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Child self-report and parent ratings of health-related quality of life in school-aged children born preterm

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CHILD SELF-REPORT AND PARENT RATINGS OF HEALTH-RELATED QUALITY OF LIFE IN SCHOOL-AGED CHILDREN BORN PRETERM

by

Thomasin E. McCoy

An Abstract

Of a thesis submitted in partial fulfillment
of the requirements for the
Doctor of Philosophy degree in
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Thesis Supervisors: Professor Elizabeth Altmaier
Professor Lynn Richman

ABSTRACT

Recent progress in science and medicine is that regions such as the United States, Canada, Australia, and Western Europe have witnessed dramatic declines in infant morbidity and mortality. The most significant of these declines has occurred among infants born prematurely and low birth weight (LBW)—the cohort that represents the highest proportion of illness and death among infants Despite these medical advances, recent longitudinal studies have provided clear evidence of physical health problems; cognitive and neuropsychological dysfunction; and other social, emotional, and behavioral problems among children born prematurely. A number of studies have indicated that premature and LBW infants are still at risk for psychosocial, physical, and mental problems despite the immediate contributions of post-natal interventions to their increased chance for survival.

The extant research has demonstrated that children born prematurely and LBW are at risk for problems in health, neuropsychological functioning, learning, academic achievement, behavior, and psychosocial adjustment. Research has further demonstrated that a variety of physical and psychological conditions are associated with poorer QOL among children. However, few studies have examined pediatric QOL among preterm school-aged children. Moreover, existing studies have not explored the relationship between cognitive, academic, and social/emotional functioning and QOL. The current study compared child and parent ratings of health-related quality of life among school-aged children born preterm (n = 26) and full-term (n = 28). Given the increased rates of physical, psychological, and cognitive problems among the preterm population, it was

hypothesized that children born prematurely would have significantly poorer proxy-reported and self-reported QOL than children born preterm.

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CERTIFICATE OF APPROVAL

PH.D. THESIS

This is to certify that the Ph.D. thesis of

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has been approved by the Examining Committee for the thesis requirement for the Doctor of Philosophy degree in Psychological and Quantitative Foundations at the December 2010 graduation.

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LIST OF SYMBOLS AND ABBREVIATIONS

α	Alpha: Cronbach's index of internal consistency
df	Degrees of freedom: number of values free to vary after certain restrictions have been placed on data
F	Fisher's *F* ratio: A ratio of two variances
M	Mean: the sum of a set of values divided by the number of values in the set
N	Statistical notation for sample size
p	Probability of obtaining the observed value or a more extreme value if the null hypothesis is true
r	Pearson product-moment correlation
SD	A statistical measure of variability in a data set; the square root of the variance
t	Computed value of a *t* test demonstrating distance from the mean
<	Less than
=	Equal to

CHAPTER I

INTRODUCTION

Advances in scientific research and medical practices have significantly altered the nature of both health care and disease within the last few decades, resulting in a dramatic decrease in rates of morbidity and mortality associated with a number of severe illnesses and conditions. One of the most significant medical improvements in the United States and other developed, industrialized nations is evident in infant, child, and maternal health care. As a result of rapid scientific advances in, for example, ultrasound, fetal heart monitoring, and genetic screening, patients have had access to increasingly sophisticated diagnosis and treatment of infant and maternal disease. One markedly positive consequence of recent progress in science and medicine is that regions such as the United States, Canada, Australia, and Western Europe have witnessed dramatic declines in infant morbidity and mortality. The most significant of these declines has occurred among infants born prematurely and low birth weight (LBW)—the cohort that represents the highest proportion of illness and death among infants (Spreen, Risser, & Edgell, 1995).

Definitions and Prevalence

According to the World Health Organization (1961), an infant is considered premature if born before 37 weeks gestation and LBW if born weighing less than 2500 grams. Further distinctions are made between very low birth weight (VLBW) infants, who are born weighing between 750 and 1499 grams, and extremely low birth weight infants (ELBW), who are born weighing less than 750 grams (Aylward, 1997). In North America and Europe, prematurity is estimated to occur among 5 to 8% of infant births (Aylward, 1997). In affluent societies, approximately two-thirds of LBW infants are also

born prematurely. In many cases, LBW and premature delivery are mediated by another event or set of events such as prenatal medical complications, disease, or multiple birth membership (Spreen et al., 1995), which has created confusion and inconsistency in the use of terminology. In most cases, research definitions of LBW and prematurity are unclear or inconsistent, while other definitions have failed to draw any distinction among gestational age, prematurity, and birth weight (e.g., Schiatriti et al., 2007).

Research indicates that the distinction between birth weight and gestational age is crucial because, although highly correlated, there is not a one-to-one relationship between gestational age and prematurity (Aylward, 1999). The term small-for-gestational-age (SGA) is reserved for infants whose birth weights are below the 10% percentile for their estimated gestational age (Steward & Moser, 2004). By definition, these infants would also be classified as LBW. Preterm SGA is further distinguished from preterm—appropriate-for-gestational-age (AGA), which refers to infants born prematurely with birth weights greater than 2500 grams. In comparison to preterm-SGA, these infants are thought to be at minimal risk for problems based upon the rate of their fetal growth (Steward & Moser, 2004).

Intrauterine growth retardation (IUGR) is another classification that is distinct from but related to birth weight. This condition is typically diagnosed in utero via ultrasound when reduction in expected fetal growth is thought to have occurred as a consequence of inadequate nutritional availability (e.g., protein and fat) to the fetus during the third trimester (Steward, 2001; Steward & Moser, 2004). In other words, the growth potential of the developing infant is inhibited by a disruption of central nervous system processes (Robson & Cline, 1998). Research suggests that IUGR accounts for the

majority of LBW infants in developing countries due to high rates of inadequate maternal nutrition and prenatal care in these regions (Barros et al., 1992). Although IUGR is described as the most frequent case of preterm-SGA, it would technically be possible for continued growth and weight gain throughout the remainder of fetal development to ultimately raise the infant's birth weight above the 10th percentile- or 2500 gram-threshold. According to Steward (2001), diagnosing IUGR when birth-weight is less than the 10th percentile may underestimate the prevalence of IUGR in full-term, healthy birth-weight infants.

Medical Treatments for Prematurity and LBW

Advances in technology, medical research, and health care practices have dramatically increased survival rates of at-risk infants in neonatal intensive care units. For example, neonatal incubators, certain methods of oxygen treatment, and Cesearean section deliveries have enhanced rates of survival among high-risk pregnancies and deliveries, many of whom are classified as VLBW, ELBW, and/or are members of a multiple birth (Aylward, 1997, 2002). Other medical advances that have increased survival rates of at-risk infants include antenatal corticosteroid treatment, surfactant replacement therapy, and neonatal blood transfusion. Transfusion is an increasingly common method of oxygen (i.e., red blood cell) restoration following significant blood loss due to pre- or peri-natal brain trauma and/or anemia secondary to premature delivery (O'Keefe et al., 2002). Brain trauma and anemia are typically mediated by oxygen and iron deficiency and are now often detected through neonatal ultrasound (Bhutta et al., 2002; Stevenson et al., 1994).

Despite these medical advances, recent longitudinal studies have provided clear evidence of physical health problems; cognitive and neuropsychological dysfunction; and other social, emotional, and behavioral problems among children born preterm. A number of studies have indicated that preterm infants are still at risk for psychosocial, physical, and mental problems despite the immediate contributions of post-natal interventions to their increased chance for survival (Hoff, Hansen, Munck, & Mortensen, 2004; Miceli, Goeke-Morey, Whitman, Kolberg, Loncar, & White, 2000; Nadeau, Tessier, Boivin, Lefebvre, & Robaey, 2003).

Research suggests that one of the reasons specific deficits persist in spite of rigorous medical interventions is related to the increased vulnerability of the preterm infant during fetal development. Preterm infants are at increased risk for both direct and indirect exposure to harmful events during the prenatal period due to biological and environmental risk factors (Aylward, 1997). A second source of vulnerability to the preterm infant is related to underdeveloped central nervous and immune system functioning, which will in turn decrease the likelihood that the infant will be able to compensate to the same degree as a full-term, health-birth-weight infant for the effects of trauma, iron-deficiency, or other disease. Thus, despite increased rates of survival and decreased rates of severe morbidity among preterm infants, it is clear that the potential for less severe but more highly prevalent risks for long-term problems in physical, psychological, and cognitive functioning do exist (Taylor et al., 2000).

Risks for Prematurity and LBW

Preterm risk factors include environmental variables such as income; maternal intelligence (IQ) and education; the presence of psychosocial stress; the quality of home

environment; and the availability of adequate nutrition, health care, and social support. The interaction of environmental risk factors with individual (or biological) risk factors, such as the number and severity of perinatal medical complications (e.g., cerebral damage) and genetic vulnerability is associated with the degree of overall risk for infant prematurity and LBW (Aylward, 1997; Steward, 2001). However, the complicated and multifaceted pathway from risk to prematurity and LBW makes it extremely difficult to predict neonatal and long-term developmental outcomes for any given individual.

Developmental Outcomes of Infants Born Prematurely and LBW

The incidence of surviving premature and LBW infants has increased dramatically due to improvements in medical practices and prenatal care; however, the long-term consequences of prematurity for infants who survive the immediate postnatal period are still relatively unclear. It is estimated that severe impairments such as intellectual disability, cerebral palsy, seizures, blindness, and deafness occur among 14-17% of VLBW infants (Aylward, 2002; Hack et al., 1995). Although medical advances in prenatal, perinatal (NICU), and postnatal care have resulted in a decrease in the prevalence of preterm infants with severe impairments, more recent studies have shown that these infants are still at significantly greater risk than full-term infants for specific, high-prevalence, low-severity deficits in memory, language, reading, concept formation, executive functioning, vocabulary, motor, visuomotor, and perceptual abilities (Alyward, 2002; Spreen et al., 1995; Taylor et al., 2000). Studies have estimated that specific neuropsychological deficits that result in learning, attention, and/or behavior problems occur in 50-70% of children born VLBW (Aylward, 1997, 2002; Taylor et al., 1998,

2000). According to Breslau (1995), children born prematurely are also at risk for problems in balance, coordination, and gait. Furthermore, although premature and LBW infants are not at as great a risk as they once were for reduced global intelligence, they have been shown to perform, on average, around 10 points lower than children born full-term on standardized tests of intellectual functioning (Goyen et al., 1998).

The relationship between preterm status and neurocognitive outcomes has been well documented. In one study, for example, Litt and colleagues (2005) compared neuropsychological functioning and academic achievement among a full-term group and two groups of preterm children: one group comprised of preterm children born weighing less than 750 grams and the other comprised of children born between 750 and 1,499 grams. They found significantly poorer reading and math achievement as well as poorer perceptual-organization skills among children born at a birth weight of less than 750 grams in comparison to both the 750 to 1,499 gram and full-term groups. Estimated intellectual ability was also significantly lower in the less than 750 gram group than in full-term controls. No significant differences in neuropsychological function or academic achievement were found between the full-term group and the 750 to 1,499 gram. The findings of Litt et al. (2005) demonstrate that specific neuropsychological deficits resulting from neonatal trauma to preterm infants are predictive of academic achievement deficits in both reading and math.

Prematurity and LBW as Risks for Poor Quality of Life

One significant outcome of recent advances in science and health care is that a greater proportion of preterm infants are surviving into childhood and adolescence.

However, this increased survival is accompanied by increased risk for significant impairment. Not only are premature infants at risk for neurocognitive impairments, but they are also at greater risk for difficulties related to physical health, growth, and neurocognitive development (Aylward, Pfeiffer, Wright, et al., 1989; Hack, Flannery, Schluchter, et al., 2002). In other words, children born prematurely are more likely than their full-term peers to experience problems in physical or mental functioning that may interfere with their ability to navigate academic, social, and home environments. These difficulties may also affect psychological well-being and quality of life. Childhood quality of life (QOL) is of particular importance because it reflects not only the degree to which impairment may be present in the domains in which children are expected to function, but also the extent to which children are able to cope with the stress, demands, or circumstances pertaining to their abilities in those areas relevant to them.

Preterm children have been identified as an at-risk population due to their increased risk for problems in physical and mental health. The limited research that does exist shows a relationship between HQOL and physical, psychological, and neurocognitive functioning. Psychiatric diagnosis, learning disabilities, and executive function deficits (e.g., Attention-Deficit/Hyperactivity Disorder; ADHD) predict lower childhood QOL (Klassen, Miller, & Fine, 2004; Matza et al., 2004; Sawyer et al., 2002; Sherman, Slick, & Eyrl, 2006).

