

Childbearing Age Women with PKU:

Assessment of Care Needs and Preferences

DNP Final Project

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By

Kimberly R. Regis RN, MS, CPNP

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DNP Project Committee:

Professor Mary Margaret Gottesman, PhD, RN, CPNP, FAAN, Advisor

Professor Thelma Patrick, PhD, RN

Professor Barbara Polivka, PhD, RN

**Acknowledgments**

Dr. Dennis W. Bartholomew

Metabolic Team, Nationwide Children's Hospital

Section of Molecular and Human Genetics, Nationwide Children's Hospital

Sabrina Horton, Sponsored Projects Officer, Nationwide Children's Hospital

Dr. Christopher Holloman, Statistician

Monica Cienga, RD, Vitaflo

Andrea R. Cooper

Jimia M. Thompson

Laverne Morris

Dori Klemanski, DNP

John Chovan, DNP

Love Zion Baptist Church Family

**Dedication**

I give the highest praise to my Lord and Savior Jesus Christ for being my comfort and my strength along this journey. I also am very thankful for my husband Kerry, my children Imara and Safia, my mother Rena Logan, and all of my family, friends, and prayer warriors that have supported me over the many years. Last but not least, I dedicate this degree and project to the loving memory of my father, Myles Logan, for I know that he would have told the whole world about what his baby girl did. I miss you, Dad.

### Abstract

**Purpose:** The purpose of this project was to describe the care needs and preferences of adult women of childbearing-age with PKU. **Methods:** A descriptive design using open-ended questions and forced choice responses was used to collect data through patient phone interviews. A Health Demographic Information Form, and the Maternal PKU Knowledge Test (Shiloh, St. James, & Waisbren, 1990) were also used. **Analysis:** Demographic data were analyzed with descriptive statistics using SPSS (IBM, 2011). Relationships among select variables and MPKUT scores were examined using Spearman's correlation. Content analysis of the phone interviews was done to identify themes and sub-themes.

**Results:** The sample consisted of 6 adult women with early-treated PKU (mean age 29 years). All participants stated that PKU was integrated into their daily lives. Preconception planning and pregnancy increased their concern in regard to dietary management of PKU in order to avoid negative outcomes for their infants associated with poor metabolic control. Various methods were used to manage the PKU diet, with family support an essential component of achieving dietary adherence. Barriers to dietary adherence included financial constraints prohibiting the purchase of medical foods. A basic knowledge of PKU and Maternal PKU was demonstrated. Some desired mental health, OB/GYN, and social work services as part of their PKU care. PKU clinic staff was described as friendly and supportive; however suggestions offered included written educational materials and implementation of multiple and more frequent communication modalities. **Conclusion:** Participants consistently identified PKU as an important part of their life with increased concern during the preconception period and pregnancy. Family support and clinic support were described as essential but in need of expansion and enhanced communication modalities.

## **Chapter One: Nature of the Project**

### **Introduction and Purpose**

Phenylketonuria (PKU) is an inborn error of metabolism in which there is a deficiency or absence of an enzyme required to effectively metabolize natural sources of protein. Untreated PKU results in elevated concentrations of phenylalanine and phenylalanine metabolites in the blood of affected individuals. The result of elevated blood phenylalanine is severe to profound mental disability, behavior disorders, rashes, seizures, skin pigment dilution, and an unusual body odor (Committee on Genetics, 2008; Harding, 2008). PKU, an autosomal recessive disorder, occurs in 1/10,000 to 1/12,000 infants born in the United States (Moyle, Fox, Arthur, Bynevelt, & Burnett, 2007). With the inception of newborn screening for PKU and the development of effective treatment, the neurologic devastation and severe mental retardation associated with PKU have been virtually eliminated. However, even with early treatment, PKU is not entirely without risk to the affected individual, with many individuals experiencing some level of cognitive deficits as adherence to diet waxes and wanes. In particular, affected women have a unique disease-related risk as they reach childbearing age, known as maternal PKU (MPKU), which poses significant risks to the fetus for mental retardation and other disorders. .

The purpose of this project was to describe the care needs and preferences of adult women with PKU of childbearing-age. Gaining a better understanding of the ways in which a children's hospital-based metabolic specialty clinic may best serve them, should lead to optimization of their health outcomes and those of their children.

### **Pathophysiology of PKU**

Phenylalanine is an essential amino acid that cannot be synthesized by mammals and, thus, must be obtained from dietary sources. The average adult consumes 2 to 3 grams of protein/kg daily, and utilizes about 10% of the phenylalanine consumed for anabolic needs (Harding, 2008). The remaining 90% of phenylalanine is converted to tyrosine which is involved in the synthesis of compounds such as melanin for skin color and the production of neurotransmitters such as dopamine and norepinephrine, essential for mood regulation and cognitive function (2008).

The primary defect in persons with PKU is that phenylalanine cannot be sufficiently converted to tyrosine due to the deficiency of the enzyme phenylalanine hydroxylase (PAH). Phenylalanine and its by-product, phenylpyruvic acid, accumulate in the body with some excreted in urine as phenylpyruvate. The detection of phenylpyruvate in the urine of two siblings with mental retardation who were brought for medical care led to the description of PKU in 1934 by a Norwegian physician, Dr. Ashbjorn Folling (Wappner et al, 1999).

In 1953 researchers found that a phenylalanine restricted diet in individuals affected with PKU reversed the clinical manifestations of PKU with the exception of the cognitive impairments (Harding, 2008). This finding spurred pursuit of a means for early detection.

The Guthrie Method (Bacterial Inhibition Assay) developed in the late 1960's made detection of PKU and initiation of early treatment a reality. The Guthrie method also made implementation of a universal newborn screening program possible. Implementation of widespread screening permitted appropriate dietary management to begin soon after birth with the goal of limiting the adverse neurologic and cognitive effects of PKU.

The gene responsible for phenylalanine hydroxylase production was isolated and in the 1980 and since that time over 500 mutations in the gene have been identified. Affected individuals fall along a spectrum from mild disease (often referred to as hyperphenylalanemia) to severe (classic) phenylketonuria (Harding, 2008). Classification of PKU is based on blood phenylalanine concentration while on a regular diet (which is the case at the time of newborn screening and follow-up testing). A phenylalanine level under 10 mg/dL is considered to be hyperphenylalanemia, while a level greater than 20 mg/dL is classic PKU. Individuals who have levels between these two extremes require treatment; however, there is no distinct classification for these individuals (Committee on Genetics, 2008).

Treatment of PKU consists of restriction of natural protein intake and supplementation with medical foods, such as metabolic formulas, in which phenylalanine has been removed. The PKU diet is largely fruits and vegetables with limited amounts of starchy vegetables such as potatoes and peas, and

limited amounts of grains. Meat, dairy foods, eggs, peanuts, and soy products are prohibited for most affected individuals due to their high protein content.

Maintenance of dietary therapy was thought to be needed only for the first 6 to 7 years of age (Hurst & Stullenbarger, 1986; Committee on Genetics, 2008). It was a common belief that the restrictive diet could be discontinued when brain growth was largely complete at seven years of age. However, studies have identified the long-term adverse consequences of elevated phenylalanine levels after diet discontinuation in individuals treated early in life. National guidelines now recommend diet therapy for life (NIH, 2001).

### **Maternal PKU**

With early screening, identification and treatment, neuro-cognitive deficits can be minimized. Persons with PKU are now more likely to enter adulthood seeking traditional life experiences, including parenting. Women with PKU have a unique burden of disease related risk that impacts them as they reach childbearing age, maternal PKU (MPKU). Phenylalanine is teratogenic to the fetus whether or not the fetus has PKU. Animal studies have shown that the placenta naturally selects amino acids that are in higher concentrations, thus there is an active transplacental phenylalanine gradient during pregnancy in affected women leading to high levels in the fetus's circulation (Hoeks, den Heijer, & Janssen, 2009). Women who have poorly controlled PKU and who become pregnant, risk their offspring having microcephaly (72%) and mental retardation (93%) (Brown et al., 20002; Hoeks, den Heijer, & Janssen, 2009; MMWR, 2002). Other risks associated with fetal exposure to elevated phenylalanine levels in the mother include congenital heart defects, facial dysmorphism, intrauterine growth retardation, and developmental delay (2009). Thus the single-gene defect in the mother can have a profoundly detrimental impact on her offspring if management of this condition is not strictly adhered to prior to conception and during pregnancy.

The occurrence of MPKU is not an absolute. The offspring of some women with poor control of phenylalanine levels do not necessarily experience detrimental effects, while women with well-controlled PKU may have less desirable newborn outcomes. These data suggest that elevated phenylalanine levels

are not the sole factor impacting fetal outcomes. Perhaps some women have protective genetic factors that others do not. Regardless, the risks associated with elevated phenylalanine levels are considerable and should be minimized (Hoeks, den Heijer, & Janssen, 2009).

When the risk of MPKU for women with PKU is coupled with the neurocognitive changes experienced by patients discontinuing diet therapy, the effective education and care of this patient population become even more critical and challenging. Multiple factors must be considered when developing interventions to prevent the occurrence of MPKU. Practitioners must recognize that physiological and psychological factors interact and can have a powerful effect on the patient's ability to comprehend and execute the self-management strategies required to achieve optimal general and reproductive health outcomes. Although gene therapy is not available currently, identification of system level factors that both impede and facilitate dietary adherence and planned pregnancies make it possible to modify interventions and remove barriers to care, allowing health professionals to support patients in choosing healthier behaviors and improving their health outcomes and those of their children.

### **Significance of the project to nursing and health care**

#### **National Agenda**

It is important to recognize that the healthcare needs of women with PKU are not isolated from the priorities of the nation (U.S. Department of Health and Human Services, 2011). Healthy People 2020, a science-based approach to improving the health of Americans, have identified topics to be addressed over a 10-year period. Within each topic goals and objectives are outlined. The topic areas in alignment with this project include: 1) maternal, infant, and child health with an objective to increase the proportion of women delivering a live birth who received preconception care services and practiced key recommended preconception health behaviors 2) family planning with an objective to increase the proportion of pregnancies that are intended and increase the proportion of sexually active persons who received reproductive health services, and 3) access to care with an objective to reduce the proportion of individuals who are unable to obtain insurance and thus delay obtaining necessary medical care.

### **Observations in Practice**

According to Goodman, Mendez, Throop, and Edwards (2002), up to 15,000 patients  $\geq 21$  years may seek inpatient care at a pediatric facility annually. This stems from the increasing ability of health professionals to sustain life and limit disabilities in individuals diagnosed with childhood diseases which previously led to a shortened life span, including inborn errors of metabolism such as PKU. Treatment of these conditions in adulthood often remains the responsibility of pediatric facilities since health professionals caring for adults rarely learn to manage these diseases. The end result is that adult patients receiving care in pediatric facilities may fail to receive healthcare addressing the breadth of adult health issues impacted by management of their condition, or patients receive suboptimal care from adult practitioners with little knowledge of their special health care needs (Britto, 2006; Kennedy & Sawyer, 2008).

Pediatric Nurse Practitioners who are educated to provide holistic care are in a prime position to advocate for age-appropriate care as their patients with chronic illness age into adulthood (Watts et. al., 2009). The involvement of nursing in the proactive management of patients with chronic illness is increasing.

Cumbie, Conley, and Burman (2004) point out that nursing is guided by a “humanistic philosophy” (p. 72). This approach to care by advanced practice nurses encompasses the ability to provide flexible, individualized care to persons with chronic illnesses through all phases of illness and development. And it is this care philosophy within nursing that lends itself to addressing the gaps in care for women with PKU.

