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Exploring and Expanding Resources for the Phenylketonuria (PKU) Population Through  
Community Survey and Recipe Testing with HowMuchPhe.org

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Exploring and Expanding Resources for the Phenylketonuria (PKU) Population Through  
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**Background:**

Phenylketonuria (PKU) is an inborn error of metabolism, inherited genetically and characterized by decreased capacity to metabolize the essential amino acid, phenylalanine (Phe). Consequently, Phe accumulates in the blood, and toxic Phe exposure to the brain ensues. Treatment for PKU requires strict adherence to a diet low in Phe and is extremely restricted in natural protein sources. Failure to treat or a delay in treatment of PKU results in irreversible neurocognitive impairment and severe developmental delay.

**Nutrition Problem of Focus:**

Normal growth and development for children and adolescents with PKU requires strict adherence to a low-protein (LP) diet. Managing the diet is often associated with mental, emotional, and financial stress for both the individual with PKU and his or her family. Challenges with PKU management include obtaining LP medical foods, tolerance of the often unpalatable nature of LP food, tracking Phe-intake throughout the day, additional cooking to accommodate both LP and non-diet portions, and preparation and consumption of a necessary Phe-free amino acid supplement multiple times per day.

**Project Description:**

HowMuchPhe.org (HMP) is an online diet-management platform for PKU, founded in an effort to support individuals and families navigating the LP diet. Its features include diet-tracking, phe-calculations for over 7000 foods, tracking and graphing of height, weight, and blood phe levels, and graphing of results for export to be shared with medical providers. The organization guides a mission to support diet adherence while promoting healthy and affordable maintenance of the PKU diet.

In light of the daily obstacles to promoting basic health as well as the threats posed by diet non-adherence, efforts to facilitate lifestyle improvements to the PKU community are important. In 2017, HMP announced its plans to merge with another instrumental PKU resource, CookForLove.org (CFL). CFL is an online resource consisting of Phe-tested, LP recipes. The site's mission is to empower individuals and families managing PKU with control over their health through the food they eat. The HMP-CFL partnership is founded in an effort to expand resources for the PKU community. The end product will be a community-driven recipe site with an expanded set of resources to build community, ease daily stressors, and promote diet adherence.

This capstone project aimed to obtain a thorough understanding of the resources presently available to the PKU community, barriers to those tools, as well as additional needs perceived by this group. By acknowledging where gaps exist, new initiatives and improvements to existing resources can be made in ways best tailored to those who will utilize and be impacted by them. The project entailed survey development and administration to 432 members of the PKU community; recipe testing, Phe-calculations, and food photography of over 50 LP recipes to be included in the new resource; and leadership of a focus group at a PKU family camp to solicit parent input to guide resource development.

**Conclusion:**

Survey administration to the online PKU community produced the following key recommendations: promote increased discussion of existing resources for PKU during metabolic clinic visits, establish partnerships between HMP and metabolic clinics to address cost of the resource as the top perceived barrier to its utilization, and include a variety of specified functions and tools within the upcoming community-driven recipe site. The new resource remains in development mode and is expected to launch in 2018. Next steps include recipe-testing completion and continued resource development, which includes implementation of the outlined recommendations to be executed by CFL, HMP, and future student projects.

## **Chapter I: Introduction**

Phenylalanine hydroxylase (PAH) deficiency, traditionally known as phenylketonuria (PKU), is an autosomal recessive inherited disorder, resulting in the accumulation of phenylalanine (Phe) in the blood of affected individuals. The *PAH* gene is located on chromosome 12, and mutations to the gene cause errors in coding for the PAH enzyme, affecting its activity level. Each individual's unique genotype predicts his or her metabolic phenotype. Disorder severity among individuals with PKU is on a continuum and is dependent on the degree of genetic mutation, with an estimated 850 mutations of the *PAH* gene identified.<sup>1</sup> In patients whom the *PAH* mutation causes PAH activity to be severely reduced or absent, the condition is known as "classical PKU." Individuals with this phenotype exhibit untreated blood Phe levels of >1200  $\mu\text{mol/L}$  (mean normal level: 60  $\mu\text{mol/L}$ ).<sup>2</sup> Mutations in the *PAH* gene that allow the enzyme to retain some function result in variant-PKU, which are milder versions of the disorder.<sup>3</sup>

Phe is an essential amino acid, meaning it is not produced by the body but rather must be consumed in the diet. Phe metabolism is initiated by PAH in the liver. In unaffected individuals, Phe is first converted to tyrosine (Tyr) by PAH with its cofactor tetrahydrobiopterin (sapropterin, or BH4). Sapropterin increases PAH activity, consequently decreasing blood Phe-levels.<sup>4,5</sup> When PAH is absent or insufficient, Phe is not converted to Tyr. This block in the normal metabolic pathway causes a Tyr deficiency and Phe accumulation in the blood. Consequently, toxic amounts of Phe cross the blood-brain barrier and cause cognitive deficits, behavioral and physical abnormalities, and mental retardation.<sup>6,7</sup>