In one study, Schiariti and colleagues (2007) examined health outcomes of preschool children born before 38 weeks gestational age (n = 50) and between 28 and 32 weeks gestational age (n = 201). Parent ratings of child health status using the Preschool Version of the Health Status Classification System revealed significant differences

between the 28-32 week preterm group and full-term group in all health-related domains, including physical abilities, growth and development, pain and discomfort, temperament and moods, and change in health. Parent responses to the Infant and Toddler Quality of Life Questionnaire also revealed an increased number of problems associated with health status (i.e., problems associated with neurosensory and motor functioning) among the 28-32 week preterm group. Behavioral outcomes were similar across all three groups of preschoolers. These findings point to an association between preterm birth and children's health status and QOL.

Limitations of the Existing Research

A number of limitations exist in the existing preterm and QOL literature. For example, studies are limited by the use of outdated instruments or normative data (Lih et al., 2000). Comparisons across studies are also limited by inconsistent definitions of the construct and wide variation in instruments used to measure QOL (Coghill, Danckaerts, Sonuga-Barke, Sergeant, & the ADHD European Guidelines Group, 2009). The validity of using parent or caregiver reports as proxy measure of child QOL, or subjective perceptions of the child regarding the impact of health status on different areas of life functioning, has also been challenged (Chien, Chou, Ko, & Lee, 2006).

The majority of existing studies are also limited by the age of children at follow-up assessment. Studies that report cognitive, behavioral, and QOL of life outcomes for very young (i.e., toddler and preschool age) children (Chien et al., 2006; Laucht, Esser, & Schmidt, 1997) may not fully reflect the impact of health status on daily functioning in preterm individuals due to the fact that the low-severity, high-prevalence deficits that are

common in this population may not be detected until children reach school ages (Taylor et al., 2000).

At present, there is a lack of consensus regarding the immediate prognosis and long-term outcomes of infants born prematurely and LBW. According to Gooi, Oei, and Lui (2003), misconceptions about premature and LBW infants' chances for survival and QOL may have a negative impact on physician's treatment decisions and the quality of care provided infants at the extremes of prematurity (i.e., less than 500 grams or 24 weeks gestation). In one study, Morse et al. (2000) found that physicians were less likely to make decisions to use corticosteroids, perform c-sections, or transfer mothers to perinatal treatment centers when they felt more pessimistic about the outcome for the infant. In a survey of physicians' attitudes about premature and LBW infants' future outcomes, Martinez et al. (1998) found that 90% of the responding obstetricians rated the QOL of infants born before 24 weeks to be "dismal." Based upon existing literature, it is clear that more information about the QOL of surviving premature and LBW infants is needed to inform not only obstetricians' decisions about treatment, but also the content of information presented parents when they are counseled about the decision-making process in high-risk situations such as premature and LBW deliveries.

Hypothesis for the Current Study

The current study examined health-related QOL among form preterm school-aged (i.e., 7-16 years of age) children and adolescents. Research has shown that chronic health conditions (e.g., asthma, epilepsy) and executive function deficits (e.g., Attention-Deficit/Hyperactivity Disorder) are significant predictors of QOL (Escobar et al., 2005; Devinsy et al., 1999; Klassen et al., 2004; Sherman et al., 2006). Research has

also documented an association between premature birth and poor HRWL in children at 42 months of age (Schiariti et al., 2007).

Preterm infants are at increased risk for health problems, cognitive impairments, learning, attention, and behavior problems, as well as for social and emotional difficulties—cognitive and psychosocial sequelae that in turn place children at risk for problems in physical, emotional, social, and school functioning (Aylward, 1992, 1997; Taylor et al., 2000). However, no research has examined the effects of premature birth on QOL in children beyond preschool age. In addition, generalization of existing findings is limited by non-uniform terminology, inconsistent classification of premature and low birth-weight infants, and the use of parents' ratings as the sole outcome measure.

The purpose of the current study was to assess differences in QOL among school-aged children who were born preterm and full-term. Based upon the increased risks for cognitive, academic, behavioral, and social-emotional difficulties experienced by the preterm children, it was hypothesized that QOL ratings (both parent and self-report) of children born preterm would be significantly lower than for full-term children across all QOL domains: total scores, physical, psychosocial, emotional, social, and school functioning.

CHAPTER II

LITERATURE REVIEW

Infants are considered low birth weight according to the World Health Organization (WHO, 1961) if they are born below 2500 grams and premature if born before 37 weeks gestation. In North America and Europe, approximately 5-8% of infants are born prematurely and of low birth weight. In affluent societies, low birth weight is often a secondary consequence to prematurity, whereas intrauterine growth retardation (IGUR) often results from inadequate nutrition or prenatal care and accounts for the majority of low birth weight infants in developing countries (Aylward, 1997, 2002). Prematurity is of particular interest due to the increasing number of infants who are surviving due to improvements in neonatal intensive care units; however, the long-term consequences of prematurity for infants who survive the immediate postnatal period are still relatively unknown. Research has shown higher rates of major handicaps in LBW compared to full-term infants, and this disparity increases in inverse proportion with the birth-weight of the infant (i.e., the highest incidence of major handicaps is noted for ELBW infants) (Alyward, 2002). Futhermore, high prevalence/low severity dysfunctions such as learning disabilities, intellectual disability, ADHD, and specific neuropsychological deficits occur in 50%-70% of VLBW infants (Alyward, 2002; O'Callaghan et al., 1996).

Environmental Risk Factors for Prematurity and LBW

Research has demonstrated that infants born prematurely and LBW (i.e., preterm infants) share a number of interrelated environmental and biological risk factors

(Aylward, 1997, 2002; Bacharach & Baumeister, 1998; Laucht, Esser, & Schmidt, 1997). Environmental variables such as low socioeconomic status (i.e., social class), low pre-pregnancy weight, inadequate weight gain during pregnancy, and poor previous pregnancy outcomes are associated with increased risk for preterm birth (Aylward, 1997, 2002).

Despite overwhelming evidence of the contribution of environmental factors to developmental outcomes, research has indicated that the negative consequences of environmental risk are not equally distributed across specific neurocognitive functions. For example, although research has demonstrated that environmental factors negatively affect expressive and receptive verbal performance and cognitive processing, the impact of environmental risk on gross and fine motor and sensory functions has been shown to be negligible. In other words, while environmental risks have the greatest potential to affect overall cognitive and verbal functioning, biological risks have the greatest potential to affect neurological and perceptual-performance (Alyward, 1997).

Other environmental variables associated with neurocognitive and developmental outcomes among preterm infants include availability of social support, accessibility of resources, quality of the child's home environment, and the presence of the father in the child's life (i.e., the marital or relationship status of the mother) (Bradley & Casey, 1992). However, research suggests that parents of preterm infants may develop different or less attentive response patterns as a result of their infants' biological characteristics (e.g., decreased responsiveness to the environment; increased negative emotionality) which may compound difficulties with behavior and attention seen later in development (Robson & Cline, 1998). These and other similar findings support the interactive nature

of environmental and biological risks to the preterm infant, and suggest that interventions targeted at improving the parenting of at-risk infants (Patteson & Barnard, 1990) may off-set some of the long-term developmental consequences of prematurity (Blair, 2002).

Biological Risks Factors for Prematurity and LBW

A second and equally important category of risk refers to direct or indirect exposure by the developing fetus to a potentially harmful event. Examples of biological risks include prenatal exposure to toxins, sedatives, hypnotics, local anesthetics, or anticonvulsants; maternal alcohol/drug use; and exposure to environmental toxins such as lead or carbon monoxide (Alyward, 1997). Decreases and increases in cerebral blood flow, fluctuations in cerebral blood flow, hemorrhaging, asphyxia (i.e., the loss or complete reduction of oxygen flow to the brain), and increased pressure within the venous cavity represent a number of biological events that increase the risk to the developing brain of the preterm infant (Aylward, 1997).

Results of insult, trauma, or disease for full-term infants vary in nature and degree in this population. In early stages of development, the blood-brain barrier (which protects the brain from chemical toxins in the blood) is not yet fully developed, which leads to increased vulnerability during the prenatal period (Spreen et al., 1995). Furthermore, infants born prematurely are at significantly greater risk than full-term infants for neuropsychological damage during prenatal, labor, and postnatal periods due to more immature development of systems within the central nervous system (CNS) (Spreen et al., 1995). Neuroplasticity of visual, motor, and language systems serves as a reparative function at the synaptic level in response to early brain damage (Lenn, 1991); however,

the degree to which plasticity can compensate for CNS damage depends on the nature, location, and timing of the insult. According to Lenn (1991), severe and acute insults occurring earlier in brain development are least likely to be fully compensated for by neuroplasticity.

Periventricular hemorrhage (PVH) and intraventricular hemorrhage (IVH) are common among infants born before 32 weeks gestation. Hypoxic-ischemic encephalopathy (HIE), or oxygen deprivation to the brain due to decreased oxygen and blood flow, differentially affects the developing white matter of the preterm brain, often leading to white matter cell death. Cell death in the areas surrounding the lateral ventricles, or periventricular leukomalacia, most frequently occurs among preterm infants born at 27-30 weeks gestation. Periventricular infarction, which is defined by white matter cell death through hemorrhage, typically occurs asymmetrically in the periventricular white matter of frontal, parietal, and occipital regions.

Infections of the preterm infant's brain tissue or membrane enclosing the brain are also linked with neuropsychological outcomes and are thought to result in damage to the axons or dendrites of the infant brain. For example, viral disease (e.g., cytomegalovirus) and congenital rubella are commonly associated with IUGR. Exposure to environmental toxins and maternal drug use may also result in direct or indirect damage to the CNS of the developing infant, although the effects of toxins vary according to a number of factors, making it difficult to predict both concurrent and long-term health and neuropsychological outcomes (Aylward, 1997).

Maternal malnutrition during the early stages of pregnancy (often secondary to drug use and disease and/or related to environmental factors and conditions) often results

in reduced overall cell number, inhibited synapse formation, and interference with cell migration. Other effects, secondary to the metabolic disruption to vulnerable brain regions during gestation as a result of these conditions, include hemorrhage, reduction of blood flow to the brain, and other disruptions of cerebral blood flow. Results of these events may include both white and gray matter damage, commonly leading to neuropsychological deficits in motor control and memory.

Neurocognitive Outcomes of Children Born Prematurely

Studies have documented cognitive and neuropsychological differences in children born prematurely and LBW as compared with children born full-term. In a study by Litt and colleagues (2005), the authors examined neuropsychological function and academic achievement among three groups of children (mean age = 11 years) at long-term follow-up. The sample consisted of 31 children who were born weighing less than 750 grams; 41 who weighed between 750 and 1,499 grams; and 52 full-term, normal birth-weight controls. Neuropsychological outcomes were categorized according to prorated IQ (using the Wechsler Intelligence Scale for Children, Third Edition) and three additional factors: perceptual planning, verbal list learning, and verbal working memory. Academic achievement for reading and math was evaluated using the Woodcock Johnson Test of Achievement Revised and Wechsler Individual Achievement Test. Children were identified as Learning Disabled on the basis of either low achievement in reading, math, or both, or IQ-achievement discrepancies where children demonstrated low achievement for reading or math despite intellectual functioning within the average range.

Results of this study indicated significantly poorer reading and math achievement and perceptual-organizational skills among children born < 750 grams in comparison to children born between 750 and 1,499 grams and full-term controls. Estimated intellectual functioning was significantly lower in the < 750 gram group than in full-term controls. No significant differences in neuropsychological function or academic achievement were found between children born 750 to 1,499 grams and full-term controls. Findings demonstrate that specific neuropsychological deficits resulting from neonatal trauma (e.g., periventricular leukomalacia, intraventricular hemorrhage) are predictive of academic achievement deficits in both reading and math.

In another study, Hack et al. (1994) compared cognitive, neuropsychological, and academic outcomes among children born weighing less than 750 grams (n= 68), 750 to 1499 grams (n=65), and full-term controls (n= 61). Neuropsychological, academic achievement, and demographic data were collected for the three groups; group age means and standard deviations at follow-up were reported as 6.7 (0.9), 6.9 (0.9), and 7.0 (0.9) respectively. Results revealed significantly poorer outcomes for the less than 750 gram group for neurosensory, physical, and developmental outcomes. Neuropsychological assessment revealed significantly poorer academic achievement as well as poorer cognitive, language-processing, gross motor, visual motor, and attention skills in the less than 750 gram group compared to the 750 to 1499 gram group. The less than 750 gram group was also significantly poorer on measures of behavior and social skills, adaptive behavior, and teacher or parents' ratings of school performance. Developmental outcomes were mediated by neonatal complications including respiratory distress, apnea of prematurity, necrotizing enterocolitis, patent ductus arteriosus, and septicemia.