Generally speaking, clinicians agree that in order to optimize health outcomes, patients with PKU should remain on a restrictive diet for life (NIH, 2001; Hoeks, den Heijer, & Janssen, 2009). However, there are few studies providing evidenced-based strategies and interventions to facilitate continuing dietary management into adulthood. One possible approach to facilitating dietary adherence for women of child-bearing age who have PKU is to replicate interventions utilized for smoking cessation and weight

loss such as support groups, computer-based interventions, and telephone support (Dale, Caralau, Lindenmeyer, & Williams, 2009). However, prior to implementing an intervention aimed at meeting the needs of this specific population, further data are needed to direct changes in care. Thus, rather than pursue best practice via trial and error, assessment of the needs of this population is a first logical step. This project gathered data on the needs and preferences of adult women of childbearing age with PKU, so that an effective evidenced-based intervention may be developed to improve the quality of care received by pediatric facilities.

### **Project Objectives**

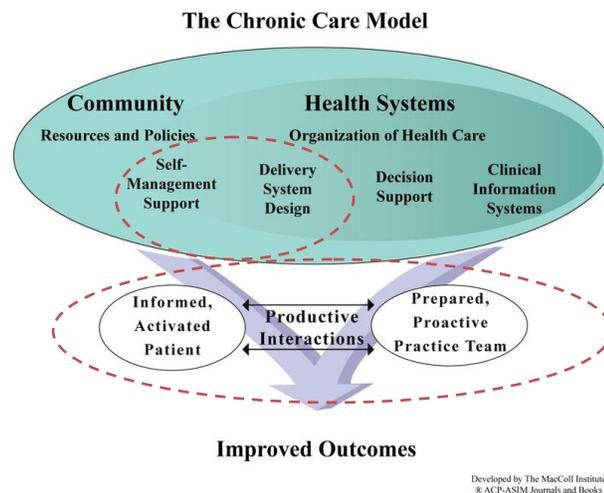
The purpose of this project was to describe the care needs and preferences of adult women of child-bearing age with PKU. While most of the research in this area has been conducted utilizing surveys and camp-based programming, this study used semi-structured interviews to learn about their needs from the women themselves. The aim of this project was to gain a better understanding of the overall concerns of adult women with PKU related to management of their condition and its influence on reproductive health and family planning decisions. Specifically, there were six questions of interest:

1. How does having PKU influence daily life?
2. What strategies are used for dietary management?
3. What support systems do participants have that either help or hinder adherence to dietary management?
4. What is the knowledge level of the participants regarding PKU and Maternal PKU?
5. How does knowledge level regarding PKU impact decisions regarding birth-control and family planning?
6. From the participants' perspectives, what can be done to improve support for ongoing dietary management within the clinic service?

## Chapter Two: Review of Literature

### Conceptual Framework

The Chronic Care Model (CCM) provided useful guidance for this project (Wagner, 1998). Watts et al. (2009) described the match between the skills of nurse practitioners and elements of the CCM; specifically, nurse practitioners value and develop expertise in patient self-management support, decision support, and delivery system change. The CCM model illustrates the variety of factors that must be considered in order to improve patient outcomes and modify the system in order to address the needs of patients (see Figure 1 for an illustration of the CCM).



*Figure 1.* Chronic Care Model. This figure illustrates the elements of focus for the project which are circled with a dashed line.

The CCM addresses self-management support, function of the team and health care delivery system, use of evidenced-based guidelines to support interactions, and enhanced systems of care to facilitate these processes and provide data for performance evaluation (Wagner, 1998). All of these factors are important to the delivery of care of those with chronic illnesses, however, addressing all of them was outside the scope of this project. The elements of the model that focus on the practitioner and patient interaction, delivery system design and self-management support were selected for this study and are circled with a dotted line above (See Figure 1). The primary focus of the project was the assessment of the needs of the patients as a means to delineate the current level of satisfaction with the services

provided and to elicit suggestions for improving delivery system design and self-management support.

### **Related Research**

National guidelines provide specific recommendations for treatment of PKU up to age 12 years. All children are screened at birth, and if PKU is identified, a restrictive diet limiting phenylalanine intake is begun immediately. Maintenance of blood phenylalanine levels between 2 to 6 mg% is recommended from birth to age 12 years. After 12 years of age, higher blood phenylalanine levels up to 15 mg% are deemed acceptable. However, beyond early childhood, approaches to care vary. Some believe that the existing guidelines are of limited use in the treatment of adults and a call for new guidelines has been made (van Spronsen & Burgard, 2008). This is especially true in light of newer research that has shown higher phenylalanine levels result in cognitive impairment and an increased incidence of psychiatric conditions such as depression and anxiety (Moyle et al., 2007; 2008).

Reports as early as 1937 demonstrated that the children of women with PKU were more likely to be institutionalized and to have PKU themselves (Jervis, 1937). However, the focus of these reports was on the inheritance pattern of PKU rather than the clinical status of the offspring. There were no data reported on the children who did not have PKU born to these women (1937). Approximately 20 years later, three children were reported to have mental retardation despite not having PKU, but it was not until a series of articles published from 1963 to 1966 that researchers recognized the teratogenic effects of high phenylalanine levels on the developing fetus (Mabry, 1964, 1966,). In the decade following these reports, subsequent literature on maternal PKU included case reports and retrospective data collection to further characterize fetal outcomes (Levy, 2003). The momentum of research increased with the development of the Guthrie method in 1963 to screen for PKU and subsequent implementation of a national newborn screening program and effective early treatment. Women with PKU having normal or close to normal intelligence have greater potential to bear healthier children (Harding, 2008). In order to better understand the preventative measures needed to protect the fetus, the literature shifted from case studies and retrospective analyses to large, prospective cohort studies.

From the late 1970's through the 1990's several published studies prospectively examined fetal outcomes of offspring born to women with PKU (Koch et al., 2003; Lee, Ridout, Walter, & Cockburn, 2004; Rohr, Doherty, Waisbren, Bailey, Ampola, Benacerraf, & Levy, 1987). The primary focus of these studies was to describe the management strategies that resulted in optimal fetal outcomes. Other factors studied included assessment of barriers to dietary adherence for the mothers and maintenance of diet adherence postpartum. For the infants, physiological and neuropsychological outcomes from poor dietary adherence were evaluated. These studies clearly demonstrated that strict dietary management, especially in the preconception period, resulted in the best outcomes for offspring. Thus, a subset of literature focusing on not only the pathology of maternal PKU, but also on the woman with PKU began during this time period.

Pueschel and Yeatman (1977) tested a program offering education on both PKU in general and content specific to maternal PKU. These sessions were held in a series of 5 bi-weekly meetings beginning with education on the inheritance of PKU and the biochemical basis for the disorder. As the sessions progressed, maternal PKU was discussed with the participants who included teenage girls and their parents. Although no formal assessment was reported of how these sessions impacted the choices of the families involved, it was concluded that the parents, teenagers, and staff alike felt that the program allowed for open discussion and reinforcement of the need for active family planning and collaboration with the specialty clinic providers.

Tice, Wenz, Jen, and Koch (1980) conducted similar programs for adolescents with PKU reporting on the content and guidelines they established for counseling, but the success of the intervention was not reported. This may have been due to the lack of validated evidence that strict dietary restriction resulted in healthy birth outcomes. The content of their programs included education about maternal PKU, use of films to educate patients on reproductive anatomy and use of birth-control, and discussion on resuming strict dietary management. These sessions were provided both individually and in a group visit. One aspect that particularly stood out is that the authors made it clear the patients should receive this

education from providers they trust, assigning this responsibility to the nursing staff. The overall goal of the program was to provide organized reproductive counseling so that adolescents could make informed decisions.

Recognizing that the education of women with PKU played a pivotal role in preventing maternal PKU syndrome, Shiloh, St. James, and Waisbren (1990) developed and tested a Maternal PKU Knowledge Test to screen for and identify individuals and groups who might benefit from further education. Specifically the test was utilized to characterize the knowledge of women with PKU and to better delineate the learning needs of this population.

Waisbren et al. (1991, 1995) conducted a five-year longitudinal, prospective study of women with PKU and two comparison groups, one comprised of female acquaintances and another of women with diabetes mellitus. The focus of these studies was to identify factors that predicted dietary adherence to treatment in maternal PKU and factors that influenced prevention of unplanned pregnancies. Variables studied included knowledge of PKU and reproductive decision-making, personality, attitudes/beliefs, and social support. The results of these studies showed that the women with PKU were at almost twice the risk of inconsistently using birth control and, therefore, having unplanned pregnancies and poor metabolic control compared to each of the comparison groups. The variables most strongly associated with adherence were social support and the positive attitude of women with PKU towards dietary management. The role of the healthcare professional also emerged as an important part of facilitating adherence if the provider was open to discussing reproductive decision-making and helped the patient feel supported in their decision-making (1991, 1995).

While the above studies looked at the intrinsic factors that influenced dietary adherence in women with PKU, the role of the healthcare provider was only briefly mentioned. Thus, the question remains of how to best support and deliver services to this patient population. Of the published studies in which interventions were developed and implemented with the aim of facilitating dietary adherence in maternal PKU, the central theme was most often that of education with the goal of equipping individuals to self-manage their condition.

One successful program implemented with pregnant women who have PKU found that pairing women with “Resource Mothers” trained to provide social support and practical assistance to women with PKU resulted in improved outcomes for the women and their infants (Rohr et al., 2004). Many of the women adhered to a strict diet throughout their pregnancy, but the majority of them discontinued the diet after giving birth. The researchers posited that the negative attitude of the women towards the diet and formula regimen was influenced by long histories of family stress and disordered eating related to their diagnosis of PKU (2004). Adherence to diet requires social support, positive attitude, and perception of treatment as manageable. The results of this study were successful in regard to the goal of improving dietary adherence during pregnancy; however, the success was short-lived, with many of the women discontinuing diet shortly after delivery. Furthermore, there still remained the concern of preconception planning and gaining metabolic control prior to becoming pregnant (2004).

A commonly used intervention in the PKU population is camp-based programming. These programs typically consist of diet education, disease education, and maternal PKU education for female patients due to the risks associated with maternal PKU (Singh, Kable, Guerrero, Sullivan, & Elsas, 2000; Waisbren et al., 1997). The results of such programs show success in increasing knowledge of the disease process and skill in self-management reflected in decreases in serum phenylalanine levels. Yet, the effects of the interventions are not long-lasting with many participants returning to baseline in terms of their serum phenylalanine levels within a year of attending camp (Singh, Kable, Guerrero, Sullivan, & Elsas, 2000). While such programming is beneficial to participants, interventions that are ongoing may better aid participants in sustaining the progress made from attending intensive camp programs (Waisbren et al., 1997).

Durham-Shearer, Judd, Whelan, and Thomas (2008) conducted a study in which they provided educational resources to participants in their preferred format, and using a pre- and post-test control group study design, assessed change in knowledge and management related to PKU. The results of this study found that there was a significant increase in knowledge, however, this did not translate into increased dietary adherence. These findings are similar to those of camp-based programming and show that

knowledge alone is insufficient to support dietary adherence in PKU patients. Education is part of the services provided in clinics caring for this population, but education alone is often ineffective in changing behavior, indicating the need for more innovative ways of conveying knowledge and inspiring dietary adherence in adult women with PKU. This is especially true in light of the research findings that these patients, even when treated early and effectively, often suffer from neurocognitive deficits and disorders.

