MQP-BIO-DSA-1615
MQP-BIO-DSA-6822

CORRELATIONS BETWEEN SEVERE NEONATAL INTRAVENTRICULAR HEMORRHAGE AND NEURODEVELOPMENTAL COMPLICATIONS

A Major Qualifying Project Report

Submitted to the Faculty of the

WORCESTER POLYTECHNIC INSTITUTE

in partial fulfillment of the requirements for the

Degree of Bachelor of Science

in

Biology and Biotechnology

by

_____ _____

Hannah Israel Kristin Newell

April 28, 2011

APPROVED:

_____ _____

Robin Adair, Ph.D.
Developmental/Behavioral Pediatrics
UMASS Medical Center
Major Advisor

David Adams, Ph.D.
Biology and Biotechnology
WPI Project Advisor

ABSTRACT

Intraventricular hemorrhaging (IVH) is surprisingly common in premature infants, and may cause neurodevelopmental problems. However, demonstration of this correlation has been difficult to obtain at UMass Memorial Medical Center due to a communication disconnect between the Neonatal Intensive Care Unit where IVH is usually first diagnosed, and the Follow-up Clinic where subsequent developmental problems would be identified. To bridge this disconnect, standardized forms were developed to allow physicians to obtain medical follow-up data on infants. The results of a sample analysis of severe IVH show that severe IVH in premature infants born under 1000g correlates with neurodevelopmental problems such as cerebral palsy, cognitive impairment, and various sensory impairments.

TABLE OF CONTENTS

Signature Page ……. 1

Abstract …… 2

Table of Contents ……..…… 3

Acknowledgements …….. 4

Background …….. 5

Project Purpose ……...……. 25

Methods ……...…… 26

Results ……...….. 30

Discussion ……...… 39

Bibliography …… 42

Appendix ……... 53

ACKNOWLEDGEMENTS

We would like to thank UMass Memorial Medical Center, especially Robin Adair, MD and Alan Picarillo, MD, for sponsoring this project and for their help and guidance throughout our entire project. We would also like to thank Mary Naples for providing us with IS support throughout this project. Lastly, we would like to thank Professor David Adams for advising us on this project, and for all of his help in initiating and editing this project.

BACKGROUND

Vermont Oxford Network

The Vermont Oxford Network (VON) is a worldwide non-profit organization, consisting of 850 neonatal intensive care units. Yearly, VON acquires data on approximately 50,000 infants. VON is a voluntary service of health care professionals working to improve the safety and quality of newborn infants' medical care. The network holds an Annual Quality Congress of Neonatology for all participating institutions (Vermont Oxford Network, 2011).

These health care professionals conduct numerous clinical trials, long-term follow-up studies, as well as outcome and epidemiologic research. This data is contained in a network database and is used to determine information about how newborn infant care influences their outcomes. The results of these studies are published by the network in scientific articles, peer reviewed medical journals, network publications, and on their website (Vermont Oxford Network, 2011).

The VON database contains information on very low birth weight (VLBW) infants as well as others that fit their requirements. VON is able to take information from the database from the participating hospitals and provide an analysis and report confidentially on those hospitals. This allows hospitals to see which areas can be improved for quality assurance purposes (Vermont Oxford Network, 2011). Quality assurance opportunities are also available through collaboration with other hospitals through face-to-face contact or through web-based conferences (Vermont Oxford Network, 2011).

Prematurity

Infants born before 37 weeks gestation are considered premature. The more preterm an infant is born, the greater the risk that the infant will experience complications of prematurity. High rates of morbidity and mortality in preterm infants can be attributed to complications associated with prematurity. Approximately one third of infant deaths can be associated with prematurity. Extremely premature infants have a mortality rate around 50 percent (the highest of any gestational age group), as well as having the greatest risk of morbidity in the long-term. Prematurity accounts for 25 percent of children with hearing or cognitive impairments, 35 percent of those with visual impairments, and 45 percent of children with cerebral palsy (Eichenwald & Stark, 2008).

Three standard subdivisions classify underweight infants and three are designated for the degree of immaturity (approximate gestational age at birth). Infants born weighing less than 1000 g are considered to be extremely low birth weight (ELBW). An infant born weighing between 1000 g and 1500 g is considered to be very low birth weight (VLBW). Infants born weighing between 1500 g and 2500 g are considered to be low birth weight (LBW) (WHO, 2011). An infant born before 25 weeks gestation is referred to as being extremely preterm (Nicolas et al., 2000). Infants born between 25 and 32 weeks gestation is referred to as being very preterm. An infant born from 32 to less than 37 weeks gestation is referred to as being late preterm (Pamela et al., 2004).

Major NICU Advancements

Advancements in antenatal medicine and neonatal care have improved the rates of preterm infant survival. However, this improved rate of survival was not followed by

proportional decreases in neurological disabilities (Stephens and Vohr, 2010). Three major advancements in neonatology contributing to this increased survival of preterm infants are the implementation of antenatal steroids, surfactant therapy, and high frequency oscillation ventilator use.

Antenatal Steroids

Antenatal steroids are a type of steroid administered intramuscularly to mothers when her baby is between 24 and 34 weeks gestation and is at risk for premature birth. Treatment consists of two doses of 12 mg of betamethasone or four doses of 6 mg dexamethasone. Antenatal steroids are the most effective 24 hours after administration, and the effects last for seven days. Antenatal corticosteroids, administered to pregnant women, cross the placenta to induce cellular differentiation. Increased cellular differentiation results in significant reductions in neonatal mortality, respiratory distress syndrome (RDS), and intraventricular hemorrhage (IVH) (Norwitz et al., 2010).

Antenatal steroids aid fetal brain development by supporting the maturation of the germinal matrix microvasculature and reducing blood-brain barrier permeability. This increases the brain's resistance to stress, decreasing the risk of IVH (Stonestreet et al., 1998).

Corticosteroids are essential to fetal lung development. During late gestation, the concentration of circulating corticosteroids increases as the lungs mature (Ballard and Ballard, 1995). Infants born preterm miss this increase in corticosteroids. Fetuses exposed to antenatal steroid treatment have increased alveolar volume, closer alignment of alveoli to vessels, and thinner alveolar walls compared with non exposed fetuses of a similar gestational age. This leads

to better gas exchange and an enhanced response to postnatal surfactant treatment (Bonanno and Wapner, 2009).

Surfactant Therapy

Surfactant is a lipoprotein complex, found in the lungs, which reduces alveolar collapse by forming a layer between the alveolar surface and the alveolar gas in the lungs, reducing surface tension (Berry, 1991). Very premature infants are often not able to produce their own surfactant because their type II alveolar epithelial cells, where surfactant is produced, have not matured. Without surfactant, the alveoli may not inflate or collapse on expiration, which can lead to respiratory distress syndrome (RDS) (Berry, 1991). Exogenous surfactant is the primary life-saving therapy for RDS in preterm infants (Ramanathan, 2009). There are two strategies for surfactant administration; prophylactic (or preventative) treatment, and rescue or therapeutic treatment (Ramanathan, 2009).

High Frequency Oscillation Ventilator

High frequency oscillatory ventilation (HFOV) is a mechanical ventilator that uses constant distending pressure, with pressure variations oscillating around the mean airway pressure. This ventilation strategy produces small tidal volumes, in contrast to conventional ventilators, which induces large pressure changes and gas volumes, and is associated with ventilator induced injury. HFOV uses alternative mechanisms of gas exchange, such as molecular diffusion. Consequently, HFOV has become the most accepted mode of ventilation support for RDS in VLBW infants, and has been shown to improve survival without an increase

in the incident of chronic lung disease (Moriette et al., 2001; Johnson et al., 2002; Kessel et al., 2010).

Short Term Complications of Prematurity

It is important to quickly stabilize infants in the delivery room to reduce their risk of developing short term complications (Lemons et al., 2001). Short term complications of prematurity are defined as those occurring during the neonatal period (Eichenwald & Stark, 2008). Premature infants are increasingly susceptible to developing short term complications with decreasing birth weight and gestational age, and are the result of anatomical or functional immaturity (Faranoff et al., 2007).

Retinopathy of prematurity (ROP) is a condition occurring around 34 weeks postmenstrual age, and occurs when the retina of premature infants is incompletely vascularized. ROP generally spontaneously resolves, but requires treatment when ROP is severe and does not resolve spontaneously (Palmer et al., 1991). Infants with ROP are more likely to have vision impairment or poor ocular outcome (Trese and Droste, 1998; Moshfeghi et al., 2004; Prenner et al., 2004; Lakhanpal et al., 2005; Repka et al., 2006).

Many VLBW infants need resuscitation at birth, most requiring endotracheal intubation and others only need resuscitation medications. Prophylactic administration of surfactant reduces the risk of respiratory complications, such as respiratory distress syndrome (RDS), pulmonary interstitial emphysema, and pneumothorax (Lemons et al., 2001). Other complications include bronchopulmonary dysplasia (BPD), and apnea of prematurity (Henderson-Smart, 1981; Frank and Sosenko, 1987). Respiratory distress syndrome (RDS) results from insufficient surfactant production prior to birth (Frank and Sosenko, 1987) and occurs about 93 percent of the time

(Stoll et al., 2010). A symptomatic patent ductus anteriosus (PDA) occurs in about 46 percent of VLBW infants (Stoll et al., 2010). BPD is a chronic lung disease defined as dependence upon oxygen at 36 weeks postmenstrual age, occurring late in the neonatal period (Shennan et al., 1988; Marshal et al., 1999) in approximately 42 percent of infants (Stoll et al., 2010). Apnea of prematurity occurs in about 25 percent of premature infants (Henderson-Smart, 1981).

Necrotizing enterocolitis (NEC), a gastrointestinal complication, increases the risk of neurodevelopmental disabilities (Rees et al., 2007; Schulzke et al., 2007) and growth delay later in life (Hintz et al., 2005).

Late-onset sepsis, or a positive blood culture occurring after three days of age, occurs in about 21 percent of VLBW infants (Stoll et al., 2002). Neonatal sepsis is also associated with an increase in growth impairment and poor neurodevelopmental outcomes later in life (Stoll et al., 2004).

Short term cardiovascular complications include a patent ductus anteriosus (PDA) and systemic hypotension (Faranroff et al., 2007; Seri and Noori, 2005). PDA causes increased blood flow through pulmonary circulation and decreased blood flow through systemic circulation by shunting the blood from left to the right side of the heart (Rudolph, 1970). If a significant amount of shunting occurs, symptoms such as respiratory distress, apnea, or heart failure may present (Thibeault et al., 1975; Cotton et al., 1978; Jacob et al., 1980; Mahony et al., 1982; Cassady et al., 1989; Schmidt et al., 2001). Systemic hypotension, occurring immediately after birth, can lead to the development of IVH (Seri and Noori, 2005; Osborn et al., 2007; Miletin and Dampsey, 2008).

Overall, the more short term complications seen in an infant, the greater the chances that the child will experience long term complications of prematurity (Eichenwald and Stark, 2008).

Preterm Brain Complications

A child born very preterm uses different regions of the brain to process information than those regions a term infant uses. When an infant is born prematurely, the brain compensates for being underdeveloped to function properly in its new environment. These changes can have detrimental effects in long term (Jobe, 2010). The preterm infant born at 24 weeks gestational age has a brain weight around 100g with a smooth surface with no external architecture (gyri). While at full term, an infant's brain weighs about 350g and has a convoluted surface and great complexity (Ment et al., 2009). The brain of an ELBW neonate grows, but the surface structure is less complex than the full term brain (Ajayi-Obe et al., 2000). A preterm brain has a lower volume of deep nuclear grey matter, which can be further damaged by white matter injury (Inder et al., 2005).

New born brain injury occurs as often as 1 in 4000 live births. Greater than 95% of infants who survive a brain injury survive until adulthood, but many suffer motor and cognitive disabilities (Nelson and Lynch, 2004). Therefore, it is important to examine the brain complications of preterm infants whose susceptibility for brain injury is higher than that of term infants. Neonatal brain injury is difficult to detect in VLBW infants due to the absence of some common signs of brain injury, including lethargy, hyperexcitability, and stupor (Mercuri et al., 2003).

Preterm infants are predisposed to brain injury due to factors including hypoxia, ischemia, hyperoxia, and maternal-fetal infection. Perinatal impacts to the brain can result in inflammation, excitotoxicity, and oxidative stress. Genetic factors cause some infants to be more

susceptible to these complications. These factors contribute to encephalopathy of prematurity, which is white and grey matter damage of the premature brain (Kaindl et al., 2009).

The most common brain injury in preterm infants is periventricular white-matter injury. Periventricular white matter injury is the primary cause of chronic neurological morbidity (Deng et al., 2008). Periventricular leukomalacia (PVL), the most common type of white matter injury, is marked by microglial activation and depletion of premyelinationg oligodendrocytes (Kaindl et al., 2009). Neuropathological studies have found that diffuse white matter damage is characterized by a lack of white matter, thinning of the corpus callosum, and delayed myelination. This is caused by death of late oligodendrocyte progenitor cells (Back et al. 2001).

White-matter damage is accompanied by neuronal loss and impaired neuronal guidance. Some preterm infant complications result from reduced connectivity between areas of the brain needed for integrating information (Kadhim et al., 2003; Kesler et al., 2006; Leviton and Gressens, 2007; Okoshi et al., 2007).

The neonatal brain is vulnerable to oxidative damage because of its high concentrations of unsaturated fatty acids, high rates of oxygen consumption, low concentrations of antioxidants, and availability of redox-active iron (Halliwell, 1992). In the immature brain, oligodendrocyte progenitor cells are susceptible to the depletion of antioxidants and exposure to free radicals, while mature oligodendrocytes are extremely resistant to this stress (Baud et al., 2004). This vulnerability gives reason to white matter injury occurring more often in preterm infants. Oxidative stress can lead to ischemic damage to the neonatal brain. Ischemia is a decrease in the blood supply caused by constriction or obstruction of blood vessels. This leads to tissue damage because of a lack of oxygen and nutrients (Kanold et al., 2003).

Excitotoxicity is also a factor in ischemic damage to the preterm brain. Excitotoxicity is the excessive activation of glutamanergic neurotransmitters leading to cell death (Olney, 2003). This cell death in the neonate brain may be triggered by the impairment of the uptake of glutamate by glia causing overactive receptors (McDonald and Johnston 1990). The expressions of these glutamate receptors dictate the reaction of a newborn to brain injury. Blocking these receptors protects against hypoxic-ischemic injury to the white matter (Deng et al., 2004).

Maternal infection is another factor associated with white matter disease in the premature brain. Chorioamnionitis, inflammation of the amnion and chorion due to bacterial infection, is a risk factor for preterm infants (Wu et al., 2003). The problem with this association is that it is difficult to define chorioamnionitis, as it is rare to document it by histological examination of the placenta. This condition can be as vague as maternal fever (Khong et al., 2000).

Neonatal strokes often originate arterialy, and are caused by ischemic damage, but about 30 percent are caused by sinovenous thrombosis (deVeber et al., 2001; Wu et al., 2004). Risk factors of neonates with stroke due to cerebral venous thrombosis include coagulation abnormalities, certain genetic mutations and polymorphisms (Mercuri et al., 2001). The risk of reoccurring neonatal stroke is low at 5 percent, and is associated with complications of systemic disorders (Kurnik et al., 2003).

Intraventricular Hemorrhage

A decline in the incidence of intraventricular hemorrhage (IVH) has been seen since the 1980s where IVH occurred 50 to 80 percent of the time. It now occurs at the rate of 10 to 15 percent. The increased survival of extremely premature infants ensures that IVH remains a

significant problem in infants. Intraventricular hemorrhage, in premature infants, is a leading cause of brain injury (Volpe, 2001).

Intraventricular hemorrhage, as its name implies, is bleeding in or around the ventricles of the brain, which function to store cerebral spinal fluid. There are four grades of IVH. In Grade 1 IVH bleeding occurs on the edge of the ventricles but does not extend into the ventricles. In IVH Grade 2 bleeding has progressed into the ventricles. In Grade 3 IVH the ventricles have become enlarged due to the bleed. Grade 4 IVH, the most severe, is present when bleeding is so severe that blood is forced into the tissue surrounding ventricles. IVH Grades 1 and 2 typically do not result in further complications. IVH Grades 3 and 4 (severe IVH) are less common, and can result in permanent damage to the brain (Lucile Packard Children's Hospital at Standford, 2011). Infants with severe IVH face a mortality rate near 20 percent, with more than 50 percent developing progressive ventricular dilation (Volpe, 2001).

IVH most commonly occurs in infants less than 1500 g or less than 32 weeks gestation. Ninety percent of IVH occurs within the first three days of life (Volpe, 2001). IVH is rarely isolated, and is often accompanied by periventricular leukomalacia (PVL) (Armstrong et al., 1987) a contributing factor of IVH (Guzetta et al., 1986). Other contributing factors include periventricular hemorrhagic infarction, and parenchymal injury (Guzetta et al., 1986).