The overall results of Hack et al.'s study revealed significantly poorer developmental outcomes among very-low-birth-weight infants (i.e., those weighing less than 750 grams) in comparison to those born weighing 750 to 1499 grams and full-term controls. These infants demonstrated a significantly greater proportion of global cognitive impairments (including intellectual disability), visual motor, gross motor, and adaptive functioning deficits, academic difficulties, attention problems, and neurosensory impairments (including cerebral palsy and visual disability). Ultrasonographic abnormality and perinatal dependence on oxygen were associated with intellectual disability and cerebral palsy in both groups of low-birth-weight infants. Social disadvantage, maternal age, marital status, race, and educational attainment, which made up an index of social risk, were not associated with developmental outcomes. These findings highlight the developmental risks to premature and low-birth-weight infants, and further demonstrate that these risks increase significantly not only as birth-weight decreases, but also as a function of neonatal complications.

Social, Emotional, and Behavioral Outcomes of Children Born Prematurely

Increased risks for social, emotional, and behavioral problems have been documented among children born prematurely and LBW. Animal research has demonstrated a relationship between iron deficiency and oxygen deprivation (which may affect dopamine transmission in brain areas such as the prefrontal cortex and striatum) and neurobehavioral outcomes characterized by both behavioral inhibition (i.e., anxiety, withdrawl, and decreased motor activity) and behavioral activation (i.e., hyperactivity and disinhibition) (Beard, Erikson, & Jones, 2002; Erikson, Jones, & Beard, 2000; Lou,

Rosa, Pryds, et al., 2004). These findings provide insight into possible behavioral outcomes of premature and LBW infants given the increased risks of iron and oxygen deficiency to the underdeveloped neonate (Alyward, 1997, 2002).

Research on the behavioral and social development of children born prematurely and LBW has documented increased risks for hyperactive behavior (Hoff, Hansen, Munck, & Mortensen, 2004). Hoff et al. (2004) reported that findings of increased outward reacting and hyperactive behavior and poorer social skills were associated with lower performances on measures of global cognitive functioning. In addition, emotional availability and the ability to accurately interpret their children's needs (as measured by the Parental Sensitivity Assessment Scale) were associated with decreased outward reacting and hyperactivity. Studies have also documented increased rates of somatization (Grunau, Whitfield, Petrie, & Fryer, 1994) and poorer self-esteem (Witgens, Lepine, Lefebvre, Glorieux, Gauthier, & Robaey, 1998) among children who were born prematurely compared to full-term controls.

In one longitudinal study, Nadeau et al. (2003) examined outcomes in a sample of 162 children (96 VLBW and premature; 66 full-term controls) at 18 months (age corrected for premature birth), 5 years 9 months, and 7 years. Social variables were assessed in school settings using the Revised Class Play (French, condensed version); parents' and teachers' reports of behavioral variables were gathered using the Child Behavior Checklist and Teacher's Report From. Results of this study demonstrated significant relationships between VLBW status and both social and behavioral outcomes. In other words, after controlling for variables associated with family environment (e.g.,

family adversity at the time of the infant's birth), birth status was still positively and significantly related to isolation, social withdrawal, and attention problems at age 7.

Academic Outcomes of Children Born Prematurely

Due to their increased vulnerability for cognitive, neuropsychological, social-emotional, and behavioral problems, premature and LBW children are also at increased risk for academic difficulties. In a study by Hack et al. (1994), results of achievement testing using the Woodcock-Johnson Tests of Achievement, Revised (Word Identification, Dictation, Applied Problems, and Calculation subtests) and teacher ratings of academic outcomes (using the Academic Performance Rating, Teacher's Report Form and Academic Skills Rating) indicated significantly poorer achievement among school-age children born VLBW. Moreover, 45% of VLBW children in this sample were receiving special education services. Another study by Hagen et at. (2006) reported significantly poorer math achievement among VLBW children (based upon standardized test results using the Wisconsin Knowledge and Concepts Exam and teacher rating of academic outcomes using the Achenbach Teacher Report Form) born during an era in which surfactant therapy was used to enhance the survival of extremely premature neonates. The authors interpreted this finding to suggest that one consequence of medical treatments that have increased the survival rates of VLBW infants may be poorer academic achievement among these children at school ages.

Achievement discrepancies between LBW and control children have also been reported by Litt et al. (2005), the most significant of which a moderate effect size difference in math scores obtained on the Woodcock-Johnson Test of

Achievement-Revised. However, Litt and colleagues (2005) did not find significant differences between LBW and control groups in rates of education assistance (i.e., special education placement and remedial services). In a study by O'Callaghan, Burns, Gray, and Harvey (1996), teachers reported significant problems in the academic areas of reading, spelling, and mathematics among ELBW children. Moreover, ELBW children were approximately three times more likely to be delayed in all academic areas by at least one year compared with full-term controls. In addition, approximately half of ELBW children received remedial academic assistance (46%) or special education services (4%).

Overall, research on achievement outcomes of premature and LBW infants at school age indicates poorer general academic functioning in addition to more specific areas of weakness, such as mathematics (Hack et al., 1994; Hagen et al., 2006; Litt et al., 2005; O'Callaghan et al., 1996). Differences in academic achievement between VLBW and full-term children appear to be mediated by specific deficits in neuropsychological functioning such as memory, language, perceptual-organizational, or executive functioning problems (Lih et al., 2005) that, although considered less severe, are estimated to be highly prevalent among the preterm infant population (Alyward, 2002; Spreen et al., 1995; Taylor et al., 2000). These deficits are often not recognized in early development, but rather are identified as a result of learning difficulties that emerge during the first few years of formal education. Early identification of learning difficulties among this population is crucial, however, given the potential for academic problems to lead to additional problems in psychosocial and behavioral domains.

Health-Related Quality of Life

In 1991, The Department of Health and Human Services published a report entitled *Healthy People 2000*, which outlined United State's policymakers' goals for improving health and preventing diseases. The primary objectives of this report included increasing the quantity of life (i.e., increasing lifespan) and enhancing the quality of one's existence (Erickson, Wilson, & Shannon, 1995). Research in the last several decades has demonstrated the importance of understanding the impact that mental, physical, and social difficulties can have on the quality of an individual's daily life. Developments in science and medicine have provided methods of prevention and treatment for once-common and fatal illnesses, prolonged the average human lifespan, and drastically changed the nature of daily living in that a much larger proportion of individuals in developed countries are not struggling to meet basic survival needs. However, research has called quantitative measures of life such as age and income into question, and posited that such indices are insufficient and potentially inaccurate predictors of subjective experiences of well-being (Campbell, 1976).

Much of the current QOL research can be traced to breast cancer treatment studies of the late 1970s. The findings of one such study indicated that women who had undergone outwardly similar experiences in terms of physical trauma and medical interventions perceived the event and experienced ensuing emotional distress very differently (Meyerowitz, Sparks, & Spears, 1979). Although exogenous events were associated with increased potential for emotional distress, the impact of these events on daily functioning was more associated with women's subjective perceptions of these

events and with their perceptions of the availability of psychosocial support than with the nature or severity of the cancer diagnosis.

Subjective reports of well-being inherently depend on gathering individuals' perceptions of their ability to function in critical life domains as well as their feelings and attributions about their daily lives and experiences. How to reliably and validly measure subjective perceptions of well-being has become an important challenge in psychological health research. In one early article, Shaw (1977) argued that physicians should not simply consider physical and intellectual characteristics of an individual when estimating his or her QOL. Shaw (1977) posited that QOL is better represented by a formula that takes into account both a person's physical and intellectual characteristics as well as both the contributions that individual's family make to him or her and the contributions the individual makes to society. According to Shaw (1997), "a person's quality of life, whether it be a baby born with an intestinal obstruction or an octogenarian with terminal cancer, may be determined to a significant degree by factors physicians frequently fail to consider" (p. 11).

Since the emergence of early definitions of the concept, QOL research has extended beyond adults with cancer to individuals representing a broad range of ages and illnesses. However, researchers have yet to agree upon a common definition of concept, which has been assessed by a variety of different procedures and instruments. One of the most commonly utilized definitions regards the "impact of disease and disability upon daily functioning" (Kaplan, 1985, p. 116). Health-related definitions of QOL specifically address the ways in which health status affects aspects of physical (e.g., mobility,

capacity to care physically for oneself) and psychosocial (e.g., social interaction, emotional behavior, communication) well-being (Kaplan, 1985).

Research in the field of health psychology has demonstrated that the same event (e.g., illness) can have different effects on individuals' daily functioning. In other words, it is now understood that the degree to which illness, disease, and trauma affects a person depends on the individual's personal traits/attributes as well as social/environmental circumstances (Kaplan, 1985; Shaw, 1977). Research has also demonstrated that the relationship between health/disease status (as measured by prevalence and incidence rates of a given medical condition) and QOL is mediated by cognitive (e.g., intellectual), social (e.g., coping, social support), and environmental (e.g., exposure) variables (Cohen et al., 1980; Sarason et al., 1983). These and other similar findings from research in public health, health psychology, and medicine prompted renewed exploration of the standards by which medical (and psychological) treatments are considered effective. In order for painful, costly, and time-consuming interventions to be deemed worthwhile, it would be necessary to demonstrate that the treatment not only prolonged, but enhanced subjective, day-to-day experience of the patient (Kaplan, 1985).

Health-Related Quality of Life

Outcomes among Children

Research has documented poorer QOL among children with chronic physical illness, Attention-Deficit/Hyperactivity Disorder (ADHD), mood disorders, behavior disorders, and psychiatric illnesses (Klassen, Miller, & Fine, 2004; Matza et al., 2004; Sawyer et al., 2002; Sherman, Slick, & Eyrl). In one study (Klassen, Miller, & Fine,

2004), 165 parents of children with ADHD (mean age = 10) from the ADHD Clinic in British Columbia completed the parent version of the Child Health Questionnaire (CHQ-PF50) and the Child/Adolescent Symptom Inventory (CSI). Parents of children with ADHD rated their children significantly lower than parents of non-ADHD children for all psychosocial domains, including: psychosocial health, family activities, family cohesion, and psychosocial summary. Effect sizes for psychosocial health deficits ranged from moderate (e.g., -0.66; self-esteem) to large (e.g., -1.98; psychosocial summary score).

Moreover, ratings of psychosocial health for children with comorbid diagnoses of Oppositional Defiant Disorder and Conduct Disorder (but not Learning Disorders) were significantly lower than in children without comorbid diagnoses. Parent reports of ADHD symptom severity were negatively correlated with psychosocial domains of health-related QOL. These findings suggest a strong relationship between poor QOL and ADHD; however the study is limited by the use of a clinical ADHD sample, cross-country comparison of data from a Canadian-based sample with United States and Australian norms, and reliance on parent-proxy ratings of ADHD symptoms and QOL.

Sawyer and colleagues (2002) considered health-related QOL among children and adolescents diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD), Major Depressive Disorder (MDD), or Conduct Disorder (CD). Participants included 3,597 respondents to a national survey of Australian parents with children and adolescents between 6 and 17 years of age. Mental disorders were identified in children and adolescents based upon parent responses to the parent version of the Diagnostic Interview Schedule for Children Version IV (DISC-IV). In order to assess QOL, parents also

completed the parent version of the Child Health Questionnaire. Results revealed significantly poorer QOL among children meeting DISC-IV criteria for MDD, ADHD, and CD, indicating that parent CHQ scores for children with mental disorders were significantly lower than for children with no disorder. Parents perceived mental health to interfere more greatly with their children's lives in family activities, peer and school activities, and daily lives than did parents of children with physical (but not mental) disabilities. The results of this study indicate the profound impact that mental disorders can have on child and adolescent domains of functioning. One notable limitation of this study, however, was the use of parent reports to assess both the presence of mental disorders in their children as well as their children's QOL.