The neurocognitive deficits experienced by persons who have discontinued dietary management of PKU cannot be overlooked, as this has implications for any intervention geared toward improving self-care management in this population. Over two decades ago, Koch, Azen, Hurst, Friedman, and Fishler (1987) described issues with school performance in children who discontinued dietary management for PKU (blood Phe consistently above 14.4 mg/dL). Similarly, Gassio et al. (2005) found that in comparison to a control group, even children with PKU who were treated early and continuously had more school problems and required more “global” tutoring than controls, versus tutoring in specific subjects. The PKU students were of normal intelligence but, on average, tested 10 IQ points lower than the controls. The authors provided two hypotheses for this phenomenon: 1) dysfunction of the prefrontal cortex due to low dopamine concentrations caused by decreased levels of tyrosine in the brain and/or 2) high phenylalanine concentrations in the brain destabilizing myelin already formed, with demyelinated axons reverting to an immature state leading to neuronal dysfunction (p. 270). Radiologic studies of adults who were treated early and who subsequently relaxed their diets as adults have revealed white matter abnormalities on structural magnetic resonance imaging (2009).

Moyle et al. (2007) conducted a meta-analysis to examine the neuropsychological symptoms seen in adults and adolescents with PKU. The results of this analysis showed that adults and adolescents with PKU differ significantly in tests of attention, inhibition, cognitive processing speed, and motor control when compared to the matched control group. Differences in abstract reasoning, executive functioning, and attention have also been identified as weaknesses in those discontinuing dietary management (Hoeks, den Heijer, & Janssen, 2009).

In addition to cognitive deficits, behavioral problems have also presented in this population. The behavioral problems include attention deficit hyperactivity disorders (ADHD), adjustment disorder with depressed mood, phobias, and oppositional defiant disorder. The cognitive deficits and behavioral problems that have been identified are not isolated to PKU patients with poor dietary adherence. Brumm, Bilder and Waisbren (2010) report that PKU patients who were treated continuously and appear to be well adjusted to living with PKU have less positive emotions, described as fewer expressions of joy and less self-confidence.

In adults with PKU, similar disorders to those identified in young children have been found, as well as many others. In adults who discontinued treatment, symptoms of obsessive compulsive disorder and social introversion are reported (Brumm, Bilder, & Waisbren, 2010; Ris, Weber, Hunt, Berry, Williams, & Leslie, 1997; Simon, E., Schwarz M., Roos, J., Dragano, N., Geraedts, M., Siegrist, et al., 2008; Waisbren & Zaff, 1994). Across all studies looking at psychological disorders related to PKU, depression was the most widely reported (Brumm, Bilder, & Waisbren, 2010; Waisbren & White, 2010).

While, young adults with PKU described themselves as happy and healthy individuals, evidence shows that they are delayed in mastering a major task of adolescence, becoming autonomous (van Spronsen & Burgard, 2008). Young adults with PKU leave home later, have fewer long-lasting relationships, and less achievement motivation than similar young adults without PKU (2008). What is not clear is whether this is a result of the disease process or the parenting environment. However, it is known that with discontinuation of diet therapy, which is common in adolescence as the peer group becomes more influential, neuropsychological issues arise for many individuals (2008).

### **Summary**

Over several decades, PKU research has continued to uncover the importance of dietary management and adherence across the life-span. Researchers shifted from describing PKU, to focusing on the treatment and prevention of mental retardation associated with untreated PKU. In more recent years, the revelation that women with PKU, who were not adhering to strict dietary management, placed their future children at risk for mental retardation and other birth defects caused a shift in the literature to

focus on establishing guidelines to prevent harm to the fetus. Education of affected women about maternal PKU has been the avenue by which many researchers and institutions have attempted to mitigate the occurrence of maternal PKU syndrome in children and prevent unplanned pregnancies. Although education programs provide some benefit to participants, the results of such programs show that while there are short-term gains in improved dietary control and knowledge, long-term benefits in terms of planned, safe pregnancies have not been demonstrated (Unger, Weigel, Stepan, & Baerwald, 2009).

Establishing the self-identified need of women with PKU may result in better maternal-fetal outcomes. Doing so may provide a better understanding of the areas of concern from the participants' perspectives (Krueger & Casey, 2009). Subsequent program development can then be tailored to their specific needs.

### **Chapter Three: Methods**

#### **Project Design and Sample**

A descriptive design using open-ended questions and forced choice responses was used to collect data through patient interviews.

#### **Setting**

Nationwide Children's Hospital Regional Genetics Clinic was the clinic from which the study participants were drawn. The clinic provides services that include diagnostic evaluations for patients with known or suspected genetic diseases, genetic and prenatal counseling for families, and treatment of genetic disorders, especially inborn errors of metabolism (Nationwide Children's Hospital, 2010). Some of these services are provided within subspecialty clinics, one of which is the Metabolic Clinic that diagnoses and treats children and adults with inborn errors of metabolism, primarily identified through the state newborn screening program.

The healthcare team for the Metabolic Clinic is multidisciplinary and includes three medical doctors who are certified in biochemical genetics, a nurse practitioner, registered dietician, and a medical assistant. The physicians are primarily responsible for patients who have disorders with the potential to result in acute crises requiring frequent hospitalization. The dietician is the common thread for all patients as dietary therapy is the treatment for the majority of the disorders. The medical assistant serves as a clinic coordinator and the nurse practitioner sees primarily patients with chronic stable conditions with well-established treatment protocols and low risk for acute crisis. One such population, and one of the largest in the metabolic clinic, is that of patients with PKU, with over 100 patients receiving care. Patients in the clinic range in age from newborns to 50 years of age. The majority of the patients were identified and treated early in life, however, there are a small number of patients born before 1965 and left untreated, who suffer from irreversible brain damage. The clinic is held in three weekly half-day sessions.

### **Inclusion Criteria**

The inclusion criteria were:

1. Women between 18 and 46 years of age.
2. A confirmed diagnosis of PKU demonstrated by serum hyperphenylalanemia by laboratory report.
3. A record of previous treatment in a metabolic specialty clinic.
4. Ability to read and speak English.

### **Exclusion Criterion**

The exclusion criterion was a diagnosis of mental retardation/intellectual disability.

### **Sample Selection**

All patients cared for in the genetics clinic at Nationwide Children's Hospital are entered into an Access (Microsoft Corporation, 2010) database housing demographic information, appointments, and diagnoses. The subjects for this project were identified through this database by the primary investigator, who is an employee of Nationwide Children's Hospital in the Metabolic Clinic and directly cares for the PKU patients in the role of nurse practitioner. The primary investigator, because of her employment status and role in the Metabolic Clinic has full rights and privileges to the patient information in the database and accesses it daily as part of normal job duties. One of the sole purposes of the database is data collection to apply for state grant monies to supplement clinic services, as well as, identifying potential participants for clinical trials. Twenty patients seen in the Metabolic Clinic met the initial query criteria. Of the 20 patients, 17 women met the inclusion/exclusion criteria.

### **Recruitment**

Using the most current patient contact information available, all eligible patients were mailed a letter that briefly explained the project. Three of the letters were returned by the postal service because of an incorrect residential address; however a working phone number was available for one of the three women, but a message could not be left on the unidentified voice messaging system. Within two weeks of receiving the letter, all potential participants were contacted by the co-investigator via phone. Due to

failure of eight women to respond to five or more messages, the list of potential participants decreased further. Six women agreed to participate out of the 14 women who were contacted (42.9% response rate). The original project design was to host focus groups as the primary means of data collection with phone interviews being a secondary option for those unable to participate. However, all six women opted to participate via phone interview.

## **Measures**

### **Demographic Form**

Individual participant information was collected using a demographic health information form developed by the primary investigator. Information of interest included age, educational level, diet history and reproductive/sexual health history. Please see Appendix A for a copy of the demographic form.

### **Maternal PKU Knowledge Test**

The Maternal PKU Knowledge Test (See Appendix B) is a 10-question, multiple-choice test written at a 7<sup>th</sup> grade reading level. Each question has one correct answer and covers content related to the cause, treatment, and complications associated with maternal PKU. The Maternal PKU Knowledge Test is the only evidenced-based test for assessing Maternal PKU Knowledge that could be located in the literature. The test was administered originally as part of a longitudinal study of psychosocial factors that influenced decision-making in women with PKU in regard to dietary management and family planning. The sample consisted of 49 women with PKU ranging in age from 16-30 with a mean IQ of 85 as determined by the Wechsler Adult Intelligence Scale-Revised (Shiloh, James, & Waisbren, 1990). The sample had a mean educational level of 12.5 years. Time to complete the test was not limited; however the majority completed the test within 5 minutes. The average test score was 7.1 (SD = 2.11). The level of difficulty for each question was determined by the proportion of women who answered the question correctly. Level of difficulty ranged from 51% to 89% with question 10 being the easiest (89% answered correctly). Questions 1 and 5 had the greatest level of difficulty, with only approximately half of the participants answering correctly (Shiloh, St. James, & Waisbren, 1990).

The test's validity was determined by analyzing the relationship between IQ and test score. This yielded a Pearson product-moment correlation of 0.40 with  $p < 0.01$ . Furthermore, participants who had previously participated in education groups scored higher on the test than those who had not ever attended an educational session ( $t = 2.55$ ,  $p = 0.02$ ).

The authors determined discriminant power by point-biserial correlation between each question's score and the total test score. From this it was deduced that questions 5, 7, and 10 were poor discriminators of overall knowledge. However, the questions were retained because of the importance of the content of the questions. The Cronbach's alpha reliability coefficient was 0.62, which the authors felt was reasonable in light of the small number of items on the test. Thus, they concluded that the test was able to reliably measure the concept of interest, knowledge of maternal PKU (1990).

### **Phone Interview Questions**

Needs and preferences for clinic support were assessed during the scheduled phone interviews. Predetermined questions derived from the six specific research questions were used to guide the discussion. These questions included:

1. How does having PKU influence daily life?
2. What strategies are used for dietary management?
3. What support systems do participants have that either help or hinder adherence to dietary management?
4. What is the knowledge level of the participants regarding PKU and Maternal PKU?
5. How does knowledge level regarding PKU impact decisions regarding birth-control and family planning?
6. From the participants' perspectives, what can be done to improve support for ongoing dietary management within the clinic service?

These six research questions were the key foci anchoring the discussion during the phone interviews. A complete script of the questions used for the phone interviews are in Appendix C.

In addition to these key areas, participants were asked to provide additional comments about issues important to them that were not previously addressed.

### **Procedure**

After agreeing to participate in the project, participants were mailed a packet that contained the informed consent form, the demographic health information form, and the Knowledge of Maternal PKU Test in a separate, sealed envelope with instructions to not open the test envelope until the scheduled phone interview appointment time.

The co-investigator called the participant at their scheduled time and conducted the phone interview using the script in Appendix C. All interviews were digitally recorded and uploaded to a secure website for a transcriptionist to transcribe yielding de-identified manuscripts.

After obtaining verbal consent, the interview began and, on average, lasted approximately one hour. The interviewer, which was primarily the co-investigator and one additional key personnel, asked the participant to read along while the demographic health form was read aloud and filled in the answers provided by the participant. The participant was then asked to provide their answers to the Maternal PKU Knowledge Test. The interviewer did not answer questions about the test or provide any input in regard to correct and incorrect answers until the participant had given all of their responses and the responses were validated. The actual interview was then completed.

At the conclusion of the interview, a summary to validate the participant's responses was provided to the participant. The participant was also given the opportunity to ask questions and to clarify answers. The participant was mailed a \$35 gift card and formula samples from the project sponsor along with a sample request form.

