The Financial Burdens Associated with Managing PKU Dietary Needs as an Adult

Melissa C. Bernzen

This research is a product of the graduate program in Nutrition and Dietetics at Eastern Illinois University.

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The Financial Burdens Associated with Managing PKU

Dietary Needs as an Adult

(TITLE)

BY

Melissa C. Bernzen

THESIS

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ABSTRACT

This study was designed to identify the financial burdens associated with purchasing medical foods and the impact this has on the dietary management of adults with PKU. PKU is a genetic disorder in which the body cannot metabolize the amino acid, phenylalanine, which occurs in all foods with protein. Dietary treatment of foods low in protein along with medical supplementation is required for the treatment of PKU. If PKU is left untreated this can lead to severe neurological damage. Medical guidelines indicate that dietary treatment is needed for the duration of one’s life, but the medical foods needed are expensive and individuals receive minimal to no insurance coverage. An online questionnaire survey was designed to identify different financial barriers associated with the cost, PKU treatment modalities and how identified barriers affect the management of the medical nutrition therapy in adults with PKU. Sixteen participants were included in this study and descriptive statistics were used to analyze the collected data. The results showed that participants paid out-of-pocket for alternative medical protein products and modified low-protein foods the most, ranging from $100-$500. The results also showed that participants perceived the cost of medical foods to be expensive, and felt that insurance coverage was inadequate. Further research is needed to continue investigating adult patient barriers to medical foods across the country.
DEDICATION

I dedicate this to everyone in the PKU community: to all the individuals and parents of children managing or trying to re-establish dietary treatment; to the dietitians, physicians, and other health care professionals aiding in the management of treatment and advocating for access to better coverage of medical foods, along with the support from family members and loved ones. I would also like to dedicate this work to my parents, Bob and Liz. You taught me the importance of how to embrace having PKU rather than be dictated by my disorder. Without you, I would not be where I am today.
ACKNOWLEDGEMENTS

First, I would like to thank my boyfriend, Eduardo, for all his love and support throughout this whole process. Even though he was 5,000 miles away, he was always there for me, reassuring me, and cheering me on.

Second, I would like to thank Kim Kowalczyk for giving me the opportunity to become more involved in the PKU community. Lobbying for the Medical Nutrition Equity Act - a bill currently in congress that will aid in the financial coverage for medical nutrition for individuals of all ages with PKU and other inborn errors of metabolism – was the most gratifying and inspiring experiences throughout my entire education that strengthened my desire to finish this research study. In the short time I’ve known her, she has been so supportive and encouraging. I cannot thank her enough.

Lastly, I would like to thank my committee members. Dr. Burns, my thesis advisor, had so much patience, kindness, and guidance for me during this study. Her constant availability gave me the continued support I needed while I was trying to complete this project and my internship at the same time. I am truly grateful for all she has done for me. Dr. Hugo was essential in helping me learn how to set up my questionnaire and use data analysis software. Dr. Shaw recognized my immense passion for this topic of study and provided great insight on how stay focused. Thank you all for your constant advise and support.
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Chapter 1

Introduction

Phenylketonuria (PKU) is an inborn error of metabolism that causes a deficiency in the enzyme phenylalanine hydroxylase which is essential for the conversion of phenylalanine into tyrosine. Without the function of this enzyme, the blood becomes saturated with phenylalanine and there is decreased production of the essential amino acid tyrosine (Vockley, Anderson, Antshel, Braverman, Burton, Frazier, Mitchell, Smith, Thompson, Berry, &; For the American College of Medical Genetics and Genomics Therapeutics Committee, 2014). Lower levels of tyrosine result in decreased production of dopamine causing neurological, behavioral, and psychological problems, as well as other medical implications. This includes hyperactivity, irritability, inability to sit, sleep disturbances, psychomotor agitation, uncontrollable attacks of rage, erratic or aggressive behavior, poor ability to learn new things, psychotic behavior, destructiveness, self-injury, self-mutilation, autistic-like behavior, mental retardation, seizures, tremors, muscular hypertonicity or hypotonicity, spastic paraplegia, eczema, sensitivity to sunlight, and body odor (Brumm & Grant, 2010; Dolan, Koch, Bekins, & Schuett, 2017; Jahja, van Spronsen, de Sonneville, van der Meere, Bosch, Hollak, Rubio-Gozalbo, Brouwers, Hofstede, de Vries, Janssen, van der Ploeg, Langendonk, & Huijbregts, 2016). Increased amounts of phenylalanine also cause neurological damage as it changes the myelination of the white matter of the brain and inhibits other essential amino acids from crossing the blood brain barrier (Vockley et al., 2014). Due to the severity of this disorder, newborn screening protocols have been implemented in order to diagnose and treat individuals within the first two weeks of life (Vockley et al., 2014).
The treatment of this disorder focuses on decreasing blood phenylalanine levels in an individual through the decreased consumption of phenylalanine in the diet (MacLeod & Ney, 2010; Vockley et al., 2014). This is achieved with a diet composed of foods naturally low in protein, such as fruits and vegetables; the incorporation of specialized low-protein medical foods; and a nutritional supplement, often in the form of a liquid formula or an alternative medical protein product. The supplement provides essential amino acids, vitamins, and minerals that are not available from natural sources. Individuals who do not maintain proper treatment are also at risk for neurological damage, further strengthening the need for individuals with PKU to maintain dietary treatment for life (Vockley et al., 2014).

With this strict dietary protocol, individuals with PKU are only able to consume foods such as fruits and vegetables, and small amounts of low-protein snack and cracker items. They also have the complex task of measuring the amount of food consumed daily to determine the units of grams of dietary phenylalanine and total calories. The severity of the dietary restrictions, and required attention to detail often leads to compliance issues, which affect the overall nutritional statuses and neurological development of the individual with PKU (Hafid & Christdoulou, 2015). In order to provide a wider variety of food choices, the use of low-protein medical foods has been incorporated into the dietary treatment of PKU. However, the price of these low-protein medical foods can cost a patient anywhere from $2,275 annually during the first few years of life to $12,438 at the beginning of adulthood (Huntington & Buist, 2009).
Statement of the Problem

The financial burden is one of the main barriers to managing the dietary needs of an adult with PKU. Insurance coverage and reimbursement for patients and families is often inconsistent and limited (Berry, Brown, Grant, Greene, Jurecki, Koch, Moseley, Suter, van Calcar, Wiles, Cederbaum, 2013a; Berry, Kenney, Harris, Singh, Cameron, Kraszewski, Levy-Fisch, Shuger, Greene, Lloyd-Puryear, & Boyle, 2013b; Camp, Lloyd-Puryear, & Huntington, 2012; Huntington & Buist, 2009; Weaver, Johnson, Singh, Wilcox, Lloyd-Puryear, & Watson, 2010). State mandates have been put in place to ensure that medical needs are being met, but there are “loopholes” that leave patients and families paying out of pocket for treatment expenses (Berry et al., 2013b; Weaver et al., 2010). The insurance providers that do cover treatment needs usually set age limits, restricting access to coverage for most individuals over the age of 18 (Berry et al., 2013a; Huntington & Buist, 2009; Weaver et al., 2010). However, PKU is a lifelong disease with treatment required for every age and stage of life.

Purpose of the Study

The purpose of this study was to identify the financial burdens associated with purchasing medical foods and the impact this has on the dietary management of adults with PKU.

Significance of Study

There have been very few studies conducted that research the financial aspects associated with maintaining the treatment of PKU. There is even less research that examines how adults with PKU are affected financially. This study helps identify how adults with PKU are affected financially while managing their dietary treatment.
Research Questions

The following research questions guided this study.

1. What were the financial responsibilities associated with managing the treatment of an adult with PKU in regard to purchasing medical foods?

2. To what extent does the state of residence, in regard to purchasing medical foods, influence the financial responsibilities associated with managing the treatment of an adult with PKU?

3. To what extent does the purchase site of the medical foods influence the financial responsibilities associated with managing the treatment of an adult with PKU?

4. To what extent do the financial responsibilities, in regard to purchasing medical foods, for the patient managing the treatment of PKU impact their dietary management? If so, how?