IVH typically occurs in the frail germinal matrix (Fanaroff et al., 2007; Stoll et al., 2010). The germinal matrix is the richly vascularized and highly cellular layer of the subependymal subventricular zone, region of the brain that gives rise to glia and neurons during infant development (Sidman et al., 1982). Infants are predisposed to hemorrhage if the structural support of the germinal matrix is insufficient (Grunnet, 1989). Astrocytic support of blood

vessels in the germinal matrix at 27 weeks gestation is minimal, and at 31 weeks is much more prominent (Gould and Howard, 1987).

The best method for preventing IVH would be to prevent a premature birth, but antenatal corticosteroid administration significantly reduces the risk of the IVH when premature birth cannot be prevented (Crowley, 2000). Some common preventative measures include maintaining hemodynamic stability, efforts to prevent conditions that disrupt cerebral autoregulation, and appropriate and timely resuscitation (Jim et al., 2005). Clamping the umbilical cord after thirty seconds following birth is also associated with a decrease in the incidence of IVH (Rabe et al., 2004; Mercer et al., 2006).

Risk factors for IVH include prolonged resuscitation, respiratory distress syndrome (Palta et al., 2008), pneumothorax, seizures, and necrotizing enterocolitis (Goddard-Finegold et al., 1997; Jen et al., 2006). Additionally, infants younger than 33 weeks gestation, whose mother had chorioamnionitis show an increased risk of developing severe IVH (Soriasham et al., 2009).

Infants born prematurely are less able to regulate cerebral blood flow which results in a pressure passive circulation in which a rise in systemic blood pressure results in an increase in cerebral blood flow, damaging the delicate germinal matrix (Papile et al., 1978; Perlman et al., 1981; Wallin et al., 1990). As infants mature, the range of blood pressures over which they are able to autoregulate increases (Papile et al., 1985). Autoregulation can be impaired due to asphyxia (Pryds et al., 1990), hypoxia, hypocarbia, hyperoxia, and hypercarbia (Jim et al., 2005).

Activities such as movement, feeding, and crying, medical interventions such as suctioning and endotracheal intubation as well as pathologic states including seizures (Goddard-Finegold et al., 1997; Volpe, 2001) and pneumothorax can all induce hypertension (Goddard-Finegold et al., 1997) resulting in an increased chance of developing IVH. Premature infants

who have spontaneous motor activity or undergo intensive care procedures resulting in an increase in their systemic blood pressure are more likely to develop IVH.

It is uncommon for severe IVH to occur in term infants, occurring in them most frequently with the rupture of a vascular malformation (Heafner et al., 1985), alloimmune thrombocytopenia (Mao et al., 1999), sinvenous thrombosis (Wu et al., 2003), trauma, such as abdominal compression (Wehberg et al., 1992), and a diagnosis of hemophilia (Tarantino et al., 2007).

IVH presentation can be catastrophic, saltatory, or (in 25-50 percent of cases) clinically silent. Catastrophic presentation of IVH is the least common, and is characterized by inappropriate antidiuretic hormone (ADH) secretion, bradycardia, hypotension, falling hematocrit levels, and a bulging anterior fontanel. Other signs of catastrophic IVH include cranial nerve abnormalities, such as the pupils being fixed to light, generalized tonic seizures, decerebrate posturing, flaccid weakness, irregular respirations such as, apnea or hypoventilation, and coma or stupor. In a saltatory presentation of IVH, respiratory function is sometimes affected as well as the presence of hypotonia, an altered level of consciousness, and a decrease in subtle, spontaneous, or elicited eye movements. Saltatory presentation of IVH typically occurs within hours to several days (Tarby and Volpe, 1982).

Diagnosis of IVH is most commonly done via cranial ultrasound. Cranial ultrasounds of IVH Grades 1, 2, 3 are shown in **Figures 1, 2, 3 and 4**, respectively below. Cranial ultrasound screening for IVH is routinely performed on premature infants because nearly half of all incidences of IVH are clinically silent (Ment et al., 2002). Another diagnostic measure used to detect IVH is a lumbar puncture. With a lumbar puncture, the cerebral spinal fluid (CSF) of an

individual with IVH would contain high protein concentrations and red blood cells (Volpe, 2001).

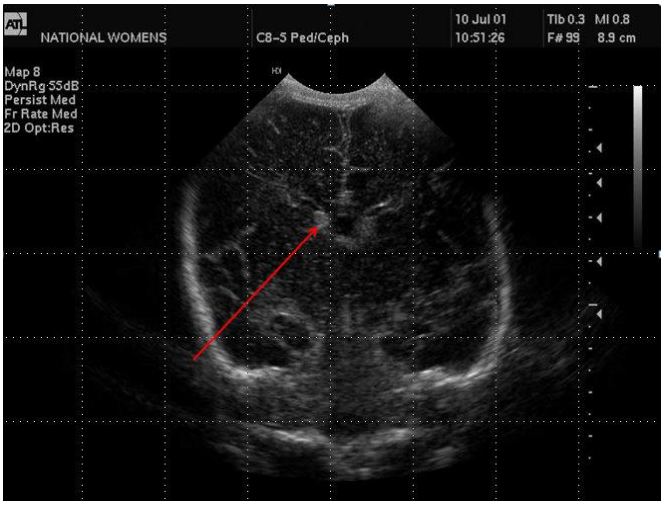

Figure 1: Cranial ultrasound of Grade 1 IVH (coronal view). The ultrasound shows bleeding in the germinal matrix but does not extend into the ventricles. (© Auckland. http://www.adhb.govt.nz/newborn/TeachingResources/Radiology/HUSS/Images/IVH/Grade1/Grade%201%20coronal.jpg)

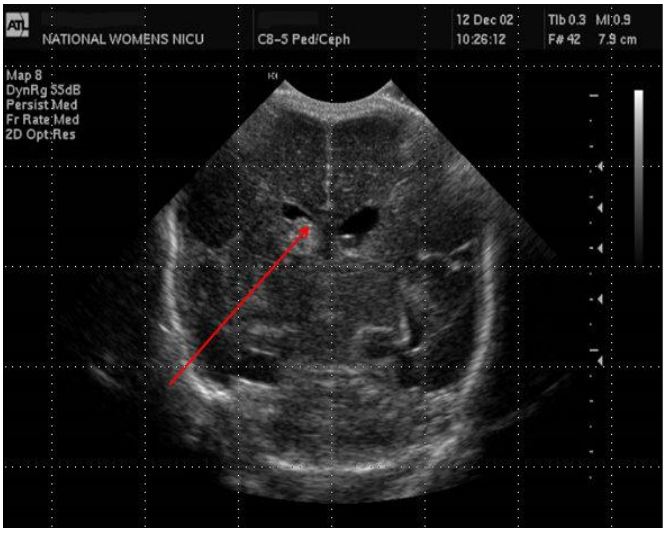

Figure 2: Cranial ultrasound of Grade 2 IVH (coronal view). The ultrasound shows bleeding extending into the ventricles, but does not result in extension of the ventricles. (© Auckland http://www.adhb.govt.nz/newborn/TeachingResources/Radiology/HUSS/Images/IVH/Grade2/Grade2Coronal2.jpg)

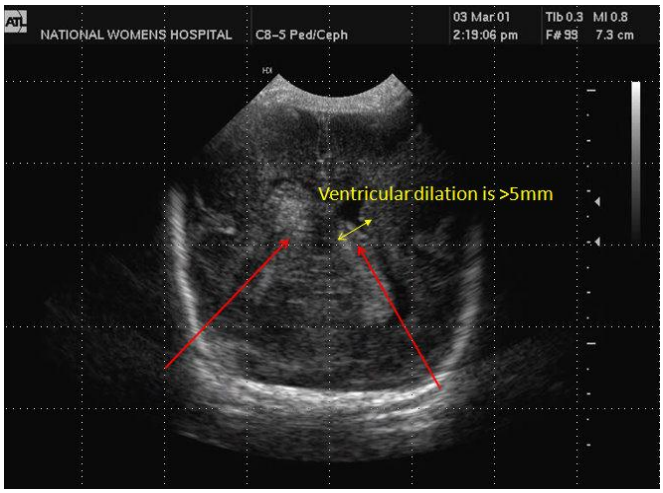

Figure 3: Cranial ultrasound of Grade 3 IVH (coronal view). The ultrasound shows a bilateral bleed causing extension of the ventricles. (© Auckland http://www.adhb.govt.nz/newborn/TeachingResources/Radiology/HUSS/Images/IVH/Grade3/Day%202b.jpg)

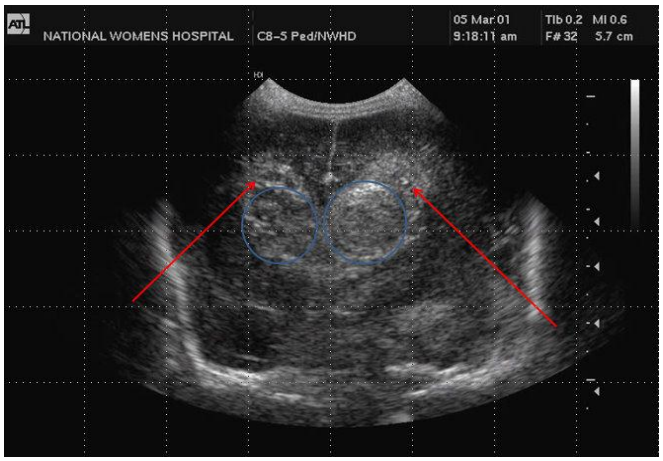

Figure 4: Cranial ultrasound of Grade 4 IVH (coronal view). The ultrasound shows a bilateral bleed extending past the ventricles into the brain tissue. (© Auckland http://www.adhb.govt.nz/newborn/TeachingResources/Radiology/HUSS/Images/IVH/Grade3/Day%204a.jpg)

Supportive treatment to limit the damage of IVH includes aiming to minimize further complications, as well as preserving cerebral perfusion. Treatment can include providing nutritional, fluid and metabolic support, as well as maintaining systemic blood pressure to prevent hypertension or hypotension, and the use of supportive oxygenation and ventilation techniques (Volpe, 2001).

The severity of the long term outcomes increases with the severity of IVH as well as decreasing gestational age and birth weights (Sherlock et al., 2005). Some of the long term complications of IVH include cognitive dysfunction, cerebral palsy, major neurosensory disabilities (Sherlock et al., 2005), and intellectual disability (formerly reported as mental retardation) (Luu et al., 2009). Other complications include posthemorrhagic hydrocephalus, and major cognitive impairments, as well as other developmental disabilities (Pinto-Martin et al., 1999; Murphy et al., 2002). Many children with these complications require special education services in school (Vhor et al., 2003). Adverse neurodevelopmental outcomes are greatest among those ELBW infants having severe IVH (Adams-Chapman et al., 2008; Brouwer et al., 2008).

Long Term Complications of Prematurity

Premature children generally have a lower body mass index, are shorter, lighter, and have a smaller head circumference than those born full-term due to reduced growth (Bracewell et al., 2008). Children born preterm have increased prevalence of chronic medical conditions such as gastroesophageal reflux (Omari et al., 1998), bronchopulmonary dysplasia (Jobe & Bancalari, 2001), as well as having an increased risk of hearing (Thompson et al., 2001) and vision impairments (Knight-Nanan & O'Keefe, 1996; Hebbandi et al., 1997; Repka et al., 1998; Quin et al., 1998; Holmstrom et al., 1999) and sudden infant death syndrome (Verma & Sridhar, 2003).

Premature infants are more likely to be rehospitalized for recurrent illnesses including feeding problems (Korvenranta et al., 2009), surgical issues (Harper et al., 1975; Peevy et al., 1986; Powell et al., 1986; Rajput et al., 1992; McCourt & Griffin, 2000), infections, notably respiratory syncytial virus infection (Nachman et al., 1997; McCormick & Tubman, 2002), and respiratory problems including asthma compared to infants born full-term (Koivisto, 2005;

Underwood et al., 2007). Premature children also have an increased risk of having impaired lung function, which may result in an increase in respiratory symptoms, and a reduced exercise and lung capacity (Smith et al., 2008).

In ELBW children, neurodevelopmental complications result in more functional limitations such as developmental, growth and motor delay, as well as decreased social skills, limited physical ability, and sensorineural deficits. Children born ELBW are also more likely to require equipment or help for activities of daily life such as washing, dressing and feeding, as well as increased medication use. In addition, ELBW children are at increased risk of requiring additional services such as educational programs individualized to their needs, other special school arrangements, and acute care visits to specialized health care professionals than children born at a normal birth weight (Stein et al., 2006).

As adults, those born prematurely seem to be more likely to have higher blood pressure and an increased resistance to insulin compared to adults born full-term (Hovi et al., 2007; Rotteveel et al., 2008). During their late teens, ELBW adults score higher on measures of inattention, anxiety, depression, withdrawn behavior, and social problems. In addition, VLBW adults in the same age group report lower rates of alcohol and drug use, sexual activity, and pregnancy than adults born at normal birth weight (Hack et al. 2004). An association can be made between decreased reproduction in adulthood and prematurity compared to the reproductive rates of full-term adults. Additionally, women who were preterm also have a higher risk of having a preterm child. However, men born prematurely have no increased risk of their children being born prematurely (Swamy et al., 2008).

Neurodevelopmental Outcomes of Premature Infants

Common neurological impairments associated with prematurity include mental retardation (cognitive impairment), cerebral palsy (CP), blindness, and hearing impairments. These are the highest in ELBW infants (Hack and Farnaroff, 2000). Research centers and hospitals have reported a range of occurrences of neurological impairment. The variability of this data can be contributed to rates of neonatal morbidities and differences in treatment management style (Vohr et al., 2004).

The most common neurological impairment is cognitive impairment, which is defined as a score more than two standard deviations below the mean on standardized cognitive tests (Bayley, 1993). Rates of cognitive impairment are inversely proportional to gestational age and birth weight. While testing of cognition is done during infancy, it is not always predictive of cognitive function later in life (Jobe, 2010).

ELBW and VLBW school age children have lower Intelligence Quotient (IQ) scores and higher rates of cognitive impairment compared with their normal peers (Marlow et al., 2005). Compared with their normal peers, VLBW and ELBW children have impairments of executive functioning, visual-motor skills, and memory. Infants born LBW are also more likely to develop learning disabilities such as attention deficit disorder or attention deficit hyperactivity disorder (Hack et al., 2002).

Other neurological impairments of prematurity affect motor functions. The main concern here is cerebral palsy (CP). Cerebral Palsy is defined as "a disorder of movement and posture that involves abnormalities in tone, reflexes, coordination and movement, delay in motor milestone achievement, and aberration in primitive reflexes (Vohr et al., 2005)." The most common form of CP is spastic diplegi: spastic quadriplegia, and hemiplegia (Bracewell and

Marlow, 2002; Vohr et al., 2005; Stephens and Vohr, 2010). Some LBW infants develop soft neurological signs of motor impairment. Soft signs include deviations in speech, balance, coordination, gait, tone, and fine motor or visual motor tasks that do not signify localized brain dysfunction (Breslau et al., 2000). Standard evaluations of motor function include muscle tone, strength, reflexes, joint angles, and posture.

Neurosensory disabilities are not as common as cognitive and motor impairments, but are prevalent in ELBW infants. Visual impairments include unilateral or bilateral blindness, myopia, and strabismus. Hearing impairments requiring amplification occur in 1% to 9% of ELBW infants (Vohr et al., 2004). Mild hearing impairments are more common (Hack et al., 2005).

Prematurity, especially VLBW infants, has been associated with many behavioral and psychological diagnoses and disabilities. Evaluation of behavior is often obtained by parents and teachers and measures behavior, attention, adaptive skills, and depression. There is concern that low birth weight and gestational age presents a risk for autism spectrum disorders, but the true risk is unknown (Schendel and Bhasin, 2008).

Diagnostic Developmental Tests

The Bayley Scales of Infant Development - Second Edition (BSID-II) is a developmental test of both cognitive and motor skills for infants one month to 42 months (Bayley Scale, 2011). BSID-II has three characterized scales evaluating the mental (mental scale), motor (motor scale), and behavioral development (behavioral scale) of a child (BSID-II, 2011). The mental scale gives a normalized Mental Developmental Index (MDI) and Psychomotor Development Index (PDI) standard score (BSID-II, 2011). The motor scale tests large muscle coordination, degree of body control, fine manipulatory skills involving he fingers and hands as well as stereognosis,

dynamic movement, dynamic praxis, and postural imitation (BSID-II, 2011). The behavioral scale is an assessment of the child's ability to perform the mental and motor tests looking at motor quality, orientation/engagement, attention/arousal, as well as emotional regulation and is used as a supplementary scale to the mental and motor scales (BSID-II, 2011).