### **Data Management**

Each participant was assigned a subject number and no patient identifiers were used on any tools used for data collection purposes. A tracking sheet was used with the participants' names in order to verify participation and prevent duplication. The tracking sheet was also used to distribute patient

incentives. The digital recordings were transcribed by a professional transcriptionist not involved in data collection or analysis. The transcripts were de-identified of both names and ID numbers.

### **Data Analyses**

#### **The Demographic Health Information Form and Maternal PKU Test**

The raw data were reviewed by the principle investigator and co-investigator prior to and during the analysis process. The author also consulted with a statistician in the Department of Statistics regarding use of SPSS (IBM, 2010) for data analysis. The statistician assisted with setting up the template for data entry and advising the author on the types of statistical tests needed for answering the project questions. The data from the health demographics form and maternal PKU test were entered into SPSS. The raw data were reviewed by the same consulting statistician. The analysis of the data from the health demographics form and maternal PKU test used descriptive techniques to characterize the sample and to describe test scores. Correlations between the data collected on the health demographics form and the maternal PKU test scores were performed to partially answer the project question, “How does knowledge level and having PKU impact decisions regarding birth-control and family planning?” For ordinal variables such as type of birth-control used, marital status, education status, protein intake and formula intake, Spearman correlations were calculated. For the remaining interval data, Pearson product-moment correlations were calculated.

#### **Phone Interview Data**

Data analysis of the phone interviews was done by using each interview question as a guide. From the transcripts the responses of each individual were pooled together into Microsoft OneNote (Microsoft Corporation, 2010) and organized by tabs for each question. Themes were then identified under each question by reading through the transcripts several times until no unique themes were found. Overriding themes were then made into separate sections. Under each theme, sub-themes were identified to maintain the richness of the data and to minimize exclusion of important concepts. In order to facilitate validation of the themes and sub-themes an outline was provided to the author’s graduate committee in a word processor document. The committee member with expertise in analyzing interview data then

reviewed the transcripts and themes identified. Following, review the committee member and author agreed on the themes that best represented the participant's responses. Whenever possible, direct quotes that summed up the experience of the group or those that showed variation in the group were used to provide a more accurate depiction of the participant's experience.

### **Chapter Four: Findings**

This chapter presents the responses obtained from the 6 early-treated women with PKU who participated in the project. The data collected via the health demographic form, maternal PKU knowledge test, and individual phone interviews are reported.

The sample consisted of 6 adult women with early-treated PKU ranging in age from 19 to 35 years of age (mean age 29 years). Table 1 summarizes demographic information and diet information as reported by the participants. As anticipated all participants were Caucasian.

The participants were evenly distributed in regard to marital status, with one-third being single, partnered, and married respectively. Four of the women had at least a high school diploma, and two out of the six had attended college.

In terms of reported protein intake, four of the women rated their intake as high, one rated her intake as medium, and one rated her intake as low. All but one participant reported drinking formula. The most recent serum phenylalanine levels ranged from 2.6 mg% to 19.9 mg% with a mean of 12.1 mg% for the group (See Table 2).

Table 2

*Most recent phenylalanine levels of participants*

Phenylalanine range in mg%	Number of Participants (n = 6)
2 to 6	2 (33.3%)
7 to 11	1 (16.7%)
12 to 16	1 (16.7%)
17 to 21	2 (33.3%)

**How does having PKU influence daily life?**

Table 3 shows the theme and subthemes identified. Participants consistently stated that having PKU was an important aspect of their lives, but full understanding of the disease and the rationale for the treatment was not clear to them as children. Now having grown into adulthood, their perspectives have changed and as one woman stated, *“It’s something I don’t mind having. I don’t feel like you know, I wish I never had this. It’s something that is just my lifestyle.”*

Although PKU was described as being an important part of their lives, the women also were in agreement that having PKU was not something they thought about continuously. There was one exception to this, during pregnancy. *I don’t think about it on a day to day basis. When I’m pregnant, obviously that is my main focus and probably my only focus throughout the day. But when I’m not, it doesn’t really even cross my mind.*

The majority of the participants (n=4) stated that having PKU did not impede their ability to work or take care of their loved ones. Two participants however, stated that having PKU did impede their ability to work. *“I’m not very good with money with being around people like in the public if I’m in a working environment.”* The other participant stated that sometimes she has trouble thinking clearly and also experienced fatigue.

Table 3

*Effects of PKU on Daily Life*

Theme	Sub-themes
PKU is a part of everyday life	<ul style="list-style-type: none"> <li>a. As a child did not understand PKU it was just a part of life</li> <li>b. Having PKU is not something that is thought about continuously</li> <li>c. Having PKU does not affect work or the ability to care for loved ones</li> <li>d. Having PKU causes fatigue and inability to think clearly</li> <li>e. Having PKU impedes ability to handle finances and being around people in public</li> <li>f. Notice PKU more during pregnancy</li> </ul>

**What strategies are used for dietary management?**

Dietary management is the mainstay of treatment for PKU. Thus, several themes and sub-themes were identified in regard to dietary management. Table 4 provides a detailed outline of the themes identified.

Participants consistently expressed difficulty in maintaining the diet with a wide range of underlying circumstances that influenced their ability to be consistent and to eat a well-rounded diet. Two participants stated that they never ate breakfast for different reasons. One stated, *“I really don’t eat*

*breakfast because the only stuff I can put for milk on my cereal is Coffee Rich. And sometimes it's hard to find Coffee Rich to put a little bit on there for my cereal".* While another participant who reported routinely drinking metabolic formula stated, *"If I drink the formula I really have a hard time eating because it fills me up".* For this participant, lack of eating extended beyond breakfast and she expressed that she was only able to eat salads and raw vegetables when and if she did eat. Her eating pattern resulted in a 10 pound weight loss when coupled with an exercise regimen, which she was happy about. This participant also commented that she sometimes has trouble drinking the formula, *"I just got so tired of having that plain old nasty no-flavored powdered stuff. It was awful. And I kept telling myself, I have to drink this."* To cope with this, she changes flavors of formula.

Environmental changes were identified as an influence on dietary management. Social outings, holidays, and vacations presented challenges for some. With the exception of one participant, it was consistently reported that maintaining the PKU diet was easier to do when at home. The participants who maintained their diet away from home relied heavily on strategies such as frequenting restaurants that had salad buffets. Other participants planned ahead and packed their own meals to take with them.

*I always pack food on my own, bring it. And we try to do vacations more where we don't have to eat out a lot. We try to get accommodations like that have kitchenettes or condos or we stay with someone. That type of thing.*

Specific strategies for diet management were individualized and varied, including measuring the amount of all foods eaten, ordering commercially available low-protein medical foods, and closely reading labels before buying or eating foods, and in general avoiding meat and dairy products because of their high protein content. One participant in particular stated that a lot of time was put into planning what was to be eaten.

*I usually plan the day before, how I'm going to have my lunch. I have a set range of milligrams that I allow myself to eat during the lunch. I don't allow myself to really go over 120 so that I*

*have 150 allowed for the rest of the afternoon and evening. And then when I come home, my husband is mainly the cook, so I just kind of talk with him. I was like, "What are you planning to cook?" And he's like, "This is what I planned for you. And this is what I planned for me and (child's name)." And we go from there.*

Most of the participants commented on the necessity of obtaining non-formula medical foods to maintain the PKU diet. However, for many the cost of these foods was viewed as a major barrier.

*I can't afford that food. It's a lot of money. And then they charge you another 15-20 dollars on top of your order for shipping and handling. I can't afford that.*

*And like I said, they don't know if your insurance will cover it. There's an application that you can fill out to see if the insurance will cover it.*

One participant shared a strategy for using foods in the grocery store to overcome the financial burden of purchasing low-protein medical foods that involved enlisting her husband to help read the ingredients that are in the medical foods and finding similar foods in local markets.

*We found some noodles that were available at Kroger in the Asian section that are made with tapioca starch. And I brought it up to my dietician, and she's like, "Well, allow for this amount until we get your next level back and we can see." And it actually ended up being lower. She's like, "Being that it's made with tapioca starch like the other ones are, I imagine that they're pretty low."*

This same participant also uses different shopping lists when going to the grocery store, one for herself, one for her daughter and one for her husband. This enables her to stay organized and ensure that everyone in the household's nutritional needs are met.

While participants recognized that the use of medical food was important to maintaining the PKU diet, there was a lack of understanding as to how to obtain medical foods and sources of payment for

medical foods in Ohio. One participant, not realizing that PKU formula is provided free of charge to Ohio residents, stated:

*I haven't been getting formula either. I have formula still back there, but I haven't found formula for a long time because I don't have insurance to pay for it. I've been waiting on the medical card so I can maybe get that again.*

Another participant held the view that non-formula medical food was provided by the clinic. This participant repeatedly stated that she would like the clinic staff to be more forthcoming about medical food and providing samples.<sup>1</sup>

*My mom had a suggestion of something that they could do: Start the kids out on the medical food as early as possible so that they would grow up liking it, I guess. Cuz I guess I wasn't like that or something. They didn't introduce it right away. Yeah, so I liked table food, like what I wasn't supposed to have, and then by the time they introduced me to the other PKU food, I didn't like it.*

Along the same lines of misunderstanding sources for payment of medical foods, participants also demonstrated a lack of utilizing the reference resources that were available to them. They also were unaware that updated versions of frequently used reference resources were available.

*We have a book, but I don't know where it's at right now. The phes and all that [phenylalanine content of all common foods listed in book]. I have a little small book they gave me about a year ago.*

*It's very hard because the food lists are very outdated. The book I have was published in 1995 and there is no recent works out there to the best of my dietician's knowledge. So it's really kind of hard because there's so many new things available in the market.*

<sup>1</sup>Medical foods are not provided by the PKU clinic. Sample availability is limited.

Managing dietary therapy coupled with the many strategies that are required to achieve adherence, ongoing planning, and the lack of knowledge and use of available resources translated into many of the participants expressing that there is an emotional toll to maintaining the diet.

One participant pointed out that she has to educate her daughter and her daughter's classmates and teachers about the PKU diet.

*And this upcoming Friday, she has "Moms and muffins" at her school. So I told her teacher, "I'm coming, but I'm going to bring a banana. Don't order me a muffin." I have to kind of explain to a bunch of 4-year-olds why Paige's mom isn't having the same muffin. And in layman's terms, I just kind of say, "you know, I have an allergy where I can't eat it." Rather than go into the whole lengthy thing.*

For many participants, coping with cravings was a concern, with some expressing frustration.

*Sometimes it just makes me frustrated. Like when we were low on the foods I'm allowed to eat and there's a bunch of things I'm not allowed to eat left right there in my face.*

*It makes it hard to see other people eating things I know I'm not allowed to have.*

*Sometimes it gets annoying because you can't have what other people have*

The frustration that participants experienced was further compounded by anxiety during pregnancy or when planning to conceive. When asked whether experimenting with new foods was problematic during pregnancy one participant stated:

*Yeah, you always wonder. That's why we're pretty much not doing it now because what if it was a food that isn't PKU-friendly like we thought? And it raises your level and then two weeks later—Oh, guess what? I'm pregnant, and I ate that food.*

Another participant expressed distress over the financial burden of purchasing medical foods and its impact on her ability to plan for pregnancy.