In the mid-1960s, newborn screening for PKU by heel-prick in the United States (US) was introduced and mandated nearly nationwide.<sup>8</sup> Today, all 50 states require newborn screening along with many other countries. Elevated Phe without elevated Tyr observed on tandem mass spectrometry (MS/MS) during newborn screening indicates a need for further testing.<sup>9</sup> The diagnostic testing that follows includes urine pterin analysis and red blood cell DHPR assay to look for pterin defects. Pterin is the heterocyclic ring component of sapropterin, and pterin defects result in the event of sapropterin insufficiency. Health care providers may also recommend DNA testing to more specifically identify the *PAH* mutation causing PKU. DNA

testing is not required for diagnosis; however, it may be useful for determining the best treatment plan.<sup>10,11</sup>

Treatment by dietary intervention should be initiated as soon as the disorder is identified to prevent adverse outcomes and allow for normal brain development.<sup>4</sup> The goal of treatment is to keep blood Phe levels within a safe range, between 120-360  $\mu\text{mol/liter}$ . This requires strict adherence to a diet low in Phe and natural protein sources. Patient age and growth rate, varying degrees of residual PAH activity, and sapropterin-responsiveness help determine each individuals' unique dietary Phe-tolerance. Dietary tolerance, quantified in milligrams Phe or grams protein per day, is determined using blood Phe levels.<sup>2</sup>

Sapropterin-responsiveness as a determinant of Phe-tolerance refers to a relatively new advancement in PKU treatment: Kuvan (KUVAN<sup>®</sup>, BioMarin Pharmaceutical Inc.). The first and only pharmaceutical treatment for PKU, Kuvan was approved by the United States Food and Drug Administration (FDA) in 2007 and by the European Union in 2008. As a pharmaceutical formulation of sapropterin, the mechanism of Kuvan is to stimulate activity of residual PAH, promoting metabolism of Phe to Tyr and effectively lowering blood Phe levels and increasing dietary tolerance for some patients. Not all forms of PKU are responsive to Kuvan; the only way to test whether an individual is responsive is through taking the drug. Kuvan is not a replacement for dietary management of PKU, but rather is to be used in conjunction with the LP diet.<sup>12</sup>

The LP diet restricts high-protein foods and includes foods naturally low in protein. High-protein food groups such as meat, fish, cheese, milk, legumes, nuts and seeds, among others, are excluded on the PKU diet. Included are foods like fruits, many vegetables, sugars, fats and oils, and specially formulated LP breads and pastas (prepared from cereal starches, sugar, and vegetable oils).<sup>13</sup> Individuals must also consume a vitamin and mineral fortified Phe-free amino acid supplement (VM Phe-free supplement) drink three to four times per day, which is combined with vitamins, minerals, fatty acids, and Phe-free L-amino acids to supplement for the absence of protein in the diet. Failure to consume adequate amounts of VM Phe-free supplement can result in a catabolic state.<sup>14</sup> Among those with classical PKU, the VM Phe-free supplement provides up to 85% of an individual's protein intake and a significant majority of

vitamin and mineral intake.<sup>2,13</sup> If not properly supplemented, commonly observed micronutrient deficiencies include zinc, iron, and vitamin B12.<sup>13</sup>

Failure to treat or a delay in treatment of PKU results in irreversible neurocognitive impairment and severe developmental delay.<sup>15</sup> Clinical symptoms include behavioral problems, Parkinsonian-like symptoms, gait abnormality, features of autism, IQ < 50, seizure disorder, and reduced melanin synthesis which leads to hypopigmentation of hair, skin, and iris.<sup>2,16,17</sup> Sub-optimal metabolic control contributes to cognitive deficits, behavioral difficulties, and poor academic achievement.<sup>18</sup>

With life-long dietary adherence, the adverse consequences with PKU can be prevented; however, research has demonstrated that even with strict diet adherence, consequences like memory, behavioral, and executive function deficits can be observed among some individuals with PKU. Secondary outcomes of the disorder can include feelings of isolation or withdrawal, anxiety and depression, and disordered eating behaviors.<sup>19</sup>

Historically, liberalization of the Phe-restricted diet as individuals transition into adulthood was regarded as safe; however, this thinking has since been refuted.<sup>2</sup> Collaborative research projects largely funded by the National Institute of Health (NIH) consistently demonstrate outcomes supporting lifelong management of blood Phe levels in order to prevent complications with PKU. For example, individuals with PKU who discontinued Phe-restriction prior to age 10 have lower rates of college graduation than those who remained on the diet.<sup>5</sup> Psychiatric symptoms such as anxiety, depression, hyperactivity, and aggression in addition to symptoms related to executive functioning are commonly seen even when Phe control is simply relaxed. Relaxed diet adherence refers to periods when individuals with PKU are less stringent with controlling their Phe/protein intake and Phe levels deviate from the recommended range of 120-360  $\mu\text{mol/liter}$ . In a breakout question and answer session with teenagers at PKU Family Camp, interviewees described experiencing trouble focusing, hyperactivity, and agitation during periods of diet relaxation. These deficits present challenges to educational achievement and barriers to socioeconomic status. Additionally, neurocognitive impairment that occurs when dietary goals are not achieved can make future adherence to the diet more challenging, perpetuating the problem.<sup>2</sup>