The BSID-II was normalized to a sample of 1,700 children randomly selected infants between the ages of one month to 42 months (BSID-II, 2011). The manual for the BSID-II provides information about specific groups as reference, including children who have the HIV antibody, Down's syndrome, are developmentally delayed, are autistic, have frequent ottis media, were asphyxiated at birth, who were prenatally exposed to drugs, or were born prematurely (BSID-II, 2011).

The Bayley Scales of Infant and Toddler Development --Third Edition (Bayley-III) also tests children from one month to 42 months of age (Bayley-III, 2011). The Bayley-III is similar to the BSID-II in the fact that they are both testing the same basic aspects of development; however the Bayley-III is a bit more comprehensive. The Bayley-III has five scales corresponding to the five developmental domains in which the children are evaluated: social-emotional, adaptive behavior, cognitive, motor, and language development (Bayley-III, 2011). The Bayley-III focuses on the developmental skills the child possesses, but also has scores children with a scaled and composite score in the fields of cognition, motor (fine and gross motor), and language (both receptive and expressive language) (Bayley, 2006).

The social-emotional domain of the Bayley-III is meant to monitor emotional and social functioning, the progress of early intervention, as well as determining if the child has mastered the early aspects of their social-emotional growth, age related milestones and detecting developmental social-emotional problems or deficits (Bayley-III, 2011).

The adaptive behavior domain of the Bayley-III includes self-care, self-direction, health and safety, home living, leisure, functional pre-academics, social, motor, communication, and community use (Bayley-III, 2011).

The cognitive domain of the Bayley-III includes exploration and manipulation, habituation, memory, concept formation, object relatedness, sensorimotor development, visual preference, visual acuity, as well as object permanence and other cognitive processing abilities, as well as age-appropriate cognitive skills (Bayley-III, 2011). The motor domain of the Bayley-III includes gross motor and fine motor skills on which the children are evaluated (Bayley-III, 2011). The language domain of the Bayley-III is comprised of two communication groups: expressive communication and receptive communication (Bayley-III, 2011).

The manual for the Bayley-III includes reference material on children who are premature, small for gestational age, at-risk, have Down's syndrome, pervasive developmental disorder, cerebral palsy, language impairment, and FAS/polysubstance use (Bayley-III, 2011). The scores generated by the Bayley-III include information on percentiles, age equivalents, T score, and cut scores (Bayley-III, 2011).

PROJECT PURPOSE

The purpose of this project was to bridge the information disconnection between the neonatal intensive care unit (NICU) at the UMass Memorial Medical Center (where IVH is first likely to be diagnosed) and their Developmental and Behavioral Pediatric Follow-Up clinic (where subsequent developmental outcomes are first identified). Physicians from the NICU at UMass Memorial Medical Center require information for parents facing the decision as to whether to continue life sustaining care premature infant when he/she has a particular neonatal complication. Standardized health and developmental follow-up forms are needed for physicians in the NICU to attain follow-up data on children who suffered from similar conditions in the NICU. With this information parents can understand what complications their premature infant my face later in life and will be better able to make an informed decision on whether to continue to provide life-sustaining care to their infants with severe IVH who may be neurologically devastated. In this project, an analysis of infants with severe IVH born under 1000g was performed to demonstrate potential correlations with neurodevelopmental follow-up statistics. Physicians can use this information to show parents the neurodevelopmental outcomes of severe IVH infants at UMass and the chances of their Infant with IVH developing neurological impairments.

METHODS

Pediatric Follow-Up Form Development

Standardized Follow-up Health Status and Developmental Status forms were created for use by the UMass Pediatric Developmental and Behavioral Follow-up Clinic and neonatal intensive care unit (NICU) to track the development of children after discharge from the NICU. These forms were based on the Vermont Oxford Network (VON) Forms (Appendicies 1a & b) and altered to fit the needs of UMass Memorial Medical Center (UMMC). VON evaluates infants between 18 and 24 months but the follow-up clinic sees children of all ages, thus there is a wider range of information to collect.

Dr. Robin Adair of the UMass follow-up clinic and Dr. Alan Picarillo of the UMass NICU were interviewed to identify what information needed to be captured during follow-up visits. These discussions provided insight on which data the follow-up clinic captures for children at different ages, and what information is necessary for neurodevelopmental diagnosis. Developmental and Behavioral Pediatric Follow-up appointments were observed to better understand the process of diagnosis.

The UMMC Follow-up Health Status and Developmental Status forms were designed for a relatively new database system at the follow-up clinic, AllScripts. The forms were designed with Microsoft Word, and numerically coded for electronic entry. A total of seven forms were developed and are listed in **Table 1**.

Table 1: UMass follow-up Clinic Forms

Form	Age Range (Months . Days)
Developmental Status	0.0 – 15.29
Developmental Status	16.0 – 26.0
Developmental Status	26.1 – 42.0
Developmental Status	>42.1
Health Status	0.0 – 15.29
Health Status	16.0 – 26.0
Health Status	>26.1

Severe IVH Database Setup

Infants born under 1000g with severe IVH (grades 3 and 4) were studied to determine trends in neurodevelopment. An Excel database was set up including all infants with severe IVH, born under 1000 grams, at the UMMC NICU from 2003 to 2009 (n = 17). Because past information was not recorded on the newly developed follow-up forms, data was extracted from paper files and was recorded in the excel database. Independent variables included all perinatal conditions. Dependent variables were all neurodevelopmental follow-up conditions. Neurodevelopment conditions were determined by the physicians at the UMMC Pediatric Follow-up Clinic. A list of the independent and dependent variables used in data analysis are provided in **Table 2**.

Table 2: Severe IVH Independent and Dependent Variables

Independent Variables ***(Perinatal Conditions)***	**Dependent variables** ***(Neurodevelopmental)***
Grade of IVH	Early Intervention
Mode of Delivery	Cerebral Palsy (CP)
Antenatal Steroids	Rehospitalization
	Bayley II MDI scores
	Bayley III scores
	Prescription Glasses
	Hearing Impairment

A comprehensive list of variables collected can be found in Appendix 2.

Data Analysis

The data collected in the severe IVH database (n=17) was compared to infants born at UMMC between 2003 and 2009 that were under 1000g but did not have severe IVH (n = 179) and infants born between 2003 and 2007, under 1000g in the VON data base (n = 85175). A two tailed Fisher's Exact Test, (Quick Calcs, 2005), was used to compare the occurrence of the neurodevelopmental outcomes in the different populations. The two tailed Fisher's Exact Tests are listed in **Table 3**.

Table 3: Two Tailed Fisher's Exact Tests

1. Cerebral Palsy: Severe IVH Infants vs. No Severe IVH Infants (UMass)
2. Severe Cognitive Impairment vs. No Severe Cognitive Impairment: Severe IVH Infants vs. No Severe IVH Infants (UMass)
3. Moderate Cognitive Impairment vs. No Cognitive Impairment: Severe IVH Infants vs. No Severe IVH Infants (UMass)
4. Eyeglasses: Severe IVH Infants vs. No Severe IVH Infants (UMass)
5. Hearing Impairment: Severe IVH Infants vs. No Severe IVH Infants (UMass)
6. Rehospitalization: Severe IVH Infants vs. No Severe IVH Infants (UMass)
7. Grade of Severe IVH (3 or 4): Use of Antenatal Steroids
8. Grade of Severe IVH (3 or 4): Mode of Delivers (Vaginal Delivery or Cesarean Section)

The occurrence of severe IVH and cerebral palsy in infants born under 1000g at UMMC and in VON was compared. The occurrence of severe IVH was compared to see how UMMC compares to the average NICU that submits data to VON. The occurrence of cerebral palsy was used as a positive control in which to compare UMMC and VON. A Two Tailed Fisher's Exact Test could not be used for these comparisons because of the large number of infants, so a Chi Squared Analysis with a Yates Correction was used for these comparisons.

The cognition levels of these children were determined by examining their Bayley II and III test scores completed between ages 14 and 26 months. Some children were given either the Bayley II or III. If both test were administered the Bayley III was used for analysis. The Bayley II has one index score for cognition termed the Mental Development Index (MDI) score. Scores of 85 or above are considered normal, scores 70 to 84 are considered moderately impaired and scores below 70 are considered severely impaired. The Bayley III test produces multiple scores so as advised by Dr. Robin Adair and Dr. Alan Picarillo, the Cognitive Index scores and Language Index scores were averaged to determine an equivalent MDI score. The average of these scores was used to determine the degree of cognitive impairment. Again, scores of 85 or above are considered normal, 70 to 84 are considered moderately impaired and scores below 70 are considered severely impaired. All other neurodevelopmental outcomes were found directly in the patients' paper charts.

The Fisher's Exact Test was used to compare the occurrence of neurodevelopmental outcomes in different infant populations, calculate the probability that a difference in two categories is a significant difference or a coincidence (not significant). The Fisher's Exact Test calculated P values for each comparison. The P value is the probability that a difference will be observed that is as large as or larger than observed if the null hypothesis were true. The Null hypothesis for each of these comparisons was that there is no difference between the groups. A P value of 0.05 or less is considered to suggest a significant difference between two groups. Meaning there is only a 5% chance that the difference is insignificant.

RESULTS

This project helped bridge the information disconnection between the neonatal intensive care unit (NICU) at the UMass Memorial Medical Center (UMMC) and their Developmental and Behavioral Pediatric Follow-UP Clinic. Physicians from the NICU will now be able to more efficiently acquire information from the Follow-Up Clinic from the developed Health and Developmental Status Forms, which will be used in the AllScripts database. The new Health and Developmental Status Forms can be found in Appendices 3a-g. This information will enable parents to understand what complications their premature infant may face later in life.

An analysis if infants with severe intraventricular hemorrhage (IVH) under 1000g was conducted to demonstrate the advantages of the Health and Developmental Status Forms in the attainment of neurodevelopmental follow-up statistics. The results show that severe IVH in premature infants born under 1000g correlates with certain neurodevelopmental complications. All but one of the severe IVH infants received Early Intervention to assist in their neurodevelopment.

A positive control was performed to ensure that UMass and the Vermont Oxford Network (VON) had accurate follow up data. As a positive control, the occurrence of cerebral palsy (CP) in ELBW infants, from 2003 to 2007, was compared between UMMC and VON. The occurrence of CP was used because it is a possible neurodevelopmental outcome of any ELBW infant. A Two-tailed Fisher's Exact Test indicated no difference in the occurrences of CP in either population. Because there is no significant difference between the two populations, the positive control indicates that these two populations are comparable, and therefore the results of

the statistical analysis between the groups are reliable. A Graph of the Occurrence of CP in ELBW infants at both UMass and Von is displayed in **Figure 5**.

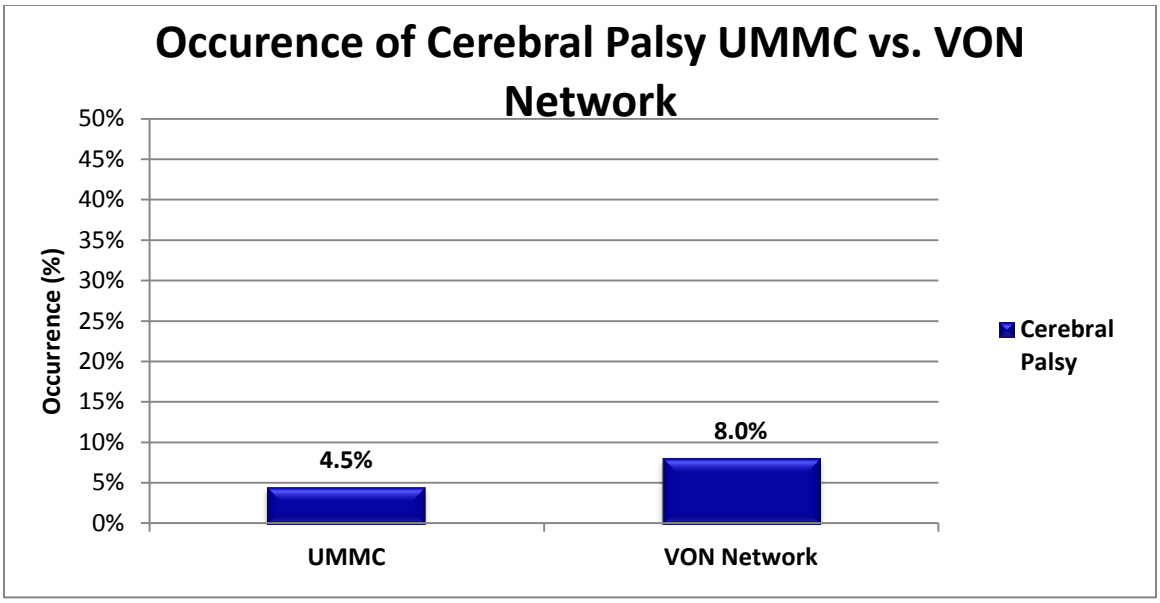

Figure 5: Occurrence of Cerebral Palsy in ELBW Infants: UMass vs. VON.
The occurrence of cerebral palsy at UMass compared to the VON Network. This functions as a positive control showing no statistical difference in the overall occurrence of cerebral palsy at UMass (n=187) compared to the VON Network (n=4007) with a P value of 0.0692.

To determine how well UMMC is stabilizing ELBW infants and preventing severe IVH, The occurrence of severe IVH in ELBW infants, between 2003 and 2007, was compared between UMMC and VON using a Chi Squared analysis with Yates correction. The analysis showed that the occurrence of severe IVH in ELBW infants at UMass was statistically significantly lower than infants reported to the national Vermont Oxford Network database. A Graph of the occurrence of severe IVH at UMass and VON is displayed in **Figure 6**.

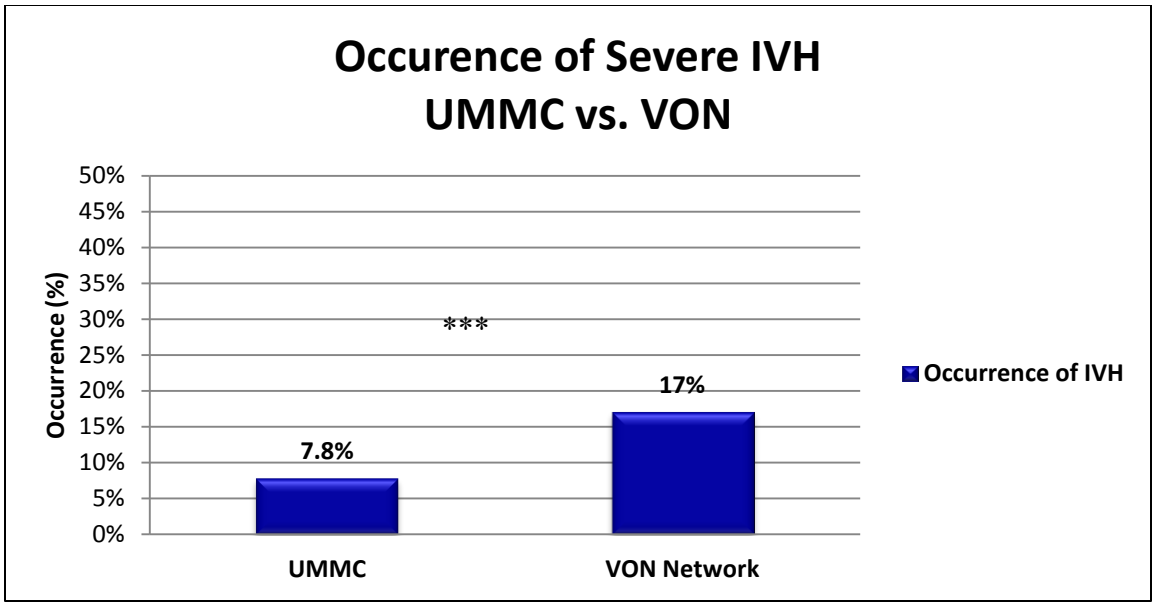

Figure 6: Occurrence of Severe IVH: UMass vs. Von.
The occurrence of severe IVH in preterm infants at UMass (n=218) was compared to the occurrence in preterm infants in the Vermont Oxford Network (n=85175). The occurrence of IVH was extremely statistically significantly lower (***) at UMass than in the Vermont Oxford Network with a P value of 0.0004.

One possible neurodevelopmental complication is cerebral palsy. To determine if severe IVH correlates with cerebral palsy, a Two-tailed Fisher's Exact Test was performed for ELBW infants from the UMMC NICU with and without severe IVH, from 2003 to 2009. ELBW infants with severe IVH were 22% more likely to develop cerebral palsy than ELBW infants without IVH. A Graph of the Occurrence of Cerebral Palsy in Infants with Severe IVH and Infants without severe IVH is displayed in **Figure 7**.