*The insurance covers the formula; "why not the low-protein food?" I don't want to try to get pregnant again and go through what I went through before. There's no sense trying to do that and have high levels. It's just not right.*

Table 4

*Facilitators and Barriers to Dietary Adherence*

Themes	Sub-themes
Difficulty maintaining diet therapy	<ul style="list-style-type: none"> <li>a. Avoidance of eating breakfast because dietary restrictions</li> <li>b. Avoidance of eating because of being full from formula consumption</li> <li>c. Weight loss associated with consuming formula and eating less</li> <li>d. Tired of drinking the same formula flavor</li> <li>e. Maintenance of diet changes from day to day</li> <li>f. When on vacation and during holidays difficult to maintain diet</li> </ul>
Individual strategies are needed to maintain dietary therapy	<ul style="list-style-type: none"> <li>a. Alternative foods consumed in place of medical foods</li> <li>b. Measure everything</li> <li>c. Planning meals ahead of time</li> <li>d. Eat a lot of salads and vegetables</li> <li>e. When off of the diet avoid meat and dairy</li> <li>f. Labels are closely read before buying or eating foods</li> <li>g. Pack food for trips or functions where food will be provided</li> <li>h. Diet well maintained in the home environment</li> </ul>
Financial constraints impact ability to maintain dietary therapy	<ul style="list-style-type: none"> <li>a. Inability to afford medical foods</li> <li>b. Lack of knowledge concerning sources for payment of non-formula and formula medical food in Ohio</li> <li>c. Lack of use of available resources for diet management</li> </ul>
There is an emotional toll to maintaining a PKU diet	<ul style="list-style-type: none"> <li>a. Coping with cravings is difficult</li> <li>b. Frustration from not being able to eat what everyone else is eating</li> <li>c. Experimenting with new foods creates anxiety, especially if pregnant</li> <li>d. Importance of medical foods to manage diet during pregnancy</li> <li>e. Need to educate children about own dietary restrictions</li> </ul>

**What support systems do participants have that either help or hinder adherence to dietary management?**

Family was consistently reported as a source of support for all of the participants (See Table 5 for themes and subthemes). Family members were involved in every aspect of dietary management. Again, the participants' mothers were routinely regarded as being supportive.

*My mother has always been a big support in understanding because she was my main caregiver when I was younger and provided my special diet meals along with my formula.*

*My mom would always make all different kinds of special meals for me. And we would buy the low-protein baking mixes and she'd make all kinds of things for me so I could eat like the same thing with my batter instead of the regular batter. Like she made homemade onion rings before and we would buy the low-protein baking mix and all that stuff. So I was allowed to eat it. She would make my bread too—low-protein bread.*

One participant identified buy-in from her husband and daughter in that they now eat more fruits and vegetables than they used to and her husband utilizes cookbooks and does research to find new recipes to cook for her.

*But one thing, since my husband has been in my life even with baby and stuff, he's definitely become more knowledgeable. He's a label reader now. And the thing for the kids is they eat fruits and vegetables and stuff because he makes kind of two separate meals. And he never really was much of doing a lot of vegetable dishes. But now he is.*

Another participant stated that her family provides financial support by helping her purchase medical foods.

*And I have a lot of low-protein food also because my family bought it for me. So they help out with that. So that helps me. They buy me the pastas and the cookies. And I've been trying all different kinds of new stuff that they have. They have like these like these pizza pockets. And I get*

*the pizza crust when I make my homemade pizza when they order pizza. And some of it's already pre-cheesed with low-protein cheese.*

In general there were no concerns expressed about lack of support from family members. One participant stated that although her husband is not unsupportive, he sometimes is sympathetic and enables her to eat foods that she should not.

*.....my husband would feel very bad about him enjoying something that he knew I really enjoyed—like I loved seafood. And we went to this restaurant that had this huge salad bar and it was a South American cuisine which I didn't have any of the meats of course. But they had like oysters on there and he was just like, "You're not trying yet. What is one oyster going to hurt?" And I'm like, "No. It's not helping me." And it's just because he knew how much I enjoyed that when I had an open diet.*

Table 5

*Family Support for Dietary Adherence*

Theme	Sub-themes
Family support is critical to maintaining dietary therapy	<ul style="list-style-type: none"> <li>a. Family members help buy medical foods</li> <li>b. Use different shopping lists and menus for each family member</li> <li>c. Family members help with preparing for meals, modifying their own diets, as well as providing alternative dishes during special occasions.</li> </ul>

**What is the knowledge level of the participants regarding PKU and Maternal PKU?****Maternal PKU Knowledge Test**

Overall the participants scored well on the maternal PKU knowledge test, with scores that ranged from 7 to 10 correct answers out of a total of 10 questions. As shown in Table 6 the majority of the questions were answered correctly by 83% of the participants (n=5), while question number 7 elicited a variety of responses. Question 7 assessed the participant's knowledge of the risk of their unborn child inheriting PKU. Only one participant answered this question correctly and incidentally this participant went to college and also has had two successful pregnancies with good health outcomes for her children.

Table 6

*Maternal PKU Knowledge Test: Results*

MPKU Test	Percent Correct (n = 6)
1. PKU is.....	83% (n = 5)
2. Mental retardation in babies born to mothers with PKU is likely caused by _____?	83% (n = 5)
3. The best known treatment for maternal PKU to prevent damage to the baby is?	83% (n = 5)
4. In addition to mental retardation, other problems that have been seen in babies born to mother with PKU include....	83% (n = 5)
5. Twenty mg/dl is considered a high blood phenylalanine level. On a low phenylalanine diet during pregnancy, blood phenylalanine levels should be controlled to what level?	83% (n = 5)
6. Which of the following snacks has the least amount of phenylalanine?	100% (n = 6)
7. Children born to mothers with PKU...	16.7% (n = 1)
8. The problems that are seen in babies from untreated pregnancies in mothers with PKU...	100% (n = 6)
9. After a child is born to a mother with PKU, it is important...	83% (n = 5)
10. The best advice to give a young woman with PKU who thinks she might be pregnant is to...	100% (n = 6)

As shown in Table 7, one major theme emerged from discussing maternal PKU knowledge with the participants. Most of the participants stated they were introduced to the topic of maternal PKU as a teenager. Maternal PKU was not discussed prior to that time. The information that was provided was often vague and oversimplified, lacking detail about the physiologic basis for poor fetal outcomes when diet therapy is not maintained.

*And they said if I was sexually active and then wear condoms, it was a possibility that I would get pregnant. And if I wasn't on my diet well, the baby would likely have retardation.*

When participants were asked who provided the maternal PKU education, the sources varied with most being from the clinic staff and the participant's parent. Specifically, mothers were most often identified as the person in the home environment to discuss maternal PKU with their daughters. The discussion from parents was also introduced during the teen years.

*My mother just always emphasized that if I wanted to be active, just to take precautions because if I were to become pregnant accidentally and I didn't find out soon enough it would harm the baby. I was probably 16 or 17 when she brought that to my attention to kind of think about those things.*

One participant stated that she had never been taught about maternal PKU. When probed further she stated that neither her family nor the clinic staff ever broached the subject. She specifically stated, "I don't even remember having the conversation".

Table 7

*Maternal PKU Education: Age introduced and content of education*

Theme	Sub-themes
Maternal PKU education when introduced is often vague and occurs at a late age	<ul style="list-style-type: none"> <li>a. Learned about MPKU in early to mid-teens</li> <li>b. Lack of being educated about MPKU</li> <li>c. Content of MPKU education emphasized being cautious and the importance of diet</li> <li>d. Educational content of MPKU is oversimplified</li> </ul>

**How does knowledge level and having PKU impact decisions regarding birth-control and family planning?**

As assessed using the Maternal PKU Knowledge test, the participants demonstrated a basic understanding of PKU and Maternal PKU. Correlations between test scores and phenylalanine levels yielded no significant relationships. However, as shown in Table 8 the participants' total scores on the Maternal PKU Knowledge test were positively correlated with their level of education ( $r = 0.853$ ,  $p > 0.05$ ). No other statistically significant correlations were identified. Moderately positive correlations between higher test score, number of live births, and number of healthy children were found and a moderately negative correlation was identified between a high test score and condom use. Women with higher test scores were less likely than low scoring women to use condoms as a method of birth control.

Table 8

*Correlation between Maternal PKU Knowledge scores and Demographic and Family Planning Factors*

Characteristic	Correlation coefficient with Participants' Total Score (n = 6)
Education	.853*
Marital Status	.739
Condom Use	-.781
Live births	.698
Healthy Children	.866

\*Correlation is significant at the 0.05 level

Table 9 summarizes the reproductive decision-making of participants. All but one participant was sexually active at the time of the interview. All participants reported using some form of birth control with only one participant reporting use of both a barrier method and a hormonal method (condom and oral contraceptive). Two of the participants used condoms as their only method of birth control. Lastly, one participant, who began being interviewed and had to resume the interview at a later time, learned that she was pregnant prior to the second interview session. The pregnancy was unplanned and thought to be the result of condom failure.

Table 10 shows the pregnancy history of the participants. Four of the six participants reported being pregnant either currently (n = 1), or in the past. Observation of the number of pregnancies compared to the number of actual births reveals that although the participants together had a total of 12

pregnancies, the pregnancies only resulted in 4 live births. The highest number of pregnancies occurred in one participant, having a total of five pregnancies. This participant had 3 miscarriages, 1 live birth, and 1 unaccounted for pregnancy. The child of this participant was reported to the interviewer as having learning disabilities and needing to be in special education classes at the age of 9 years.

Table 9

*Birth-control and Reproductive Decisions*

Characteristic	Participants (n = 6)
Sexually Active	
Yes	5 (83.3%)
No	1 (16.7%)
Trying to Conceive	
Yes	3 (50.0%)
No	3 (50.0%)
Birth Control	
Condoms	3 (50.0%)*
Pill	3 (50.0%)*
IUD	1 (16.7%)
Pregnant Now	
Yes	1 (16.7%)
No	5 (83.3%)

\*indicates one participant reported two methods of birth control use

Table 10

*Pregnancy Outcomes*

Characteristic	Participants (n = 6)
No. of Pregnancies	
None	1 (16.7%)
One	2 (33.3%)
Two	1 (16.7%)
Three	1 (16.7%)
Five	1 (16.7%)
Total Pregnancies	12*
No. of Live births	
One	2 (33.3%)
Two	1 (16.7%)
Total live births	4
Miscarriages	
One	1 (16.7%)
Three	1 (16.7%)
Total Miscarriages	4

\*Includes participant who was pregnant at time of interview. Thus 12 pregnancies, 4 live births, 1 current pregnancy, and 4 miscarriages = 3 unaccounted for pregnancies

The discussions with the participants included their feelings about how PKU influenced their decision to have or not have children, their families' perspective on whether they should have children, and the pregnancy experiences of those who had conceived. Table 11 summarizes the themes and sub-themes that emerged.

All participants consistently reported that having PKU strongly influenced their decisions about whether or not to have children. One participant explicitly stated that she was afraid to have children because of the possible outcomes. For another participant, she felt that she was happy having already had two healthy children and did not plan to have more. Amongst all of the participants, concerns regarding dietary management during pregnancy were a major focus.

*They say that's like the best part of being pregnant is that you get to eat whatever you want. You don't have to worry about your weight pretty much cuz it's a good thing to gain weight. I have to follow a strict diet. You have cravings, and you can't eat it.*

One participant stated that she always wanted to have a large family, but once she became pregnant and realized how difficult it was to maintain the PKU diet her family plans changed.

*Being though that the road was so difficult in the beginning; we went from wanting 3 to 2. I never thought growing up that I could never had kids. I always had the big family in my head—5 kids, 4 kids. The road got a little harder, just not so much PKU-wise, but everything else that was entailed. So we worked it down to two.*

In regard to family support, all of the participants stated that their families were supportive of their family planning decisions. In particular the participants' mothers were mentioned as a major support person in their lives. In one instance, a participant commented on her spouse as being supportive of her decisions.

