as the CBCL may have altered the current study findings (Bender et al., 2008). The present study employed the BASC-2 as it was the only measure of internalising behaviour accessible. Further, the externalising problems composite has robust psychometric properties (Reynolds & Kamphaus, 2004).

The current study employed a cross-sectional study design, therefore controlling for additional covariates was difficult. It is increasingly being acknowledged that prenatal substance exposed children, are typically exposed to other poly substances (Lester et al., 2001; Nygaard et al., 2015), and that early variables such as gestational age and birth weight

are key covariates for predicting developmental trajectories. This potentially compromises the validity of the current study; however, term data was not accessible in the present study.

8.6 Implications of the Current Study

The current thesis investigates language abilities, externalising problems, and internalising problems in 9.5 year-old children born to mothers enrolled in the methadone maintenance treatment. The current study findings strengthen the existing literature and confidently provide an in-depth analysis on language, externalising problems, and internalising problems in school aged ME children. As such, this research may contribute to target interventions in order to support these children and their families.

The present study findings propose that children born to mothers maintained on methadone during their pregnancy experience greater language difficulties, externalising problems, and internalising problems relative to their peers. These findings are noteworthy as difficulties in developmental areas place children at a higher risk of mental health difficulties (Howard & Williams, 2018; Liu et al., 2011; Selinus et al., 2016), social problems *i.e.* criminality, employment (Dodge et al., 2006; Hughes et al., 2008; Liu et al., 2011), and poor academic achievement (Arguedas et al., 2016; Howard & Williams, 2018; Pedersen et al., 2019). Further, deficits in one developmental domain significantly impact other areas of development (Lee et al., 2020; Roben et al., 2013; St Clair et al., 2011). With this knowledge, it is a necessity for these children and their families to receive additional support to guide positive developmental trajectories.

Research on parenting interventions for women maintained on methadone is scarce (Peisch et al., 2018); however, it is probably beneficial for these women to receive parenting support during the initial stages of being caregivers. Given interventions should focus on support systems for the child in terms of facilitating education programmes coupled with parenting interventions and individualised support (Peisch et al., 2018).

Parent-implemented language interventions have been shown to significantly improve children's expressive and receptive language abilities (Roberts & Kaiser, 2011). A recent study explored Enhanced Milieu Teaching (EMT; Hart & Rogers-Warren, 1978), a language intervention which involves coaching caregivers to use a set of language facilitation strategies. For example: *i.* noticing and responding to child communication; *ii*. modelling language and expanding child utterances; *iii.* using specific language prompts in response to the child's requests (Curtis et al., 2017). Studies have reported that EMT language interventions have had improved child communication, caregiver responsiveness and child-caregiver relationship quality (Curtis et al., 2017; Wright & Kaiser, 2017), improved expressive language (Hatcher & Page, 2020; Roberts & Kaiser, 2015), receptive language (Hancock & Kaiser, 2002; Kaiser et al., 2017; Kashinath et al., 2004), and lowered levels of externalising and internalising behaviour difficulties (Curtis et al., 2017; Hancock et al., 2002).

An early dissertation reported that substance exposed children's verbal abilities and ability to communicate improved after attending EIM (Peterson, 2000). Further, families from impoverished backgrounds showed that EIM improved caregiver responsiveness, a child's ability to communicate, and length and quality of utterance (Hancock et al., 2002; Hatcher & Page, 2020). Studies have highlighted the earlier onset of educational interventions such as EIM are the most advantageous in re-directing children onto a positive developmental trajectory. While research on EIM in substance exposed children is limited, it warrants further investigation as it may be of value for guiding ME children and their families onto positive trajectories.

8.7 Future Research

The current study findings provide preliminary evidence of language, externalising problems, and internalising problems at age 9.5 years in children born to mothers maintained

on methadone. Clearly further research is required to address the following gaps in the literature.

Firstly, future research should examine the impact caregiver verbal input, caregiver responsivity, child-caregiver relationships, parenting practices and stimulating activities have on language, externalising problems, and internalising problems developmental outcomes. Previous literature has indicated that these factors are important during preschool years; however, it is not well documented whether these factors still play a key role at age 9.5 years in ME children (Lugo-Gil & Tamis-LeMonda, 2008; Smith et al., 2018).

Secondly, a key direction for future studies would be to examine developmental outcomes of ME adolescents. It is possible that language outcomes will continue to deviate over time between ME children and comparison children (Church, 2015; Hart & Risley, 1995; Stothard et al., 1998). To date there are no studies that examine language outcomes between ME adolescents and comparison adolescents. In addition, the demand for self-regulation also continues to increase through adolescent years, therefore it would be of value to identify developmental trajectories in ME adolescence.