Assumptions

Several assumptions were made throughout this study. The researcher assumed PKU organizations and clinics would participate in this study and that participants would find this study interesting and relevant to their personal lives. A second assumption was that participants would be willing to complete the questionnaire due to potential long-term benefits this may have for them as PKU patients. The researcher also assumed that participants would be able to read and comprehend the questionnaire and consent form. Finally, it was assumed that participants would answer questions honestly and to the best of their knowledge.

Definition of Terms

Terms used throughout this study include:
1. Medical food – a broad term describing three different components based on the Food and Drug Administration (FDA) definitions: medical formula, alternative medical protein products, and modified low-protein medical foods as energy sources and alternative energy products (Huntington & Buist, 2009).

2. Medical formula – formulas designed as the main alternative to natural protein, but lacking selected nutrient(s) that must be restricted in the diet of persons with inborn errors of metabolism (Huntington & Buist, 2009).

3. Alternative medical protein products – products excluding specific amino acids for the use of persons with inborn errors of metabolism and contain amino acids in a variety of forms: tablets, bars, gels, frozen sticks, and sauces (Huntington & Buist, 2009).

4. Modified low-protein medical foods – “products that come in the form of baking mixes, pastas, rice, sauces, and premade items that are designed to be as similar to their normal counterparts as possible, but supply negligible protein” (Huntington & Buist, 2009).
Chapter 2

Review of Literature

This section presents the current literature related to the management of PKU, including disease diagnosis and progression, the dietary management required to treat PKU, consequences of untreated or undiagnosed patients, the different treatment options available, and insurance coverage discrepancies that can negatively impact the treatment of PKU.

Disease Diagnosis and Progression

PKU is an inherited autosomal recessive disorder that hinders the metabolism of phenylalanine (Vockley et al., 2014). This genetic disorder results from both parents being carriers of the gene. According to the National PKU Alliance [NPKUA] (2016a), the prevalence of being a carrier of the gene is 1 in 50, and the likelihood of two carriers having a child together is about 1 in 2,500. When both parents are carriers of the gene, there is a 25% chance that their child will have PKU (Mitchell, Trakadis & Scriver, 2011). While PKU is extremely rare, it is considered one of the most common inborn errors of metabolism affecting 1 in every 10,000-15,000 births (Vockley et al., 2014). Of the 3.2 million people in the United States, there are about 15,000 people who have PKU (United States Census Bureau, 2016; Vockley et al., 2014).

Individuals with PKU have a deficiency of the phenylalanine hydroxylase enzyme, which is responsible for the conversion of the amino acid phenylalanine into another amino acid, tyrosine. Phenylalanine is obtained through dietary protein as well as through transamination, which result in an endogenous protein source (Mitchell et al., 2011; Vockley et al., 2014). The metabolic pathway of phenylalanine catabolism is
essential because tyrosine is an amino acid that cannot be produced by the body and must be obtained from food through the conversion of phenylalanine. The deficiency of the phenylalanine hydroxylase enzyme causes a decreased production of tyrosine and a build up of phenylalanine. If PKU is left undiagnosed or untreated these nutrient imbalances will cause severe and irreversible behavioral, psychological, and neurological problems, such as hyperactivity, irritability, inability to sit, sleep disturbances, psychomotor agitation, uncontrollable attacks of rage, erratic or aggressive behavior, poor ability to learn new things, psychotic behavior, destructiveness, self-injury, self-mutilation, autistic-like behavior, mental retardation, seizures, tremors, muscular hypertonicity or hypotonicity, spastic paraplegia, eczema, sensitivity to sunlight, and body odor (Brumm & Grant, 2010; Dolan et al., 2017; Jahja et al., 2016; Mitchell et al., 2011; Vockley et al., 2014). Thus, further strengthening the necessity to maintain the dietary treatment for life (). The consequences of an individual with PKU being undiagnosed or untreated was unacceptable for Dr. Robert Guthrie, as his son was born with developmental disabilities and his niece was diagnosed with PKU (Koch, 1997).

In the 1960’s, Dr. Guthrie developed the bacterial inhibition assay test that could detect high levels of phenylalanine in patients’ blood (Koch, 1997; Mitchell et al., 2011; Vockley et al., 2014). When the blood is drawn, the amount of phenylalanine concentration is tested to determine the presence and severity of PKU. This test was used to screen newborns shortly after birth in order to provide an early diagnosis and prevent future brain damage (Koch, 1997; Mitchell, 2011). Eventually, this test influenced the development of newborn screening tests for other inborn errors of metabolism, which is now a Federal policy that newborns be screened.
Testing has now advanced to analyzing the specific genetic mutation of the phenylalanine hydroxylase enzyme associated with PKU. Analysis of the genetic mutation is not a standard of care, but according to the American College of Medical Genetics and Genomics (ACMG) Practice Guidelines, recommendations include that individuals get tested (Vockley et al., 2014). Understanding the genetic mutation of individuals with PKU will provide a better understanding about PKU and promote further research into new treatments (Mitchell, 2011). Depending on the type of genetic mutation, individuals with PKU have different tolerance levels of phenylalanine (NIH U.S. National Library of Medicine, 2017; Vockley et al., 2014).

PKU can be separated into four different classifications based on the severity of the disorder: classic PKU, moderate PKU, mild PKU, and mild hyperphenylalaninemia (MHP). The most common and severe form of PKU is called classic PKU (Blau, van Spronsen, & Levy, 2010; Mitchell et al., 2011; Vockley et al., 2014). Individuals with classic PKU are identified as having severely reduced or absent enzyme activity and blood phenylalanine levels greater than 1200 umol/L or 20 mg/dL while normal phenylalanine levels are 60 umol/L or 1 mg/dL (Blau et al., 2010; Mitchell et al., 2011; Vockley et al., 2014). Moderate PKU is considered a moderate level of the disorder with a phenylalanine concentration range of 900-1200 umol/l or 15-20 mg/dL. Mild PKU is classified as having blood phenylalanine levels with a range of 600-900 umol/L or 10-15 mg/dL, and MHP the lowest level of PKU with phenylalanine levels ranging from 120-600 umol/L or 2-10mg/dL (Blau et al., 2010). The less severe forms of PKU including moderate PKU, mild PKU, and MHP have some enzyme activity, which is why phenylalanine tolerance is higher than classic PKU.
Dietary Treatment of PKU

The treatment of PKU requires individualized medical nutrition therapy that restricts the intake of dietary phenylalanine (MacLeod & Ney, 2010). Due to the spectrum of this disorder, every patient’s dietary phenylalanine tolerance differs from each other. Patients with classic PKU can tolerate no more than 250-350 mg of dietary phenylalanine, whereas patients with MHP PKU have little to no restriction with phenylalanine intake. Individuals with MHP PKU are able to maintain plasma phenylalanine concentrations less than 600 µmol/L on a normal diet (Mitchell et al., 2011). According to guidelines, dietary phenylalanine intake may change depending on age and gender (MacLeod & Ney, 2010). A metabolic physician and registered dietitian nutritionist determine the specific amount of dietary phenylalanine a patient is allowed to consume per day, in order to keep plasma phenylalanine concentrations within the therapeutic range of 120-360 µmol/L (2-6 mg/dL) (MacLeod & Ney, 2010; Vockley et al., 2014).