*And my husband was very supportive and said, "If you can do the diet and the formula, great. If you don't think you can because I definitely could never," then we would just adopt and go from there. So my family's been very supportive.*

For the participants who had experienced pregnancy one stated that, *The way I look it is, there's no greater reward for my will power and being strict than a healthy child.* However, the majority of the discussion regarding the pregnancy experience elicited concerns about dietary management and the difficulty of maintaining the diet. As one participant stated:

*Well, it was very hard. I was sick most of the time. And my doctor got on me about my weight because—well, I kept throwing up the formula that I was on. And then I wasn't eating and they said I had to gain weight—because when she was born, she was only 5 pounds. And I only weighed 100 pounds. So they were concerned about my weight. And I said, "Well, what am I supposed to do? I can't have nothing to eat.*

Another participant stated that her family would question whether she knew how to manage the diet. *Like "are you doing the right thing? Should you be eating that?" So I would say cautionary and then during the pregnancy, questioning, just making sure that I knew what I was doing.*

A unique concern that was expressed by one participant was she had to explain to others why she was on a strict diet.

*We all expect that most people just don't know. They don't know what's all entailed when it comes to PKU and your diet. So you just have to let them know cuz they don't know that—for them, most people don't know what's dangerous [when] development takes place and why it's so important that I stay the course and stuff. So I mean, I find it's a lot harder.*

Table 11

*Feelings and Experiences around Conception and Pregnancy*

Theme	Sub-themes
Decisions to have children strongly influenced by having PKU	<ul style="list-style-type: none"> <li>a. Afraid to have children</li> <li>b. Have healthy children and not planning to have more</li> <li>c. Returning to PKU diet in order to conceive</li> <li>d. Desire to have large family swayed by PKU diet</li> </ul>
Families support the decision to have/or not have children	<ul style="list-style-type: none"> <li>a. Spouse supportive of having children or adopting children</li> <li>b. Mother has always been a big support person</li> <li>c. Decision is personal but are supportive and believe they can be successful</li> </ul>
Pregnancy can be rewarding but difficult to manage	<ul style="list-style-type: none"> <li>a. Having a healthy child is the reward of maintaining the diet</li> <li>b. Following a strict diet and coping with cravings is difficult during pregnancy</li> <li>c. Have to educate others about why maintaining diet during pregnancy is important</li> <li>d. Issues with gaining weight because of diet restrictions and formula aversion</li> <li>e. Family members concerned about proper eating and food choices</li> </ul>

**From the participants' perspective, what can the clinic do to improve support for dietary management?**

Table 12 provides a detailed outline of the themes and sub-themes that were identified regarding suggestions for improvement in clinic services. While participants were generally satisfied and perceived the PKU clinic as supportive and friendly, they did express some dissatisfaction and offered suggestions for improvement. The responses to questions regarding the clinic staff varied with half of the participants stating that the staff listened to concerns about diet and introduced new formulas during clinic visits, while others stated they had to inquire about new medical foods and treatments and felt the level of support from the staff had decreased over time.

*Right now I'm still just in the monthly stages of taking my level every month, and that's pretty much all that I hear from my nurse. And I never really hear from my dietician other than when I call her to order formula. So I feel like I got more communication along the way than the previous team that I had. But I am also someone who's already been through this, so maybe that's why because I have most of the knowledge already. But I think that if this was my first time around, I would feel a little unsure and uneasy because I didn't have the type of communication all the time that I had with the other team.*

Participants voiced that communication had diminished over time. When questioned about the preferred method of communication, responses varied. All participants noted that phone follow-up was desired but the timeframe varied from every week to every month. In terms of email, it was discovered that not all participants had email accounts or access to a computer. The only modality that the participants consistently requested was a newsletter from the PKU clinic, which they considered a trusted source for information.

*Any type of newsletter, any type of community—kind of just get together, especially if there are other women who have had babies who have PKU and are currently on diet or anything, just*

*getting the kids together and then having the parents with the PKU just socializing and that kind of thing.*

In line with the concern that communication had changed over time, the participants also voiced the desire for more written information at visits. Clinic visits were considered helpful, but participants left without reference materials. One participant directly stated that the clinic staff do not come across as supportive nor provide individualized advice.

*I don't know if it's because I'm a second-timer, but I wasn't handed the information like I was the first time around. I got a little folder that said—it had somewhat of a food list on it. And then they pretty much said—these are our new formula options. And I had to ask about the pill because that's something that was taught to me before, but it was in clinical trial.*

Physical space was deemed appropriate and accommodating for bringing children to the visit. There were no concerns expressed regarding having appointments at a pediatric institution. However, several participants suggested having earlier appointment times available. Participants stated they are required to fast prior to their appointment to have their serum phenylalanine level drawn, and fasting all day was difficult.

When asked about their interest in support groups, participants expressed enthusiasm. With more than one stating, *“I have never met anybody before. I feel like I'm the only one.”* Although enthusiastic about support groups, barriers were identified.

*I get these letters in the mail and to come to these outings and stuff like they have. But the only thing it's like so far away from home. And like I said, I'm two hours away from Columbus.*

*I used them as—growing up I had pen pals from camps. I think that's always very important, but right now where I live, it's not really anything that I can get to, especially with a 4-year-old because I would have to have a support group that would have daycare provided or something for the children.*

The need for additional services was discussed during the interviews and the possibilities presented to the participants were mental health services, OB/Gyn services, and social work services as part of their routine visits to the PKU clinic. Responses varied widely with two participants expressing a desire for all three services specifically stating that mental health services would be helpful because of ongoing issues with depression and agoraphobia. In regard to OB/GYN services, some felt this was not appropriate while others stated it would be good to have an expert with whom to discuss birth-control and pregnancy. Lastly, social work services were perceived as valuable by two participants as a resource they could use for themselves, while the other participants stated they were not in need of such services but understand that some women may benefit.

Table 12

*Suggestions for the PKU Clinic*

Themes	Sub-themes
While PKU clinic was generally perceived as friendly and supportive; concerns exist	<ul style="list-style-type: none"> <li>a. Clinic staff talk and listen about diet and diet concerns, introduce us to new formulas, and communicate with other providers</li> <li>b. Obtaining information about new medical foods and treatments requires inquiry</li> <li>c. Clinic staff are willing to answer questions</li> <li>d. Clinic support has changed over time</li> </ul>
Providing timely, clear, supportive, educational discussions and materials is a key service component	<ul style="list-style-type: none"> <li>a. Lack of written information provided at visits</li> <li>b. Have good discussions at visits about diet planning</li> <li>c. Do not come across as supportive nor provide individualized advice</li> </ul>
Physical space and appointments are adequate	<ul style="list-style-type: none"> <li>a. Appointments are easy to obtain, but time of day inflexible</li> <li>b. Visit room is comfortable</li> </ul>
Additional services (social work, OB/Gyn, mental health) are important to holistic health care	<ul style="list-style-type: none"> <li>a. Mental health services important to aid with depression and agoraphobia</li> <li>b. Gynecologist services helpful for discussing pregnancy and birth control, but not welcomed by all</li> <li>c. Varying opinions regarding usefulness of social worker</li> </ul>
Multiple communication strategies needed to assure information dissemination	<ul style="list-style-type: none"> <li>a. Phone follow-up is desired but timeframe for follow-up is variable</li> <li>b. Email access is not universal</li> <li>c. Newsletter from the clinic would be helpful for updates from a trusted source</li> </ul>
Suggestions for improving services	<ul style="list-style-type: none"> <li>a. Clinic should provide more information on medical foods</li> <li>b. Ordering formula in a timely</li> </ul>

Support groups/group visits/conference calls would be a valued addition

- manner
- c. Resolving patient questions, concerns, and lab results in a timely manner
  - a. Some prefer one-on-one visits
  - b. Many never meet anyone else with PKU
  - c. Interested in being connected with someone locally with PKU
  - d. Travel and childcare are barriers to attending support groups and events

### **Discussion**

The CCM elements of delivery system design and self-management support aim to provide patient-focused care that promotes interaction between the healthcare team and the patient, supporting the patient and family to assume effective self-care (Wagner, 1998; Watts et al., 2009). The assessment of the care needs and preferences of the women who participated in this project identified areas for improvement in the delivery of care which have the potential to improve their ability to manage their disease and optimize their health in general.

The current system provides care to patients using a multi-disciplinary team. The literature supports providing care to patients with chronic illness in comprehensive care clinics. Additionally, advantages for improved outcomes stem from the use of nurse-led models of care for delivery (Watts et al., 2009). Based on feedback from project participants, additional team members would better meet the needs of women with PKU. A prime example was the need for mental health services to address issues with depression and agoraphobia, which are common among persons with PKU.

The participants in this project scored above those reported by Waisbren et al., (1991, 1995) indicating a higher than expected level of PKU knowledge. However, participants consistently expressed the need for support beyond education to cope with barriers to dietary adherence and the psychosocial issues related to dietary management.

Despite the strong scores on the MPUT and similar to findings by Waisbren et al. (1991, 1995), over half ( $n = 4$ ) of the participants had poor metabolic control with an average serum phenylalanine level of 12.1 mg% compared to a desirable level of  $\leq 12$  (See Table 2). However, in contrast to her findings, the women in this project reported consistent use of birth-control. These findings must be interpreted with caution given the small sample size and the reported number of pregnancies and miscarriages versus live births (See Table 10). Also a finding that was consistent with Waisbren's studies is that the women felt that the clinic staff members played an important role in facilitating adherence to the PKU diet; participants desired for the clinic staff members to be more involved in their management.

Adherence to dietary management required social support, positive attitude, and the perception that the diet is manageable (Rohr et al., 2004). The results of this project reinforce the need for a delivery system designed to provide support and practical assistance to women with PKU in developing strategies to manage their diet. Although education alone was shown to be insufficient for maintaining dietary adherence, a central theme that emerged across interviews was that providers assumed participants were knowledgeable about PKU once they assumed responsibility for their own care. However, this may be an erroneous assumption on the part of health care providers given that parents are the major target for dietary management information throughout the infancy, childhood, and teen years. It should not be assumed that parents passed along this knowledge accurately and thoroughly.

### **Conclusions**

In summary the participants consistently identified PKU as an important part of their life, but it was regarded as just another component of themselves. One exception that emerged, during the preconception period and pregnancy, PKU and dietary management of PKU became the main focus of their lives because of their desire to avoid the negative outcomes for their babies associated with poor metabolic control.

A variety of methods were used for dietary management, with family support an essential component. Additionally, clinic staff was described as supportive. However, several areas for improvement were identified with participants communicating a need for ongoing PKU and Maternal

PKU education, dietary management support using diverse methods, and the need for developing a support network among women affected with PKU.

### **Limitations**

Although every effort to minimize bias and maintain rigor were implemented in the planning and conduct of the project, however there were some limitations that could have impacted the project outcomes. The sample size for the project was small. Of the 17 women who met the inclusion/exclusion criteria and were mailed the initial recruitment letter, three of the letters were returned by the postal service because of an invalid residential address. Additionally, the three women were not able to be contacted by phone. Of the 14 women for whom valid contact information was available, six women agreed to participate and eight of them failed to respond to five or more messages (42.9% response rate). This was not entirely detrimental to the project in that saturation of content was obtained from the six interviews that were conducted.

The 11 women, who that met the inclusion/exclusion criteria, but who did not participate in the project, had serum phenylalanine levels that ranged from 7.2 to 21.2 mg%, with a mean of 12.7mg%. Additionally, the age range for the women was 18 to 41 years, with a mean age of 26.9 years. Overall, the nonparticipant group tended to be younger and had a slightly higher average serum phenylalanine level than the six women who chose to participate. Thus, the possibility that the nonparticipants input would have differed from the project participant remains.