An association between deficits in executive function and poor QOL was demonstrated by Sherman et al. (2006). Participants in this study were 121 children with epilepsy (mean age = 11.9 years) seen for neuropsychological evaluations at British Columbia's Children's Hospital. Clinical data included age of epilepsy onset, duration of epilepsy, number of anti-epileptic drugs, number of failed anti-epileptics, seizure frequency, and level of adaptive behavior (determined by parents' ratings of the child's ability to function independently in a number of domains using The Scales of Independent Behavior—Revised [SIB-R]). Executive function was assessed using the Behavior Rating Inventory of Executive Function (BRIEF). Health-related quality of life was assessed using The Impact of Childhood Illness Scale (ICI), a questionnaire completed by parents that assesses the general impact of the illness and its treatment on child development and adjustment, parents, and family.

Sherman et al.'s (2006) results indicated that the number of antiepileptic drugs taken currently by the child, the previous number of antiepileptic drugs taken, and the child's adaptive level were significant predictors of QOL. The authors also reported clinical-level impairments in executive function in 45.2% of children. Deficits in executive function were significantly correlated with poorer QOL. Overall, findings suggest that impairment in executive function is an important indicator of risk among children, and that risks may be compounded for children with low adaptive levels and for those with neurological conditions that require long-term pharmacological treatment. The results of this study should be interpreted with caution, however, given the use of a behavior rating inventory rather than a neuropsychological battery to assess executive function.

In another study, Matza, Rentz, Secnik, Swenson, Revicki, Spencer, & Kratochvil (2004) examined health-related QOL among 297 outpatient children (mean age = 11.2 years) diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD). Participants were randomly assigned to one of three atomoxetine treatment groups (0.5, 1.2, and 1.8 mg/kg) or a placebo-control group. Symptoms of ADHD were assessed using both the ADHD Rating Scale-IV; Parent Version (ADHD-RS) and the Clinical Global Impressions-ADHD-Severity (CGI-ADHD-S). The parent form of the Child Health Questionnaire (CHQ-PF50) was used to assess QOL. Mean symptom and QOL ratings for the four groups were compared at baseline, endpoint, and in terms of the 8-week change scores. Results revealed statistically significant improvements among all four groups in ADHD symptoms. Participants were then classified into mild, moderate, and severe groups based upon their ADHD-RS total score. Mean scores for the psychosocial

scales of the CHQ-PF50 (Role Limitations-Emotional/Behavioral, Behavior, Mental Health, Self-Esteem, Parental Impact-Emotional, Parental Impact-Time, Family Activities, and the Psychosocial Summary Score) were reported as 1.5 standard deviations (SDs) below average at baseline and 1.0 SDs below average at endpoint.

Results of the Matza et al. (2004) study indicated a negative correlation between ADHD symptoms and QOL. Specifically, mean scores for psychosocial scales varied as a function of ADHD symptom severity (mild, moderate, and severe). Results demonstrated that psychosocial problems among children with ADHD persist beyond clinical symptom reduction. However, a number of limitations exist. For example, although participants were originally randomly assigned to atomoxetine treatment or control groups, these groups were collapsed for the purpose of the current analyses, yielding mean scores for the entire sample. No comparisons were made between groups. The authors also failed to report means and SDs for the population with which mean samples scores were compared.

Research has also examined the relationship between QOL and psychiatric symptoms. Bastiaansen, Koot, and Ferdinand (2005) assessed 126 child psychiatric outpatients from 7 to 19 years of age (mean age = 12.3 years) with diagnoses of Attention-Deficit/Hyperactivity, Anxiety, Mood, Pervasive Developmental or Other Disorders. Parent ratings of child behavioral and emotional problems (i.e., psychiatric symptoms) were obtained at initial assessment (Time 1) and at one-year follow-up (Time 2) using the parent form of the Child Behavior Checklist (CBCL); parent ratings of quality of life were obtained using the parent-proxy form of the Pediatric Quality of Life Inventory (PedsQL).

Bastiaansen and colleagues' (2005) results revealed statistically significant improvements between Time 1 and Time 2 in psychiatric symptoms and quality of life; 33.3% of participants showed clinically significant improvement in both domains. Results also demonstrated clinically significant improvements in QOL among 22.6% of children for whom psychiatric symptoms remained high across time. Prognosis for participants was defined on the basis of Time 2 clinical scores within the normal range of functioning on the CBCL, PedsQL, or both measures. Results indicated poor prognosis for 38.1% and moderate or good prognosis for 61.9% of the total sample at follow-up. Prognosis was unrelated to diagnostic category. Overall, findings indicate a moderate relationship between quality of life and child/adolescent psychopathology. Implications for clinical practice with children and adolescents include the potential benefits of addressing quality of life in the context of child and adolescent interventions. However, this study was limited by reliance on parent-proxy ratings to assess psychiatric symptoms and pediatric quality of life.

As previously mentioned, Schiatriti and colleagues (2007) examined the health outcomes of 251 preschool children born before 28 weeks gestational age (n = 50) and between 28 and 32 weeks gestational age (n = 201). Questionnaires were mailed to families in British Colombia; response rates were 57% for parents of neonatal intensive care unit graduates and 56.3% for parents of healthy infants. Parents rated their children's health status using the Preschool Version of the Health Status Classification System (HSCS-PS); QOL was measured by parent ratings using the Infant and Toddler Quality of Life Questionnaire (ITQOL). Behavioral, social, and emotional outcomes were measured using the parent form of the Child Behavior Checklist (CBCL).

In the Schiatriti et al. (2007) study, results of parent ratings revealed significant differences between the 28-32 week preterm group and full-term infants in all health-related domains, including: physical abilities, growth and development, pain and discomfort, temperament and moods, and change in health. Ratings of ITQOL were similar between preterm groups. Results also revealed an increase of reported problems related to health status (i.e., problems associated with neurosensory and motor functioning) among the 28-32 week preterm infants. Behavioral outcomes were similar across all three groups of preschoolers at follow-up. Overall, findings suggest the need for early intervention with children born prematurely, particularly for those children born before 28 weeks gestational age. One limitation of this study, however, was the use of parent reports as outcome measures for health status, quality of life, and behavior. In addition, the use of 'gestational age' versus 'birth-weight' as the selection criterion is questionable given the fact that birth-weight and gestational age, although correlated, are differentially related to long-term neuropsychological and behavioral outcomes (e.g., Alyward, 2002).

Key Considerations in QOL Assessment

A number of conceptual and methodological problems have emerged in QOL assessment, including vague or non-uniform definitions of the construct and the use of parents or teachers to estimate child QOL. A study by Hays et al. (1995) found overall agreement between self and proxy ratings of QOL to be moderate (from $r = 0.29$ to 0.56). However, level of agreement was also associated with the domain of functioning assessed. For example, agreement was best for domains of functioning that were

observable in nature and worst for subjective areas of functioning. Proxies in this study reported better cognitive functioning and worse health perceptions than self-reporters, and overall agreement between self and proxy reports was found to be indirectly related to patient education.

In a Danish study by Theunissen et al., 1998, children's self-reports of QOL were significantly lower than the parent proxy reports for physical complaints, motor functioning, autonomy, cognitive functioning, and positive emotions. Other researchers have reported similar findings, suggesting that adolescents self-reports also differed from parent-proxy reports on more subjective (and likely less observable) measures such as emotional functioning (Saigal, Rosenbaum, Hoult, Furlong, Feeny, Burrows, & Stoskopf, 1998), pain/physical symptoms, and social functioning (Verrips, Vogels, den Ouden, Paneth, & Verloove-Vanhorick, 2000).

Conclusion

The extant research has demonstrated that children born prematurely and LBW are at risk for problems in health, neuropsychological functioning, learning, academic achievement, behavior, and psychosocial adjustment. Research has further demonstrated that a variety of physical and psychological conditions are associated with poorer QOL among children. However, few studies have examined pediatric QOL among preterm school-aged children. Moreover, existing studies have not explored the relationship between cognitive, academic, and social/emotional functioning and QOL.

Hypothesis

The purpose of the current study was to assess differences in QOL among

school-aged children who were born preterm and full-term. Based upon the increased risks for cognitive, academic, behavioral, and social-emotional difficulties experienced by the preterm children, it was hypothesized that QOL ratings (both parent and self-report) of children born preterm would be significantly lower than for full-term children across all QOL domains: total scores, physical, psychosocial, emotional, social, and school functioning.

CHAPTER III

METHODS

Participants

Participants included 54 children (26 preterm; 28 full-term) and their guardians volunteering to participants in a longitudinal research study at the University of Iowa Hospitals and Clinics (UIHC) on the long-term impact of different hematocrit thresholds for red blood cell transfusion (Bell, Strauss, Widness, Mahoney, Mock, & Seward et al., 2005). Eligible preterm participants were born prematurely (i.e., before 37 weeks gestation), had birth weights between 500 and 1300 g, received neonatal care at the University of Iowa Children's Hospital between December, 1992 and June, 1997, and received one or more packed red blood cell transfusions during the neonatal period. Infants were excluded from participation in the initial study if they had alloimmune hemolytic disease, congenital heart disease, other major birth defects requiring surgery, or a chromosomal abnormality; if their parents had strong philosophical or religious objections to transfusion; if they were thought to face imminent death; if they had received greater than two red blood cell transfusions prior to enrollment in the study; or if they were already enrolled in a clinical study that might interfere with the conduct or outcome of this study.

Assessments of full-term and preterm children began in 2005, approximately 13 years following the onset of the longitudinal research study. Parents/guardians of preterm children were contacted by research nurses and asked if they would be interested in having their child participate in a study on the effects of RBC transfusion on brain structure and function in children born prematurely, as a follow-up to the original

transfusion study. Parents who expressed interest were asked screening questions. None of the children who could be located met any of the exclusion criteria: significant hearing loss and history of epilepsy, brain tumor, or head injury resulting in unconsciousness or concussion. A total of 46 preterm subjects from the original sample did not participate in the follow-up study: 3 were deceased, 12 declined to participate, and 31 were unable to be contacted. A death index search was conducted on those children who were lost to follow-up. These children did not match any death records through 2007. The Score for Neonatal Acute Physiology (SNAP; Richardson et al., 1993) was recorded on the day of birth and once daily through the first week of life.

Preterm participants for the current study met the initial entrance criteria for participation in the Iowa Trial and did not, by parent report and review of their medical records meet any of the exclusion criteria at the time of follow-up. All participants, both full-term and preterm, provided written and verbal assent for participation and were observed by a licensed psychologist and/or doctoral graduate assistant to be capable of adequately understand the statements in the QOL questionnaire. In some instances, it was necessary for the examiner to provide further assistance if children had difficulty reading a word or needed further explanation in order to answer the questionnaire accurately.

Full-term control children and their guardians were recruited via advertisements in local newspapers across the state of Iowa. Efforts were made to recruit healthy, full-term children from across who would be most representative of the general population. Telephone interviews were conducted with parents/guardians who responded to advertisements in order to determine eligibility. Potential controls were excluded based upon parent/guardian reports of the following:

1) If the child reportedly had a history of learning problems or learning disability diagnosis;
2) If the child had ever been retained a grade in school;
3) If the child had a history of mental/psychiatric illness, had received or was receiving counseling for mental/psychiatric illness and/or had taken or was currently taking medication for mental/psychiatric illness;
4) If the child had been given a diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD);
5) If the child had any medical problems (e.g., heart defects);
6) If the child had major illness requiring ongoing medical care;
7) If the child had a history of epilepsy, brain tumor, or brain trauma.

Procedures

Guardians of participants were reimbursed for travel, lodging, and meal expenses and child participants were compensated monetarily. Guardians were asked to accompany their children to the hospital, and informed consent was obtained in writing from one or both guardians prior to their child's participation. Guardians completed a demographic questionnaire designed for this study that included questions regarding academic performance and socioeconomic status. Children completed a battery of cognitive, neurologic, behavioral, and social-emotional tests (administration lasted approximately 160-180 minutes). All assessments were conducted by licensed psychologists and psychology graduate assistants who were blind to the transfusion group of the children.

Parents of preterm participants were contacted by UIHC nurses between 2005 and 2007 and asked if they would be interested in participating in a study on the effects of red blood cell transfusion on brain structure and function among children born prematurely. Parents who expressed interest were placed on a mailing list and received phone calls regarding scheduling. Consenting parents of the surviving preterm children were asked to accompany their children to the UIHC to complete a battery of cognitive, neurologic, behavioral, and social/emotional tests lasting from 9:00 am until approximately 3:30 pm. Parents were informed that they would be reimbursed for travel, lodging, and meal expenses, and that compensation for participation in the amount of $100.00 would be provided to participating children.