Table 1

Recommended Dietary Phenylalanine Intake Based on Diagnosis

<table>
<thead>
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<th>Diagnosis</th>
<th>Diagnostic Plasma Phenylalanine Concentration</th>
<th>Recommended Dietary Phenylalanine Intake</th>
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<tr>
<td>Classic</td>
<td>&gt;1200 µmol/L (20 mg/dL)</td>
<td>&lt;250-350 mg</td>
</tr>
<tr>
<td>Moderate</td>
<td>900-120 µmol/L (15-20 mg/dL)</td>
<td>350-400 mg</td>
</tr>
<tr>
<td>Mild</td>
<td>600-900 µmol/L (10-15 mg/dL)</td>
<td>400-600 mg</td>
</tr>
<tr>
<td>MHP</td>
<td>120-600 µmol/L (2-10 mg/dL)</td>
<td>Little to no restriction</td>
</tr>
</tbody>
</table>
**Dietary Management.** Parents are tasked with extra and unfamiliar responsibilities for caring for their child from day one. Immediately following diagnosis, generally around 8-10 days old, measuring and recording the amount of food consumed each day is essential in order to track the intake of phenylalanine. This can be achieved using the book, “Low protein food list for PKU”, or using the app, “How Much Phe?” (Schuett, 2010). Both of these products give patients and families the phenylalanine content in foods and beverages. Along with daily monitoring of food intake, patients are required to send in monthly blood samples using a dried blood spot test in order to assess phenylalanine concentration (Vockley, 2014; Williams, Mamotte, & Burnett, 2008). Patients are also required to attend annual outpatient clinic visits from their physician, dietitian, and any other necessary health professionals. This visit includes a dietary check-up involving a 24-hour food recall, a routine blood phenylalanine and tyrosine analysis, and an overall examination from the physician checking for physical signs of noncompliance with the diet such as hand or tongue tremors (MacLeod & Ney, 2010; Vockley, 2014; Willaims et al., 2008).

**Components of PKU Diet.** In order to satisfy nutritional needs, patients need to use a phenylalanine-free synthetic medical formula that is fortified with amino acids, calories, fat, vitamins, and minerals (MacLeod & Ney, 2010; Rohde, von Teeffelen-Heithoff, Thiele, Arelin, Mütze, & Kiener, Gerloff, Baewald, Schultz, Heller, Müller, Kiess, & Beblo, 2013; Vockley et al., 2014). Depending on the nutritional composition of the medical formula product prescribed, physicians may also recommend additional vitamin and mineral supplementation. Without consumption of medical food products, patients
could develop extreme nutrient deficiencies (MacLeod & Ney, 2010; Rohde et al., 2013; Vockley et al., 2014).

Alternative medical protein products have been recently introduced as new sources of protein as well. Like the medical formulas, these products also contain the necessary amino acids and nutrients required for treatment. However, these products are in the form of tablets, bars, gels, sauces, and frozen sticks (Huntington & Buist, 2009; MacDonald, 2000). Gylcomacropeptide (GMP) products are an alternative medical protein product that is popular among individuals with PKU.

GMP is a whey protein that naturally occurs in bovine milk and does not contain phenylalanine. However, GMP comes from cheese whey and when isolated, it becomes contaminated with b-lactoglobulin and a-lactalbumin (Hafid & Christodoulou, 2015; MacLeod & Ney, 2010; van Calcar & Ney, 2012). Both of these contain phenylalanine, which results in 2-5 mg of phenylalanine per gram of protein in commercially sold GMP products (van Calcar & Ney, 2012). According to MacLeod & Ney (2010), GMP foods and beverages will ultimately result in 5-15 g of protein and 15-25 mg of phenylalanine. For someone with classic PKU, who is allotted less than 350 mg phenylalanine, this amount of dietary phenylalanine would still be within the therapeutic range.

GMP products also offer an increase in protein retention and utilization compared to that of a synthetic amino acid-based diet (i.e. use of medical formula). Patients using GMP products as their source of nutrients receive about 70% of protein needs from the intact protein in GMP, fruits and vegetables. The other 30% of protein needs are from supplemented synthetic amino acids found in alternative medical products or medical formula (MacLeod & Ney, 2010; van Calcar & Ney, 2012). In contrast, patients on an
Amino acid-based diet receive only 20% of protein needs from intact protein found in fruits and vegetables. The remaining 80% is from the supplemented synthetic amino acids (MacLeod & Ney, 2010; van Calcar & Ney, 2012). Overall, GMP products, along with other alternative medical protein products, offer patients an effective way to achieve normal growth and health maintenance (Hafid & Christodoulou, 2015; Huntington & Buist, 2009; MacDonald, 2000; MacLeod & Ney, 2010; van Calcar & Ney, 2012).

Modified low-protein medical foods are also used in the treatment of PKU. Individuals with PKU are restricted from consuming natural sources of protein. Maintaining a severely restricted diet for a long period of time is extremely difficult. Even non-PKU individuals who voluntarily limit their food intake for personal reasons struggle with diet maintenance. Patients with PKU have dietary limitations throughout the duration of their life, but unlike non-PKU persons, they do not have the option to stop dietary treatment without suffering from severe health consequences. Modified low-protein products offer patients a variety of food choices including, but not limited to, breads, cereals, baking mixes, meat alternatives, and pastas (Cambrooke Therapeutics, 2016). These medical foods also provide patients with additional calories and satiety (Vockley, 2014).

**Consequences of PKU Diet.** Reducing dietary phenylalanine intake requires patients to decrease the intake of natural protein sources, which includes the elimination of meat, fish, poultry, egg, milk, grain, legume, and nut products, as well as limited consumption of higher protein vegetable items (MacLeod & Ney, 2010). This leaves patients consuming a diet of low-protein vegetables, fruits, and foods that are high in sugar and fat. The PKU diet is lacking a majority of natural food sources putting patients at a higher
risk for nutrient deficiencies (Hafid & Christodoulou, 2015; MacLeod & Ney, 2010; Robert, Rocha, van Rijn, Ahring, Bélanger-Quintana, MacDonald, Dokoupil, Gokmen, Lannardo, Goyens, & Feillet, 2013; Rohde et al., 2013).

Vockley et al. (2014) states the importance of assessing the nutrient status of patients routinely through tests including a full panel of plasma amino acids, albumin, complete blood count, ferritin, vitamin D, vitamin B12, essential fatty acids, trace minerals, vitamin A, and a comprehensive metabolic panel. Vockley et al (2014) also recommends implementing routine DEXA scans to monitor bone density. Common nutrient deficiencies seen in patients with PKU include vitamin B6, B12, folate, calcium and iron. Individuals following the PKU diet also consume less total fat compared to a regular diet. This leads to a decreased consumption of long-chain polyunsaturated fatty acids (LC-PUFAs). Docosahexaenoic acid (DHA) is especially important because this LC-PUFA supports normal brain and visual development (MacLeod & Ney, 2010). Adequate intake of folate, vitamin B6, and B12 are also important due to their role in reducing the risk of thrombosis, atherosclerosis, and stroke (Hafid & Christodoulou, 2015; MacLeod & Ney, 2010; Robert et al., 2013). PKU patients also have a higher risk of osteopenia, osteoporosis, and fractures. Researchers are unclear whether this is the result of an individual’s genotype or poor utilization and absorption of phosphorus, calcium, and vitamin D, but consumption of adequate levels of these nutrients are vital to compensate for reduced absorption and metabolism associated with an elemental diet and to prevent future complications (Hafid & Christodoulou, 2015; MacLeod & Ney, 2010).
Barriers of PKU Diet

In order to decrease the risk of the developing nutrient deficiencies and neurological dysfunction, individuals with PKU are required to follow strict dietary guidelines (Hafid & Christodoulou, 2015; MacLeod & Ney, 2010; Vockley et al., 2014). However, managing the dietary treatment of PKU is very challenging. There are multiple barriers to overcome in order to successfully achieve and maintain proper dietary treatment including compliance issues, high cost of medical foods, and seemingly inadequate insurance coverage (National Organization for Rare Disorders [NORD], 2015; Berry et al., 2013a; Berry et al., 2013b; Camp, Lloyd-Puryear, & Huntington, 2012; Hafid & Christodoulou, 2015; Huntington & Buist, 2009; MacLeod & Ney, 2010; Weaver et al., 2010). These barriers are especially difficult for adult patients with PKU (Berry et al., 2013a; Berry et al., 2013b; Hanley, 2004; MacLeod, & Ney, 2010; Schuett, Gurda, Brown, 1980).

Compliance Issues. Compliance with the prescribed dietary treatment is extremely important in order to avoid any cognitive or nutrient deficits. Dietary compliance starts with learning management skills and responsibilities and implementing these practices at a young age. However, children often face challenges with compliance as they grow older due to peer influences, independence of food selection, and developed taste preferences (MacLeod & Ney, 2010). The three main reasons for noncompliance in individuals with PKU include age of maintaining dietary treatment, palatability, and social influences.