Individuals and families affected by PKU face dietary challenges that profoundly impact day to day lifestyle.<sup>2</sup> Normal growth and development for children and adolescents hinges on precise adherence to the diet. The potential negative outcomes associated with excessive Phe intake place immense pressure on affected individuals and their caretakers (i.e. parents, grandparents, etc.). Monitoring of other nutritional indices becomes increasingly important given the diet is devoid of a vast list of foods and consequently, inadequate in specific nutrients. Individuals with PKU must be compliant in preparing and drinking their VM Phe-free supplement multiple times per day so they are not at risk for various vitamin and mineral deficiencies, inadequate polyunsaturated fatty acid (PUFA) levels, as well as lower than ideal bone mineral density given low calcium intake from the absence of dairy on the LP diet.<sup>4</sup> Additional burdens of PKU management include factors like routine blood draws for monitoring Phe levels, obtaining low-protein medical foods (LPMFs), tolerance of the often unpalatable nature of LP food, tracking Phe-intake throughout the day, and additional cooking to accommodate both PKU affected and non-affected individuals in the household.<sup>5,20</sup> These elements of disorder management often cause not only mental and emotional stress for families, but also financial stress. LPMFs tend to be expensive, and time required to prepare LP foods can feel daunting and/or be unrealistic for many families.<sup>14</sup>

Adolescents and young adults with PKU often struggle with noncompliance. Increased independence from parents, desire for social normalcy, temptations for “forbidden foods,” familial norms, decreased supervision, rebellion, and lack of motivation are some factors that contribute to this age group’s non-adherence to Phe-restriction or going off diet entirely. Self-monitoring and self-regulation to a medically-prescribed diet can also be challenging at this age. As previously detailed, irreversible neurological damage develops with diet non-adherence and when blood Phe levels exceed the safe range. These risks are especially problematic among young individuals given the vast amount of growth and development that occurs during this life phase.<sup>21</sup>

The multi-dimensional PKU management challenges present barriers to maintaining basic health on a daily basis. In light of this, there exists a need for strategies to alleviate some of the burdens associated with PKU. This project aims to obtain a more thorough understanding

of the resources presently available to the PKU community, the barriers to those tools, and other perceived needs of this group. By identifying where gaps exist, new initiatives and improvements to existing resources can be made. Understanding barriers to utilization of existing resources available to the PKU population and provision of cooking tips and recipes represent a couple of the potential ways to better understand and cater to the daily challenges of the PKU community. Providing support around diet adherence leaves less room for the detrimental outcomes that come with non-adherence.

### ***Chapter II: Social Determinants of Health and Lifestyle Management Considerations Among Individuals with PKU***

Dependent on the country of origin, PKU affects between 1 in 10,000 and 1 in 20,000 individuals.<sup>22</sup> The disorder occurs in all ethnic groups around the world, but is more prevalent in individuals of Northern European, Native American, and Turkish descent. PKU is less commonly observed in African, Japanese, and Ashkenazi Jewish groups.<sup>23</sup> In the US, the incidence is estimated between 1 in 12,000 and 1 in 20,000. Today, an estimated 16,500 individuals are living with PKU in the US. The disorder appears to proportionately affect males and females.<sup>22</sup>

PKU is a lifelong disorder, thus individuals of all ages are living with PKU today. Since widespread mandate of newborn screening in the 1960's, most all cases of PKU are diagnosed and odds of preventing mental disability are significantly improved.<sup>2</sup> The first individuals diagnosed with PKU through neonatal screening in the 1960s are middle-aged today.<sup>24</sup> As individuals with PKU live longer and severity of developmental disabilities has decreased, the age demographics will continue to shift.<sup>2</sup>

A variety of measures and screening tools exist to assess the health of individuals with PKU. Most often, screening tools are utilized in metabolic or pediatric clinics as individuals must regularly be seen to ensure blood-Phe levels are within treatment goal range. Assessing health markers early on allows for monitoring and evaluation of individuals over time. Adult- and pediatric-specific Quality of Life (QoL) questionnaires are an example of screening tools used. The following domains of health are tested and monitored over time in the PKU population: medical, metabolic, emotional, nutritional, cognitive, behavioral, and social. Measures above

certain thresholds within each of these domains may warrant referral to a specialized provider for a more in-depth neuropsychological assessment.<sup>25</sup>

Some of the screening tools available for assessing behavioral, neuropsychological, and mood disorders may be self-administered or completed by parents. Such at-home screening instruments can help justify insurance coverage for more intensive neuropsychological assessment and/or services such as consultation with a psychiatrist as necessary.<sup>25</sup>

Collecting qualitative data to inform social determinants of health and nutritional and health status among individuals with PKU often relies upon voluntary participation and provision of information through patient registries and/or research studies. Consequently, selection bias with the inclusion of more compliant, socially-adjusted patients becomes a significant limitation to obtaining data representative of the entire group. This reality presents challenges to drawing concrete conclusions about the health and nutrition status of the overall group of individuals living with PKU.<sup>20</sup>