The current author and another investigator reviewed the components of the study, including information regarding confidentiality and risks, with families upon their scheduled visit to the UIHC. Parental consent and child assent documents were also reviewed and signed at this time. Children completed the cognitive assessment in approximately 90 minutes. Children also completed a packed of self-report questionnaires, which typically required 30-40 minutes, depending on their age and reading ability. Parents completed a packet of information that will include demographic, behavioral, health, and QOL measures. The time required to complete this packet is approximately 30-40 minutes.

Instruments

Demographic Questionnaire

Participants' guardians reported the following demographic information: age, sex, and social class of parents. Sex was coded as a dichotomous variable (male/female). Age

was a continuous variable recorded to the thousandths of the year. Race and social class were coded as categorical variables consisting of 5 or more categories. Ethnic identity was coded as follows: (1 = White; 2 = Asian American; 3 = Black/African American; 4 = Hispanic/Latino; 5 = American Indian/Alaska Native; 6 = Hawaiian/Pacific Islander; or 7 = Multiracial).

The term "social class" is used in place of "socioeconomic status" in the current paper because (1) it refers to participants' guardians' ratings of their perceived social rank and (2) theoretical distinctions between the terms have not been clearly drawn (Liberatos, Link, & Kelsey, 1988; Liu, Fridman, & Hall, 2008; Oakes & Rossi, 2003), and therefore one term does not convey any more significance than the other. Based upon the recommendations by Hollingshead (1958), social class of participants and their guardians was assessed in the current study using the following 5-point scale:
1 = Families of wealth, education, top-rank social prestige (Highest Social Rank);
2 = Families in which adults hold college/advanced degrees; in professional or high-rank managerial positions (High Social Rank); 3 = Small businessmen, white collar and skilled workers; high school graduates (Middle Social Rank); 4 = Semi-skilled workers, laborers, education below secondary level (Low Social Rank); and 5 = Unskilled and semi-skilled workers; elementary education (Lowest Social Rank). Guardians were asked to circle the number corresponding to the description they perceived to best match their social class. Means and standard deviations were computed for preterm and comparison groups and for the two groups combined, with a lower mean score indicating higher ratings of social class rank. Demographic questionnaires were completed by the guardian of all but two

participants in the current study (one full-term; one preterm). The time required to complete this form is approximately 5 minutes.

Cognitive Functioning

It has been well-established that preterm status is correlated with specific cognitive deficits that may increase the risk for academic, behavioral, and psychosocial difficulties. However, the relationship between cognitive ability and quality-of-life has not thoroughly been investigated among school-aged children, at which time difficulties in behavioral, social, and academic functioning are often first observed (Taylor et al., 2000). Cognitive functioning was assessed using the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV; Wechsler, 2003a, 2003b). The General Ability Index (GAI) is a composite of verbal and perceptual domains that was used as an estimate of global cognitive ability. In addition, prorated index scores were obtained for the Verbal Comprehension Index (VCI) using Similarities and Vocabulary subtests; Perceptual Reasoning Index (PRI) using Block Design and Matrix Reasoning subtests; and Processing Speed Index (PSI) using Digit Symbol-Coding and Symbol Search subtests.

Index scores for each of the four intellectual domains are computed from standard scores (Mean = 100; Standard Deviation = 15) according to procedures, which are outlined in the manual, that allow comparison of the participants' performance with that of same-age peers. This procedure for estimating general intellectual functioning using prorated IQ scores is widely used in both clinical and research settings and is established as a valid and reliable method of estimating global cognitive abilities. Internal reliability ($r = .79$ to $.90$) and test-retest reliability ($r = .76$ to $.92$) for these subtests is excellent, as are internal reliability estimates for the GAI ($r = .96$) (Raiford et al., 2005). Standard

scores for GAI, VCI, PRI, and PSI were used in the analyses. The time necessary to complete these subtests is approximately 90 minutes.

Quality of Life

The Pediatric Quality of Life Inventory; PedsQL (Children's Hospital and Health Center, San Diego, California) was administered to assess subjective perceptions of well-being (Varni, Seid, & Kurtin, 2001; Varni, Seid, & Rode, 1999). The PedsQL inventories were originally developed from a cancer and designed to measure the effects of pain on daily functioning (Varni et al., 2001); it has been recently revised to reflect functional status in the core domains of health outlined by the WHO (i.e., physical, mental, and social) (WHO, 1948). The most recent of these revisions is the PedsQL (Version 4.0 Generic Core Scales), which was developed through focus groups and parent interviews as a non-categorical measure of health-related QOL to be used with healthy community and acute or chronically ill pediatric populations (Varni et al., 2001; Varni et al., 1999). This measure is available in parent proxy, young child (ages 5-7), child (ages 8-12), and adolescent (ages 13-18) forms and can be compared to general population or disease-specific norms. The time estimated to complete this measure is approximately 5-10 minutes.

The PedsQL is preferable to previous instruments that relied primarily on the ratings of health care providers and parent-proxies as estimate of children's QOL (Theunissen et al., 1998). The PedsQL (Version 4.0 Generic Core Scales) also reflects an improvement from previous QOL instruments that have failed to take into account the cognitive limitations of very young children as well as overlooked potential normative

differences between chronically or acutely ill and healthy child populations (Erickson et al., 1995; Kaplan, 1985; Saigal et al., 1998; Spieth & Harris, 1996).

The PedsQL (4.0 Generic Core Scales) is comprised of 23 items, which are grouped into four scales: Physical Functioning (8 items), Emotional Functioning (5 items), Social Functioning (5 items), and School Functioning (5 items) (Varni et al., 2001). Both child and proxy raters are asked to respond to items on a 1 to 5 scale, where 0 = "never a problem"; 1 = "almost never a problem"; 2 = "sometimes a problem"; 3 = "often a problem"; and 4 = "almost always a problem". The wording and response format of the young child version have been simplified to account for developmental differences in cognitive ability and reading ability. The reading level of the child and young child versions ranges from below-first to mid-second; the adolescent version is consistent with third to sixth grade reading levels (Varni et al., 2001).

Normative data were obtained from pediatric health care settings and are based upon a total sample of 963 children and 1,629 parent proxies (Varni et al., 2001; Varni et al., 1999). Internal consistency reliability coefficients for the individual scales of the self-report version range from .68 (School Functioning) to .83 (Psychosocial Health). Internal consistency reliability for the Total Score scale is .88. Coefficients for the proxy-report version range from .75 (Social Functioning) to .88 (Physical Health); reliability for the Total Score scale is .90.

Validity evidence for the PedsQL (Version 4.0 Generic Core Scales) suggests higher quality of life among healthy children than children who are chronically and acutely ill (Varni et al., 2001). Research also demonstrates moderate correlations between child self-reports and quantitative data regarding the number of days of required care

(r = -.24 for the Total Score scale) in the past 30 days and number of school absences (r = -.22 for Total Score). In addition, parent reports are correlated with data on number of work days missed (r = -.30 for Total Score), and with their reports on the impact of their child's functioning on both their work routine (r = -.44 for Total Scale) and work concentration (r = -.50 for Total Scale). Effect sizes for concordance between parent and child reports for each subscale range from medium (.30) to large (.50). Inter-correlations for individual scales are as follows: Physical Functioning = .50, Emotional Functioning = .36, Social Functioning = .37, and School Functioning = .41 (Varni et al., 2001; Varni et al., 1999).

As described by Varni et al., 2001, scaled scores are computed by dividing the sum of items within a given subscale by the total items completed. Scale scores are not computed for scales in which greater than 50% of items were not completed (Varni et al., 2001). Linear transformation to a 0 to 100 scale (e.g., 0 = 100; 1 = 75; 2 = 50; 3 = 25; 4 = 0) and reverse-scoring are used in order that higher scores correspond to higher ratings of QOL (Varni et al., 2001).

CHAPTER IV

RESULTS

This chapter will outline the results of the statistical analysis performed in the current study. All analyses were performed using SPSS 17.0 for Windows (SPSS Inc., Chicago, Illinois). The relationship of birth status (i.e., preterm vs. full-term) to child QOL ratings on the dependent measures (i.e., four subscales: physical, emotional, social, and school) were assessed using five separate repeated measures ANOVAs for each of the respective QOL scales. The alpha level was adjusted with the Bonferroni correction (0.05/5) to control for multiple comparisons, yielding an alpha level of 0.01.

Descriptive Statistics

Of the 100 preterm infants originally enrolled in the Iowa Trial, 54 participated in the follow-up assessment. Of these participants, 26 completed the PedsQL measure and were included in the repeated measures ANOVAs. Data from parent proxy report are available for all preterm participants and all but one full-term participant (the child self-report data for the full-term participant without corresponding proxy data were included in the present analyses). Table A1 of the Appendix provides demographic information for the 54 participants (28 full-term; 26 preterm) included in the analyses. Overall, the sample was predominantly male (53.7%), white (74.1%), and of middle or high social rank (89%).

Participants were between the ages of 7 and 16 (mean age = 11.78 years, SD = 2.16) and enrolled in first through eleventh grades (mean grade = 5.75, SD = 2.27). A little more than half (54%) of participants were elementary school students

(i.e., enrolled in grades one through six), while the rest (46%) were enrolled in seventh through eleventh grades (see Appendix, Table A1).

Descriptive statistics, including means and standard deviations for the preterm group, full-term group, and total sample for age, tanner (i.e., developmental) stage, cognitive ability (GAI), and each of the dependent measures (i.e., physical, emotional, social, school, and psychosocial PedsQL scales), are presented in Table A2 of the Appendix.

Sample means and standard deviations can be compared to means and standard deviations for chronically ill, acutely ill, and healthy children reported by Varni et al. (2001), which are also presented in Table 1. Qualitative comparisons indicate that the current data are generally consistent with those obtained previously. Of note, however, means and standard deviations of the current preterm and full-term samples are generally larger than those reported previously (Varni et al., 2001). In addition, when compared to previous data, the preterm means for physical, emotional, social, and school subscales in the current sample exceed those of not only chronic and acutely ill subgroups, but also the healthy subgroup, while full-term means in the current sample are generally lower than the means of Varni et al.'s (2001) healthy subgroup. Finally, the preterm group achieved higher mean parent and child ratings on all except the emotional scale (see Appendix, Table A2).

Preliminary Analyses

Independent-samples *t* tests were conducted to compare preterm and full-term groups on the demographic variables of social class, age, and the dependent variable of

cognitive ability (i.e., GAI). Significantly lower social class was found in the preterm group (M = 2.96, SD = .63) compared to the full-term group (M = 2.33, SD = .48), $t(50) = -4.06$, $p < .001$. The preterm group was also significantly younger (M = 11.13, SD = 2.51) than the full-term group (M = 12.48, SD = 1.44), t(52) = -2.39, p = .02). Cognitive ability was significantly lower in the preterm group (M = 93.62, SD = 20.84) compared to the full-term group (M = 107.04, SD = 14.61), $t(52) = 2.76$, $p = .008$. Differences in sex and ethnicity between preterm and full-term groups were analyzed using separate Chi-square tests. Preterm and full-term groups did not differ in sex $\chi^2 = 1.24$ (1, 54) or ethnicity $\chi^2 = 3.89$ (1, 51). Sample means and standard deviations for child and proxy ratings on each of the subscales are consistent with those reported elsewhere (e.g., Varni, Seid, & Kurtin, 2001).

Variable Inter-correlations

Table A3 of the Appendix displays Pearson r values for correlations between all variables, including Social Class, which was included as a covariate in subsequent analyses. Results indicate a number of significant relationships exist between birth status, HRQL ratings, GAI, and Social Class (the covariate). For example, birth status, or group membership, was significantly related to ratings of parent Social Class (i.e., lower Social Class ratings were associated with preterm group membership). Birth status also shared a significant negative relationship with GAI (i.e., lower GAI scores were associated with preterm group membership). Birth status was also significantly related to HRQL proxy physical, social, school, and total ratings (i.e., preterm birth was related to higher parent ratings of HRQL in physical, social, and school domains and for total functioning). Cognitive ability, or GAI, was negatively correlated with parent ratings of social

functioning (i.e., higher GAI was associated with lower proxy ratings in the social domain). Significant positive relationships were also observed for parent and child reports of physical, emotional, and school functioning, and for parent and child total scores. Participant sex was significantly associated with child physical, emotional, psychosocial, and total scores (i.e., female sex was associated with higher HRQL scores). (see Appendix, Table A3).