Children with poor management skills experience greater challenges complying with dietary restrictions through adulthood. MacLeod and Ney (2010) describe how
challenging it can be for adults trying to re-establish the low phenylalanine diet after periods of noncompliance. Since an adult with PKU does not show physical symptoms or an immediate reaction the same way someone with a food allergy does, the primary cause for discontinuing the diet was decreased motivation (MacLeod and Ney, 2010; Schuett, Gurda, & Brown, 1980). While noncompliance during adulthood may not cause irreversible damage the same way it does during childhood, it does still cause neurological problems including irritability, increased incidence of anxiety and depression, difficulty concentrating, and headaches (Brumm & Grant, 2010; Jahja et al., 2016; Hafid & Christodoulou, 2015; MacLeod & Ney, 2010; Vockley, 2014).

Adults who have experienced long-term noncompliance are more likely to be born before 1970. Schuett, Gurda, & Brown conducted a study in 1980 that examined the diet discontinuation policies and practices of PKU clinics in the U.S. The results indicated that policies of PKU clinics varied widely across the country. Recommendations included that children over the age of 10 stop dietary treatment altogether (Schuett, Gurda, & Brown, 1980). For patients who grew up believing that treatment cessation was acceptable, reinstituting the low phenylalanine diet is even more difficult (MacLeod & Ney, 2010).

Another reason for noncompliance is the palatability of the diet (Hafid & Christodoulou, 2015; van Calcar & Ney, 2012). The synthetic amino acid medical formula is a challenge for some patients to consume due to the taste of the products. MacDonald (2000) reported that 20% of adult patients had stopped consuming the prescribed protein substitute, but were still following a low phenylalanine diet. Multiple studies have shown low levels of acceptability for the prescribed protein substitutes,
especially among adults (Kemper, Brewer, & Singh, 2010; MacDonald, 2000). Kemper, Brewer, & Singh (2010) conducted a study evaluating the perspectives of dietary adherence among women with inborn errors of metabolism and identified common themes of barriers to dietary adherence such as taste, social isolation, and expense. Results indicated participants reporting decreased acceptance of taste and smell of the medical formulas and modified low-protein foods (Kemper, Brewer, & Singh, 2010).

New products have been created in order to help improve the taste, thus increasing diet acceptance (van Calcar and Ney, 2012). Medical formulas now come in a variety of brands and flavors. Alternative medical protein products such as bars, tablets, capsules, gels, and other flavored powders and beverages have been introduced into the diet as well. GMP products were evaluated based on appearance, odor, taste, texture, and overall acceptability with scores indicating positive responses. “Ten of 11 subjects believed the GMP foods were better tasting and added variety to the low phenylalanine diet compared with their usual amino acid formula” (van Calcar & Ney, 2012, p. 6). Alternative medical protein products are proving to be even more beneficial for adults because the daily consumption of formula in place of food has shown to be challenging for patients as they age (van Calcar & Ney, 2012).

Mealtimes are another challenge for compliance with the diet (MacDonald, 2000). Individuals with PKU cannot eat a majority of food included in a typical American diet. Dining at restaurants is even more challenging due to the limited menu options. French fries, baked potatoes, salad, and other side vegetables may be the only options individuals with PKU can choose from. Depending on the individual’s confidence or beliefs about the diet, having such restrictions can cause feelings of isolation or “being different”
Modified low-protein medical foods not only provide nutritional support, but can offer the sense of inclusion. Individuals would be able to enjoy bread, pastas, baked goods, meat alternatives, and other substitute foods with the rest of their families and friends (Cochrane, Schwahn, Galloway, Robinson, & Gerasimidis, 2014; MacDonald, 2000). Kemper, Brewer, and Singh (2009) found that patients with inborn errors or metabolism appreciated having low-protein medical foods during social gatherings and around other peers. Cochrane et al (2014) conducted a study exploring patient’s beliefs and acceptability of modified low-protein medical foods and found that 78% of adult patients reported using low-protein foods to add variety in their diet and 74% of adult patients reported that using low-protein foods helped satisfy their appetite. Medical foods are not only used to provide adequate nutrition, but have been proven to help overcome compliance issues with the extremely strict dietary treatment of PKU. However, access to medical foods is challenging for most patients, and is even harder for adults to obtain due to increased cost and lack of insurance coverage.

**Cost of Medical Foods.** The cost of medical foods causes a financial burden on most individuals and families with PKU. Huntington & Buist (2009) estimated the average annual cost of medical formula increases from $2,275 during infancy to $12,483 at the age of 18. This is an average cost of about $7,100 per year and $220,000 from infancy through the age of 24 years, which does not include the cost of alternative protein products or modified low-protein medical foods. Medical formula is not easily affordable as the wholesale cost is about 30% higher than the retail cost of regular infant formula (Huntington & Buist, 2009). This is an issue because most non-PKU families stop purchasing infant formula after about 6 months to 2 years of age, whereas families and
patients with PKU need medical formula for their entire life. The continuous increase in cost of medical formula is hindering for patients as they get older and adds greater stress for compliance as they are already faced with other additional barriers.

According to Huntington and Buist (2009), the use of low-protein medical foods is necessary to include in the PKU diet as a source of energy because the amino acid products, i.e. medical formulas, are the most expensive products and too costly to be used as the main energy source. Using medical formula as the primary energy source was calculated to cost 170% more than the use of low-protein medical foods combined with the medical formula, which is a difference of more than $8,000 per year (Huntington & Buist, 2009). However, modified low-protein medical foods are also expensive, with these low-protein food products costing anywhere from 2 to 8 times more than the retail cost of the regular counterpart food items. For example, the retail cost of spaghetti is $0.37 per 100 grams and the wholesale cost of low-protein pasta is $2.20 per 100 grams (Huntington & Buist, 2009). The cost of low-protein medical foods is also going to cost more than regular food items due to supply and demand. There are only 16,445 patients in the United States requiring low-protein medical foods, which results in a significant markup of cost.

Since the demand for low-protein food items is so low, these products are often not supplied in commercial grocery stores, leaving families and individuals no choice but to make purchases through third-party companies and pharmacies, further increasing the cost (Camp, Lloyd-Purdyear, & Huntington, 2012; Huntington & Buist, 2009). Retail prices are higher than wholesale prices, and pharmacies typically add a markup of 200% to 300% of wholesale cost (Camp, Lloyd-Purdyear, & Huntington, 2012; Huntington &
Furthermore, most third-party companies are online stores with policies requiring a minimum cost of purchase (Cambrooke Therapeutics, 2016). For example, Cambrooke Therapeutics, a popular PKU food distributor, requires a minimum purchase of $50 for any cold shipped items and a minimum of $30 for any dry shipped items. After making that minimum purchase, shipping rates ranging anywhere from $40-$50 still apply (Cambrooke Therapeutics, 2016).

**Inadequacies of Health Care Coverage.** The high cost of medical foods is of significant concern because unlike most treatments or prescriptions, PKU medical foods are not adequately covered by health insurance, leaving most patients and families to pay out-of-pocket (Berry et al., 2013a; Berry et al., 2013b; Camp, Lloyd-Puryear, & Huntington, 2012; Huntington & Buist, 2009; Kemper, Brewer, & Singh, 2010; Weaver et al., 2010). Berry et al. (2013b) found that 60% of parents with children of inborn errors of metabolism paid for modified low-protein foods out-of-pocket, with 48% paying more than $100 per month and 5% paying more than $500 per month.

One of the main problems contributing to lack of health care coverage for patients with PKU is the way medical foods are defined. The Food and Drug Administration (FDA) defines a medical food as “a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements based on recognized scientific principles are established by medical evaluation” (section 5(b) of the Orphan Drug Act [2] U.S.C 360ee (b) (3))). This definition is inadequate because it describes medical food closer to that of general food than that of a prescription or treatment. According to Weaver et al. (2010), the FDA
could not define medical foods as pharmaceutical agents because the population of disorders treated by medical foods was too small to perform clinical trials, in part due to ethical considerations. Since, by the FDA’s definition, medical foods are not considered pharmaceutical agents, there is no need for a doctor’s prescription, which is one reason insurance companies are not required to provide reimbursement or coverage (Weaver et al., 2010).