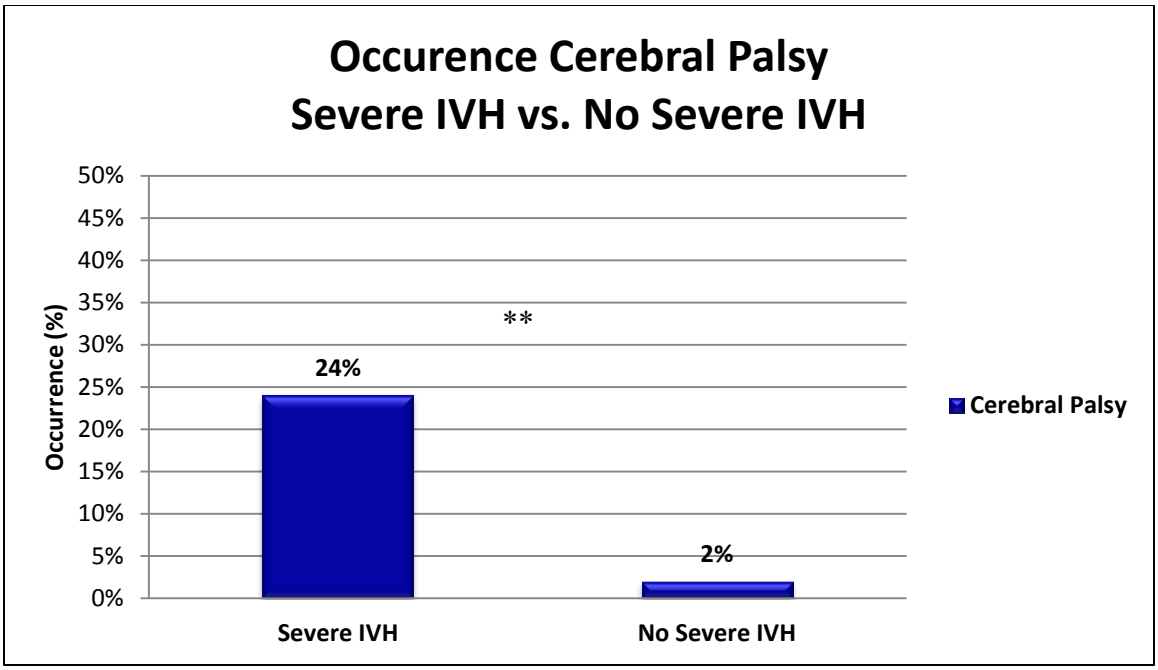

Figure 7: Occurrence of Cerebral Palsy: Severe IVH vs. No Severe IVH.
The occurrence of cerebral palsy in preterm infants with severe IVH (n=17) was s found to be very statistically significantly higher (**) in the severe IVH infants than in the no severe IVH infants with a P value of 0.0032.

Another possible neurodevelopmental complication is cognitive impairment. To determine if severe IVH correlates with moderate or severe cognitive impairment a Two-tailed Fisher's Exact Test was performed for ELBW infants from the UMMC NICU with and without severe IVH, from 2003 to 2009. ELBW infants with severe IVH were 38% more likely to become moderately cognitively impaired than ELBW infants without IVH. Severe IVH infants are no more likely to develop severe cognitive impairment than infants without severe IVH. A Graph of the Occurrence of cognitive impairment in Infants with Severe IVH and Infants without severe IVH is displayed in **Figure 8**.

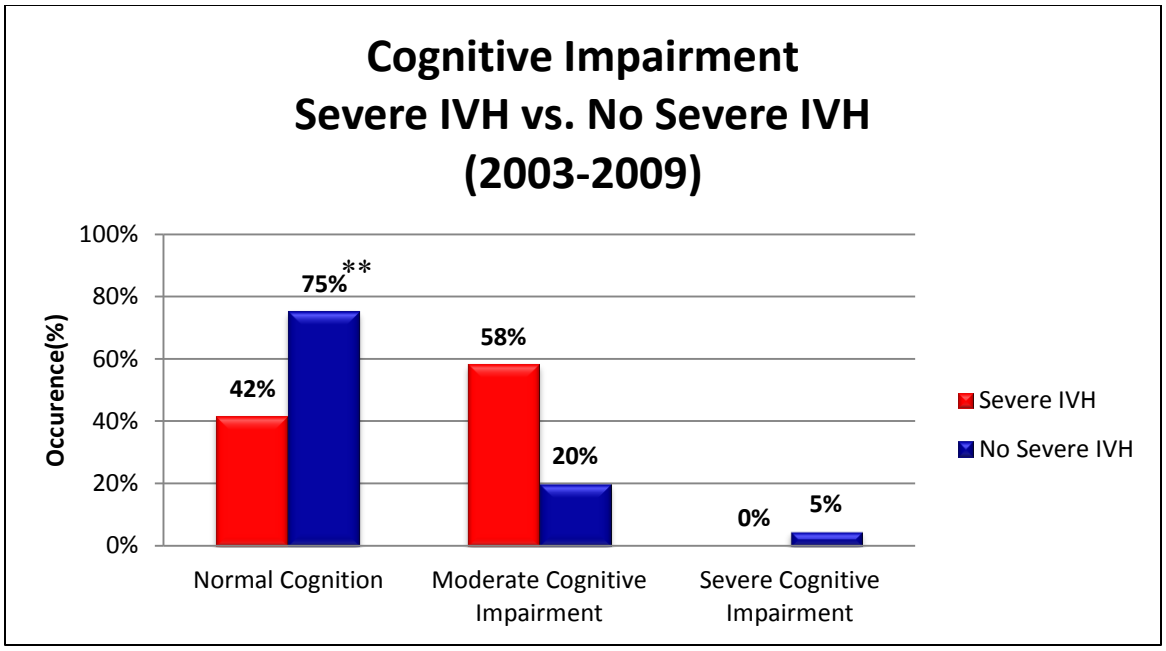

Figure 8: Cognitive Impairment: Severe IVH vs. No Severe IVH.
The Cognition of preterm infants with severe IVH (n=17) was compared with the cognition of preterm infants without severe IVH (n=158). All Cognition tests were performed between 14 and 26 months corrected age. There was no statistical significant difference in the occurrence of severe cognitive impairment in either the severe IVH group or the no severe IVH group with a P value of 1. The infants with severe IVH had a very statistically significantly (**) higher occurrence of moderate cognitive impairment than infant without IVH with a P value of 0.0036.

To determine if there is a correlation between sensory impairment, particularly sight and vision, a Two-tailed Fisher's Exact Test was run to compare the need for eyeglasses and any hearing impairment in ELBW infants with and without severe IVH between 2003 and 2009. These sensory impairments were found to correlate with severe IVH. ELBW infants with severe IVH were 30% more likely to need eyeglasses than infants without severe IVH. ELBW infants with severe IVH were also 13% more likely to have a hearing impairment. A graph of the occurrence of sensory impairments in infants with and without severe IVH is displayed in **Figure-9**.

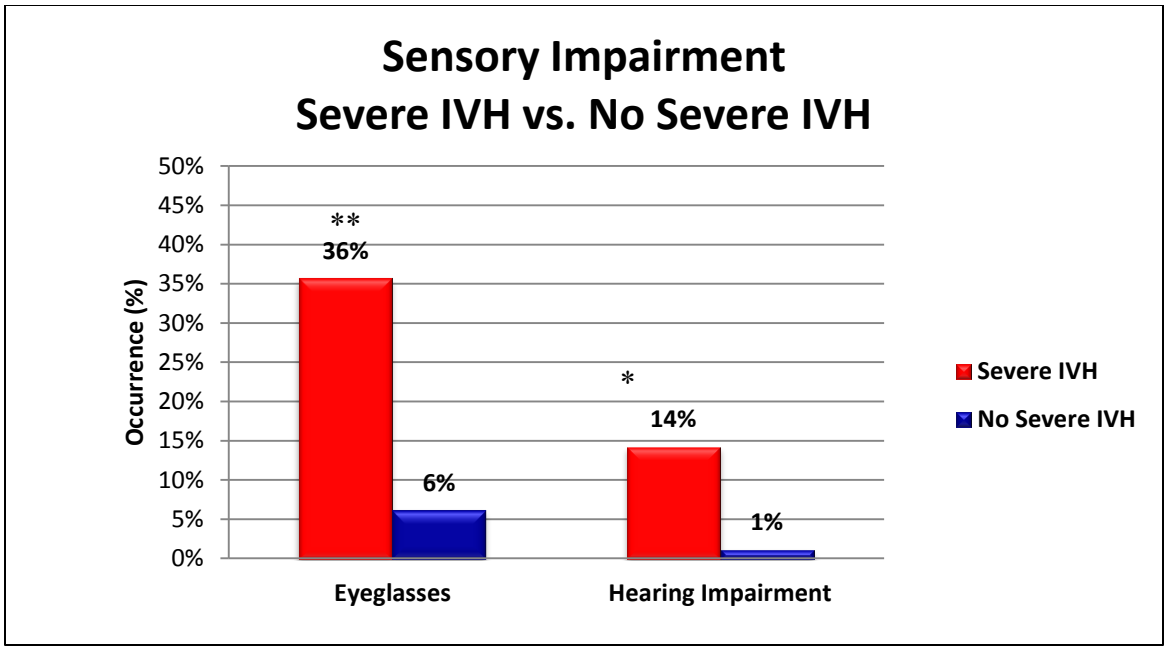

Figure 9: Sensory Impairment: Severe IVH vs. No Severe IVH.
The occurrence of sensory impairments, the need for eyeglasses and any hearing impairment, in premature infants with severe IVH (n=17) was compared to the occurrence in infants without severe IVH (n=165). Premature infants with severe IVH had a very statistically significantly (**) higher occurrence of the need for eyeglasses with a P value of 0.0027. Severe IVH Infants also had a statistically significantly (*) higher occurrence of hearing impairment than did infants without severe IVH.

The occurrence of rehospitalization of ELBW infants with and without severe IVH, between 2003 and 2009, was compared using a Two-tailed Fisher's Exact Test. There was no significant difference between the rehospitalization of infants with and without severe IVH. No correlation between severe IVH and rehospitalization was found. A graph of the occurrence of rehospitalization is displayed as **Figure 10**.

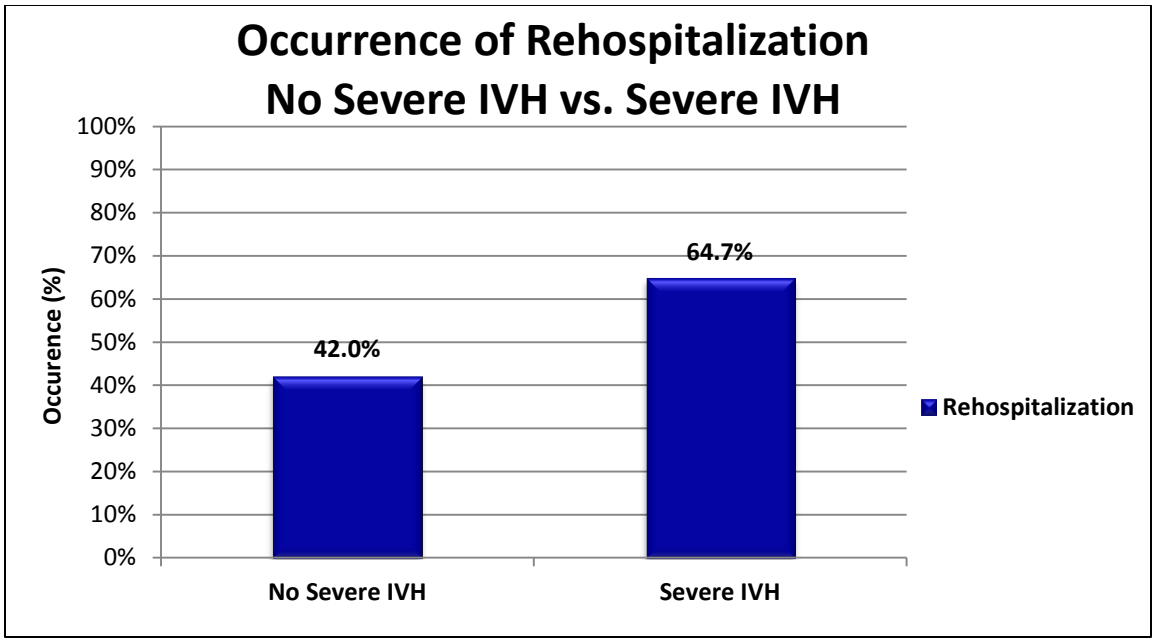

Figure 10: Occurrence of Rehospitalization: No Severe IVH vs. Severe IVH.
The occurrence of rehospitalization after discharge from the NICU of preterm infants with severe IVH (n=17) was compared to its occurrence for preterm infants without IVH (n=162). The Occurrence of rehospitalization was found not to be statistically different in the severe IVH infants than in the no severe IVH infants with a P value of 0.1213.

To determine whether mode of delivery, either vaginal delivery or cesarian section, correlates with the grade of severe IVH, a Two-tailed Fisher's Exact Test was performed. There was no significant difference between the grade of IVH with vaginal delivery or cesarian section. Thus, no correlation was found between mode of delivery and severity of IVH. A graph of this comparison can be found in **Figure 11**.

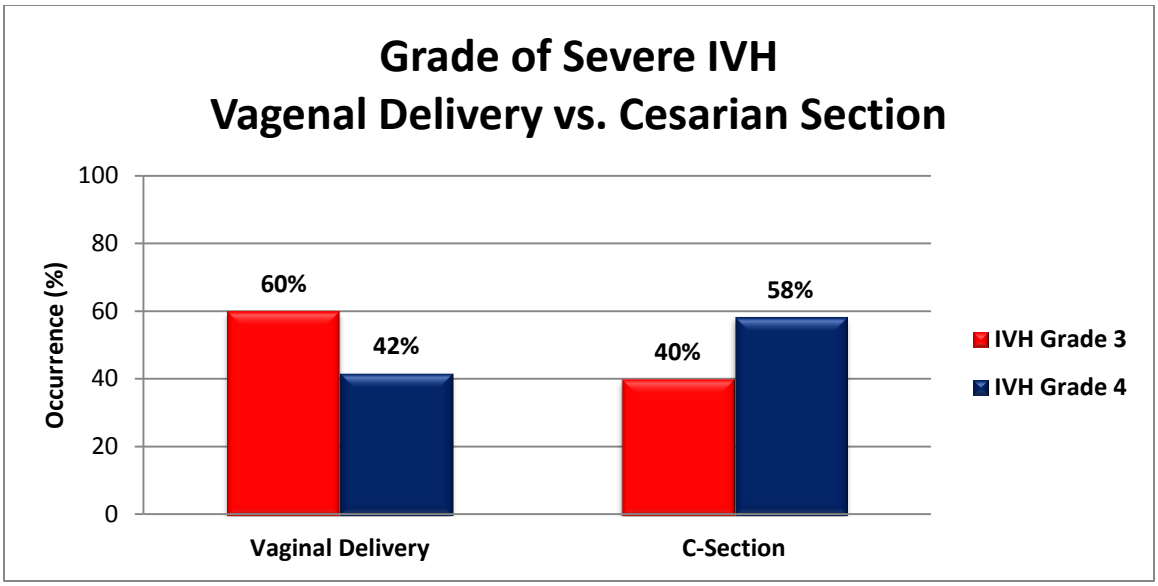

Figure 11: Severity of IVH Compared to Mode of Delivery.
The severity of IVH, grade 3 (n=8) or grade 4 (n=9), was compared to the mode of delivery, vaginal or cesarian section. No statistically significant difference in grade of severe IVH was found based on the mode of delivery, with a P value of 0.6199.

The severity of IVH was compared to the administration of antenatal steroids with a Two-tailed Fisher's Exact Test. No significant difference in severity of IVH was found with or without the use of antenatal steroids. These results can be seen in **Figure 12**.