In regard to the methods and procedures, none of the participants opted to be part of the proposed focus groups, primarily citing travel as a barrier to attending. While the phone interviews were informative, the possibility exists that having the women face-to-face with each other may have elicited different responses to the interview questions. Also, the participants were recruited from one clinic in one location. Thus results may not be generalizable to the larger population of adult women with PKU.

## **Chapter 5: Summary, Recommendations and Implications**

### **Summary**

The purpose of this project was to describe the care needs and preferences of adult women of childbearing age with PKU in order to gain a better understanding of the ways in which a children's hospital-based metabolic specialty clinic may best serve them to optimize their health outcomes and those of their children.

There were six questions of interest:

1. How does having PKU influence daily life?
2. What strategies are used for dietary management?
3. What support systems do participants have that either help or hinder adherence to dietary management?
4. What is the knowledge level of the participants regarding PKU and Maternal PKU?
5. How does knowledge level regarding PKU impact decisions regarding birth-control and family planning?
6. From the participants' perspectives, what can be done to improve support for ongoing dietary management within the clinic service?

A descriptive design using open-ended questions and forced choice responses was used to collect data through patient interviews. Additionally, data were collected using a Demographic Health Information form, and The Maternal PKU Knowledge Test (Shiloh, St. James, & Waisbren, 1990). Descriptive statistics were used to describe the sample. Correlations were used to examine the relationship between maternal PKU knowledge, birth-control, and family planning. Interview data were transcribed and analyzed for themes and subthemes using each project question as a guide.

Of the 17 women meeting inclusion/exclusion criteria, 14 were contacted and six agreed to participate. The sample ranged in age from 19 to 35 years of age with a mean age of 29 years. One-third of the sample was single, one-third partnered, and one-third married. Four of the women had at least a

high school diploma, and two of the six had attended college. Serum phenylalanine levels ranged from 2.6 mg% to 19.9 mg% with a mean of 12.1 mg%.

The principal findings of the study were that participants were more knowledgeable about PKU and Maternal PKU compared to previously reported studies. The women consistently identified PKU as important, but integrated into their daily life. Participants stated that during preconception and pregnancy they became more vigilant about dietary management. A variety of dietary management strategies were identified with family support essential to dietary adherence. Clinic staff were identified as supportive, and several suggestions for improving clinic services were provided. These included the need for written education materials, more frequent phone follow-up, facilitation of patient-to-patient interaction, and communication using diverse modalities. Several recommendations were made to address the barriers to care identified by the project participants.

### **Recommendations**

Based on the findings of this study, the author proposes the following recommendations in regard to improving care offered in the Metabolic Clinic for adult women with PKU during their childbearing years.

1. Develop and disseminate written, age-appropriate educational materials addressing various topics, including: medical foods, pregnancy, and birth-control.
2. Assess patient knowledge at each visit to provide individualized patient education.
3. Develop education documentation tool to track patient learning.
4. Develop a formal, written transition plan for assuming responsibility for care as an adult.
5. Initiate discussions about birth-control and family planning at patient visits.
6. Explore ways to facilitate patient-to-patient interaction.
7. Determine preferences for follow-up by asking the patient at each visit their preferred method of contact and preferred interval (monthly, bi-weekly etc.).

### **Implications for Nursing Practice**

The American Nurses Association, in collaboration with the International Society for Nurses in Genetics published a scope and standards of practice for genomics and genetics in nursing (2007). The “essential attributes” of genetics/genomic nursing were defined as: 1) attention to the full range of human experiences and responses to health and illness, 2) application of genetics knowledge to processes of nursing care, education, and research, 3) integration of objective data with knowledge gained from an understanding of the client’s subjective experience, and 4) a caring relationship that facilitates health and healing with consideration of ethical, legal, and social issues (p. 10). In addition to these essential attributes, the ANA/ISONG standards encourage advanced practice nurses to pursue doctoral level education, both PhD and practice doctorates that include courses focused on clinical and research genetics content.

This project addressed the essential attributes set forth by the ANA/ISONG scope and standards of practice (2007) and allowed the student to explore and develop competency in the Doctorate of Nursing Practice Essentials for advanced nursing practice. Specifically, the student was able to delineate the scientific underpinnings for practice including the pathophysiology and psychosocial components of caring for women with PKU; clinical scholarship and analytical methods for evidenced-based practice as applied to the development of the project and the analysis of the data collected into a format useful for implementing change; and clinical prevention and population health for improving the nation’s health (AACN, 2006).

This project serves as a first step in the long-term planning of programming to address the needs of women of childbearing age with PKU as a distinct population with the shared risk of having offspring with disabilities as a result of their genetic disorder. Thus, this project is only the inauguration of a career dedicated to increasing the presence and contribution of nurses in genetic/genomic clinical practice and evidence-based intervention development.

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Appendices

Appendix A

**Demographic and Health History Questionnaire**

All questions contained in this questionnaire are strictly confidential and will be used for project purposes only.

<b>Age:</b>					
<b>Marital status:</b> <input type="checkbox"/> Single <input type="checkbox"/> Partnered <input type="checkbox"/> Married <input type="checkbox"/> Separated <input type="checkbox"/> Divorced <input type="checkbox"/> Widowed					
<b>Highest Level of Education:</b> High School_____ College graduate_____ (indicate degree:    ) Some College _____ Other_____					
<b>Diet</b>					
# of meals you eat in an average day?					
Rank protein intake		<input type="checkbox"/> Hi	<input type="checkbox"/> Med	<input type="checkbox"/> Low	<input type="checkbox"/> None
Rank formula intake		<input type="checkbox"/> Hi	<input type="checkbox"/> Med	<input type="checkbox"/> Low	<input type="checkbox"/> None
<b>Tobacco</b>		Do you use tobacco?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	

<b>Reproductive Health</b>						
<b>Sex</b>	Are you sexually active?				<input type="checkbox"/> Yes	<input type="checkbox"/> No
	If yes, are you trying for a pregnancy?				<input type="checkbox"/> Yes	<input type="checkbox"/> No
	If not trying for a pregnancy circle the contraceptive method used: abstinence/ condoms/ diaphragm/ pill/ ring/ IUD/ tubal ligation/ other_____					
Number of pregnancies		Number of live births				
Number of miscarriages if any						
Are you pregnant?					<input type="checkbox"/> Yes	<input type="checkbox"/> No
Are you breastfeeding?						
If you have children are they all healthy? If no, please explain below.					<input type="checkbox"/> Yes	<input type="checkbox"/> No

## Appendix B

**Knowledge of Maternal PKU**

Date:

Subject Number:

Circle the best answer.

1. PKU is \_\_\_\_\_.
  - A. a blood disease
  - B. an enzyme deficiency
  - C. a kidney disorder
  - D. a protein deficiency
  - E. an iron deficiency
  
2. Mental retardation in babies born to mothers with PKU is likely caused by \_\_\_\_\_?
  - A. an enzyme deficiency in the baby
  - B. PKU in the baby
  - C. high blood phenylalanine
  - D. the father carrying the gene for PKU
  - E. too little protein in the mother's diet during pregnancy
  
3. The best known treatment for maternal PKU to prevent damage to the baby is \_\_\_\_\_.
  - A. following a well-balanced diet
  - B. following a vegetarian diet
  - C. following a high protein diet during pregnancy
  - D. following a low phenylalanine diet after a positive pregnancy test
  - E. following a low phenylalanine diet before conception and throughout pregnancy
  
4. In addition to mental retardation, other problems that have been seen in babies born to mothers with PKU include \_\_\_\_\_.
  - A. low birth weight
  - B. heart problems
  - C. small head size
  - D. all of the above
  - E. none of the above

5. Twenty mg/dl is considered a high blood phenylalanine level. On a low phenylalanine diet during pregnancy, blood phenylalanine levels should be controlled to what level?
- A. Less than 1 mg/dl
  - B. 2-6 mg/dl
  - C. 6-8 mg/dl
  - D. 10-15 mg/dl
  - E. 16-20 mg/dl
6. Which of the following snacks has the least amount of phenylalanine?
- A. Chocolate chip cookies
  - B. An apple
  - C. A hamburger
  - D. Potato chips
  - E. A bagel with jelly
7. Children born to mothers with PKU \_\_\_\_\_.
- A. never have PKU
  - B. have a 1 in 1000 chance of having PKU
  - C. have a 1 in 100 chance of having PKU if the father carries the gene for PKU
  - D. have a 50-50 chance of having PKU if the father carries the gene for PKU
  - E. will always have PKU
8. The problems that are seen in babies from untreated pregnancies in mothers with PKU \_\_\_\_\_.
- A. are entirely reversible
  - B. can be corrected by surgery
  - C. can be corrected by treating the baby with a low phenylalanine diet
  - D. generally result in the child having mental retardation, learning difficulties, birth defects, and the need for special services
  - E. go away as the child grows older
9. After a child is born to a mother with PKU, it is important \_\_\_\_\_.
- A. to place the child on a high protein diet

- B. to perform newborn screening for PKU with special care and consideration so that if the child has PKU, he or she can begin dietary treatment
- C. to hold off on newborn screening for PKU for a month since the baby has had enough stress
- D. for the mother to be on a high protein diet
- E. to immediately place the child on a low protein diet.
10. The best advice to give a young woman with PKU who thinks she might be pregnant is to \_\_\_\_\_.
- A. wait and see if it is true
- B. wait, but stop eating meat in the meantime
- C. wait, but start using birth control
- D. immediately contact the PKU Clinic for guidance
- E. contact her friends for guidance

Answers: 1b, 2c, 3e, 4d, 5b, 6b, 7d, 8d, 9b, 10d

## Appendix C

**Phone Interview Script**

Hello [insert participant name]. First let me thank you for your participation today and also allow me to reintroduce myself to you. My name is Dr. Mary Margaret Gottesman [Dr. Barbara Polivka, Dr. Thelma Patrick] and I am the primary investigator/key personnel for this study. As we spoke about before the purpose of this interview is to learn how PKU impacts your life as an adult female. We also are interested in learning about the care you get at the Nationwide Children's Genetics Clinic and how it can be improved. This phone call is being recorded to ensure that the informed consent was completed and that all of your comments are recorded during the interview.

This study is being conducted by the Ohio State University College of Nursing and Nationwide Children's Hospital Genetics Clinic and is being paid for by \_\_\_\_\_.

*Participant has had all forms previously mailed to them with ID numbers written on folder and forms beginning with PI and numbered sequentially starting with 001. The MPKU knowledge test is in a sealed envelope. At this time the PI will ask if the participant has the packet that was mailed to them with them, and ask that the pull out the agenda that shows the order the interview will be conducted. Participant is also asked to have a pen for writing with them at this time.*

*[Order of events: consent form, demographic form, MPKU test, and interview questions]*

The first thing we will do is review the informed consent form. In order for you to participate in the study, you will need to sign the consent form. You have the form in front of you. I will now read the form. Please ask any questions you may have as I read the form.

*<READ INFORMED CONSENT FORM OUT LOUD and HIPPA Regulations- answer any questions. Request that the participant sign the form and put it inside the postage paid envelope in their packet.*

Next on the agenda is the demographic form that is included in your packet. Please take a few minutes to fill it out and let me know if you have any questions.