Language is also an issue regarding state policies and mandates. State policies and mandates are put in place to ensure that health care needs are being met. “The main themes addressed in the laws include (1) who is responsible for covering the individual (e.g. health insurance, health department, or state funds), (2) what disorder(s) is/are covered, (3) the benefit limit of what is covered, (4) whether the medical food must be order by a physician, (5) until what age the coverage is applicable, (6) whether deductibles and copayments are applicable, and (7) income eligibility requirements for public programs” (Weaver et al., 2010, p. 366). State policies and mandates are different across the country though with some states using specific terms and definitions, while other states using broader terms and definitions. Due to the variability of coverage, some states provide different coverage than others and even families within the same state may receive different coverage (Huntington & Buist, 2009; Weaver et al., 2010).

The administrative language used for coding health services is also inadequate. Insurance companies evaluate reimbursement eligibility based on a system of coding. PKU would be classified under inborn errors of metabolism, but there are no classified codes for this category of disorders (Huntington & Buist, 2009). B codes and S codes are used as replacement codes, however, they do not properly define the products and
services utilized. The three types of B codes specify administration of medical foods enterally (Huntington & Buist, 2009). Unless a patient with PKU has a specific need for enteral or parenteral tube feedings, medical foods are consumed orally. The two S codes used are more appropriate in definition, but can only be successfully used in a small number of states because certain providers don’t recognize it for reimbursement (Huntington & Buist, 2009). This aligns with the variability of language with state policies and mandates.

Medicare, ERISA, and TRICARE regulations impact state mandates that decrease eligibility status for health care coverage. Most patients with PKU consume medical foods orally, unless required otherwise as directed by a physician, and Medicare does not provide coverage for enteral solutions (e.g. medical formula) unless administered enterally. ERISA is an act that abolished state regulation of employee benefit plans through self-insured employers (Huntington and Buist, 2009). Employment-based health plans provide private insurance coverage and because of ERISA, these plans are exempt from state insurance laws. TRICARE is a federal insurance program provided for U.S. Armed Forces military personnel and military retirees that is also exempt from state insurance laws, but this year a bill was passed from the House to includes the use of medical foods for treatment and management of rare disorders, including PKU (National PKU Alliance, 2016b). The passing of this bill will help raise awareness to other insurance providers about the importance of coverage of medical foods for patients with PKU and other inborn errors of metabolism.

Access to health care coverage for adults with PKU is especially difficult because state and private insurance companies usually have a designated age cutoff at 18 to 21
years of age (Berry et al., 2013b; Hanley, 2004; Huntington & Buist, 2009; Weaver et al., 2010). Berry et al. (2013a) examined the mandated coverage of treatment for adults with PKU by state and found only 8 states provided coverage for medical formula. Twenty-five states covered medical formula and low-protein medical foods and 1 state covered the use of low-protein medical foods only (Berry et al., 2013a). Six states only had pediatric mandates in place and of those 6 states, 1 state indicated a cutoff age of 24 years. Overall, 18 states did not include mandates about health care coverage for adults with PKU and 30 states did have mandates in place (Berry et al., 2013a). However, even with state mandates in place for adult health care coverage, the variability of language used in creating these policies may deny adults eligibility for coverage or reimbursement (Berry et al., 2013a; Huntington & Buist, 2009; Weaver et al., 2010).

Quality access to and health care coverage of medical foods is important for the management of PKU. Kemper, Brewer, & Singh (2010) found that women with inborn errors of metabolism indicated that lack of insurance coverage led to compliance issues. Without insurance coverage for medical foods, participants reported not having adequate access to food and thus, would be tempted to eat foods higher in protein that were more readily available.

Conclusion

In summary, compliance with the diet, cost of medical foods, and inadequate health care coverage are all barriers associated with managing the dietary treatment of PKU as an adult. Medical foods help support dietary adherence due to improving taste, palatability, and sense of social inclusion and acceptance (Hafid & Christodoulou, 2015; Kemper, Brewer, & Singh, 2010; MacDonald, 2000; van Calcar & Ney, 2012). The cost
of medical foods is extremely expensive compared to the cost of regular foods and there is a lack of health care coverage for most adults, which restricts access to necessary treatment (Berry et al., 2013a; Berry et al., 2013b; Camp, Lloyd-Puryear, & Huntington, 2012; Huntington & Buist, 2009; Kemper, Brewer, & Singh, 2010; Weaver et al., 2010). The inadequate access to medical foods dangerously hinders dietary compliance and leads to other health complications such as nutrient deficiencies and neurological problems, further solidifying the need to address these financial burdens associated with managing PKU dietary needs as an adult (Brumm & Grant, 2010; Jahja et al., 2016; Hafid & Christodoulou, 2015; MacLeod & Ney, 2010; Vockely, 2014).
Chapter 3

Methodology

The purpose of this study was to identify the financial burdens associated with purchasing medical foods and the impact this has on the dietary management of adults with PKU. Four research questions guided this research study:

1. What were the financial responsibilities associated with managing the treatment of an adult with PKU in regard to purchasing medical foods?

2. To what extent does the state of residence, in regard to purchasing medical foods, influence the financial responsibilities associated with managing the treatment of an adult with PKU?

3. To what extent does the purchase site of the medical foods influence the financial responsibilities associated with managing the treatment of an adult with PKU?

4. To what extent do the financial responsibilities, in regard to purchasing medical foods, for the patient managing the treatment of PKU impact their dietary management? If so, how?

Research Design

The design of this study was a mixed method, non-experimental, survey design using an online questionnaire to identify different financial barriers associated with the cost, PKU treatment modalities and how identified barriers affect the management of the medical nutrition therapy in adults with PKU. Currently there are no standards for health care coverage and each state has its own mandates about providing insurance coverage, reimbursement, and any other type of financial assistance (NORD, 2015). Missouri and Illinois are two states that offer different financial assistance for those diagnosed with
PKU, which is why the financial barriers for adult with PKU were examined in both Missouri and Illinois. Permission to conduct this study was obtained from Eastern Illinois University Institutional Review Board (IRB number 16-127).

Sample

A non-probability, purposive sample was used due to the focus of this study evaluating individuals with PKU. The original sample size was intended to be between 50 and 100 participants in total from both Missouri and Illinois. There are currently no reports indicating the population of adult PKU patients per state, so this was a very rough estimate of how many adults with PKU might participate.

Recruitment. Recruitment of prospective subjects first started with recruiting participation from registered dietitians and board members (point persons) from PKU organizations and clinics in Missouri and Illinois. Due to HIPPA laws, point person participation was vital in order to send out the survey to PKU patients. Point persons from the NPKUA, the PKU Organization of Illinois, the University of Illinois at Chicago Medical Center, RUSH Hospital, Lurie Children's Memorial Hospital, St. Louis Children's Hospital, SSM Health Cardinal Glennon Children's Hospital, and the University of Missouri Health Care were contacted via email by the researcher explaining the purpose of the study and the importance of participation. Each hospital selected has a known PKU clinic, and the organizations listed are widely known community organizations involved in supporting families and individuals with PKU. Due to the small population of adults with PKU, a point person from the University of Iowa Hospitals and Clinics was also recruited to establish a sample for a pilot study. Establishing point
person participation required IRB approval from both the Eastern Illinois University and the participating hospital.

Recruitment of prospective subjects occurred after participation of point persons were confirmed. An email was distributed to each participating point person that was to be forwarded to patients and members of hospitals and organizations. The email invited anyone with PKU who was 18 years of age or older to take the anonymous survey. The email included how this study could benefit participants directly, included a link to the online questionnaire, and listed contact information for anyone that had questions or concerns about the study or survey. Participants were excluded from the study if they were not from Missouri or Illinois, and if they were a parent of a child with PKU.