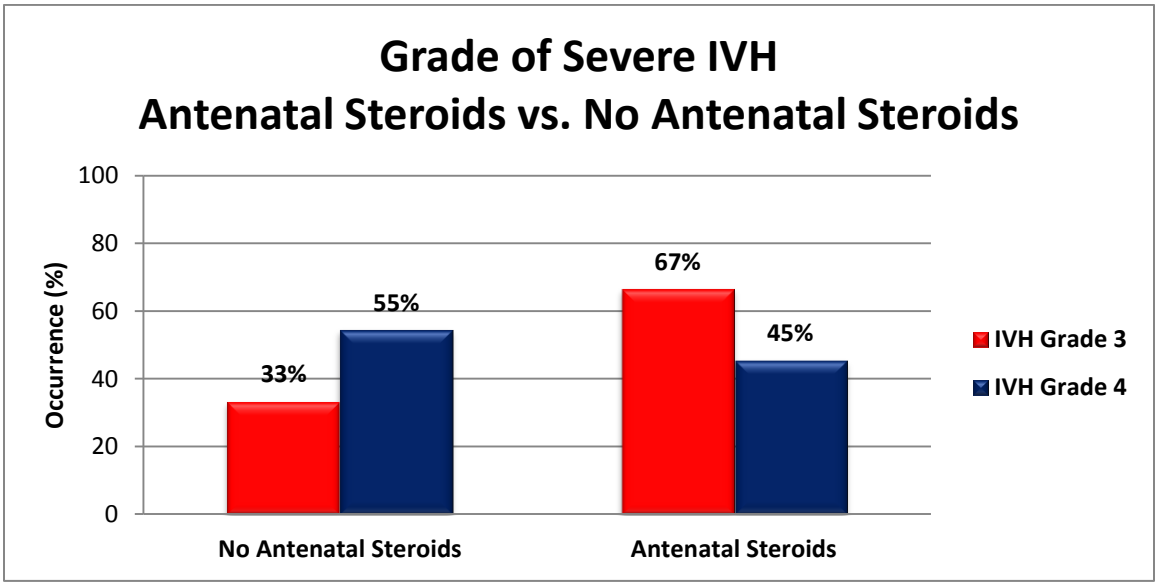

Figure 12: Severity of IVH Compared to Use of Antenatal Steroids.
The severity of IVH, grade 3 (n=8) or grade 4 (n=9), was compared to the use of antenatal steroids. No statistically significant difference in grade of severe IVH was found based on the use of antenatal steroids, with a P value of 0.6199.

Severe IVH was found to have correlations with cerebral palsy, moderate cognitive impairments, as well as impairments but not with rehospitalization or severe cognitive impairments at UMMC. No correlation was found between the severity of IVH and the mode of delivery or use of antenatal steroids at UMMC. This information can be used to inform parents and aid in the difficult decision of resuscitation and continuation of medical care for their ELBW infant.

DISCUSSION

To compare different variables recorded in this severe IVH study, two statistical analytic tests were performed, including two-tailed Fisher's exact test and Chi Squared analysis with Yates correction. A Chi Squared analysis with Yates correction shows that there are significantly fewer cases of severe IVH at UMass Memorial Medical Center (UMMC) compared with the VON Network as a whole. This data suggests that the NICU at UMMC is doing a better job stabilizing babies born <1000g than the average VON Network center. The chi squared analysis with Yates correction was performed for this comparison because the Fisher's exact analysis could not be performed because of the large population size. Fisher's exact tests were used for all other statistical analyses. Statistical analysis shows a very strong correlation between babies with severe IVH and the development of moderate cognitive impairment later in life. However, no correlation was found with severe cognitive impairment. At UMMC, there is a very strong correlation between babies who had severe IVH and the development of cerebral palsy as an infant. In addition, a very strong correlation was found between babies who had severe IVH needing eyeglasses later in life due to visual impairments. A strong correlation was found between babies, at UMMC, who had severe IVH and the occurrence of hearing impairment. These correlations indicate that severe IVH increases the risk of poor neurodevelopmental, motor and sensory outcomes.

According to the Fischer's exact test there is no statistical significance between the incidence of CP at UMMC compared to the VON network, which acts as a positive control, showing that UMass Memorial Medical Center is comparable to the VON Network. There was also no significant difference in rehospitalization in children who had severe IVH compared to

those who did not have severe IVH at UMMC. This indicates that infants at UMMC with severe IVH are not at an increase risk of rehospitalization compared to those who did not have severe IVH. Other analyses showing no statistical significance were the administration of antenatal steroids compared to the grade of severe IVH (grade 3 vs. grade 4), the mode of delivery compared to the grade of severe IVH, and the occurrence of cerebral palsy compared to the grade of severe IVH. These comparisons likely did not show statistical significance due to small sample sizes (Grade 3 IVH, n=8; Grade 4 IVH, n=9). If the populations were larger, likely there would be a greater chance of these differences being significant.

Had the sample sizes been larger for the comparisons of the grade of severe IVH and mode of delivery or antenatal steroid use a correlation would likely have been found since these correlations have been found with larger populations. The lack of a correlation between severe IVH and increased incidence of rehospitalization is also interesting because the expectation would be that a correlation would exist between the two, based on previous research. This begs the question of whether trends found from analyzing single hospitals with a small population size of interest are reliable. If data is pooled over 30 years in order to get a large enough populations, size the results of analysis will likely be unreliable due to advances in patient care during those 30 years. It would be most beneficial to pool data from multiple hospitals for analyzing trends in order to have a large enough sample size to obtain reliable correlations over a shorter time period.

The forms created for UMass will allow physicians in the NICU to find these types of correlations for babies with various NICU complications born at UMMC. This would allow physicians in the NICU to give parents more accurate information regarding the possible sensory, motor, neurodevelopmental or other outcomes their child faces in order to make a better

educated decision about whether to continue to provide life-sustaining care to their infants who may be neurologically devastated.

BIBLIOGRAPHY

Adams-Chapman I, Hansen NI, Stoll BJ, Higgins R (2008) NICHD Research Network. Neurodevelopmental outcome of extremely low birth weight infants with posthemorrhagic hydrocephalus requiring shunt insertion. *Pediatrics* **121**: e1167.

Ajayi-Obe M, Saeed N, Cowan FM, Rutherford MA, Edwards AD (2000) Reduced development of cerebral cortex in extremely preterm infants. *Lancet* **356**: 1162–1163.

Armstrong DL, Sauls CD, Goddard-Finegold J (1987) Neuropathologic findings in short-term survivors of intraventricular hemorrhage. *Am J Dis Child* **141**: 617.

Back SA, Luo NL, Borenstein NS, Levine JM, Volpe JJ, Kinney HC (2001) Late oligodendrocyte progenitors coincide with the developmental window of vulnerability for human perinatal white matter injury. *Journal of Neuroscience*. **21**(4): 1302-1312.

Ballard PL, Ballard RA (1995) Scientific basis and therapeutic regimens for use of antenatal glucocorticoids. *Am J Obstet Gynecol* **173**: 254-262.

Baud O, Greene AE, Li J, Wang H, Volpe JJ, Rosenberg PA (2004) Glutathione peroxidasecatalase cooperativity is required for resistance to hydrogen peroxide by mature rat oligodendrocytes. *Journal of Neuroscience* **24**: 1531-40.

Bayley N (1993) Bayley Scales of Infant Development-II. San Antonio (TX): Psychological Corporation.

Bayley Scale of Infant and Toddler Development -- Third Edition (Bayley-III) Product Summary (2011) Pearson Education Inc. http://www.pearsonassessments.com/HAIWEB/ Cultures/en-us/Productdetail.htm?Pid=015-8027-23X&Mode=summary.

Bayley Scales of Infant Development -- Second Edition (BSID-II) Product Summary (2011) Pearson Education Inc. http://www.pearsonassessments.com/HAIWEB/Cultures/en us/Productdetail.htm?Pid=015-8028-007.

Bayley, Nancy (2006) Bayley Scales of Infant and Toddler Development, Third Edition. San Antonio, TX: NCS Pearson, Inc.

Berry D (1991) Neonatology in the 1990's: surfactant replacement therapy becomes a reality. *Clin Pediatr* **30**(3): 167-170.

Bonanno C, Wapner RJ (2009) Antenatal Corticosteroid Treatment: What's happened since Drs Liggins and Howie. *American Journal of Obstetrics and Gynecology* **200**(4): 448-457.

Bracewell M, Marlow N (2002) Patterns of Motor Disability in Very Preterm Children. *Ment Retard Dev Disabil Res Rev* **8**(4): 241-248.

Bracewell MA, Hennessy EM, Wolke D, Marlow N (2008) The EPICure study: growth and blood pressure at 6 years of age following extremely preterm birth. *Arch Dis Child Fetal Neonatal Ed* **93**: F108.

Breslau N, Chilcoat HD, Johnson EO, et al. (2000) Neurologic Soft Signs and Low Birth Weight: Their Association and Neuropsychiatric implications. *Biological Psychiatry* **47**(1): 71-79.

Brouwer A, Groenendaal F, van Haastert IL, et al. (2008) Neurodevelopmental outcome of preterm infants with severe intraventricular hemorrhage and therapy for post-hemorrhagic ventricular dilatation. *J Pediatr* **152**: 648.

Cassady G, Crouse DT, Kirklin JW, et al. (1989) A randomized, controlled trial of very early prophylactic ligation of the ductus arteriosus in babies who weighed 1000 g or less at birth. N *Engl J Med* **320**: 1511.

Cotton RB, Stahlman MT, Kovar I, Catterton WZ (1978) Medical management of small preterm infants with symptomatic patent ductus arteriosus. *J Pediatr* **92**: 467.

Crowley P (2000) Prophylactic corticosteroids for preterm birth. Cochrane Database Syst Rev:CD000065.

Deng W, Pleasure J, Pleasure D (2008) Progress in periventricular leukomalacia. *Arch Neurol*. **65**(10): 1291-1295.

Deng W, Wang H, Rosenberg PA, Volpe JJ, Jensen FE (2004) Role of Metabotropic glutamate receptors in oligodendrocyte excitotoxicity and oxidative stress. *Proc Natl Acad Sci USA* **101:** 7751-7756.

deVeber G, Andrew M, Adams C, et al. (2001) Cerebral sinovenous thrombosis in children. *New England Journal of Medicine* **345**: 417-423.

Eichenwald EC, Stark AR (2008) Management and outcomes of very low birth weight. *N Engl J Med* **358**: 1700.

Fanaroff AA, Stoll BJ, Wright LL, et al. (2007) Trends in neonatal morbidity and mortality for very low birthweight infants. *Am J Obstet Gynecol* **196**:147.e1.

Frank L, Sosenko IR (1987) Development of lung antioxidant enzyme system in late gestation: possible implications for the prematurely born infant. *J Pediatr* **110**: 9.

Goddard-Finegold J, Hansen TN, McIntosh N, WB Saunders (1997) Pharmacologic prevention of intraventricular hemorrhage. In: *Current Topics in Neonatology,* p.170.

Gould SJ, Howard S (1987) An immunohistochemical study of the germinal layer in the late gestation human fetal brain. *Neuropathol Appl Neurobiol* **13**: 421.

Grunnet, ML (1989) Morphometry of blood vessels in the cortex and germinal plate of premature neonates. *Pediatr Neurol* **5**: 12.

Guzzetta F, Shackelford GD, Volpe S, et al. (1986) Periventricular intraparenchymal echodensities in the premature newborn: critical determinant of neurologic outcome. *Pediatrics* **78**: 995.

Hack M, Farnaroff AA (2000) Outcomes of children of extreamly low birthweight and gestational age in the 1990's. *Seminars in Neonatology* **5**(2): 89-106.

Hack M, Flannery DJ, Schluchter M et al. (2002) Outcomes in Young Adulthood for Very-Low Birth Weight infants. *New England Journal of Medicine* **246**(3): 149-157.

Hack M, Taylor HG, Drotar D, et al. (2005) Poor predictive Validity of the Baley Scales of infant development for cognitive function of extremely low birth weight children at school age. *Pediatrics* **116**(2): 333-341.

Hack M, Youngstrom EA, Carter L, et al. (2004) Behavioral Outcomes and evidence of Psychopathology among Very Low Birth Weight Infants at age 20 years. *Pediatrics* **114**(4): 932-940.

Hack M, Taylor HG, Drotar D, et al. (2005) Chronic conditions, functional limitations, and special health care needs of school-aged children born with extremely low-birth-weight in the 1990s. *JAMA* **294**: 318.

Halliwell B (1992) Reactive oxygen species and the central nervous system. *Journal of Neurochemistry* **59**: 1609-1623.

Harper RG, Garcia A, Sia C (1975) Inguinal hernia: a common problem of premature infants weighing 1,000 grams or less at birth. *Pediatrics* **56**: 112.

Heafner MD, Duncan CC, Kier EL, et al. (1985) Intraventricular hemorrhage in a term neonate secondary to a third ventricular AVM. Case report. *J Neurosurg* **63**: 640.

Hebbandi SB, Bowen JR, Hipwell GC, et al. (1997) Ocular sequelae in extremely premature infants at 5 years of age. *J Paediatr Child Health* **33**: 339.

Henderson-Smart, DJ (1981) The effect of gestational age on the incidence and duration of recurrent apnoea in newborn babies. *Aust Paediatr J*, **17**: 273.

Hintz, SR, Kendrick, DE, Stoll, BJ, et al (2005) Neurodevelopmental and growth outcomes of extremely low birth weight infants after necrotizing enterocolitis. *Pediatrics*; **115**: 696.

Holmström G, el Azazi M, Kugelberg U (1999) Ophthalmological follow up of preterm infants: a population based, prospective study of visual acuity and strabismus. *Br J Ophthalmol* **83**:143.

Hovi P, Andersson S, Eriksson JG, et al. (2007) Glucose regulation in young adults with very low birth weight. *N Engl J Med* **356**: 2053.

Inder TE, Warfield SK, Wang H, Huppi PS, Volpe JJ (2005) Abnormal Cerebral Structure is Present at Term in Premature Infants. *Pediatrics* **115:** 286-294.

Inder TE, Volpe JJ (2000) Mechanisms of perinatal brain injury. *Semin Neonatol* **5**: 3.

Jacob J, Gluck L, DiSessa T, et al. (1980) The contribution of PDA in the neonate with severe RDS. *J Pediatr* **96**: 79.

Jen HC, Graber JJ, Hil JL, et al. (2006) Surgical necrotizing enterocolitis and intraventricular hemorrhage in premature infants below 1000 g. *J Pediatr Surg* **41**: 1425.

Jim WT, Chiu NC, Chen MR, et al. (2005) Cerebral hemodynamic change and intraventricular hemorrhage in very low birth weight infants with patent ductus arteriosus. *Ultrasound Med Biol* **31**: 197.

Jobe AH (2010) "Miracle" Extremely Low Birth Weight Neonates. *Obstetrics and Gynecology* **116:** 1184-1190.

Jobe AH (2001) Bancalari, E. Bronchopulmonary dysplasia. *Am J Respir Crit Care Med* **163**: 1723.

Johnson AH, Peacock JL, Greenough A, et al. (2002) High-frequency oscillatory ventilation for the prevention of chronic lung disease of prematurity. *New England Journal of Medicine* **347(**9): 633-642.

Kadhim H, Tabarki B, De Prez C, Sebire G (2003) Cytokine immunoreactivity in cortical and subcortical neurons in periventricular leukomalacia: are cytokines implicated in neuronal dysfunction in cerebral palsy *Acta Neuropathology*. **105**(3): 209-216.

Kaindl A.M., Favrais G, Gressens P (2009) Molecular Mechanisms Involved in Injury to the Preterm Brain. *Journal of Child Neurology* **24:** 1112-1118.

Kanold PO, Kara P, Reid RC, Shatz CJ (2003) Role of subplate neurons in functional maturation of visual cortical columns. *Science* **301**: 521-525.

Kesler SR, Vohr B, Schneider KC, et al. (2006) Increased temporal lobe gyrification in preterm children. *Neuropsychologia* **44**(3): 445-453.

Kessel I, Waisman D, Branet-Grinnes O, Ben Ari TZ, Rotschild A (2010) Benefits of High Frequency Oscillatory Ventilation for Premature Infants. *Original Articles* **12:** 144-149.

Khong TY, Bendon RW, Qureshi F, et al. (2000) Chronic deciduitis in the placental basal plate: definition and interobserver reliability. *Human Pathology* **31**: 292-5.

Knight-Nanan DM, O'Keefe M (1996) Refractive outcome in eyes with retinopathy of prematurity treated with cryotherapy or diode laser: 3 year follow up. *Br J Ophthalmol* **80**: 998.

Koivisto M, Marttila R, Saarela T, et al. (2005) Wheezing illness and re-hospitalization in the first two years of life after neonatal respiratory distress syndrome. *J Pediatr* **147**: 486.

Korvenranta E, Lehtonen L, Peltola M, et al. (2009) Morbidities and hospital resource use during the first 3 years of life among very preterm infants. *Pediatrics* **124**: 128.

Kurnik K, Kosch A, Strater R, Schobess R, Heller C, Nowak-Gottl U (2003) Recurrent thromboembolism in infants and children suffering from symptomatic neonatal arterial stroke: a prospective follow-up study. *Stroke* **34**: 2887-2892.

Lakhanpal RR, Sun RL, Albini TA, Holz ER (2005) Anatomic success rate after 3-port lens-sparing vitrectomy in stage 4A or 4B retinopathy of prematurity. *Ophthalmology* **112**: 1569.

Lemons JA, Bauer CR, Oh W, et al. (2001) Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network. *Pediatrics* **107**: E1.

Leviton A, Gressens P (2007) Neuronal damage accompanies perinatal white-matter damage. *Trends in Neuroscience*. **30**(9): 473-478.