Patient registries have demonstrated utility in accelerating development of treatments and improving patient outcomes in various healthcare arenas. In the PKU community, registries are developed to collect information to track nutrition, health, and other characteristics over time; however, this information is not readily available due to study compliance.<sup>26</sup>

Additionally, studies are performed to evaluate the Health-Related Quality of Life (HRQoL) of patients with PKU. Through combined use of PKU-specific and generic questionnaires, the aim is to evaluate effectiveness of therapeutic treatment and support as it relates to emotional, physical, and social outcomes among this population.<sup>27</sup> Studies of this nature from the 1990s revealed patient reports of reduced self-autonomy and a restricted social situation.<sup>20</sup> More recent findings tend to consistently demonstrate an HRQoL among individuals with PKU similar to that of the general population, especially when the disorder is diagnosed early and treated well.<sup>20,28</sup> The lack of observed significant mean differences in HRQoL across the two groups is thought to be reflective of the difficulty capturing a hidden disability, underpowered sample sizes due to rarity of the condition, and lack of long-term, longitudinal studies.<sup>28</sup> These studies also tend to come from a single country of origin, placing limits on generalizability.<sup>27</sup>

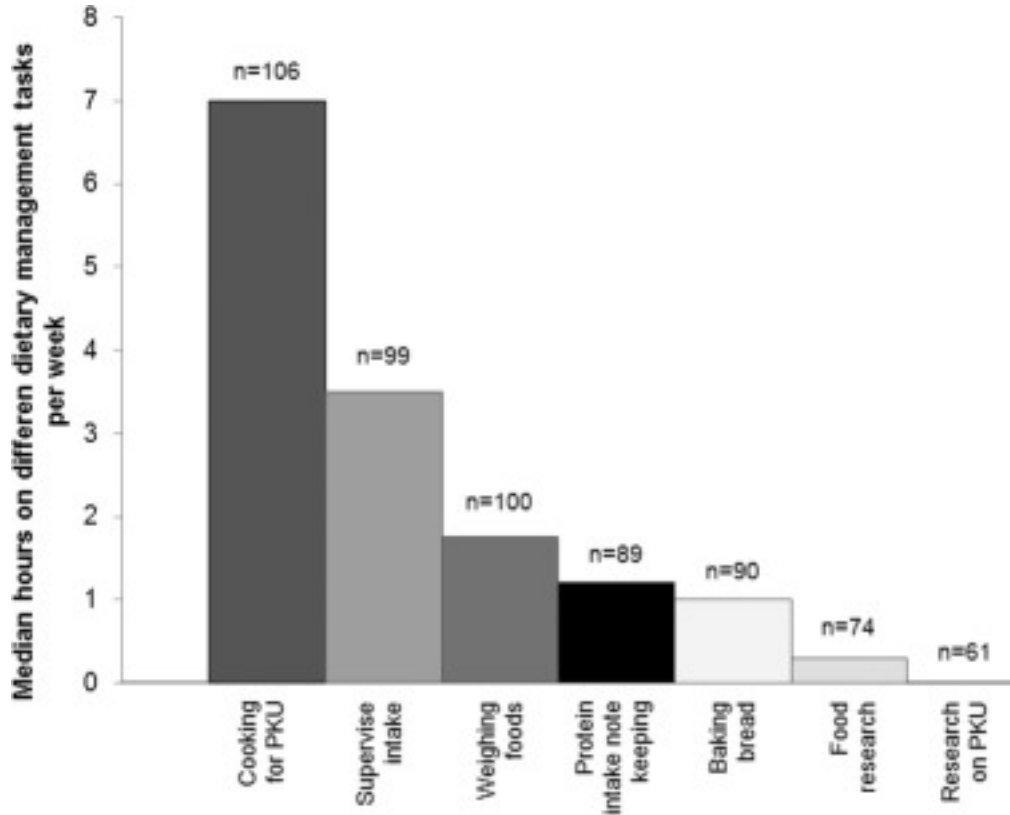
When consistent metabolic control is not maintained, individuals with PKU may be at increased risk for facing health disparities. Periods of relaxed diet adherence can contribute to reversible and irreversible mood instability, attention challenges, and poor job performance. An accumulation of these cognitive deficits over time may contribute to difficulty in the work place, which has the potential to impact income potential and socioeconomic status.<sup>29</sup>

Given the known consequences of poor metabolic control, one might expect low rates of poor- or non-adherence; however, such an expectation is not the reality. Research indicates many children and adolescents have blood-Phe levels above the recommended range. One study, which included 330 patients, demonstrated that 25% of 0-9 year-olds, 50% of 10-14 year-olds and 75% of 15-19 year-olds had Phe levels outside their recommended levels.<sup>30</sup> A variety of demographic and psychosocial determinants can play a role in making metabolic control more challenging for this population. Among the factors known to influence adherence and thus health outcomes, especially among children and adolescents, are the following: social pressures, patient age, level of educational attainment of caregiver, household income, and degree of family cohesion (i.e. marital status). Research suggests older children and adolescents are at greater risk for poor diet adherence, and children with separated or divorced parents demonstrate higher blood-Phe levels than children whose parents are married.<sup>18</sup>