**Instrumentation**

The data collection instrument was an anonymous online questionnaire survey. The questionnaire was adapted from an existing questionnaire survey that was used in a study called, “Insurance coverage of medical foods for treatment of inherited metabolic disorders”, created by Berry et al. (2013b). The questionnaire survey from Berry et al. (2013b) was developed in four different regions of the nation and then piloted in two centers in different regions. Family focus groups were held and the questions were refined based on provided feedback. A medical food reference list was also included in the survey to aid in responding to questions (Berry et al., 2013b). The validity and reliability of this tool was not discussed in the research article, nor was it disclosed to the researcher.

Modifications were made to the pre-existing questionnaire in order to meet the needs of this study. A Likert-type scale was included in the questionnaire in order to
evaluate the individual's perception of the financial burdens related to purchasing medical foods, with the medical food reference list not included based on the purposes of this study. Once the questionnaire was completed, a committee of three professors reviewed the instrument to ensure face validity. Reliability was not determined.

Upon opening the link to the survey, individuals were prompted with information about consent to participate in the study before proceeding to the questions. Participants were reminded that the survey was anonymous and advised them of any potential discomfort that may arise due to the personal nature of the questions. If individuals agreed with the terms of informed consent, they could choose to continue to the following questions within the survey. If individuals did not agree with the terms of participation, they were given the opportunity to leave the survey by exiting out of the browser. Participants were also given the option to withdrawal from the study at any point and confirmed that answers were not saved or utilized until completion of the study was submitted.

Within the survey (see Appendix A), the three different types of medical foods (i.e. medical formula, alternative medical protein products, and low-protein medical foods) were defined for participants. This was important to establish because every state has a varying definition for the term medical food, which overall affects the type of coverage provided (NORD, 2015). Each question was specific about the type of medical food.

The survey consisted of six questions divided into three sections labeled A, B, and C. Section A examined the participants' source of medical foods. The first question verified state of residence and the second question assessed purchase site of medical
foods. Section B included questions pertaining to the payment of medical foods such as how products are paid for, how much insurance pays and how much participants pay out-of-pocket. Lastly, Section C included a Likert-type scale evaluating participants' perceptions about their health care coverage and dietary management. At the end of the questionnaire, space was provided for participants to leave additional comments about the survey or their personal experiences with health care coverage for the treatment of PKU.

**Pilot Study**

A pilot study was conducted for this research in December 2016 using Qualtrics. The purpose of the pilot study was to evaluate the duration of the study, and the clarity and readability of the questions. After the final question of the survey, participants were redirected to questions about completion the survey. Face validity of the pilot study questions were reviewed by a committee of three professors. Reliability was not determined. If participants did not agree that the survey was clearly written or easy to understand, they were prompted with follow-up questions indicating which questions were an issue. There was also additional space for participants to leave comments or suggestions about clarification of instructions or improvement of format of the survey. The survey was piloted with five patients from the University of Iowa Hospitals and Clinics. The survey reportedly took patients about five to ten minutes to complete. All five patients agreed that the survey was clearly written and easy to understand. Only one participant made suggestions and adjustments were made accordingly.

**Data Collection**

Of the eight PKU organizations and clinics, three agreed to participate in this study. Data collection occurred over the span of two weeks, however, the survey was
opened at three separate occasions to accommodate to the needs of the point persons regarding IRB approval from their facility. The survey was first opened to patients at Cardinal Glennon Children's Hospital in December 2016. The second opening of the survey occurred between January and February 2017 for patients at Lurie Children's Memorial Hospital. The third and final opening of the survey was in February 2017 for members of the PKU Organization of Illinois. The survey was opened over a two-week time frame to ensure potential participants had enough time to receive the invitation email and complete the survey.

First, the invitation email was sent to the point person the night before the survey opened. Point persons were then able to distribute the invitation email to their adult patients and members. After one week of opening the online survey, a follow-up email was sent to the point person from each organization and hospital asking to forward reminders about participation in the survey. A final follow-up email was sent as another reminder for participation in the survey 24 hours before closing the survey. At the end of the two weeks from the final survey opening, the researcher assessed each participant's response to the questionnaire.

**Data Analysis**

Data were analyzed using basic descriptive statistics, which was achieved through reports from Qualtrics. Data were exported from Qualtrics and imported into Microsoft Excel. Responses to questions in sections A and B were analyzed using a measure of frequencies and percentage statistics. Data from survey item 5 was not reported due to the number of null responses. Responses to questions in section C were based on a Likert-type scale and were analyzed by a mean of the responses to each question. At the end of
the questionnaire there was space for participants to leave additional comments regarding their thoughts and opinions. Any additional comments were analyzed comprehensively in order to determine main themes from each response.
Chapter 4

Results and Discussion

The purpose of this study was to identify the financial burdens associated with purchasing medical foods and the impact this has on the dietary management of adults with PKU. An online questionnaire including six questions and Likert-type scale was used to evaluate the financial barriers and responsibilities of adults with PKU.

Participation

Of the eight PKU organizations and hospitals that were sent email invitations, three agreed to participate in the study and shared the survey link to their patients and members. Cardinal Glennon Children’s Hospital represented individuals in Missouri, and Lurie Children’s Memorial Hospital and the PKU Organization of Illinois represented individuals in Illinois. The number of adult PKU patients and members of each hospital and organization is unknown, however, a total of 45 responses were recorded. Of the 45 responses, 24 participants completed the survey. After reviewing the completed surveys, 7 were excluded based on eligibility criteria. If participants did not reside in Illinois or Missouri, and/or was not an adult patient with PKU (i.e. a parent of a child with PKU), the survey response was excluded. A total of 17 surveys were left for review in this study. A small sample was anticipated for this study due to the population of adults with PKU. However, the reason for this unanticipated sample size was due to participation. The point person from the University of Illinois at Chicago Medical Center reported most adult patients from their clinic was involved in the PKU Organization of Illinois. Since IRB approval was not necessary from this organization, the point person explained it would be easier to send out the survey through this organization rather than wait for their
hospital’s IRB approval process. Other reasons for lack of participation from point persons included the inability to obtain IRB approval from their hospital, no response to the email invitation, and new procedures being established for contacting patients about research.

After reviewing number of responses from both Missouri and Illinois, only 1 response survey was completed from Missouri. The shortage of Missouri responses resulted in a change of design for the study. Given the ratio of responses from Missouri and Illinois, a state comparison of financial barriers and responsibilities of adult patients with PKU was unattainable. The single Missouri response was excluded from the study and responses only from surveys in Illinois were used to answer the research questions that guided this study. The final number of survey responses included in this study was 16.

**Research Questions Analysis**

**Research Question 1: What are the financial responsibilities associated with managing the treatment of an adult PKU patient in regard to purchasing medical foods?** In each survey item medical food was categorized into medical formula, alternative medical protein products, and modified low-protein foods. Survey item 3 identified how medical foods were paid for. Figure 1 shows all reported payment sources for each medical food. Individuals responded with multiple payment sources depending on the product being purchased. A state insurance program/Medicaid was most often reported as the payment method for medical formula (44%), whereas private insurance rarely contributed to coverage of medical formula (6%). Fifty percent of responses consisted of “Does not apply”, “I don’t know”, and “Other” for medical formula. Little
coverage was provided for alternative medical protein products and modified low-protein foods leaving individuals paying out-of-pocket (50, and 80% of reported sources, respectively).

**Figure 1.** Payment Sources of Medical Foods. This figure illustrates the percentage of reported payment sources used for obtaining medical foods.

Survey item 4 asked individuals to identify how much they pay out-of-pocket per month for medical foods, which is illustrated in Figure 2. Eighty-one percent of individuals spent $0 on medical formula and the remaining 19% responded as “Does not apply” or “I don’t know”. Eighty-one percent of adults paying $0 on medical formula was expected given the Illinois state mandates. Individuals purchasing alternative medical protein products (38%) and modified low-protein foods (50%) reportedly spend
greater than $100, but less than $500 per month on medical food. This result was expected since state mandates only require coverage of medical formula (NORD, 2015). Additionally, there was consistency in reports from another study identifying 60% of families with children of inherited metabolic disorders paid out-of-pocket for access to modified low-protein foods (Berry et al., 2013b). While this study was conducted on a national level, assessing coverage from most states, it is still representative of the lack of coverage for low-protein medical foods.