Lucile Packard Children's Hospital at Stanford (2011) Intraventricular Hemorrhage. http://www.lpch.org/DiseaseHealthInfo/HealthLibrary/hrnewborn/ivh.html

Luu TM, Ment LR, Schneider KC, et al. (2009) Lasting effects of preterm birth and neonatal brain hemorrhage at 12 years of age. *Pediatrics* **123**: 1037.

Mahony L, Carnero V, Brett C, et al. (1982) Prophylactic indomethacin therapy for patent ductus arteriosus in very-low-birth-weight infants. *N Engl J Med* **306**: 506.

Mao C, Guo J, Chituwo BM. (1999) Intraventricular haemorrhage and its prognosis, prevention and treatment in term infants. *J Trop Pediatr* **45**: 237.

Marlow N, Wolke D, Bracewell MA, et al. (2005) Neurological and Developmental disabilities at six years of age after extremely preterm birth. *New England Journal of Medicine* **352**(2): 9-19.

Marshall DD, Kotelchuck M, Young TE, et al. (1999) Risk factors for chronic lung disease in the surfactant era: a North Carolina population-based study of very low birth weight infants. North Carolina Neonatologists Association. *Pediatrics* **104**: 1345.

McCormick J, Tubman R (2002) Readmission with respiratory syncytial virus (RSV) infection among graduates from a neonatal intensive care unit. *Pediatr Pulmonol* **34**: 262.

McCourt MF, Griffin CM (2000) Comprehensive primary care follow-up for premature infants. *J Pediatr Health Care* **14**: 270.

McDonald JW, Johnston MV (1990) Physiological and pathophysiological roles of excitatory amino acids during central nervous system development. *Brain Res Brain Res Rev* **15**: 41-70.

Ment LR, Hirtz D, Huppi PS (2009) Imaging biomarkers of outcome in the developing preterm brain. *Lancet Neurolology* **8**: 1042–1055.

Ment LR, Bada HS, Barnes P, et al. (2002) Practice parameter: neuroimaging of the neonate: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology* **58**: 1726.

Mercer JS, Vohr BR, McGrath MM, et al. (2006) Delayed cord clamping in very preterm infants reduces the incidence of intraventricular hemorrhage and late-onset sepsis: a randomized, controlled trial. *Pediatrics* **117**: 1235.

Mercuri E, Cowan F, Gupte G, et al. (2001) Prothrombotic disorders and abnormal neurodevelopmental outcome in infants with neonatal cerebral infarction. *Pediatrics* **107**: 1400-1404.

Mercuri E, Guzzetta A, Laroche S, et al. (2003) Neurologic examination of preterm infants at term age: comparison with term infants. *Journal of Pediatrics* **142**: 647-655.

Miletin J, Dempsey EM (2008) Low superior vena cava flow on day 1 and adverse outcome in the very low birthweight infant. *Arch Dis Child Fetal Neonatal Ed* **93**: F368.

Moriette G, Paris-Llado J, Walti H, et al. (2001) Prospective randomized multicenter comparison of high frequency oscillatory ventilation and conventional ventilation in preterm infants of less than 30 weeks with respiratory distress syndrome. *Pediatrics* **107**(2): 363-372.

Moshfeghi AA, Banach MJ, Salam GA, Ferrone PJ (2004) Lens-sparing vitrectomy for progressive tractional retinal detachments associated with stage 4A retinopathy of prematurity. *Arch Ophthalmol* **122**: 1816.

Murphy BP, Inder TE, Rooks V, Taylor GA, Anderson NJ, Mogridge N, Horwood LJ, Volpe JJ (2002) Posthaemorrhagic ventricular dilation in the premature infant: natural history and predictors of outcome. *Arch Dis Child Fetal Neonatal Ed* **87**: F37-F41.

Nachman SA, Navaie-Waliser M, Qureshi MZ (1997) Rehospitalization with respiratory syncytial virus after neonatal intensive care unit discharge: A 3-year follow-up. *Pediatrics* **100**: E8.

Nelson KB, Lynch JK (2004) Stroke in newborn infants. *Lancet Neurology* **3**: 150-158.

Nicholas S. Wood, M.B., Ch.B., Neil Marlow, D.M., Kate Costeloe, M.B., B.Chir., Alan T. Gibson, Ph.D., and Andrew R. Wilkinson, M.B., Ch.B. (2000) Neurologic and Developmental Disability after Extremely Preterm Birth. *N Engl J Med*; **343**: 378-384.

Norwitz ER, Phaneuf LE, Greenberg JA (2010) Beyond Antenatal Corticosteroids: What Did Mont Liggins Teach Us? *Rev Obstet Gynecol* **3**(3): 79-80.

Okoshi Y, Mizuguchi M, Itoh M, et al. (2007) Altered nestin expression in the cerebrum with periventricular leukomalacia. *Pediatcis Neurology*. **36**(3): 170-174.

Olney JW (2003) Excitotoxicity, apoptosis and neuropsychiatric disorders. *Current Opinion in Pharmacology* **3**: 101-109.

Omari TI, Barnett C, Snel A, et al. (1998) Mechanisms of gastroesophageal reflux in healthy premature infants. *J Pediatr* **133**: 650.

Osborn, DA, Evans, N, Kluckow, M, et al. (2007) Low superior vena cava flow and effect of inotropes on neurodevelopment to 3 years in preterm infants. *Pediatrics* **120**: 372.

Palmer EA, Flynn JT, Hardy RJ, et al. (1991) Incidence and early course of retinopathy of prematurity. The Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Ophthalmology* **98**: 1628.

Palta M, Sadek-Badawi M, Carlton DP (2008) Association of BPD and IVH with early neutrophil and white counts in VLBW neonates with gestational age <32 weeks. *J Perinatol* **28**: 604.

Pamela J. Surkan, M.S., Olof Stephansson, M.D., Ph.D., Paul W. Dickman, Ph.D., and Sven Cnattingius, M.D., Ph.D. (2004) Previous and Small-for-Gestational-Age Births and the Subsequent risk of Stillbirth. *N Engl J Med*; **350**: 777-785.

Papile LA, Burstein J, Burstein R, et al. (1978) Relationship of intravenous sodium bicarbonate infusions and cerebral intraventricular hemorrhage. *J Pediatr* **93**: 834.

Papile LA, Rudolph AM, Heymann MA (1985) Autoregulation of cerebral blood flow in the preterm fetal lamb. *Pediatr Res* **19**: 159.

Peevy KJ, Speed FA, Hoff CJ (1986) Epidemiology of inguinal hernia in preterm neonates. *Pediatrics* **77**: 246.

Perlman JM, Hill A, Volpe JJ (1981) The effect of patent ductus arteriosus on flow velocity in the anterior cerebral arteries: ductal steal in the premature newborn infant. *J Pediatr* **99**: 767.

Pinto-Martin JA,Whitaker AH, Feldman JF, Van Rossem R, Paneth N (1999) Relation of cranial ultrasound abnormalities in low-birthweight infants to motor or cognitive performance at ages 2, 6, and 9 years. *Dev Med Child Neurol* **41**: 826-833.

Powell TG, Hallows JA, Cooke RW, Pharoah PO (1986) Why do so many small infants develop an inguinal hernia? *Arch Dis Child* **61**: 991.

Prenner JL, Capone A Jr, Trese MT (2004) Visual outcomes after lens-sparing vitrectomy for stage 4A retinopathy of prematurity. *Ophthalmology* **111**: 2271.

Pryds O, Greisen G, Lou H, Friis-Hansen B (1990) Vasoparalysis associated with brain damage in asphyxiated term infants. *J Pediatr***. 117**: 119.

Quick Calcs (2005) Analyze a 2x2 contingency table.
http://graphpad.com/quickcalcs/contingency1.cfm

Quinn GE, Dobson V, Kivlin J, et al. (1998) Prevalence of myopia between 3 months and 5 1/2 years in preterm infants with and without retinopathy of prematurity. Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Ophthalmology* **105**: 1292.

Rabe H, Reynolds G, Diaz-Rossello J (2004) Early versus delayed umbilical cord clamping in preterm infants. *Cochrane Database Syst Rev*: CD003248.

Rajput A, Gauderer MW, Hack M (1992) Inguinal hernias in very low birth weight infants: incidence and timing of repair. *J Pediatr Surg* **27**: 1322.

Ramanathan R (2009) Choosing a Right Surfactant for Respiratory Distress Syndrome Treatment. *Neonatology* **95**: 1-5.

Rees, CM, Pierro, A, Eaton, S (2007) Neurodevelopmental outcomes of neonates with medically and surgically treated necrotizing enterocolitis. *Arch Dis Child Fetal Neonatal Ed*; **92**: F193.

Repka MX, Summers CG, Palmer EA, et al. (1998) The incidence of ophthalmologic interventions in children with birth weights less than 1251 grams. Results through 5 1/2 years. Cryotherapy for Retinopathy of Prematurity Cooperative Group. *Ophthalmology* **105**: 1621.

Repka MX, Tung B, Good WV, et al. (2006) Outcome of eyes developing retinal detachment during the Early Treatment for Retinopathy of Prematurity Study (ETROP). *Arch Ophthalmol* **124**: 24.

Rotteveel J, van Weissenbruch MM, Twisk JW, Delemarre-Van de Waal HA (2008) Infant and childhood growth patterns, insulin sensitivity, and blood pressure in prematurely born young adults. *Pediatrics* **122**: 313.

Rudolph AM (1970) The changes in the circulation after birth. Their importance in congenital heart disease. *Circulation* **41**: 343.

Schendel D, Bhasin TK (2008) Birth Weight and Gestational age Characteristics of Children with Autism, Including Comparison with other Developmental Disibilities. *Pediatrics* **121**(6): 1155-1164.

Schmidt, B, Davis, P, Moddemann, D, et al. (2001) Long-term effects of indomethacin prophylaxis in extremely-low-birth-weight infants. *N Engl J Med* **344**: 1966.

Schulzke, SM, Deshpande, GC, Patole, SK (2007) Neurodevelopmental outcomes of very low-birth-weight infants with necrotizing enterocolitis: a systematic review of observational studies. *Arch Pediatr Adolesc Med*; **161**: 583.

Seri I, Noori S (2005) Diagnosis and treatment of neonatal hypotension outside the transitional period. *Early Hum Dev* **81**: 405.

Shennan AT, Dunn MS, Ohlsson A, et al. (1988) Abnormal pulmonary outcomes in premature infants: prediction from oxygen requirement in the neonatal period. *Pediatrics* **82**: 527.

Sherlock RL, Anderson PJ, Doyle, LW (2005) Victorian Infant Collaborative Study Group. Neurodevelopmental sequelae of intraventricular haemorrhage at 8 years of age in a regional cohort of ELBW/very preterm infants. *Early Hum Dev* **81**: 909.

Sidman, RL, Rakic, P. (1982) Development of the human central nervous system. In: *Histology and histopathology of the nervous system*, Haymaker, W, Adams, RD (Eds), CC Thomas, Springfield, IL. p.1.

Smith LJ, van Asperen PP, McKay KO, et al. (2008) Reduced exercise capacity in children born very preterm. *Pediatrics* **122**: e287.

Soraisham AS, Singhal N, McMillan DD, et al. (2009) A multicenter study on the clinical outcome of chorioamnionitis in preterm infants. *Am J Obstet Gynecol* **200**: 372.e1.

Stein RE, Siegel MJ, Bauman LJ (2006) Are children of moderately low birth weight at increased risk for poor health? A new look at an old question. *Pediatrics* **118**: 217.

Stephens BE, Vohr BR (2010) Neurodevelopmental Outcome of the Premature Infant. *Pediatric Clinics N Am* **56:** 631-646.

Stoll BJ, Hansen N, Fanaroff AA, et al. (2002) Late-onset sepsis in very low birth weight neonates: the experience of the NICHD Neonatal Research Network. *Pediatrics* **110**: 285.

Stoll BJ, Hansen NI, Adams-Chapman I, et al. (2004) Neurodevelopmental and growth impairment among extremely low-birth-weight infants with neonatal infection. *JAMA* **292**(19): 2357-2365.

Stoll BJ, Hansen NI, Bell EF, et al. (2010) Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. *Pediatrics* **126**: 443.

Stonestreet BS, Petersson GB, Pettigrew KD, Patlak CS (1998) Antenatal steroids decrease blood brain barrier permeability in the ovine fetus. *American Physiological Society* **276**(2): R283-R289.

Swamy GK, Ostbye T, Skjaerven R (2008) Association of preterm birth with long-term survival, reproduction, and next-generation preterm birth. *JAMA* **299**: 1429.

Tarantino MD, Gupta SL, Brusky RM (2007) The incidence and outcome of intracranial haemorrhage in newborns with haemophilia: analysis of the Nationwide Inpatient Sample database. *Haemophilia* **13**: 380.

Tarby TJ, Volpe JJ (1982) Intraventricular hemorrhage in the premature infant. *Pediatr Clin North Am* **29**: 1077.

Thibeault DW, Emmanouilides GC, Nelson RJ, et al. (1975) Patent ductus arteriosus complicating the respiratory distress syndrome in preterm infants. *J Pediatr* **86**: 120.

Thompson DC, McPhillips H, Davis RL, et al. (2001) Universal newborn hearing screening: summary of evidence. *JAMA* **286**: 2000.

Trese, MT, Droste, PJ (1998) Long-term postoperative results of a consecutive series of stages 4 and 5 retinopathy of prematurity. *Ophthalmology* **105**: 992.

Underwood MA, Danielsen B, Gilbert WM (2007) Cost, causes and rates of rehospitalization of preterm infants. *J Perinatol* **27**: 614.

Verma RP, Sridhar S, Spitzer AR (2003) Continuing care of NICU graduates. *Clin Pediatr (Phila)* **42**: 299.

Vermont Oxford Network (2011) Improving Care for Infants and Their Families. http://www.vtoxford.org/

Vohr BR, Allan WC, Westerveld M, et al. (2003) School-age outcomes of very low birth weight infants in the indomethacin intraventricular hemorrhage prevention trial. *Pediatrics* **111**: e340-346.

Vohr BR, Allan WC, Westerveld M, Schneider KC, Katz KH, Makuch RW, Ment LR (2003) School-age outcomes of very low birth weight infants in the indomethacin intraventricular hemorrhage prevention trial. *Pediatrics* **111**: e340-e346.

Vohr BR, Msall ME, Wilson D, et al. (2005) Spectrum of Gross Motor Function in Extremely Low Birth Weight Children with Cerebral Palsy at 18 months of age. *Pediatrics* **116**(1): 123-129.

Vohr BR, Wright LL, Dusick AM, et al. (2004) Center differences and outcomes of extremely low birth weight infants. *Pediatrics* **113**(4): 781-789.

Volpe JJ (2001) Neurology of the newborn. Philadelphia: W.B. Saunders, **4**: 912.

Volpe, JJ (2001) Intracranial hemorrhage: Germinal matrix-intraventricular hemorrhage. In: *Neurology of the Newborn*, WB Saunders, Philadelphia, **4**: 428.

Wallin, LA, Rosenfeld, CR, Laptook, AR, et al. (1990) Neonatal intracranial hemorrhage: II. Risk factor analysis in an inborn population. *Early Hum Dev*; **23**: 129.

Wehberg K, Vincent M, Garrison B, et al. (1992) Intraventricular hemorrhage in the full-term neonate associated with abdominal compression. *Pediatrics* **89**: 327.

Wu YW, Escobar GJ, Grether JK, Croen LA, Greene JD, Newman TB (2003) Chorioamnionitis and cerebral palsy in term and near term infants. *JAMA* **290**: 2677-2684.

Wu YW, March WM, Croen LA, et al. (2004) Perinatal stroke in children with motor impairment: a population-based study. *Pediatrics* **114**: 612-619.

Wu YW, Hamrick SE, Miller SP, et al. (2003) Intraventricular hemorrhage in term neonates caused by sinovenous thrombosis. *Ann Neurol* **54**: 123.

(2011) Indicator definitions and metadata. WHO Statistical Information System (WHOSIS). World Health Organization (WHO). April 12, 2011.http://www.who.int/whosis/indicators/2007 LBW/en/index.html

APPENDIX

Appendix 1a: VON Developmental Status Report

Patient's Name:_____ Medical Record:_____
(Please do not transmit information in this box.)