Hypothesis

Were parent and child ratings of QOL lower for the preterm group than for the full-term group across all domains of functioning? A total of 49 participants (24 preterm, 25 full-term) were included in the analyses of the effect of birth status on self-report and proxy QOL ratings on the dependent measures (i.e., physical, emotional, social, school, and psychosocial subscales). Research questions regarding potential differences in QOL outcome based upon birth status (i.e., preterm vs. full-term) and rater (i.e., proxy vs. child) were addressed using five independent repeated measures ANOVAS. The between group factor was birth status (preterm or full-term) and the within-group factor was rater (self or proxy). The alpha level was set at 0.01, applying a Bonferroni correction for multiple comparisons.

Results of the preliminary analyses indicated that full-term and preterm groups differed significantly in age, social class, and cognitive ability (GAI). In order to control for potential effects of group differences in social class and GAI on the dependent variables, age, social class, and GAI were initially entered into the model for each independent repeated measures ANCOVA as covariates, with type as the between subjects factor and rater as the within subjects factor. The results of these analyses

indicated that the covariates had no significant effects on the dependent variables. Therefore, only the ANOVA results for these analyses are presented (see Appendix, Table A4).

The results of these analyses showed no significant differences (alpha levels were set at 0.01) in QOL between full-term and preterm groups for any of the five QOL subscales. No significant differences in proxy and self ratings of QOL were found for any of the five subscales. In other words, the interaction between type and rater was non-significant. No differences in Physical QOL scores were found between preterm and full-term groups $F(1, 44) = 4.78$, $p = .03$, ($d = .36$) and parent proxy and child ratings of Physical QOL were also not significantly different $F(1,44) = .17$, $p = .68$. No differences between were found for preterm and full-term Emotion scores $F(1, 44) = .80$, $p = .38$ ($d = .38$) or between proxy and child ratings of Emotional QOL $F(1, 4) = .00$, $p = .99$. Overall scores for the Social domain were also not significantly different between group $F(1, 44) = .17$, $p = .69$, ($d = .11$) or between raters $(1, 44) = .03$, $p = .86$. No differences between were found for preterm and full-term groups $F(1, 44) = 2.22$, $p = .14$, ($d = .47$) for School QOL or between proxy and child ratings of School QOL $F(1, 44) = .51$, $p = .48$. Overall scores for the Psychosocial domain were also not significantly different between groups $F(1, 44) = .25$, $p = .70$, ($d = .04$) or between raters $(1, 44) = .03$, $p = .85$.

CHAPTER V

DISCUSSION

Preterm infants are at greater risk for neuropsychological deficits that in turn increase the risk for problems in emotional, social, and school functioning (Aylward, 1992, 1997; Taylor et al., 2000). Researchers have estimated that neuropsychological deficits result in learning, attention, and/or behavior problems in 50-70% of VLBW infants (Aylward, 1992; 1997; Taylor et al., 2000). Clinically significant discrepancies in measured intellectual ability have also been found between full-term and preterm infants (Goyen et al., 1998).

At present, there is limited research on the relationship between mental disorders or neurocognitive impairment and QOL. Adult studies have shown a relationship between cognitive dysfunction and QOL in human immunodeficiency virus (Lutgendorf, Antoni, Schneiderman, Ironson, & Fletcher, 1995), schizophrenia (Green, Kern, Braff, & Mintz, 2000; Meltzer, Thompson, Lee, & Ranjan, 1996), and dementia (Hoe, Hancock, Livingston, Woods, Challis, & Orrell, 2009). Research also suggests a relationship between specific cognitive abilities and QOL (Perrine, Hermann, Meador, et al., 1995). Impairments in executive functioning (e.g., sustained attention and cognitive flexibility), processing or psychomotor speed, aspects of visual and verbal memory and learning, and verbal fluency have been related to significantly poorer QOL in adults (Barker-Collo, 2006; Buchanan, Holstein, & Brier, 1994; Meltzer et al., 1996; Mitchell, Kemp, Benito-Leon, & Reuber, 2010; Wegener, Redoblado-Hodge, Lucas, Fitzgerald, Harris, & Brennan, 2005). In studies of adults with schizophrenia, however, psychopathology appears to share a stronger relationship with QOL than neurocognitive impairment

(Addington & Addington, 1999; Aksaray, Oflu, Kaptanoglu, & Bal, 2002; Heslegrave, Awad, & Vorunganti, 1997; Wegener et al., 2005).

Much less is known about the relationship between functional impairments associated with mental disorders or neurocognitive deficits and QOL in pediatric populations. Poorer QOL has been found in children with Major Depressive Disorder and Conduct Disorder (Sawyer et al., 2002), traumatic brain injury (Horneman et al., 2005), executive dysfunction (Sherman et al., 2006), and ADHD (Escobar et al., 2005; Devinsy et al., 1999; Klassen et al., 2004; Matza et al., 2004a; Sawyer et al., 2002; Schiariti et al., 2007; Secnick et al., 2004; Topolski et al., 2004). Research also suggests a relationship between overall intellectual functioning and QOL. Sabaz, Cairns, Lawson, Bleasel, and Bye (2001) found that intellectual disability--as measured by individually administered norm-referenced cognitive assessment--was independently associated with poorer health-related QOL in children with epilepsy. Many of these studies are limited; use rating scales rather than objective measures; use parent proxy ratings alone; and use the term "cognitive" loosely and inconsistently.

The purpose of the current study was to assess differences in QOL among school-aged children who were born preterm and full-term. Based upon the increased risks for cognitive, academic, behavioral, and social-emotional difficulties experienced by the preterm children, it was hypothesized that QOL ratings (both parent and self-report) of children born preterm would be significantly lower than for full-term children across all QOL domains: physical, psychosocial, emotional, social, and school functioning.

Research has shown that environmental variables such as low socioeconomic status (i.e., social class) are associated with increased risk for preterm birth (Aylward, 1997, 2002). Caregivers in the preterm group in the current study were assessed for socioeconomic status and reported belonging to a lower social class than caregivers in the full-term group. The preterm group also exhibited lower overall cognitive ability (as measured by the GAI) than the full-term group, which is also consistent with previous findings that preterm perform children, on average, around 10 points lower than children born full-term on standardized tests of intellectual functioning (Goyen et al., 1998).

The current hypothesis that QOL ratings would be significantly lower in the preterm group compared to the full-term group was not supported. No significant differences between preterm and full-term groups in child (self) report of QOL were found for any of the core scales: physical, emotional, social, school, and psychosocial functioning. Likewise, no significant differences were found between groups for proxy ratings on any of the core scales. Proxy and self ratings were also not significantly different.

The findings of the current study are in contrast with previous studies that have shown reliable and significant differences between QOL in healthy, chronically ill, and acutely ill children (Varni et al., 2001). Results of the current study also contrast with research documenting poorer QOL in children born preterm (Schiariti et al., 2007). Similar findings to the current study have been reported, however, in one study comparing adolescents born prematurely to their peers (Saigal, Feeny, Rosenbaum, Furlong, Burrows, & Stoskopt, 1996) despite the presence of greater functional impairment among those born prematurely.

Several important factors should be considered in the current study. First, only 25 of the original 54 preterm infants in the Iowa transfusion trial (Bell et al., 2005) returned for this follow-up portion of the study. This is a major limitation because it suggests that the current sub-sample of preterm infants may not be representative of the entire sample nor of the general preterm population. Furthermore, is possible that the current sample size was not large enough to detect differences in QOL between full-term and preterm groups. The results of the original power analysis, which was computed using an alpha level of .01, indicated that a minimum sample size of 66 (with a minimum of 33 participants per group) would be necessary to achieve a moderate effect size with a power of .80 or greater. However, the power estimate upon re-analysis using the current sample size of 54 was .70.

Second, the relationship between QOL and cognitive ability is unclear. Studies have reported significant relationships between cognitive dysfunction and intellectual disability and QOL (e.g., Barker-Collo, 2006; Buchanan et al., 1994; Green et al., 2000; Perrine et al., 1995; Sabaz et al., 2001). Research also suggests increasing awareness of the potential impact of subtle and/or mild cognitive deficits on QOL (Mitchell, Kemp, Benito-Leon, & Reuber, 2010). Other research suggests that psychopathology (i.e., mood, behavioral, and emotional dysfunction) has a much greater impact on QOL than neurocognitive impairment. Adult QOL studies found that the presence of negative symptoms in schizophrenia and depression in dementia were stronger predictors of poor QOL than cognitive dysfunction (e.g., Hoe et al., 2009; Wegener et al., 2004).

It is possible that self-perceived cognitive difficulties are equivalent if not better predictors of QOL than performances on standardized measures of neurocognitive

functioning (Baker, Taylor, & Hermann, 2009; Giovagnoli & Avanzini, 2000). It is not surprising that perceptions of dysfunction may be a significant predictor of poor QOL even in the absence of objective evidence of impairment given that QOL is also a measure of subjective experience. It is clear that further research exploring the relationship between both objective and perceived neurocognitive deficits and QOL in both adults and children.

Third, there may also be some evidence to suggest that positive aspects of extreme prematurity are underemphasized. For example, a study by Saigal et al. (1996) found high self-reports of QOL by former preterm adolescents, despite the experience of functional limitations. Lou, Pedersen, and Hedegaard (2009) also described a number of positive family outcomes of extremely premature birth. In this qualitative study, Lou et al. (2009) examined themes reported by 9 fathers and 11 mothers of 14 extremely premature infants in Denmark. Though the experience of negative outcomes and consequences of prematurity were not overlooked nor absent from parent reports, the authors captured several themes regarding positive experiences of parents of their children's health and development as sources of joy, pride, and love. The authors reported that themes related to life and death, complications, and concerns were prominent in parents' descriptions of the neonatal period. As time passed, however, these themes were regarded in terms of "concerns of the past." Parents described feelings of relief as children experienced developmental "catch up," were no longer in the high-risk medical category, and as parents' previous worries about their children's development proved unfounded. In fact, parents in this study generally reported few long-term functional limitations in their children.

These authors discussed the possible impact of parents' experiences of the critical early circumstances of their children on subsequent values and expectations. The influence of early expectations, information, and critical circumstances is an important context from which to view the results of parents' perspectives on their children's later functioning. As the authors discuss, it is interesting and important to consider the context in which parents of preterm infants are asked to view their current and previous experiences related to prematurity. For the parents in this study, it was relevant that they were describing their children's current functioning in the context of significant previous difficulties, many of which were not ultimately as problematic or devastating as had been anticipated, while other difficulties had begun to ameliorate over time or as a result of access to services and intervention.

As the results of the Lou et al. study demonstrate, qualitative research on long-term family outcomes may be an important source of information on positive aspects of preterm birth. It is important to consider the potential impact of highly aversive experiences, such as those experienced by parents of medically high risk infants, on one's subsequent encounters with academic, social, physical, and emotional problems. Early experiences with adversity provide a context within which later experiences, behavior, and perspectives are shaped. Early adversity may then translate to relief experienced upon encountering fewer long-term problems than anticipated and heightened confidence in the ability to cope with and remediate other difficulties encountered.

Another important consideration regards the extent to which the research process in the current study may have altered the experiences of preterm infants and their families. Because of the limited retention rate of preterm participants, it is difficult to

ascertain whether the preterm infants enrolled in the current longitudinal research study were representative of the entire sample. Therefore, the possibility that participating parents, preterm infants, and families were distinct in some way from those who did not participate cannot be ruled out. Furthermore, because the process of conducting research is in and of itself a form of intrusion that may disrupt the course of natural events, it is also possible that aspects of the health and development of a preterm infant were emphasized differentially for participants than non-participants. This, in turn, may have led to a potentially differential awareness or to differences in the degree to which parents had access to or sought our supportive or preventive services.

Implications

Implications for Medicine

Understanding of the enhanced difficulties associated with bonding and parent-child interactions following preterm birth is evident in family-centered neonatal intensive care (Griffin, 2006). As previously discussed, physicians should not simply consider physical and intellectual characteristics of an individual when estimating his or her QOL; QOL is better represented by a formula that takes into account both a person's physical and intellectual characteristics as well as both the contributions that individual's family make to him or her and the contributions the individual makes to society (Shaw, 1977). Research in the field of health psychology has demonstrated that the same event (e.g., illness) can have different effects on individuals' daily functioning. In other words, it is now understood that the degree to which illness, disease, and trauma affects a person depends on personal traits/attributes as well as social/environmental circumstances (Kaplan, 1985; Shaw, 1977). It is also clear that factors determining a given individual's

QOL can go unrecognized by physicians. It has been suggested that the relationship between health/disease status (as measured by prevalence and incidence rates of a given medical condition) and QOL is mediated by cognitive (e.g., intellectual), social (e.g., coping, social support), and environmental (e.g., exposure) variables (Cohen et al., 1980; Sarason et al., 1983).