Figure 2. Out-of-pocket Payment of Medical Foods. This figure illustrates the percentage of reported out-of-pocket expenses per month used for obtaining medical foods.
Survey item 5 was intended to describe the amount of coverage provided for medical foods, but this data was not analyzed due to the number of null responses.

Research Question 2: To what extent does the state of residence, in regard to purchasing medical foods, influence the financial responsibilities associated with managing the treatment of an adult PKU patient? Due to a lack of participation from individuals living in Missouri, state of residence was not used to compare financial responsibilities associated with managing the treatment of an adult PKU patient. Instead, results from the state of Illinois were analyzed to describe the different financial components of managing the dietary treatment of PKU. Based on current state mandates, researchers hypothesized that adults living in Missouri would have less state and private insurance coverage, and would be required to pay for medical foods out-of-pocket or through other financial assistance programs (NORD, 2015).

Research Question 3: To what extent does the purchase site of the medical foods influence the financial responsibilities associated with managing the treatment of an adult PKU patient? Figure 3 shows all reported purchase sites of medical foods. Individuals reported obtaining medical foods from a variety of sources. Some individuals had to use multiple purchase sites depending on the type of medical food being purchased. Of the 16 participants, 25 responses for purchase sites of modified low-protein foods were identified. Individuals mainly purchased modified low-protein foods from internet sources (44%). The remaining purchases took place from the manufacturer (16%) and/or a health food store (24%). Similarly, Berry et al., (2013b) identified 41% of families purchasing modified low-protein foods from online stores, 16% from health food stores, and 14% from manufacturers.
Individuals who did not respond "Does not apply", "I don't know", or "Other", identified the state or county health department as their source of medical formula (69%), which is consistent with previous responses of participants reporting having state coverage and spending $0 for medical formula. Adults using alternative medical protein products reportedly used a variety of purchase sites including online stores (29%), the state or county health department (21%), pharmacy (7%), manufacturer (7%), and a health food store (7%).

Figure 3. Purchase Site of Medical Foods. This figure illustrates the percentage of reported purchase sites used for obtaining various medical foods.
Research Question 4: To what extent do the financial responsibilities, in regard to purchasing medical foods, for the patient managing the treatment of PKU impact their dietary management? If so, how? A Likert-type scale was used to assess individuals’ varying degrees of agreement or disagreement with statements presented regarding health care coverage and how access to medical foods may impact their dietary management. Figure 4 summarizes the responses in terms of agreement, neutral, and disagreement. Of the 16 participants, 10 agreed to purchasing medical food. Ninety-four percent of participants agreed that medical food is expensive and 44% reported that medical food is easy to purchase. A total of 84% of participants agreed that the cost of medical food and lack of health care coverage is a challenge to purchasing medical food, while 0% agreed to having adequate health care coverage of medical foods.

This is an interesting perception given that most adults using medical formula receive coverage from the state and pay $0 out-of-pocket. Patients need access and coverage to modified low-protein products and alternative protein products, in addition to medical formula (Hafid & Christodoulou, 2015; MacDonald, 2000; MacLeod & Ney, 2010). Providing coverage for only 1/3 of patient’s treatment is not adequate. Lastly, 14 participants agreed that compliance with dietary management would increase if there was better access to medical foods. Kemper, Brewer, & Singh (2010) conducted a qualitative study evaluating the attitudes and beliefs of women with PKU and a common theme discussed was about inadequate insurance coverage regarding dietary adherence. A majority of participants agreed that lack of insurance coverage and cost of medical foods is an issue impacting their dietary compliance.
If cost of medical foods were not a factor, I would be more compliant with my diet.

Medical food helps satisfy my appetite.

Access to medical food improves compliance with my dietary...

I feel like I have adequate health care coverage for medical food.

The lack of health care coverage makes it challenging to purchase medical food.

The cost of medical food makes it challenging to purchase medical food.

The cost of medical food is expensive.

It is easy to purchase medical food.

I regularly purchase medical food.

Figure 4. Health Care Coverage of Medical Foods and Impact on Dietary Management.
Chapter 5

Summary, Conclusions, and Implications

Summary

The purpose of this study was to identify the financial burdens associated with purchasing medical foods and the impact this has on the dietary management of adults with PKU. Research questions were written to identify the financial responsibilities of purchasing medical foods and whether the state of residence or purchase site influences the financial responsibilities. The fourth question examined if and how one’s financial responsibilities impacted their management of dietary treatment. The study was a mixed-method, non-experimental, survey design using an online questionnaire to collect data. Forty-five participants responded to the survey and only 24 participants completed the survey. The study had a lack of participation from patients living in Missouri, resulting in examining financial burdens from residents of Illinois only. Responses from participants living in Illinois that also met the inclusion criteria resulted in a sample size of 16 participants.

Data analysis showed that reported financial barriers associated with purchasing medical foods from adult patients living in Illinois aligned with the state mandated coverage (NORD, 2015). There was no comparison of financial responsibilities from patients living in Illinois and Missouri, which would have been beneficial to illustrate differences in coverage and out-of-pocket expenses. Regardless of state coverage of certain medical foods from Illinois, the analysis also indicated that participants believe there is a lack of health care coverage for medical foods, the cost of medical food is expensive, and improved access could help with dietary compliance. Overall, these
results demonstrate that while adult patients living in Illinois have insurance coverage for certain medical foods, individuals still find inadequacies with health care coverage, which has effects on dietary compliance. Future studies need to compare insurance coverage and out-of-pocket expenses of medical foods for adults with PKU living in different states, as well as patients’ perspective on compliance to dietary treatment associated with access to medical foods.

**Conclusions**

Results of this study showed the financial responsibilities associated with managing the treatment of an adult with PKU, however, result were inconclusive regarding a comparison of financial responsibilities depending on the state of residence.

**Research Question 1: What are the financial responsibilities associated with managing the treatment of an adult PKU patient in regard to purchasing medical foods?**

Most adult patients with PKU, living in the state of Illinois, who are using medical foods for treatment of PKU, use a state insurance program/Medicaid to pay for medical formula, resulting in a $0 per month out-of-pocket expenditure. On the contrary, adult patients receive no coverage or financial assistance, and pay out-of-pocket for modified low-protein foods and alternative medical protein products. On average, an adult patient will pay out-of-pocket greater than $100, but less than $500 per month for modified low-protein foods and alternate medical protein products. The amount of coverage that is provided for medical foods is unknown due to number of null responses.

**Research Question 2: To what extent does the state of residence, in regard to purchasing medical foods, influence the financial responsibilities associated**
with managing the treatment of an adult PKU patient?

This research question was not able to produce results as only 1 participant completed the survey from Missouri a comparison of financial responsibilities between states was inconclusive.

Research Question 3: To what extent does the purchase site of the medical foods influence the financial responsibilities associated with managing the treatment of an adult PKU patient?

Most patients using medical formula receive their product from the state or county health department, which is expected since medical formula is covered through a state insurance program/Medicaid. However, the purchase site for alternative medical protein products and modified low-protein foods is variable. Of the adults using these products, online stores were most often used as a purchasing site.

Research Question 4: To what extent do the financial responsibilities, in regard to purchasing medical foods, for the patient managing the treatment of PKU impact their dietary management? If so, how?

More than half of the participants regularly purchase medical food and less than half find it easy to purchase medical food. Almost all patients agreed that the cost of medical food is expensive and that this makes it challenge to purchase medical food. Additionally, patients agreed that the lack of health care coverage for medical foods creates a barrier for purchasing medical food. Lastly, most patients agreed that access and cost of medical foods contributed to whether patients were compliant with their diet.
Limitations

Several limitations were identified throughout this research study. The sample size consisted of 16 adults diagnosed with PKU. Although, this sample size was unavoidable given that the population of individuals diagnosed with PKU is about 20,000 in the United States. This number significantly decreases when discussing only adult patients 18 years and older. Furthermore, not all adult patients are receiving care or treatment and that population is unknown, which leads into the second limitation of this study.