VERMONT OXFORD NETWORK
Extremely-Low-Birth-Weight Infant Follow-Up Project Year 2008 Cohort

DEVELOPMENTAL STATUS REPORT

Center Number:_____ **Center Name:**_____

Network ID Number:_____ **Year of Birth (YYYY):**_____

SECTION A: GROWTH PARAMETERS

1. **Corrected Age Growth Parameters Were Obtained (months/days): _____months_____days**
2. **Weight: ___ ___ . ___ ___ kg** 3. **Head Circumference: ___ ___ . ___ cm**

SECTION B: VISION & HEARING

4. **Formal Ophthalmologic Exam:** ☐ Yes ☐ No
5. **Blindness:** ☐ One eye ☐ Both eyes ☐ Not blind ☐ Unsure
6. **Prescription Glasses:** ☐ Yes ☐ No
7. **Formal Hearing Test:** ☐ Yes ☐ No
8. **Hearing Impairment:** ☐ One ear ☐ Both ears ☐ Not impaired ☐ Unsure
9. **Amplification:** ☐ Yes ☐ No

Section C: Cerebral Palsy

10. **Cerebral Palsy:** ☐ Yes ☐ No
IF Yes, a. *Impairment:* ☐ Diplegia ☐ Hemiplegia ☐ Quadriplegia
IF No, b. *Muscle tone:* ☐ Hypotonia ☐ Hypertonia ☐ Both (hypo- & hypertonia) ☐ Normal

SECTION D: GROSS MOTOR MILESTONES

11. **Sits independently:** ☐ Yes ☐ No
IF No, a. *Sits with support:* ☐ Yes ☐ No
12. **Walks ten (10) steps independently:** ☐ Yes ☐ No
IF No, a. *Walks ten (10) steps with support:* ☐ Yes ☐ No

SECTION E: DEVELOPMENTAL TESTING

13. **Bayley Scales of Infant Development:** ☐ Completed ☐ Partly completed ☐ Not performed

IF completed or partially completed,

a. *Corrected age used in scoring:* ___ ___ **months** ___ ___ **days**

b. *Results: Check (✓) all sections that apply.*

☐ **BSID-II MDI:** Raw Score: ___ ___ ___ Index Score for Corrected Age: ___ ___ ___
☐ **BSID-II PDI:** Raw Score: ___ ___ ___ Index Score for Corrected Age: ___ ___ ___

☐ **BSID-III Cognitive:** Scaled Score: ___ ___ Composite Score: ___ ___ ___
☐ **BSID-III Language:** Sum Scaled Score: ___ ___ Composite Score: ___ ___ ___
☐ **BSID-III Motor:** Sum Scaled Score: ___ ___ Composite Score: ___ ___ ___

IF partially completed or not performed,

c. *Check (✓) why:* ☐ Neurosensory impairment (blind or deaf) ☐ Too severely delayed ☐ Uncooperative ☐ Other reason

14. **Other Developmental Test Performed:** ☐ Yes ☐ No
IF Yes, a. *Abnormal results:* ☐ Yes ☐ No

SECTION F: OVERALL CLINICAL APPRAISAL

15. **Clinical Appraisal:** Cognitive Function: ☐ Normal ☐ Suspect ☐ Impaired
Language: ☐ Normal ☐ Suspect ☐ Impaired
Motor Function: ☐ Normal ☐ Suspect ☐ Impaired

ELBW Follow-Up Project-2008 Version 11.0 08/2009

Appendix 1b: VON Health Status Report

Patient's Name: _____ Medical Record: _____
(Please do not transmit information in this box.)

VERMONT OXFORD NETWORK
Extremely-Low-Birth-Weight Infant Follow-Up Project Year 2008 Cohort
HEALTH STATUS REPORT

Center Number: _____ **Center Name:** _____

Network ID Number: _____ **Year of Birth (YYYY):** _____

SECTION A: HEALTH STATUS

1. **Status at 18 - 24 Months Corrected Age:** ☐ Alive ☐ Expired ☐ Unknown
2. **Consent Obtained at the Follow-Up Visit:** ☐ Yes ☐ No
3. **Corrected Age at the Follow-Up Visit (months/days):** ___ ___**months**___ ___**days**

SECTION B: LIVING SITUATION

4. **Maternal Age at Infant Birth**: ___ ___ years ☐ Unknown
5. **Home Child Resides:** ☐ Parent/Family member ☐ Foster care ☐ Chronic care facility
6. **Caregiver(s):** *Check (✓) only one.* ☐ Single parent ☐ Two parent ☐ Single parent extended family ☐ Two parent extended family ☐ Institutional
7. **Primary Caregiver Education:** *Check (✓) only one.* ☐ Some high school or less ☐ High school degree/GED ☐ Not applicable ☐ Some college/university ☐ College/university degree ☐ Unknown

USA CENTERS ONLY:

8. **Income Below 2008 HHS Poverty Guideline:** ☐ Yes ☐ No ☐ Unknown
   See Income Appendix: 2008 PAGE 2
9. **Caregiver(s) Primary Language:** ☐ English ☐ Spanish ☐ Other

SECTION C: SUPPORT AFTER DISCHARGE

10. **Support after ultimate hospital discharge:** ☐ Yes ☐ No ☐ Unsure

a. ***If Yes:*** *Check (✓) all that apply.*

- ☐ 1. **Tracheostomy**
- ☐ 2. **Ventilator**
- ☐ 3. **Oxygen**
- ☐ 4. **Gastrostomy**
- ☐ 5. **Nasogastric Feeds**
- ☐ 6. **Apnea or Cardio-Respiratory Monitor**

SECTION D: MEDICAL RE-HOSPITALIZATIONS & SURGERIES

11. **Medical re-hospitalizations after ultimate discharge:** ☐ Yes ☐ No ☐ Unsure

a. ***If Yes,* Category:** *Check (✓) all that apply.*	**Number of Admissions**
☐ 1. **Respiratory Illness**	___ ___
☐ 2. **Nutrition/Failure to Thrive**	___ ___
☐ 3. **Seizure Disorder**	___ ___
☐ 4. **Shunt Complication**	___ ___
5. **Infections (*not respiratory or shunt infections*):**	
☐ a. **Meningitis**	___ ___
☐ b. **Urinary Tract Infection**	___ ___
☐ c. **Gastrointestinal Infection**	___ ___
☐ d. **Other Infection:** _____ *(specify)*	___ ___
☐ 6. **Other Medical Re hospitalization:** _____ *(specify)*	___ ___

12. **Surgical Procedures After Discharge:** ☐Yes ☐ No ☐ Unsure

	Number of Procedures
(P-Codes) _____	___ ___
_____	___ ___

INCOME APPENDIX: 2008
HHS Poverty Guidelines : UNITED STATES
(48 continguous states and the Distric of Columbia)

Persons in Household	
2	$ 14,000
3	$ 17,600
4	$ 21,200
5	$ 24,800
6	$ 28,400
7	$ 32,000
8	$ 35,600
Each additional person	$ 3,600

Source: Federal Register, Vol.73, No. 15, January 23, 2008. pp 3971-3972.

SURGICAL PROCEDURE CODES (P –CODES)

CODE	PROCEDURE
	Central Nervous System Surgery
P-101	Shunt or shunt revision for hydrocephalus
P-102	Other neurosurgical procedure
	Congenital Heart Defect Surgery
P-201	Cardiac surgery
	Gastrointestinal Surgery
P-301	Gastrostomy tube placement
P-302	Inguinal hernia repair
P-303	Other gastrointestinal surgical procedure
	Genitourinary Surgery
P-401	Circumcision
P-402	Other genitourinary surgical procedure
	Otolaryngology Surgery
P-501	Tracheostomy
P-502	Tympanostomy tubes
P-503	Other ENT surgical procedure
	Ophthamologic Surgery
P-601	Retinal cryosurgery or laser surgery: single eye
P-602	Retinal cryosurgery or laser surgery: both eyes
P-603	Strabismus surgery
P-604	Other ophthamological surgical procedure
P-900	**Other Surgical Procedure**

Appendix 2: Comprehensive List of Variables

Independent Variables

Gestational age (GA) (criteria: days from LMP (last menstrual period) documented by OB, or ultrasound dating

Birth weight

Weight for gestational age
1. Small for gestational age (SGA)
2. Average for gestational age (AGA)
3. Large for gestational age (LGA)

Apgar, 5 minute
1. Not applicable (N/A)
2. Score

AP5
1-10
9. Unknown

Mode of delivery
1. C-section (CS)
2. Vaginal

VAGDEL
0. No (C-section)
1. Yes
9. Unknown

Chronic Lung Disease
1. Yes
0. No
7. Not applicable
9. Unknown

Ox36
0. No
1. Yes
7. Not applicable
9. Unknown

Intraventricular Hemorrhage (IVH) (highest grade, unilateral or bilateral)
1. Grade 3
2. Grade 4

UGRADE
0-4
7. Not applicable
9. Unknown

Periventricular Leukomalacia
1. None
2. Cystic
3. Diffuse

PVL
0. No
1. Yes (Cystic)
7. Not applicable
9. Unknown

Retinopathy of prematurity (ROP)
1. None
2. < Grade 2+
3. Grade 2+ (plus disease)
4. Grade 3

5. Grade 4

ISTAGE

0-4
7. Not applicable
9. Unknown

Retinopathy of prematurity (ROP) laser treatment

1. Not applicable (N/A)
2. Yes
3. No

ROPSURG

0. No
1. Yes
7. Not applicable
9. Unknow

Hearing (BAER)

1. Pass bilaterally
2. Referred one ear
3. Referred both ears
4. Not recorded

Sepsis

1. None
2. Symptoms & blood culture (cx) positive
3. Symptoms and urine culture (cx) positive
4. Symptoms and cerebral spinal fluid (csf) culture (cx) positive

SEPSIS

0. No
1. Yes
9. Unknown

Antenatal steroids

1. None
2. Betamethasone (BMZ) or Celestone
3. Other (please note)

ASTER

0. No
1. Yes
9. Unknown

Antenatal Steroid Doses

1. Not eligible (criteria: 23-5/7 to 34-0/7 wks gest)
2. None
3. 1 dose
4. 2 doses
5. Not known

Chorioamnionitis evidence (maternal fever, other mention)

1. Yes
2. No

CHORIO

0. No
1. Yes
9. Unknown

Dependent Variables

Cerebral palsy (CP)

1. Yes
2. No

Cpalsy

1. Yes
0. No

CPImp

1. Diplegia
2. Hemiplegia
3. Paraplegia

Seizures/Epilepsy

1. Yes
2. No

SeizAdm

1. Yes
0. No

SEIZURE

0. No
1. Yes
7. Not applicable
9. Unknown

Hearing impaired

1. Yes
2. No

HearImp

0. Not impaired
1. One ear
2. Both ears
9. Unsure

HearingTest

0. No
1. Yes

Vision impaired

1. Yes
2. No

Blindness

0. Not blind
1. One eye
2. Both eyes
9. Unsure

Hospitalizations since NICU discharge

1. 0
2. 1
3. 2
4. 3
5. 4+

Surgery since NICU discharge

1. 0
2. 1
3. 2
4. 3
5. 4+

Surgery

0. No
1. Yes
9. Unknown

Bayley Scales of Infant Development II: MDI

1. Not applicable (N/A)
2. MDI score

MDI

0. No
1. Yes

MDIIndex

MDIRaw **Bayley Scales of Infant Development II: PDI** 1. Not applicable (N/A) 2. PDI score	**PDI** 0. No 1. Yes	**PDIIndex**	**PDIRaw**
Bayley Scales of Infant and Toddler Development III: Cognitive 1. Not applicable (N/A) 2. Composite score	**CogComp** 0. No 1. Yes	**CogCompIndex**	**CogCompRaw**
Bayley Scales of Infant and Toddler Development III: Language 1. Not applicable (N/A) 2. Composite score	**LangComp** 0. No 1. Yes	**LangCompIndex**	**LangCompRaw**
Bayley Scales of Infant and Toddler Development III: Motor 1. Not applicable (N/A) 2. Composite score	**MotorComp** 0. No 1. Yes	**MotorCompIndex**	**MotorCompRaw**

Appendix 3a: UMass Memorial Medical Center Developmental Status Report (0 to 15-29/30 months)

Date Last Seen (MM/DD/YYYY) ___/___/_____

SECTION A: GROWTH PARAMETERS

Corrected Age Growth Parameters Were Obtained (months/days): **__ __ months __ __ days**

Weight: __ __ . __ __ **kg**

Head Circumference: __ __ . __ __ **cm**

Length: __ __ . __ __ **cm or** __ __ . __ __ **in**

Early Intervention Received: □ Yes □ No

SECTION B: VISION AND HEARING

Formal Ophthalmologic Exam: □ Yes □ No

Blindness: □ One eye □ Both eyes □ Not blind □ Unsure

Prescription Glasses: □ Yes □ No

Formal Hearing Test: □ Yes □ No

Hearing Impairment: □ One ear □ Both ears □ Not deaf □ Unsure

Amplification: □ Yes □ No

SECTION C: CEREBRAL PALSY

Cerebral Palsy: □ Yes □ No

If Yes, a. Impairment: □ Diplegia □ Hemiplegia □ Quadriplegia

If No, b. Muscle tone: □ Hypotonia □ Hypertonia □ Both (hypo- & hypertonia) □ Normal

---

SECTION D: GROSS MOTOR MILESTONES

Sits Independently: □ Yes □ No

If No, a. Sits with support: □ Yes □ No

Walks ten (10) steps independently: □ Yes □ No

If No, a. Walks ten (10) steps with support: □ Yes □ No

SECTION E: DEVELOPMENTAL TESTING

Bayley Scales of Infant Development: □ Completed □ Partly Completed □ Not Performed

If completed or partially completed,

a. Corrected age used in scoring: __ __ **months** __ __ **days**

b. Results: Check all sections that apply.

	BSID-II			
□	**MDI:**	Raw Score: __ __ __	Index Score for Corrected Age:	__ __ __
	BSID-II			
□	**PDI:**	Raw Score: __ __ __	Index Score for Corrected Age:	__ __ __
	BSID-III			
□	**Cognitive:**	Scaled Score: __ __ __	Composite Score:	__ __ __
	BSID-III	Sum Scaled		
□	**Language:**	Score: __ __ __	Composite Score:	__ __ __
	BSID-III	Sum Scaled		
□	**Motor:**	Score: __ __ __	Composite Score:	__ __ __

BINS: □ **L**
□ **M**
□ **H**

IF partly completed or not performed,

Check why: □ Neurosensory impairment (blind or deaf) □ Too severely delayed
□ Uncooperative □ Other reason: _____

Other Developmental Test Performed: □ Yes □ No

If Yes, Abnormal results: □ Yes □ No

SECTION F: OVERALL CLINICAL APPRAISAL

Clinical Appraisal:	Cognitive Function:	□ Normal	□ Suspect	□ Impaired
	Language:	□ Normal	□ Suspect	□ Impaired
	Motor Function:	□ Normal	□ Suspect	□ Impaired

Appendix 3b: UMass Memorial Medical Center Health Status Report (0 to 15-29/30 months)

Date Last Seen (MM/DD/YYYY) ___/___/_____

Birth Weight (g): □ <1000 □ 1000-1250 □ 1251-2000 □ 2001-2500 □ >2500

Gestational Age (weeks): □ <28 □ 28 – 38 □ 30 1/7-34 □ 34 1/7 -36 6/7 □ 37 – 42 □ >42

SECTION A: HEALTH STATUS

Corrected Age at the Follow-Up Visit: (months/days) __ __ months __ __ days

---

SECTION B: LIVING SITUATION

Maternal Age at Infant Birth: __ __ Years □ Unknown

Home Child Resides: □ Parent/Family Member □ Foster Care □ Chronic care facility

Caregiver(s): (Check only one) □ Single Parent □ Single parent extended Family □ Institutional □ Two Parents □ Two parent extended family

Primary Caregiver Education: (Check only one) □ Some high school or less □ Some college/university □ High school degree/GED □ College /university degree □ Not applicable □ Unknown

Caregiver(s) Primary Language: □ English □ Spanish □ Other: _____

SECTION C: SUPPORT AFTER DISCHARGE

Support After NICU Discharge: □ Yes □ No □ Unsure

If Yes, Check all that apply

- □ **1. Tracheostomy**
- □ **2. Ventilator**
- □ **3. Oxygen**
- □ **4. Gastrostomy**
- □ **5. Nasogastric Feeds**
- □ **6. Apnea or Cardio Respiratory Monitor**

SECTION D: MEDICAL HOSPITALIZATION & SURGERIES

Medical Hospitalization After NICU Discharge: □ Yes □ No □ Unsure

If Yes, Category: Check all that apply	**Number of Admissions**		**Number of Admissions**
□ **1. Respiratory Illness**	__ __	□ **5. Infections (not respiratory of shunt infections):**	__ __
□ **2. Nutrition/Failure to Thrive**	__ __	□ **a. Meningitis**	__ __
□ **3. Seizure Complications**	__ __	□ **b. Urinary Tract Infection**	__ __
□ **4. Shunt Complication**	__ __	□ **c. Gastrointestinal Infection**	__ __
		□ **d. Other Infection** (Specify)_____	__ __

□ **6. Other Medical Hospitalizations:** (Specify)_____

Surgical Procedures After NICU Discharge: □ Yes □ No □ Unsure

	Number of Procedures
(P-Codes) _____	__ __
_____	__ __

SURGICAL PROCEDURE CODES (P-CODES)