Social status can be a predictor of success with respect to treatment adherence. Full reimbursement for PKU treatment exists in some developed countries; however, in other countries, cost remains a significant barrier and concern for families managing PKU. In the US, the National Health Service (NHS) takes some responsibility for reducing the financial burden of PKU caregivers. 60% and 10% of total NHS costs for managing a PKU patient is accounted for by the VM Phe-free supplement and LPMFs, respectively. Prescriptions and financial help platforms, such as the Disability Living Allowance, Carers Allowance, and Family Fund are among the instrumental sources of reimbursement for specialty products and VM Phe-free supplements.<sup>14</sup> For most individuals in the US, the high cost of LPMFs are not covered by insurance; an estimated four out of five patients pay out-of-pocket for LPMFs.<sup>20,24</sup>

Time burden is similarly important to consider. A study conducted in the United Kingdom (UK) sought to explore the time and financial burden for caregivers of pediatric PKU

patients. The study was performed using a questionnaire to collect information on time spent on tasks specifically related to PKU management. Figure 1 below illustrates the median hours spent per week by a caregiver on PKU-related tasks.



**Figure 1:** Median Hours Spent per Week on PKU-Related Tasks<sup>14</sup>

The study illustrated a significant time burden due to the treatment regimen, including a median 19 hours per week strictly related to dietary tasks, which was the most time consuming category compared to other categories, such as “Research on PKU” or “Supervise Intake.” These hours come in addition to the many more routine childcare tasks of a parent or guardian and can present burdensome strain for families. Situations in which this may be especially true include single parents, working parents, or parents simultaneously managing their own health complications. Almost half of all caregivers participating in this study reported their child’s PKU condition impacts their job, with 90% of that subset reporting reducing working hours or quitting a job altogether.<sup>14</sup>

Individuals with PKU and their families are subject to influence by various social

determinants of health. Examples may include the following: Proximity to grocery stores to obtain appropriate foods for supporting health on the LP diet, accessibility to reliable transportation, proximity and accessibility to healthcare services, adequate educational and/or professional opportunity and support, social norms and attitudes around a disorder such as PKU, among others. Each of these resources are essential for those with PKU to properly support their health and promote optimal outcomes. When these fundamental conditions are not met, individuals are at risk for sub-optimal health and functioning and poor quality-of-life outcomes.<sup>31</sup>

Considering patients' social outcomes is one way of measuring success of PKU management. Although early and consistent treatment ensures mostly normal intellectual outcomes, academic and professional success depend on factors beyond strictly intellect. Deviations from therapeutic Phe-range over the course of one's life can contribute to deficits, such as memory difficulties, attention deficit, and behavior abnormalities. Emotional and behavioral repercussions stemming from childhood or adolescent experiences related to living with a chronic disease may also influence academic and/or professional achievement.<sup>20</sup>

This capstone project aims to investigate lifestyle management with PKU in order to promote best possible health and quality of life outcomes for those affected by PKU. By investigating existing barriers to managing the disorder, such as lack of knowledge around food preparation or inaccessibility to resources like LPMFs, working groups in the PKU community can provide support to address them and in doing so, promote LP diet adherence and positive health outcomes. Understanding social determinants of health in this population is an essential piece in the development of the proposed community-driven recipe site. With an understanding of existing barriers and health disparities that may present, new resources can be better tailored to individuals of all circumstances.

### ***Chapter III: The Nutritional and Lifestyle Challenges of the Low-Protein Diet***

PKU is one of the few medical conditions in which nutrition functions as the primary medical treatment, and without it, individuals endure negative, irreversible consequences. Drastically restricting an entire nutrient group on the premise of preventing severe

neurodevelopmental and psychological impairments brings up challenges and questions the average person may struggle to navigate if left to his or her own devices. Successful dietary therapy requires guidance and support from a multidisciplinary team that includes a metabolic physician, nurses, and a registered dietitian nutritionist (RDN).<sup>2</sup> The metabolic disorder subspecialty is one in which RDNs are privileged to exercise their indispensable value in patient care.

The goal of dietary therapy is to maintain blood Phe levels within a safe range. To ensure Phe is being maintained within that specified range and that dietary intake is nutritionally adequate, Phe and Tyr levels must be closely monitored. Infants' levels should be checked in clinic weekly until age one. From ages one to twelve, levels should be checked one to two times per month. During adolescence and young adulthood, monthly sampling is adequate. As individuals progress through the life phases, encounter illnesses, and manage other comorbidities, dietary manipulation can become necessary to stay within target Phe ranges, reinforcing the importance of routine blood sampling. RDNs are in a critical position to help families facilitate those dietary modifications.<sup>2</sup>

Frequent blood tests for monitoring Phe levels requires routine trips to a metabolic clinic. Proximity to clinics may influence the time and effort required of families to adhere to this component of therapy. Some families travel hours by car to attend appointments and may need to stay in a hotel overnight. Further considerations include whether families have access to transportation and whether caregivers are supported by their workplace in taking time off to travel with their children to clinic appointments.<sup>32</sup>