Adults with PKU who were contacted to participate in this study were either patients of a clinic, being followed by a health care team, or were members of PKU community organizations. This creates a bias within the sample suggesting that only adults with PKU receiving treatment were recruited. Input from adults with PKU who are not receiving support, treatment, financial assistance or any other aid would have given more generalized responses for the PKU population. Inclusion of these individuals could have been achieved through online forums or social media networks such as Facebook.

Another limitation was the design of the questionnaire survey. One question asked about participant’s state of residence for the purpose of answering research question 2, but it also verified participants’ residence for inclusion in the study. There was no question verifying the age of participants or the status of their diagnosis (i.e. “I have PKU” versus “I am a parent of a child with PKU”). Initially these questions were thought to be unnecessary given the invitation email and informed consent message stated the inclusion criteria for potential subjects to take the survey. However, after review of survey responses, two surveys had comments about personal experiences dealing with
inadequate health care coverage. Within the responses, each participant verified that he or she was a parent of a child with PKU. There is no way of knowing whether the 16 participants in this study were all adults diagnosed with PKU. This would have made an even bigger difference if data were collected and analyzed from individuals living in Missouri because age limits are set on coverage mandates.

In order to accommodate to the needs of point persons, the survey was opened at three different points. This was a limitation because individuals invited to take the survey had access to the survey at each point the survey was opened; the survey link stayed the same. This would have created a bias in length of time individuals had to complete the survey. Additionally, the different time frames the survey was opened was a limitation. The first survey opening was in December during the holidays and this could have generated a low response rate, whereas opening the survey in February may have been a time when people were checking their email more frequently. There was not an equal chance for participation response indicating this study could have resulted in more or less participants than the actual sample size.

A final limitation in this study is personal bias. The researcher is an adult PKU patient who has been struggling with access, coverage, and cost of medical foods personally her whole life. To counter this bias, the researcher remained as objective as possible while conducting this study.

**Implications and Recommendations**

The results of this study did not fully answer the guided research questions regarding differentiating financial responsibilities between states. However, this is important in order to understand the variability of health care coverage, cost of medical
foods, and of out-of-pocket expenses adults with PKU are responsible for with the management of their dietary treatment. Reaching out to hospitals, clinics, and other PKU organizations is a great way to recruit participation, but utilizing other PKU forums and informal Facebook groups would be recommended for future studies in order to obtain a more generalized sample of the population.

More research is continually emerging regarding cost of medical foods, insurance coverage and state policies, but it is important to investigate the impact this has on the individual. Compliance with dietary management is often low in adults with PKU, and it is important to determine if financial responsibilities have any effect on compliance. This study showed positive results from patients agreeing that there is a lack of health care coverage for medical foods and compliance would improve if cost was not an issue. This needs to be investigated further to determine how coverage or financial assistance could help with dietary compliance. Furthermore, studies demonstrating how patients' dietary management and compliance are affected are essential to show that there is a need for treatment coverage across the country for all ages.

In a study conducted by Berry et al. (2013b), authors pointed out the importance of researching the financial barriers to access of medical foods for adults with PKU and other inherited disorders. This study aimed to investigate that need. However, further research is needed to continue investigating adult patient barriers to medical foods across the country.
References


http://dx.doi.org/10.1097/gim.0b013e3182141b48


http://dx.doi.org/10.1038/ejcn.2013.218v


http://dx.doi.org/10.1016/j.jand.2012.05.004


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http://dx.doi.org/10.1038/gim.2012.173

Appendix A

Insurance Coverage for Medical Foods Questionnaire Survey

Please read each statement carefully and answer the questions to the best of your ability.

For some questions, more than one answer is appropriate. There are no correct or incorrect answers. The survey should take about 10-15 minutes to complete.

Section A: Source of Medical Foods

1. What is your state of residence?
   a. __________________

2. Where do you get your medical foods: medical formula, alternate medical protein products, and modified low-protein foods? Check all that apply.

   Medical Formula = medical food in the form of a liquid or powder that provides essential nutrients and amino acids free of phenylalanine (e.g. Glyactin BetterMilk, Glyactin RESTORE, Vitaflo Cooler 10, PhenylAde 60, Lophelix LQ, etc.).

   Alternate Medical Protein Products = medical food in the form of drink mixes, beverages, bars, capsules, tablets, and gels that provide small amounts of phenylalanine or phenylalanine-free protein along with other essential nutrients and/or amino acids (e.g. Glyactin COMPLETE bars, Phleyx-10 Tablets, PhenylAde PheBLOC, etc.).
Modified Low-Protein Foods = medical food products in the form of baking mixes, pastas, rice, and premade items that are designed to be similar to their normal counterparts, but supply very low amounts of phenylalanine.

<table>
<thead>
<tr>
<th></th>
<th>Medical Formula</th>
<th>Alternate Medical Protein Products</th>
<th>Modified Low-Protein Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>State or county health department</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internet source</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manufacturer (for example, Mead Johnson)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home health care company</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health food store</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital/clinic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I do not know</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other: __________</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Section B: Payment of Medical Foods

3. How are your medical foods: medical formula, alternate medical protein products, and modified low-protein products paid for? Check all that apply.
<table>
<thead>
<tr>
<th>Medical Formula</th>
<th>Alternate Medical Protein Products</th>
<th>Modified Low-Protein Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>State insurance program / Medicaid/MA</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>State insurance program health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintenance organization / Medicaid HMO/MA HMO</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Private insurance (ex. CBS and AETNA) that was NOT paid for by your state</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Private health maintenance organization /HMO (for example: BlueCross Blue Shield, Kaiser Permanente) that was NOT paid for by your state</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Medigap</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Military/Veterans program (ex. TriCare, CHAMPUS, or CHAMP-VA)</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Indian Health Service</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>WIC</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Out-of-pocket</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>I do not have health care coverage</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Does not apply</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>I do not know</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>
4. How much do **YOU** pay per **MONTH** for medical foods including: medical formula, alternate medical protein products, and modified low-protein foods? Include out-of-pocket payments and insurance co-payments. **DO NOT include health insurance premiums or costs that are covered by insurance or another source.**

<table>
<thead>
<tr>
<th></th>
<th>Medical Formula</th>
<th>Alternate Medical Protein Products</th>
<th>Modified Low-Protein Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>$0 per month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than $0 but less</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>than $100 per month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than $100 but</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>less than $500 per</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Between $500 and</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$1000 per month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than $1000 per</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does not apply</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I don't know</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5. How much does your **INSURANCE COMPANY** pay per **MONTH** for medical foods including: medical formula, alternate medical protein products, and modified low-protein foods?

<table>
<thead>
<tr>
<th></th>
<th>Medical Formula</th>
<th>Alternate Protein Medical Products</th>
<th>Modified Low-Protein Foods</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All of the cost</strong></td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>(write the average amount per month that your insurance covers)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Some of the cost</strong></td>
<td>$</td>
<td>$</td>
<td>$</td>
</tr>
<tr>
<td>(write the average amount per month that your insurance covers)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>None of the cost</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>I do not know</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Section C: Health Care Coverage of Medical Foods and Dietary Management**

6. Please indicate your level of agreement or disagreement with the following statements below.

<table>
<thead>
<tr>
<th></th>
<th>Strongly Disagree</th>
<th>Disagree</th>
<th>Neutral</th>
<th>Agree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.) I regularly purchase medical food.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.) It is easy to purchase medical food.</td>
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<tr>
<td></td>
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<td>---</td>
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<tr>
<td>c.) The cost of medical food is expensive.</td>
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</tr>
<tr>
<td>d.) The cost of medical food makes it challenging to purchase medical food.</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e.) The lack of health care coverage makes it challenging to purchase medical food.</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>f.) I feel like I have adequate health care coverage for medical food.</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>g.) Access to medical food improves compliance with my dietary management of PKU.</td>
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</tr>
<tr>
<td>h.) Medical food helps satisfy my appetite.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>i.) If cost of medical foods were not a factor, I would be more compliant with my diet.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This section is for any comments you may have about this survey or your experiences with health insurance paying for medical foods including: medical formula, alternate
medical protein products, and/or modified low-protein foods. Any comments you wish to share are welcome.