*Ask the participant to put the completed demographic form in the postage paid envelope. Participant should place package in the mail within 2 business days. [remind participant again at the end of the interview and mail reminder if not received within a week].*

Next on the agenda is something called the Maternal PKU Knowledge Test, you will find it in the sealed envelope marked do not open. There are 10 questions and it is a multiple choice test. There is only one right answer for each question. Your name will not be written on the answer sheet, but your subject ID is already been written in for you. You will be mailed a copy of the test with answers after we finish today. I will read the questions and answer options out loud. Please ask if you need me to repeat all or part of the question. I cannot answer questions about the test but ask that you answer them the best you can.

Now that we have all the forms out of the way, we will now begin the interview. I would just like to remind you that this interview is part of a research project so I m digitally tape recording our discussion so we can be sure we do not miss any of your comments.

This interview is confidential and no ones names will be attached to your comments. Also, although this is confidential I would like to remind you not to share anything that you would not like to be shared on accident by another person. The topics and questions for our discussion will cover PKU and management of PKU. We will also be talking about family planning. You may choose to not answer any or all questions, and you may choose not to take part in any or all of the interview. You may stop the interview at anytime and still receive your gift certificate.

We will talk about a lot of different things that are about you as an individual, but the we are looking to learn about how as a group, women with PKU can be better cared for by the Genetics clinic. Also, please know there are no wrong or right answers.

The interview will take approximately one hour and I will do my best to stick to the time you have scheduled without going over my time. Now I will begin by asking you the first question:

#### Start Interview

**Key Question:** How does having PKU influence daily life?

- a) Is it an important part of your life
- b) How do you feel about having PKU?
- c) How have your feelings about having PKU changed from when you were a child to now?
- d) Does having PKU impact your ability to work? Or care for others?
- e) How does your family/friends/partners/spouses feel about your diagnosis of PKU and do you feel they are supportive and how do they show their support?
- f) What part of your relationships make you feel unsupported?

**Key Question:** What impact does PKU have on your daily decision-making about what you eat?

- a) What strategies do you use for dietary management? (Prompts: Have participants state whether they consider themselves on diet or off diet.)
  - a) At home
  - b) Social outings
  - c) Travel/vacation
  - d) Holidays

Because you already indicated if you use birth control on the demographic form we will not ask that again...but let's talk a little bit more about how PKU affects your family planning decisions.

**Key Question:** How does having PKU impact decisions regarding family planning?

- a) What were you told about family planning and PKU and how old were you at the time?
- b) How do your families, friends, and significant others feel about you having children?
- c) Do you think about having children?
- d) For those who have children...do you mind sharing your experience with managing your diet and the outcome of your pregnancy?

**Key Question:** From the participants' perspective, what role do you see the clinic having in supporting you and helping you with managing your health?

- b) What can the clinic do to improve support for health management?
  - a. Availability of appointments
  - b. Physical space
  - c. Education format
  - d. Counseling format
  - e. Follow-up
  - f. Number of services provided
  - g. What do you like most about the services provided?
  - h. What suggestions do you have?
  - i. How do they keep you informed of new treatments?
- c) What would the ideal clinic look like for you?
  - a. Social worker
  - b. Gynecologist
  - c. Support groups
  - d. More frequent phone follow-up
  - e. Mental health services
  - f. Other

## Conclusion

1. Clarify comments, answer questions
2. Thank participant for their time
3. Remind them to mail the consent form and demographic form
4. Remind them that a copy of the test with an answer sheet will be mailed to them along with their incentive.

## Appendix D



March 8, 2011

Kimberly Regis  
Molecular and Human Genetics

**Study ID:** IRB11-00017  
**Study Name:** Assessment of the Care Needs and Preferences of Childbearing Age Females with Phenylketonuria (PKU)

Dear Mrs. Regis,

The response to modifications requested, submitted on 3/4/2011, for the above study has been reviewed by the Institutional Review Board on 3/8/2011 - **STUDY APPROVED**.

**Date of Approval:** 3/4/2011  
**Date of Expiration:** 3/3/2012

**This approval is for one year only.** A Continuing Review Report must be approved before this study can proceed beyond the date of expiration. Please be aware that all changes to the research protocol consent form, or any other aspect of this study must receive prospective IRB approval. IRB policy requires that provisions are made for assent of subjects age nine and older.

**The Federalwide Assurance number assigned to the IRB at Nationwide Children's Hospital, Inc. is FWA00002860.**

If we can provide additional assistance, please do not hesitate to call this office at ext. 22708.

Sincerely,

Alexander Rakowsky, MD, Chair  
Institutional Review Board

*Important Warning: If the reader of this message is not the intended recipient you are hereby notified that any dissemination, distribution or copying of this information is STRICTLY PROHIBITED.*

## Appendix E

**CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY**

**STUDY TITLE:** Assessment of the Care Needs and Preferences of Childbearing Age Females with PKU

**PRINCIPAL INVESTIGATOR:** Kimberly R. Regis, Nurse Practitioner

**CONTACT TELEPHONE NUMBER:** Dr. Mary Margaret Gottesman, Co-Investigator at 614-292-4989 (Monday – Friday, between 9 am to 6 pm)

**SUBJECT'S NAME:** \_\_\_\_\_ **DATE OF BIRTH:** \_\_\_\_\_

**NOTE:** The words “you” and “your” are used in this consent form. These words refer to the study volunteer whether a child or an adult.

**1) INTRODUCTION**

We invite you to be in this research study because *you are a woman with PKU, you are of age to become pregnant, and are cared for in the Metabolic Specialty Clinic at Nationwide Children's Hospital.*

Participation is voluntary. Please learn enough about this research study, its risks and benefits, to decide whether you should agree to participate. We will explain the study to you, and give you a chance to ask questions about anything you do not understand. This process is called “informed consent”. It is up to you to choose if you want to be in this study. You may refuse to be in this study or quit this study at any time, and standard medical care will still be available here or at a doctor of your choice without a penalty or loss of benefits to you.

Before agreeing to participate, it is important to read and understand the study information in this consent form. By signing the consent form, you agree to be in this study.

You will be given an unsigned copy of the consent form to keep for your records.

**2) WHY ARE WE DOING THIS RESEARCH STUDY?**

This is a study to find out what the specialty care needs and preferences are of adult women with PKU

who are of age to become pregnant in order to provide care that helps them to best control their PKU and have healthier children if they choose to become pregnant.

**3) WHERE WILL THE STUDY BE DONE AND HOW MANY SUBJECTS WILL TAKE PART?**

This study will be done at Nationwide Children's Hospital. We hope to enroll about 20 women.

**4) WHAT WILL HAPPEN DURING THE STUDY AND HOW LONG WILL IT LAST?**

- **Discussion (Focus) Group (If applicable)**

On the scheduled date for the discussion (focus) group you will be asked to sign in and will get a name tag. The consent form will be read out loud to the group by the discussion leader. You will then be given the opportunity to ask questions regarding the consent form and study in general. After questions have been answered, you will be asked to sign the informed consent form if you wish to be part of the study. If you decide not to be part of the study, you return home.

Following the signing of the informed consent form, each person will receive a paper asking about your age and education. You will also be asked to take the Maternal PKU Knowledge Test. This will help us know how well we have taught this information to each person in the past. You will be given 15 to 20 minutes to complete the forms and return them to the discussion group leaders.

Immediately following the collection of the forms, the leader, will begin the discussion. The co-leader will take notes of the discussion, manage the recording of the discussion, and be responsible for limiting disruptions from outside the meeting room. At the end of the discussion, the co-leader will read a summary of the responses from the group to each question. You will have the chance to make any other comments that you would like to add.

Refreshments will be provided during the focus groups and will be limited to foods that are healthy for women with PKU such as fruits, vegetables, and water.

When the discussion is over, you will be given a copy of the answers to the Maternal PKU Knowledge Test and a \$25 gift card to a local grocery store and a parking token to pay for parking in the hospital's visitor garage.

- **Phone Interview (if applicable)**

The interviewer will call you on the day and at the time you have chosen to conduct the phone interview. You will be reminded that the phone call will be recorded. Also, you will be asked to be sure to mail back the two completed question forms and the signed consent form you have received in the mail in the stamped envelope included with the forms within 2 days of the interview.

The consent form will be read out loud and you will be asked to provide verbal consent, by clearly stating “Yes, I agree to participate” for the recording. You will also be asked to sign the consent form including date and time that it was sent with the question forms. Following completion of the consent process, the interviewer will ask you to read along while the personal and health information form is read aloud and the interviewer fills in your answers. You will then be asked to provide the answers to the Maternal PKU Knowledge Test. The interviewer will not be able to help you choose answers. After the personal and health information form and Maternal PKU Knowledge Test are done, the interviewer will start the discussion.

At the end of the interview, the interviewer will provide a summary of your responses and make sure the summary is right. You will have the chance to make comments and correct the summary. The interviewer will confirm that a \$25 gift card, as well as, the correct answers to the MPKU tests will be sent to you by mail.

5) **WHAT ARE THE RISKS OF BEING IN THIS STUDY?**

There is the possibility that others may be told of your responses to questions during the small discussion group. However, every effort will be taken to minimize this risk. During the informed consent process, everyone will be reminded of the importance of not sharing any other person’s responses with people outside the discussion group. Additionally, all answers will be kept separately from the medical record and any identifying information will be removed so that no one will know how any participant replied to any certain question.

6) **ARE THERE BENEFITS TO TAKING PART IN THIS STUDY?**

Possible benefits to you from being in the study might be better plans for care in the clinic for treatment of PKU based on the information learned from you. We also might learn something that could help others.

**7) WILL THERE BE ANY COSTS TO ME?**

It will not cost you anything to be in this study. For your time and inconvenience, a \$35 gift card will be mailed to you within two weeks after the study visit. Also, you will be given one parking token for the hospital visitor garage.

**8) WHOM SHOULD I CALL IF I HAVE QUESTIONS OR PROBLEMS?**

If you have questions about anything while on this study or you have been injured by the research, you may contact the Co-Investigator at 614-292-4989, Monday – Friday, between 9 AM and 6 PM.

If you have questions, concerns, or complaints about the research, questions about your rights as a research volunteer, cannot reach the Principal Investigator, or want to call someone else, please call (614) 722-2708, Nationwide Children's Hospital Institutional Review Board, (IRB, the committee that reviews all research in humans at Nationwide Children's Hospital).

Subject's Name \_\_\_\_\_

Date of Birth \_\_\_\_\_

**SUBJECT or SUBJECT'S PARENT OR PERSON AUTHORIZED TO CONSENT ON BEHALF OF THE CHILD (SUBJECT TO THE SUBJECT'S GENERAL MEDICAL CARE)**

I have read this consent form and have had a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have more questions about participation in this study or a research-related injury, I may contact the Principal Investigator. By signing this consent form, I certify that all health information I have given is true and correct to the best of my knowledge.

I have been given a copy of the Nationwide Children's Hospital Notice of Privacy Practices. I understand that my right to my patient information that is created or collected by Nationwide Children's Hospital in the course of this research can be temporarily suspended for as long as the research is in progress. I also understand that my right to access will be reinstated upon completion of this research.

I agree to participate in this study. I will be given a copy of this consent form for my own records.

**CONSENT SIGNATURES**

\_\_\_\_\_  
**SUBJECT or SUBJECT'S LEGAL REPRESENTATIVE**

\_\_\_\_\_  
**DATE & TIME AM/PM**

\_\_\_\_\_  
**PERSON OBTAINING CONSENT**

I certify that I have explained the research, it's purposes,  
and the procedures to the subject or subject's legal  
representative before requesting their signature.

\_\_\_\_\_  
**DATE & TIME AM/PM**