CODE	**PROCEDURE**
	Central Nervous System
P-101	Shunt or shunt revision for hydrocephalus
P-102	Other neurosurgical procedure
	Congenital Heart Defect Surgery
P-201	Cardiac surgery
	Gastrointestinal Surgery
P-301	Gastrostomy tube
P-302	Inguinal hernia repair
P-303	Other gastrointestinal surgical procedure
	Genitourinary Surgery
P-401	Circumcision
P-402	Other genitourinary surgical procedure
	Otolaryngology
P-501	Tracheostomy
P-502	Tympanostomy tubes
P-503	Other ENT surgical procedures
	Ophthalmologic Surgery
P-601	Retinal cryosurgery or laser surgery: single eye
P-602	Retinal cryosurgery or laser surgery: both eye
P-603	Strabismus surgery
P-604	Other ophthalmological surgical procedure
P-900	**Other Surgical Procedures**

Appendix 3c: UMass Memorial Medical Center Developmental Status Report (VON: 16 to 26 months)

Center Number: _____ **Center Name:** _____

Network ID Number: _____ **Year of Birth (YYYY):** _____ **Date Last Seen (MM/DD/YYYY):** ___/___/_____

SECTION A: GROWTH PARAMETERS

Corrected Age Growth Parameters Were Obtained

(months/days): __ __ **months** __ __ **days**

Weight: __ __ . __ __ **kg**

Head Circumference: __ __ . __ __ **cm**

Height: __ __ . __ __ **cm or** __ __ . __ __ **in**

Early Intervention Received: □ Yes □ No

SECTION B: VISION AND HEARING

Formal Ophthalmologic Exam: □ Yes □ No

Blindness: □ One eye □ Both eyes □ Not blind □ Unsure

Prescription Glasses: □ Yes □ No

Formal Hearing Test: □ Yes □ No

Hearing Impairment: □ One ear □ Both ears □ Not deaf □ Unsure

Amplification: □ Yes □ No

SECTION C: CEREBRAL PALSY

Cerebral Palsy: □ Yes □ No

If Yes, a. Impairment: □ Diplegia □ Hemiplegia □ Quadriplegia

If No, b. Muscle tone: □ Hypotonia □ Hypertonia □ Both (hypo- & hypertonia) □ Normal

---

SECTION D: GROSS MOTOR MILESTONES

Sits Independently: □ Yes □ No

If No, a. Sits with support: □ Yes □ No

Walks ten (10) steps independently: □ Yes □ No

If No, a. Walks ten (10) steps with support: □ Yes □ No

SECTION E: DEVELOPMENTAL TESTING

Bayley Scales of Infant Development: □ Completed □ Partly Completed □ Not Performed

If completed or partially completed,

a. Corrected age used in scoring: __ __ **months** __ __ **days**

b. Results: Check all sections that apply.

□	**BSID-II MDI:**	Raw Score:	__ __ __	Index Score for Corrected Age:	__ __ __
□	**BSID-II PDI:**	Raw Score:	__ __ __	Index Score for Corrected Age:	__ __ __
□	**BSID-III Cognitive:**	Scaled Score:	__ __ __	Composite Score:	__ __ __
□	**BSID-III Language:**	Sum Scaled Score:	__ __ __	Composite Score:	__ __ __
□	**BSID-III Motor:**	Sum Scaled Score:	__ __ __	Composite Score:	__ __ __

Mullen: Domain	**Age Equivalent (months)**	**Descriptive Category**					**Gains from last visit (months)**
GM	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
VR	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
FM	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
RL	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
EL	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __

ADOS: □ **No** □ **ASC** □ **AC**

BINS: □ **L** □ **M** □ **H**

IF partly completed or not performed,

Check why: □ Neurosensory impairment (blind or deaf) □ Too severely delayed □ Uncooperative □ Other reason: _____

Other Developmental Test Performed: □ Yes □ No

If Yes, Abnormal results: □ Yes □ No

SECTION F: OVERALL CLINICAL APPRAISAL

Clinical Appraisal:	Cognitive Function:	□ Normal	□ Suspect	□ Impaired
	Language:	□ Normal	□ Suspect	□ Impaired
	Motor Function:	□ Normal	□ Suspect	□ Impaired

Appendix 3d: UMass Memorial Medical Center Health Status Report (VON: 16 to 26 months)

Center Number: _____ **Center Name:** _____

Network ID Number: _____ **Year of Birth (YYYY):** _____ **Date Last Seen (MM/DD/YYYY)** ___/___/_____

Birth Weight (g): □ <1000 □ 1000-1250 □ 1251-2000 □ 2001-2500 □ >2500

Gestational Age (weeks): □ <28 □ 28 – 38 □ 30 1/7-34 □ 34 1/7 -36 6/7 □ 37 – 42 □ >42

SECTION A: HEALTH STATUS

Status at 18-24 Months Corrected Age: □ Alive □ Expired □ Unknown

Consent Obtained at the Follow-Up-Visit: □ Yes □ No

Corrected Age at the Follow-Up Visit: (months/days) __ __ months __ __ days

---

SECTION B: LIVING SITUATION

Maternal Age at Infant Birth: __ __ Years □ Unknown

Home Child Resides: □ Parent/Family Member □ Foster Care □ Chronic care facility

Caregiver(s): (Check only one) □ Single Parent □ Single parent extended Family □ Institutional □ Two Parents □ Two parent extended family

Primary Caregiver Education: (Check only one) □ Some high school or less □ Some college/university □ High school degree/GED □ College /university degree □ Not applicable □ Unknown

Caregiver(s) Primary Language: □ English □ Spanish □ Other: _____

SECTION C: SUPPORT AFTER DISCHARGE

Support After NICU Discharge: □ Yes □ No □ Unsure

If Yes, Check all that apply

□ **1. Tracheostomy**
□ **2. Ventilator**
□ **3. Oxygen**
□ **4. Gastrostomy**
□ **5. Nasogastric Feeds**
□ **6. Apnea or Cardio Respiratory Monitor**

SECTION D: MEDICAL HOSPITALIZATION & SURGERIES

Medical re-hospitalization after ultimate discharge: □ Yes □ No □ Unsure

If Yes, Category: Check all that apply	**Number of Admissions**		**Number of Admissions**
□ **1. Respiratory Illness**	__ __	□ **5. Infections (not respiratory of shunt infections):**	__ __
□ **2. Nutrition/Failure to Thrive**	__ __	□ **a. Meningitis**	__ __
□ **3. Seizure Complications**	__ __	□ **b. Urinary Tract Infection**	__ __
□ **4. Shunt Complication**	__ __	□ **c. Gastrointestinal Infection**	__ __
		□ **d. Other Infection** (Specify)_____	__ __

□ **6. Other Medical Hospitalizations:** (Specify)_____

Surgical procedures after discharge: □ Yes □ No □ Unsure

	Number of Procedures
(P-Codes) _____	__ __
_____	__ __

SURGICAL PROCEDURE CODES (P-CODES)

CODE	**PROCEDURE**
	Central Nervous System
P-101	Shunt or shunt revision for hydrocephalus
P-102	Other neurosurgical procedure
	Congenital Heart Defect Surgery
P-201	Cardiac surgery
	Gastrointestinal Surgery
P-301	Gastrostomy tube
P-302	Inguinal hernia repair
P-303	Other gastrointestinal surgical procedure
	Genitourinary Surgery
P-401	Circumcision
P-402	Other genitourinary surgical procedure
	Otolaryngology
P-501	Tracheostomy
P-502	Tympanostomy tubes
P-503	Other ENT surgical procedures
	Ophthamologic Surgery
P-601	Retinal cryosurgery or laser surgery: single eye
P-602	Retinal cryosurgery or laser surgery: both eye
P-603	Strabismus surgery
P-604	Other ophthamological surgical procedure
P-900	**Other Surgical Procedures**

Appendix 3e: UMass Memorial Medical Center Developmental Status Report (26-1/30 to 42 months)

Date Last Seen (MM/DD/YYYY) ___/___/_____

SECTION A: GROWTH PARAMETERS

Corrected Age Growth Parameters Were Obtained

(months/days): __ __ **months** __ __ **days**

Weight: __ __ . __ __ **kg**

Head Circumference: __ __ . __ __ **cm**

Height: __ __ . __ __ **cm or** __ __ . __ __ **in**

Early Intervention Received: □ Yes □ No

SECTION B: VISION AND HEARING

Formal Ophthalmologic Exam: □ Yes □ No

Blindness: □ One eye □ Both eyes □ Not blind □ Unsure

Prescription Glasses: □ Yes □ No

Formal Hearing Test: □ Yes □ No

Hearing Impairment: □ One ear □ Both ears □ Not deaf □ Unsure

Amplification: □ Yes □ No

SECTION C: CEREBRAL PALSY

Cerebral Palsy: □ Yes □ No

If Yes, a. Impairment: □ Diplegia □ Hemiplegia □ Quadriplegia

If No, b. Muscle tone: □ Hypotonia □ Hypertonia □ Both (hypo- & hypertonia) □ Normal

---

SECTION D: GROSS MOTOR MILESTONES

Sits Independently: □ Yes □ No

If No, a. Sits with support: □ Yes □ No

Walks ten (10) steps independently: □ Yes □ No

If No, a. Walks ten (10) steps with support: □ Yes □ No

SECTION E: DEVELOPMENTAL TESTING

Bayley Scales of Infant Development: □ Completed □ Partly Completed □ Not Performed

If completed or partially completed:

a. Corrected age used in scoring: __ __ **months** __ __ **days**

b. Results: Check and complete all sections that apply:

□	**BSID-II MDI:**	Raw Score: __ __ __	Index Score for Corrected Age:	__ __ __	
□	**BSID-II PDI:**	Raw Score: __ __ __	Index Score for Corrected Age:	__ __ __	
□	**BSID-III Cognitive:**	Scaled Score: __ __ __	Composite Score:	__ __ __	
□	**BSID-III Language:**	Sum Scaled Score: __ __ __	Composite Score:	__ __ __	
□	**BSID-III Motor:**	Sum Scaled Score: __ __ __	Composite Score:	__ __ __	

Mullen: Domain	**Age Equivalent (months)**	**Descriptive Category**					**Gains from last visit (months)**
GM	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
VR	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
FM	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
RL	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
EL	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __

ADOS: □ **No** module □ **1** □ **3**
□ **ASC** □ **2** □ **4**
□ **AC**

IF partly completed or not performed check why:

Check why: □ Neurosensory impairment (blind or deaf) □ Too severely delayed
□ Uncooperative □ Other reason: _____

Other Developmental Test Performed: □ Yes □ No

If Yes, Abnormal results: □ Yes □ No

SECTION F: OVERALL CLINICAL APPRAISAL

Clinical Appraisal:	Cognitive Function:	□ Normal	□ Suspect	□ Impaired
	Language:	□ Normal	□ Suspect	□ Impaired
	Motor Function:	□ Normal	□ Suspect	□ Impaired

Appendix 3f: UMass Memorial Medical Center Health Status Report (26-1/30 months and older)

Date Last Seen (MM/DD/YYYY) ___/___/_____

Birth Weight (g): □ <1000 □ 1000-1250 □ 1251-2000 □ 2001-2500 □ >2500

Gestational Age (weeks): □ <28 □ 28 – 38 □ 30 1/7-34 □ 34 1/7 -36 6/7 □ 37 – 42 □ >42

SECTION A: HEALTH STATUS

Corrected Age at the Follow-Up Visit: (months/days) __ __ months __ __ days

---

SECTION B: LIVING SITUATION

Maternal Age at Infant Birth: __ __ Years □ Unknown

Home Child Resides: □ Parent/Family Member □ Foster Care □ Chronic care facility

Caregiver(s): (Check only one) □ Single Parent □ Single parent extended Family □ Institutional □ Two Parents □ Tw0 parent extended family

Primary Caregiver Education: (Check only one) □ Some high school or less □ Some college/university □ High school degree/GED □ College /university degree □ Not applicable □ Unknown

Caregiver(s) Primary Language: □ English □ Spanish □ Other: _____

SECTION C: SUPPORT AFTER DISCHARGE

Support After NICU Discharge: □ Yes □ No □ Unsure

If Yes, Check all that apply

- □ **1. Tracheostomy**
- □ **2. Ventilator**
- □ **3. Oxygen**
- □ **4. Gastrostomy**
- □ **5. Nasogastric Feeds**
- □ **6. Apnea or Cardio Respiratory Monitor**

SECTION D: MEDICAL HOSPITALIZATION & SURGERIES

Medical re-hospitalization since last seen: □ Yes □ No □ Unsure

If Yes, Category: Check all that apply	**Number of Admissions**		**Number of Admissions**
□ **1. Respiratory Illness**	__ __	□ **5. Infections (not respiratory of shunt infections):**	__ __
□ **2. Nutrition/Failure to Thrive**	__ __	□ **a. Meningitis**	__ __
□ **3. Seizure Complications**	__ __	□ **b. Urinary Tract Infection**	__ __
□ **4. Shunt Complication**	__ __	□ **c. Gastrointestinal Infection**	__ __
		□ **d. Other Infection** (Specify)_____	__ __

□ **6. Other Medical Hospitalizations:** (Specify)_____

Surgical procedures since last seen: □ Yes □ No □ Unsure

	Number of Procedures
(P-Codes) _____	__ __
_____	__ __

SURGICAL PROCEDURE CODES (P-CODES)

CODE	**PROCEDURE**
	Central Nervous System
P-101	Shunt or shunt revision for hydrocephalus
P-102	Other neurosurgical procedure
	Congenital Heart Defect Surgery
P-201	Cardiac surgery
	Gastrointestinal Surgery
P-301	Gastrostomy tube
P-302	Inguinal hernia repair
P-303	Other gastrointestinal surgical procedure
	Genitourinary Surgery
P-401	Circumcision
P-402	Other genitourinary surgical procedure
	Otolaryngology
P-501	Tracheostomy
P-502	Tympanostomy tubes
P-503	Other ENT surgical procedures
	Ophthalmologic Surgery
P-601	Retinal cryosurgery or laser surgery: single eye
P-602	Retinal cryosurgery or laser surgery: both eye
P-603	Strabismus surgery
P-604	Other ophthalmological surgical procedure
P-900	**Other Surgical Procedures**

Appendix 3g: UMass Memorial Medical Center Developmental Status Report (42.1 months and older)

Date Last Seen (MM/DD/YYYY) ___/___/_____

SECTION A: GROWTH PARAMETERS

Corrected Age Growth Parameters Were Obtained (months/days): **__ __ months** **__ __ days**

Weight: __ __ . __ __ **kg**

Head Circumference: __ __ . __ __ **cm**

Height: __ __ . __ __ **cm or** __ __ . ____ **in**

Early Intervention Received: □ Yes □ No

SECTION B: VISION AND HEARING

Formal Ophthalmologic Exam: □ Yes □ No

Blindness: □ One eye □ Both eyes □ Not blind □ Unsure

Prescription Glasses: □ Yes □ No

Formal Hearing Test: □ Yes □ No

Hearing Impairment: □ One ear □ Both ears □ Not deaf □ Unsure

Amplification: □ Yes □ No

SECTION C: CEREBRAL PALSY

Cerebral Palsy: □ Yes □ No

If Yes, a. Impairment: □ Diplegia □ Hemiplegia □ Quadriplegia

If No, b. Muscle tone: □ Hypotonia □ Hypertonia □ Both (hypo- & hypertonia) □ Normal

---

SECTION D: GROSS MOTOR MILESTONES

Sits Independently: □ Yes □ No

If No, a. Sits with support: □ Yes □ No

Walks ten (10) steps independently: □ Yes □ No

If No, a. Walks ten (10) steps with support: □ Yes □ No

SECTION E: DEVELOPMENTAL TESTING

Mullen: Domain	**Age Equivalent (months)**	**Descriptive Category**					**Gains from last visit (months)**
GM	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
VR	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
FM	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
RL	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __
EL	__ __	□ very low	□ below average	□ average	□ above average	□ very high	__ __

ADOS: □ **No** module □ **1** □ **3**
□ **ASC** □ **2** □ **4**
□ **AC**

KBIT-2: __ __ __ **V (verbal)**
__ __ __ **N (non-verbal)**

WRAT: __ __ __ **WR (word reading)**
__ __ __ **SC (sentence comprehension)**
__ __ __ **S (spelling)**

Einstein: □ **A (Acceptable)**
□ **U (Unacceptable)**

IF partly completed or not performed, check why:
□ Neurosensory impairment (blind or deaf) □ Too severely delayed
□ Uncooperative □ Other reason: _____

Other Developmental Test Performed: □ Yes □ No
If Yes, Abnormal results: □ Yes □ No

SECTION F: OVERALL CLINICAL APPRAISAL

Clinical Appraisal:

Cognitive Function:	□ Normal	□ Suspect	□ Impaired
Language:	□ Normal	□ Suspect	□ Impaired
Motor Function:	□ Normal	□ Suspect	□ Impaired