The construct of QOL has played a key role in more recent discussions within the field of medicine. Medical advances have led to significant decreases in mortality rates for a variety of pediatric conditions. However, it has been argued that in order for painful, costly, and time-consuming interventions to be justified, it will be necessary to demonstrate that the treatments not only prolong, but also enhance the subjective, day-to-day experience (i.e., quality of life) of the patient (Kaplan, 1985). The number of small, critically ill infants who are surviving the neonatal period has dramatically increased in recent years. Yet knowledge on longitudinal outcomes of preterm infants and the impact of preterm birth on patients' subjective experiences are minimally understood. As a result of limitations in objective data from long-term outcome studies, pediatricians, neonatologists, and other health care professionals must often rely upon clinical experience and judgment. Assumptions regarding a patient's projected quality of life may thus play a pivotal role in early medical decision-making and in professional opinions presented to parents during the neonatal period.

Research suggests that misconceptions about premature and LBW infants' chances for survival and later QOL may have a negative impact on physicians' treatment decisions and the quality of care provided infants at the extremes of prematurity (Gooi et al., 2003). Studies suggesting that many physicians may view the QOL of the most

premature infants (i.e., those born before 24 weeks) to be "dismal" and that physicians may be less apt to pursue rigorous medical interventions for critically ill infants about whom they experienced greater feelings of pessimism (Moorse et al., 2000) highlights the relevancy of QOL in pediatric health care in general and within the preterm population in particular. It is evident that more information about the QOL of surviving preterm infants is needed to inform obstetricians' decisions about treatment, and also the content of information presented parents counseled about the decision-making process in high-risk situations such as premature and LBW deliveries.

Further research in the area of QOL and prematurity may greatly enhance medical decision-making and informed consent. Health-related quality of life ratings by school-aged children who were born preterm are more appropriate than physician assumptions, and are potentially invaluable data to present to parents (and future parents) to enhance their ability to make informed decisions regarding prenatal and neonatal care/treatment. Research also suggests that physician's decision-making style, when participatory in nature, can have a positive impact on patient QOL (Arora, Weaver, Clayman, Oakley-Girvan, & Potosky, 2009).

Implications for Prevention

Neurocognitive impairment and learning disabilities are among the most costly conditions afflicting this nation's youth. Research in the area of prematurity is crucial in the development of prevention programs. Studies suggest that environmental variables such as lower social class and poor previous pregnancy outcomes are associated with increased risk for preterm birth (Aylward, 1997, 2002). Many environmental risk factors, such as low pre-pregnancy weight and poor weight gain during pregnancy, are

preventable with education and prenatal care. Improvements in understanding of risk factors for prematurity provide valuable insight for targeting at-risk groups for preventive education and parent training programs. Education regarding family planning, birth control, pregnancy options and the importance of healthy lifestyle, balanced diet, vitamin supplements, and regular prenatal care may be particularly beneficial for socioeconomically disadvantaged women pre-pregnancy and during the prenatal period.

Education during pregnancy and the postnatal period may also be beneficial for parents of preterm infants. Mothers of preterm infants may be unprepared for the difficulties associated with parenting an infant who shows decreased responsiveness to the environment and increased negative emotionality (Robson & Cline, 1998). Some mothers may internalize their infants' behaviors as reflections of inadequate parenting, or may feel unable or unmotivated to bond with their infants. Research in the area of attachment and parent-child bonding suggests that early experiences between infants and their caregivers can have life-long implications for the development of healthy self-concept, successful and fulfilling interpersonal relationships, and psychological well-being. Thus, interventions targeted at improving the parenting of at-risk infants (Patteson & Barnard, 1990) may help off-set some long-term developmental consequences of prematurity (Blair, 2002).

Parents of preterm infants may also benefit from education about the ways in which their behavior and decision-making can protect their at-risk child from later difficulties. Research suggests that increased social support and access to resources, the quality of the child's home environment, and the presence of the father in the child's life (i.e., the marital or relationship status of the mother) can play a protective role, mitigating

problems in social, emotional, and school functioning (Bradley & Casey, 1992). Research also suggests that early development programs targeted at at-risk populations can have substantial impact on QOL in adolescence (Manning, Homel, & Smith, 2009).

Implications for Remediation

Quality of life research has many potential implications for counseling as well. By asking children to provide information about their perceptions of the impact of illness and disease on aspects of daily functioning, it is possible to promote their active involvement in medical assessment and intervention as well as potentially even psychological intervention (Coghill et al., 2009). By routinely assessing children's and their caregiver's perceptions about the impact of their illness on their daily functioning, physicians and psychologists may enhance their understanding of where major issues lie and modify treatment/intervention accordingly to address these aspects of functioning (Coghill et al., 2009).

Research has suggested that although ratings between children and their parents may be similar, children and physician perspectives differ significantly (Rimmer, Campbell, & Coghill, 2007). Lack of concordance between children's and physicians' beliefs about the impact of illness/disease on daily functioning is particularly problematic in pediatric psychology due to the fact that it is often the clinician making the judgment about the level of impairment and the life domains in which the impairment exists. Ideally it would be possible to obtain ratings by multiple individuals involved in various aspects of a child's daily functioning. Collaborative discussion among parents, teachers, clinicians, and child patients regarding the perceived impact of mental or physical health problems on different relevant domains would likely achieve a more comprehensive

picture of QOL than individual ratings alone. Opportunities to address differences in perspective and develop targeted intervention might be enhanced by comparing and contrasting QOL ratings completed by patients and familiar adult proxies. Assessment of QOL within clinical settings may also promote dialogue between children, their caregivers, and their health care providers; help to reduce confusion and misunderstanding; and increase satisfaction with and benefit from utilization of health care resources.

The active, problem-focused, collaborative, and transparent nature of cognitive behavioral interventions has been hypothesized to contribute to enhanced treatment outcomes for children (Kendall & Suveg, 2006). Additional research has suggested that outcomes can be enhanced when the clinician adopts the role of an "educator" or "coach" and works collaboratively with the client and parents toward mutually agreed upon goals (Reinecke et al., 2003). Research with children and adolescents has suggested that non-specific factors are modest and consistent predictors of treatment outcome (Shirk & Karver, 2003). Therefore, it is also important to address how process elements such as the client-therapist working alliance may affect outcome.

The therapist's ability to be flexible and to modify treatment based upon individual strengths, limitations, or needs is another important consideration for clinicians working with children and adolescents (Kendall & Suveg, 2006). According to Kendall and Suveg (2006), greater spontaneity and flexibility on the part of the therapist may be evaluated more positively by the client, which in turn may enhance the working alliance and improve therapy outcomes. Furthermore, the working alliance is developed by establishing rapport with the child and his or her parents and collaborating with members

of the family throughout treatment. The strength of the working alliance is affected by therapist behaviors toward both clients and clients' parents. Research has indicated that therapy outcomes can be enhanced by a strong therapist-parent alliance, which predicts both greater parent participation and client retention in treatment (Hawley & Weisz, 2005).

As discussed by Coghill et al. (2009), QOL assessment may benefit remediation efforts by helping to identify the domains of functioning most affected by mental/physical illness and target areas to prioritize within the context of intervention. Quality of life assessment may also help to identify appropriate methods for intervention with a particular individual, particularly when deciding upon one therapy versus another when previous research has demonstrated equivalent success between the two in reducing symptoms. It is of further importance that parents are made aware of their children's perspective on their own capacity to function in various life domains because parents are responsible for accessing treatments/interventions and health care for their children (Varni et al., 2001)

Overall, it is evident that the use of QOL measures, in addition to symptom rating scales and process measure, could promote involvement by the child or adolescent in his or her treatment. By promoting greater collaboration among health care providers, children, and their families, it may also be possible to strengthen the therapeutic alliance and feelings of satisfaction by parents and children with treatment outcomes. Further research into differential effects of treatments on QOL outcomes might also provide insight for reducing costs and justify the allocation of resources to a particular treatment (Coghill et al., 2009).

Implications for Education

As noted by Hack et al. (1994), it is possible that one consequence of increasing survival rates of preterm infants may be academic difficulties that emerge during the first few years of formal schooling. Academic difficulties among preterm children are evident in studies by, for example, O'Callaghan et al. (1996), in which teachers reported significant academic difficulties in reading, spelling, and mathematics among ELBW children. O'Callaghan et al. (1996) also found that ELBW children were approximately three times more likely to be delayed in all academic areas by at least one year compared with full-term controls and that approximately half of ELBW children received remedial academic assistance (46%) or special education services (4%).

Of greater concern is the possibility that preterm children may be Under-recognized as children with special needs. For example, Litt et al. (2005) did not find significant differences between LBW and full-term comparison groups in rates of educational assistance (i.e., special education placement and remedial services) but found a moderate effect size for math score differences on the Woodcock Johnson Tests of Achievement Revised. Findings of this nature ignite concern that preterm children may go unrecognized as children with special education needs. Research has shown that these children, as a group, are not likely to exhibit global deficits in cognitive functioning, but rather, are at greater risk for low-severity, high-prevalence deficits that may not be detected until children reach school age (Taylor et al., 2000). As a result, it is possible that these children continue to go unrecognized, are viewed primarily in the context of behavioral or social-emotional disturbance and not referred for thorough neurocognitive evaluation, or do not meet state criteria for learning disabilities.

It is possible that educators may not fully understand the long-term impact of preterm status on cognition and achievement. Furthermore, educators may not fully understand the link between neurocognitive functioning and behavior, social, academic outcomes. It is clear that further efforts to disseminate information about the risks of preterm status to educators are necessary. Furthermore, it is crucial that at-risk children are identified for intervention early in their development to reduce significant difficulties. Research on the cost benefits of early intervention and prevention efforts is also crucial to justify allocation of limited funds to early education programs.

Contributions to Literature

The current study addresses several areas of limitation in the existing QOL literature. First, previous research on QOL outcomes in preterm infants has been conducted for the most part with infants, toddlers, and children of preschool ages. This study was intended to fill a gap in the existing literature by examining QOL in school-aged children (mean age = 11.78 years) and by using both child and caregiver ratings as the dependent measure. As discussed previously, studies that report cognitive, behavioral, and QOL of life outcomes for very young (i.e., toddler and preschool age) children (Chien et al., 2006; Laucht, Esser, & Schmidt, 1997) may not fully reflect the impact of health status on daily functioning in preterm individuals due to the fact that the low-severity, high-prevalence deficits that are common in this population may not be detected until children reach school ages (Taylor et al., 2000).

Second, both children's and their caregivers' ratings were obtained as a measure of QOL. Existing studies examining QOL among children are often limited by the sole use of a parent or teacher proxy, which may not be a valid indicator of children's

perceptions of the impact of their health on daily functioning (Klassen et al.; Sawyer et al., 2002; Schiatriti et al., 2007). The sole use of proxy ratings is problematic because the validity and reliability of proxy ratings of QOL may be questionable. Studies have shown moderate agreement between self and proxy ratings of QOL; however, the level of agreement was also associated with the domain of functioning assessed (Hays et al., 1995; Theunissen et al., 1998). In other words, self-reports of QOL tend to differ from parent-proxy reports on more subjective (and likely less observable) measures such as emotional functioning (Saigal et al., 1998), pain/physical symptoms, and social functioning (Verrips et al., 2000).

The current study also examined QOL in school-aged children who were very early, very small, and very ill at the time of their birth and required a minimum of one packed red blood cell transfusion. These children were selected for participation in the current study based upon very stringent entrance criteria and all were both premature and low birth weight. Previous studies (e.g., Schiatriti et al., 2007) have been limited by the use of "gestational age" versus "birth-weight." This reflects a limitation because, as noted, though these definitions are correlated, they have been found to be differentially related to long-term neuropsychological and behavioral outcomes (e.g., Alyward, 2002).

The current study also incorporated cognitive data obtained via objective, individually administered, norm-referenced intellectual assessments with sound psychometric properties. Previous studies have used behavioral rating scales to estimate cognitive ability (Sawyer et al., 2002) or to diagnose mental disorders (Bastiaansen et al., 2005; Sherman et al., 2006). The use of parent rating scales in lieu of standardized, individually administered test batteries and diagnostic interviews limits our

understanding of the extent to which previous groups of acute and chronically ill children may have been at risk for significant learning and academic problems.