Suboptimal bone health is a potential complication with the LP diet. Lower bone mineral density (BMD) has been reported among PKU patients when compared to a healthy population average; however, a large, multi-national systematic review raises question to the clinical significance of such observations, as the mean-effect Z-scores for patients with PKU are still within the range for normal BMD.<sup>7</sup>

The LP diet is insufficient in selenium and coenzyme Q, which may alter an individual's antioxidant profile. Data exists to suggest individuals with PKU may exhibit more lipid peroxidation and DNA damage than those without the disorder, even in the setting of good

metabolic control. As such, there are suspicions that individuals in this group may be at risk for earlier-onset dementia; however, being that the first generation of early-treated individuals with PKU will be entering its elderly years over the next two decades, follow-up is necessary to further investigate this potential relationship.<sup>24</sup>

#### ***Chapter IV: Current Efforts Underway to Support the PKU Community***

Upstream funding for clinical and animal research studies to continue to explore a thorough understanding of disorder management, new treatment methods, gene therapy, and progress toward a cure holds massive potential for positive influences in the PKU community.<sup>27</sup>

Research into non-dietary alternatives, such as somatic gene therapy or enzymes that degrade Phe in the digestive system, is underway, but advances may be far off. Advocacy in support of this type of research can be a helpful way to increase financial support from upstream sources.<sup>19</sup>

Clinical research studies for rare genetic disorders, such as PKU, can present a number of obstacles. Such disorders are referred to as “orphan” disorders. The low incidence of orphan disorders often result in challenges with participant recruitment and retention. Additionally, pharmaceutical companies are often reluctant to invest in efforts to develop new therapies for rare disorders given these complexities and the high cost of research. A relatively small pool of patients also limits the financial gain for pharmaceutical companies in comparison to the process and cost of developing a drug, reducing their incentive. The US Food and Drug Administration (FDA) created the Orphan Drug Act of 1983 to provide support around this conflict. The system helps to reduce cost of developing such drugs and offers financial enticements, such as tax credits and marketing incentives.<sup>19</sup>

BioMarin’s Palyngiq (pegvaliase-pqpz or Peg-pal) provides an example of a successful drug under the Orphan Drug Act. Approved by the FDA in May 2018, Pegvaliase-pqpz is a recombinant phenylalanine ammonia lyase (PAL) enzyme, designed for individuals with PKU who have uncontrolled Phe concentrations greater than 600  $\mu\text{mol/L}$  while on dietary treatment. Administered through injection one time per day, the PAL enzyme functions as a substitute for the deficient PAH enzyme by converting Phe to ammonia and trans-cinnamic



acid, reducing blood-Phe concentrations to an acceptable range.<sup>33</sup> Preliminary results demonstrated that individuals treated with Peg-pal achieved a 62% improvement in blood Phe levels when compared with the placebo group.<sup>33</sup>

In 2017, Orphan Drug Designation was granted to Synlogic, a drug company in the pre-clinical stage of developing a synthetic biotic drug, SYN1618. In theory, the drug candidate is designed to be orally ingested as a pill that would provide an alternate metabolic mechanism for digesting Phe, effectively removing excess Phe from the blood. Synlogic states their goal as successful development of a novel treatment that eases the lifestyle and management of a challenging disorder.<sup>34</sup>

The PKU Foundation serves as a fundraising organization in the United States in place to support those affected with PKU. The organization seeks to raise funds to promote the cure and treatment of PKU as well as community and social awareness around the disorder. Additionally, the PKU Foundation provides support to the community in the form of providing sponsorships, literature, and other resources to affected families in addition to hosting public service conferences, national conferences, and social opportunities to promote networking and community within this group.<sup>35</sup>

Since 2009, the NPKUA has been involved in efforts to help pass federal legislation for the Medical Nutrition Equity Act, which proposes public and private insurance coverage of LPMFs and VM Phe-free supplements for all children and adults with PKU. The bill also extends to provide support for coverage of foods medically necessary for other disorders. Proponents of the bill argue that these products are medically necessary for effective management of metabolic disorders, and without them, individuals are at increased risk for suffering adverse health consequences. The average cost of necessary LPMFs to treat PKU is \$12,000-\$15,000 per year. The high cost of these products, which often aren't covered by insurance, leave families with a financial burden or inability to purchase them at all. In May of 2017, the bill was introduced into Congress.<sup>22</sup>

## **Chapter V: HowMuchPhe.org**

Lifestyle management on the PKU diet has evolved through the years as various resources have developed. Virginia Schuett, a leading RDN in PKU treatment and author of multiple LP cookbooks, started National PKU News in 1989. National PKU News began publishing a newsletter three times per year, which provided important news and updates for the global PKU community. With Facebook and an online PKU listserv, reliance on the newsletter for communication diminished and it was discontinued in 2015.<sup>36</sup>

Historically, the PKU population relied on Schuett's *Low Protein Food List for PKU (The List)*, a book containing over 7,000 foods, to determine Phe levels in foods in order to track Phe intake throughout the day. Though the book served as an indispensable resource for many years, access to *The List* assumed individuals had the book readily available at all times. In 2014, development of a new online resource, *How Much Phe?* (HMP), eliminated that inconvenience. With the mission to offer support and improve lifestyle management for families managing the LP diet, HMP provided a platform for the resource to be more conveniently accessed and continually improved and updated. More than 300 foods have been added to *The List* since the launch of HMP.<sup>36</sup>