8.8 Conclusion

Research examining the language, externalising outcomes, and internalising outcomes of ME children is essential in understanding conditions that these children are raised in. Identifying and understanding developmental areas that these children struggle in can inform appropriate interventions, to improve developmental outcomes of these children and their families.

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Appendix A

Health and Disability Ethics Committees

Health and Disability Ethics Committees
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28 November 2012

Dr Lianne Woodward
Canterbury Child Development Research Group
Psychology Department
University of Canterbury
Christchurch 8041

Dear Dr Woodward

Re:	**Ethics ref:**	**URB/07/10/042**
	Study title:	Neurodevelopmental Outcomes of Children Exposed to Methadone During Pregnancy at Ages 4.5 and 6 Years: Role of neuroanatomical and Socio-Environmental Factors.

I am pleased to advise that this amendment has been *approved* by the Southern Health and Disability Ethics Committee. This decision was made through the HDEC Expedited Review pathway.

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

Ms Raewyn Idoine
Chairperson
Southern Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix B

Canterbury Child Development
Research Group
Department of Psychology
College of Science

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

CODE NUMBER

9/ 10 YEAR FOLLOW-UP STUDY
CONSENT FORM

- I have been invited to participate with my child in a study that is comparing the development of children who were and were not born to mothers on methadone maintenance during their pregnancy. I have read and understood the Information sheet dated November 2012.
- I have had enough time to consider whether we will take part in the study, and to discuss my decision with the researcher or a person of my choice.
- I know who to contact if I have any questions about the study.
- I understand that our participation in this research is **confidential** and that no material which could identify me will be used in any study reports, or made available to anyone else without my approval in writing.
- I understand my child will be videotaped during the procedure and that this information will only be used for further observation by the named investigators and the material will be secured and kept strictly confidential.
- I also understand that my child and I can withdraw from the study at any time.
- I understand the compensation provisions for the study.
- I am willing for the research team to contact my child's class teacher to obtain information on my child's school progress during the last year. **YES/NO**
- I agree to members of the research team having access to medical information about my child for cross checking the number and dates of any major or minor illnesses that I have recorded on the study forms. **YES/NO**
- I wish to receive a summary of the results of this study. **YES/NO**

I consent to take part in this study.

Parent/s Name: _____

Signature of Parent/s: _____ **Date:** _____

I consent to my child taking part in this study.

Child's name_____ Parent/s Name: _____

Signature of Parent/s: _____ **Date**: _____

In my opinion, consent was given freely and the participant understands what is involved in this study.

Researcher's Name:_____

Signature of Researcher: _____ **Date**: _____

Canterbury Child Development
Research Group
Department of Psychology
College of Science

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

CODE NUMBER

Video Use Consent Statement (9/10) years

We are videotaping this session to help us record how your child responds to the activities, which we will do today. Most tapes are coded and scored by the Child Development Research Team and will never be seen by anyone else.

However occasionally, it is useful to be able to use short video clips for training or for presentations, with students and/or other professional workers. This may take place in Christchurch, elsewhere in New Zealand or abroad.

If you would be happy for us to use the tape of your child for this purpose, please indicate below. Your name and that of your child would always remain confidential and the videos would be presented in an anonymous way.

I **give / do not give** permission for the tape to be used for talks and presentations **in Christchurch / elsewhere in New Zealand / abroad.**
(Delete as appropriate)

Signed:_____

Name:_____
(Please print clearly)

Date:_____

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Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

CANTERBURY CHILD DEVELOPMENT STUDY
9/10-YEAR FOLLOW-UP

We would like to thank you for taking part in the 9/10 year follow-up study. We are sending this form to show your child's teacher that you have given us permission to speak to them and access information from them in regards to your child's classroom behaviour. Your signature will be shown to them in case they have concerns regarding your consent.

Parental consent to take part in this study.

Parent/s Name: _____

Signature of Parent/s: _____ **Date:** _____

I consent to my child taking part in this study.

Child's name_____

Parent/s Name:_____

Signature of Parent/s: _____ **Date:** _____

In my opinion, consent was given freely and the participant understands what is involved in this study.

Researcher's Name:_____

Signature of Researcher: _____ **Date:** _____

THIS STUDY HAS BEEN APPROVED BY THE UPPER SOUTH B REGIONAL ETHICS COMMITTEE

Reference: URB/07/10/042