Limitations

There are several limitations to the current study. First, the study is limited by its small sample size. The results of a power analysis indicated a suggested n of 76 in order to obtain a moderate (.15) effect size with a power of .80. The sample size in the current study was 54; therefore, the study may have lacked sufficient power to detect any true differences between the groups. Given the contextual nature of health-related experiences, is has been recommended that QOL be measured across a range of different life settings and age ranges (Cohill et al., 2009). This study is therefore also limited by the use of cross-sectional measurement of QOL outcomes. Another limitation of the current study is that only 26 of the original 100 preterm infants enrolled in the initial study returned for the follow-up portion. Thus, the results of this subsample may not be representative of the original sample of preterm infants who were enrolled.

The current study is limited by the lack of additional measures on behavioral, academic, and physical functioning of child participants. It would be important to ascertain whether the current sample differed from previous preterm samples in the number and severity of physical, behavioral, academic, and social problems experienced. It would also be important to determine whether the current preterm sample had received significant intervention or educational services. Such information may provide important context for interpretation of the lack of significant findings. Data indicating that the current sample experienced fewer or less severe problems in health, behavior, and academics, and/or had received more significant intervention than other preterm samples

studies may explain why the current findings are in contrast to the findings of previous studies of QOL and preterm birth (e.g., Schiariti et al., 2007).

As noted previously, the extant literature in on QOL is limited by inconsistent definitions of the construct and a wide variation in the instruments used to measure QOL (Coghill et al., 2009). It is unclear whether and to what extent QOL measures such as the PedsQL actually tap into an individual's subjective appraisal of his or her day-to-day experience as they intend to do. Though QOL instruments were designed to differ from existing instruments assessing functional outcomes or adaption (such as the Vineland, for example), these measures are often used in the literature in an interchangeable fashion. It is possible that many of the differences in QOL outcome among studies could be accounted for by the way in which the construct was defined and measured—which suggests the need for caution in comparing or contrasting the findings of the current study with studies using alternative approaches to QOL measurement.

Future Directions

Several future directions are generated by the current study. First, it will be important to obtain follow-up QOL data across time in order to determine the extent to which the absence of significant findings may have been related to the age or health experiences of the sample at the time of their participation within the study. Assessment of QOL with larger samples of preterm children at various ages will also be important, given the current study's limitations in sample size and power.

Given research on the impact of executive functioning deficits (i.e., ADHD) on QOL, it may be important to further investigate the impact of these deficits within preterm samples. Research has suggested that executive functioning problems are

common among former preterm infants assessed at school ages (Marlow, 2007). Furthermore, research also suggests that specific neurocognitive/executive abilities such as processing speed and working memory significantly predict academic achievement as well as explain significant discrepancies between lower academic performances in former preterm compared to former full-term groups (Mulder, Pitchford, & Marlow, 2010). In order to add to the existing data on executive functioning in preterm populations, assessment of executive functioning ideally would take place among former preterm children and adolescents who had reached school ages and would incorporate both individually administered and norm-referenced neuropsychological tests in addition to behavioral reports completed by parents/teachers and direct observation.

Research children born prematurely and LBW are at risk for problems in health, neuropsychological functioning, learning, academic achievement, behavior, and psychosocial adjustment. Research has further demonstrated that a variety of physical and psychological conditions are associated with poorer QOL among children. However, few studies have examined pediatric QOL among preterm school-aged children. Moreover, existing studies have not explored the relationship between cognitive, academic, and social/emotional functioning and QOL. It is clear that further research in the area of prematurity will be essential in understanding the long-term effects of this condition on patients and their families.

APPENDIX

TABLES

Table A1. Demographic Data (N = 54)

		Frequency	Percent
Type			
	Full-term	28	51.9
	Preterm	26	48.1
Gender			
	Male	29	53.7
	Female	25	46.3
Ethnicity			
	White	40	74.1
	Asian American	5	9.3
	Black/African American	1	1.9
	Hispanic/Latino	5	9.3
	American Indian/Alaskan Native	0	0.0
	Hawaiian/Pacific Islander	0	0.0
	Multiracial	0	0.0
	Missing	1	1.9
Social Class			
	Top Social Rank	0	0.0
	High Social Rank	24	44.5
	Middle Social Rank	24	44.5
	Low Social Rank	4	7.4
	Lowest Social Rank	0	0.0
	Missing	2	3.7

Table A2. Descriptive Statistics (N = 54)

Variable		*N*	Mean	Standard Deviation	Min	Max
Age						
	Preterm 26	12.48	1.44	10.08	15.17	
	Full-term	28	11.13	2.51	7.00	16.83
	Total	54	11.78	2.16	7.00	16.83
Tanner						
	Preterm	26	2.96	0.96	1	5
	Full-term	27	2.41	1.08	1	4
	Total	53	2.68	1.05	1	4
GAI						
	Preterm	26	93.62	20.84	40	139
	Full-term	28	107.04	14.61	77	142
	Total	54	100.57	18.96	40	142
Child Physical SS						
	Preterm	26	90.63	9.88	65.63	100.00
	Full-term	27	85.53	17.23	37.50	100.00
	Total	53	88.03	14.21	37.50	100.00
	Chronic Ill	*367*	*77.36*	*20.36*		
	Acute Ill	*148*	*78.88*	*19.10*		
	Healthy	*400*	*84.41*	*17.26*		
Child Emotional SS						
	Preterm	26	74.62	16.97	30.00	100.00
	Full-term	27	82.03	21.45	10.00	100.00
	Total	53	78.40	19.56	10.00	100.00
	Chronic Ill	*366*	*76.40*	*21.48*		
	Acute Ill 1	*48*	*77.33*	*20.04*		
	Healthy	*400*	*80.86*	*19.64*		
Child Social SS						
	Preterm	26	84.23	14.95	0.00	100.00
	Full-term	27	82.04	24.89	10.00	100.00
	Total	53	78.40	20.46	0.00	100.00
	Chronic Ill	*367*	*81.60*	*20.24*		
	Acute Ill 1	*48*	*82.83*	*16.66*		
	Healthy	*399*	*87.42*	*17.18*		
Child School SS						
	Preterm	26	79.42	15.51	45.00	100.00
	Full-term	27	69.84	25.60	0.65	100.00
	Total	53	74.54	21.60	0.65	100.00
	Chronic Ill	*362*	*73.43*	*19.57*		
	Acute Ill	*143*	*75.68*	*18.04*		
	Healthy	*386*	*78.63*	*20.53*		

Table A2. Continued

Variable	*N*	Mean	Standard Deviation	Min	Max
Child Psychosocial SS					
Preterm	26	79.42	13.09	43.33	98.33
Full-term	27	78.77	18.65	33.33	100.00
Total	53	79.09	16.01	33.33	100.00
Chronic Ill	*367*	*77.10*	*15.84*		
Acute Ill	*148*	*78.68*	*14.66*		
Healthy	*399*	*82.38*	*15.51*		
Child Total SS					
Preterm	26	85.02	13.09	60.73	99.17
Full-term	27	82.15	16.89	35.42	99.17
Total	53	83.56	14.04	35.42	99.17
Chronic Ill	*367*	*77.19*	*15.53*		
Acute Ill	*148*	*78.70*	*14.03*		
Healthy	*401*	*83.00*	*14.79*		
Parent Physical SS					
Preterm	26	96.13	8.48	59.38	100.00
Full-term	27	87.96	18.48	34.38	100.00
Total	53	91.89	15.00	34.38	100.00
Chronic Ill	*653*	*73.28*	*27.02*		
Acute Ill	*199*	*81.81*	*20.46*		
Healthy	*717*	*89.32*	*16.35*		
Parent Emotional SS					
Preterm	26	89.20	13.74	55.00	100.00
Full-term	27	90.37	12.40	60.00	100.00
Total	53	89.81	12.94	55.00	100.00
Chronic Ill	*661*	*73.05*	*23.27*		
Acute Ill	*199*	*78.82*	*18.00*		
Healthy	*718*	*82.64*	*17.54*		
Parent Social SS					
Preterm	26	93.20	9.78	70.00	100.00
Full-term	27	84.26	18.54	40.00	100.00
Total	53	88.56	15.51	40.00	100.00
Chronic Ill	*657*	*79.77*	*21.91*		
Acute Ill	*198*	*83.58*	*18.29*		
Healthy	*716*	*91.56*	*14.20*		

Table A2. Continued

Variable	*N*	Mean	Standard Deviation	Min	Max
Parent School SS					
Preterm	26	89.20	13.82	50.00	100.00
Full-term	27	77.78	19.48	35.00	100.00
Total	53	83.27	17.79	35.00	100.00
Chronic Ill	*601*	*71.08*	*23.99*		
Acute Ill	*167*	*74.74*	*20.95*		
Healthy	*611*	*85.47*	*17.61*		
Parent Psychosocial SS					
Preterm	26	90.53	10.46	61.67	100.00
Full-term	27	85.14	13.82	53.33	100.00
Total	53	87.21	12.62	53.33	100.00
Chronic Ill	*661*	*74.80*	*18.16*		
Acute Ill	*199*	*79.56*	*15.51*		
Healthy	*717*	*86.58*	*12.79*		
Parent Total SS					
Preterm	26	93.33	8.25	64.69	100.00
Full-term	27	86.05	14.51	50.10	100.00
Total	53	89.55	12.37	50.10	100.00
Chronic Ill	*662*	*74.22*	*18.40*		
Acute Ill	*199*	*80.42*	*15.26*		
Healthy	*717*	*87.61*	*12.33*		

Note: SS = Standard Scores; Standard Scores range from 0 to 100 and were computed for each scale based upon the normative data for healthy children of that age range. "Child" scales = self-reports completed by participants. "Parent" scales = proxy ratings by guardian. In italics: number, mean, and standard deviations for each scale by subgroup (from Varni et al., 2001). Chronic Ill = children with a parent-reported chronic health condition; Acute Ill = seen at a specialty clinic but had no parent-reported chronic health condition; Healthy = no parent-reported chronic health condition and were seen at well-child checks or assessed by telephone.

Table A3. Inter-correlations of Variables Using Pearson *r*

	Type	SC	GAI	CPSS	CESS	CSOSS	CSCSS	CPSSS	PPSS	PPESS	PSOSS	PSCSS	PPSSS	SC	GAI
Type	1	.51**	.35**	.20	-1.79	.05	.19	.01	.11	.28*	-.04	.28*	.28*	.24	.29*
SC		1	-.43**	-.20	-.01	.73	.14	.07	.03	.11	-.04	.28*	.28*	.24	.29*
GAI			1	-.07	-.13	-.23	-.00	-.12	-.10	-.11	-.13	-.28*	-.90	-.20	-.17
CPSS				1	-.52**	.68**	.41**	.71**	.92**	.40**	.16	.17	.12	.18	.33*
CESS					1	.58**	.19	.77**	.70**	-.04	.28*	.06	-.02	.12	.04
CSOSS						1	.46**	.89**	.86**	.12	.07	.17	.02	.10	.13
CSCSS							1	.64**	.57**	.16	-.11	.24	.31*	.21	.21
CPSSS								1	.93**	.11	.10	.14	.10	.14	
PPSS									1	.52**	.60**	.35**	.60**		
PESS										1	.54**	.30**	.71**		
PSOSS											.57**	.87**			
PSCSS											.82**				
PPSSS															

Note: For Type, 0 = Full-term, 1 = Preterm; SC = Social Class: scale is 1 to 5; 1 = higher social class, = lower social class; CPSS = Child Physical Standard Score; CESS = Child Emotional Standard Score; CSOSS = Child Social Standard Score; CPSSS = Child Psychosocial Standard Score; CTOTSS = Child Total Standard Score; PPSS = Parent Physical Standard Score; PESS = Parent Emotional Standard Score; PSOSS = Parent Social Standard Score; PPSSS = Parent Psychosocial Standard Score; PTOTSS = Parent Total Standard Score; *$p < .05$, **$p < .01$. Correlations are rounded to the nearest hundredth place

Table A4. Repeated-Measures ANOVAs

	df	*F*	*p*
Physical			
Type	1, 44	6.613	0.013
Rater	1, 44	0.033	0.857
Emotional			
Type	1, 44	0 .628	0.432
Rater	1, 44	2.181	0.146
Social			
Type	1, 44	0.859	0.359
Rater	1, 44	0.222	0.640
School			
Type	1, 44	2.457	0.124
Rater	1, 44	0.553	0.461
Psychosocial			
Type	1, 44	0.641	0.427
Rater	1, 44	1.099	0.300

Note: Type = Preterm or Full-term; Rater = Self or Proxy

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