HMP is an online subscription service, developed under National PKU News as a supportive resource for individuals and families managing PKU. The service provides quick and convenient access to every food item on The List as well as PKUNews.org's Baby Food List. Individuals are able to use the platform to look up Phe content of foods and track Phe intake throughout the day from their mobile or other electronic device.<sup>37</sup>

Features of HMP include the following: the ability to calculate the amount of Phe in a quantity of food using a variety of units (i.e. grams, pretzels, garlic cloves, fluid ounces, etc.); a function to track Phe, protein, calorie, and protein equivalents to stay within a day's target range; the option to graph results for export to be shared with medical providers; the ability to track and graph height, weight, and blood Phe levels; an option to have multiple profiles per subscription to allow access for all family members, caregivers, and medical providers; and the ability to input favorite foods or recipes for personal use. Users report significant stress relief and appreciation for the support provided by these tools.<sup>36</sup>

HMP is a 501c3 nonprofit organization and a service of National PKU News. The staff and leadership of HMP includes Sarah Chamberlin (Executive Director of National PKU News), Virginia Schuett (RDN; Founding Editor and Director of National PKU News; Member, Board of Directors), Jeb Haber (President, Board of Directors), Adrian Mayes (Secretary and Treasurer, Board of Directors), and Michelle Hobbs (RD). The leaders of this organization are individuals who either have PKU, are parents of a child with PKU, or are devotedly committed to work in the metabolic community.<sup>36</sup>

The subscription fee for HMP is \$45 per year and has been since the organization's inception in 2014. In 2016, 78% of HMP income was from subscription revenue, and 22% was from community donors. Revenue is used to fund general operations as well as to expand the food list through the *PKUNews' Amino Acid Analysis Program (AAAP)*. This program entails use of laboratories endorsed by industry experts to analyze amino acid content in common PKU-diet foods to determine accurate and precise Phe levels. HMP maintains a goal of increasing revenue in order to expand this program to support testing up to 50-100 new foods per year. As the food industry grows and an increasing number of food labels and products enter the market, accurate amino acid testing remains an important tool to support the community managing metabolic disorders. This technology exists in complement to the organization's dietitian-driven food analysis process, which is performed using ingredient labels and outreach to food companies to determine Phe content.<sup>36,37</sup>

HMP is available in the US and Canada, with 94% of users residing in the US and 6% in Canada. Eligibility criteria for subscription includes residence in either of these countries and payment of the annual subscription fee. HMP recognizes the cost of its services may be a barrier to use for many families, especially in the context of the numerous other added costs associated with managing PKU, so the organization established a scholarship fund to offer a number of free annual subscriptions.<sup>37</sup>

An additional important resource available to the PKU population is CookForLove.org (CFL), an online, non-profit, culinary resource with a mission to empower the metabolic community to take control of its health through the food it eats. Founded by Brenda Winiarski, a culinary chef and mother of a child with PKU, the site aims to equip individuals in the PKU

community with the recipes, skills, and education to prepare and enjoy palatable and delicious food, despite significant dietary restrictions. Brenda develops LP recipes for foods otherwise too high in protein for those with PKU to enjoy. Since its launch in 2009, CFL has been a separate organization from National PKU News and HMP; however, in 2017, CFL and HMP announced plans to merge. The merger will allow CFL to continue as a free resource but with expanded features and offerings, thanks to the more developed infrastructure provided by HMP.<sup>36</sup>

The goal behind establishing this partnership is to enhance CFL and develop the site into a community-based resource guided by an ongoing mission to improve lifestyle conditions for the PKU community. Plans for development of this tool generated high expectations and ambitious goals among individuals in both organizations. This energy created the opportunity and a vision for the capstone project at hand: to better understand the current perceived needs of the PKU community in order to develop the new resource in a way that is best tailored to the individuals who will use and be impacted by it.<sup>38</sup> This was accomplished through development of a survey, which was administered to the online PKU community. In coordination with the efforts of the survey, this project included facilitation of a focus group among parents of children with PKU at a PKU family camp in August 2017. Additionally, the project entailed preparation, phe calculations, and photography of recipes from *Apples to Zucchini's (A to Z)*, a LP cookbook written by Virginia Schuett, to be included on the new community-based resource. Chapter VI outlines further details and explanations of these processes.

### ***Chapter VI: Assessing Population Needs Through a Qualitative Survey***

As previously detailed, lifestyle management of PKU encompasses a wide variety of challenges, including financial stressors, psychosocial concerns, time constraints, among others. These added hurdles can contribute to diet non-adherence and/or burdensome stress for individuals and families. In light of this, HMP and CFL identified a need for expanding resources to provide support to these challenges through development of the community-driven recipe site previously described.

HMP and CFL envisioned the new site as a culmination of existing resources, such as the LP recipes already available on CFL, with the addition of new content and features. Schuett provided permission for the hundreds of LP recipes from her cookbooks, *Low Protein Cookery for Phenylketonuria* and *Apples to Zucchini (A to Z)*, to be included on the site. The recipes as they are found in *A to Z* are missing a total gram weight, by which to calculate the milligrams of Phe per gram of food for each dish. Another element of this project required preparation of a subset of these recipes (50 recipes total) to obtain the total gram weight of each dish in addition to a photograph to be included on the new website. Preparation of each recipe followed a step-wise process, detailed as follows:

1. Prepare grocery list, coordinating which dishes to shop for and prepare based on common ingredients.
2. Grocery shop.
3. Weigh each ingredient according to gram weight or measurement listed in recipe.
4. Prepare recipe.
5. Weigh final product.
6. Enter recipe, including ingredients, cooking instructions, number of servings, and final gram weight into HMP.
7. Upload labeled photos to a shared photo stream with HMP administrators to be uploaded to community-driven recipe site.

The photos in Figure 2 below provide examples of finished products from the process.



**Figure 2:** Starting with the top left photo and moving clockwise, the dishes are as follows: Tropical Fruit Salad, Orange-Drenched Beet Salad, Spicy-Sweet Vegetable Kabobs, and Marinated Cauliflower Salad.

This process provided insight into the time-intensive and often burdensome nature of LP cooking. The start to finish timing of the step-wise process outlined above averaged to be around 60 to 90 minutes per dish. An adjunct to this part of the project included entering 160 additional recipes from three chapters in *A to Z* (“Hot off the Grill,” “Vegetables for All Seasons,” and “Salad Celebrations”) into HMP for future use on the new resource. The process for entering a recipe into HMP includes looking up each ingredient in the database and entering its quantity, typing the recipe’s directions, and including the number of servings, serving size, and total gram weight. This process averages around seven to ten minutes per recipe.

Attendance at a PKU family camp at Washington Family Ranch in August 2017 provided the opportunity to take part in LP menu planning and mass-production LP cooking from-scratch, which provided a similar firsthand understanding of the meticulous and time-consuming nature of preparing LP food.

HMP desired to develop the community-driven recipe site according to current needs and desires perceived by the PKU community. The first step of this process included in-person discussions with teenagers and parents of children and teens with PKU at the family camp. Attendance at a break-out session with teenagers provided an opportunity to hear teens' perspectives on a variety of topics. The following table provides examples of questions asked and subsequent responses from teenagers:

**Table 1:** Example Questions and Responses from Teen Breakout Session

Question	Responses
How has your perspective on having PKU changed as you've gotten older?	-"When you grow up with PKU, it doesn't phase you." -"It's more of a burden as I get older."
How many people use HowMuchPhe.org?	-6 out of 20 teenagers raised their hands.
Tell me what it's like to drink your formula every day.	-"I finish homework at 9 at night and want to go to bed then realize I have to go make my shake." -"Formula is not the hardest part of the diet; the hardest thing is not eating the foods I want to eat." -"Traveling and having to pack all the formula is a pain."

A focus group among parents at the camp provided valuable insight from the parent perspective with respect to challenges with feeding, diet-adherence, and behavior among their children and adolescents. This gathering also provided an opportunity for brainstorming ideas related to what features would be useful as part of the new site.

The second, and more major, component of resource development as part of this project included survey development followed by its administration to the PKU community, analysis of the results, and provision of recommendations based on results. The survey objectives were:

1. To explore utilization and barriers to presently existing resources in the PKU community.
2. To gain a better understanding of barriers to lifestyle management and low-protein diet adherence with PKU.

3. To solicit feedback from the PKU community in order to learn what the community hopes to see in a community-driven recipe site.

The survey development process included establishing objectives (outlined above), researching effective techniques related to survey development (i.e. question design and language use), developing questions in line with objectives, and formatting the finalized questions into survey software (Survey Monkey). The survey development literature emphasizes the importance of setting measurable objectives and asking purposeful, concrete questions that are logically related to the survey objectives.<sup>39</sup> The appropriate number of questions for inclusion depends on what information the surveyor hopes to learn in coordination with the amount of time respondents have available to answer the questions. Questions should be designed in a straightforward way, avoiding imprecise or ambiguous words so the survey taker is only required to call on one thought at a time.<sup>40</sup>

Survey questions take one of two general forms: open- or closed-ended. Each type of question has its strengths and limitations. Open-ended questions allow for the respondent to provide unanticipated responses. This type of question proved useful in the present survey given the expected variation of perspectives across the wide sampling of survey participants, which brought unique and innovative ideas to the table. The chief limitation with open-ended questions is difficulty in comparing and interpreting responses, as these answers require time-consuming categorization and interpretation. Closed-ended questions are more simply interpreted; however, respondents are limited only to the answer choices offered. These questions can be helpful in larger surveys with higher numbers of participants and responses.<sup>40</sup>

The survey encompassed both open- and closed-ended questions. A number of open-text questions were included as well as two types of closed-ended questions: multiple choice and Likert scales. Likert scales offer respondents an opportunity to respond to a scaled question based on how true or untrue a statement is or how likely or unlikely one might be to utilize a resource feature. Below is an example of a Likert scale question included in the survey:



- ❖ The following are potential elements of a community-driven recipe site. Please indicate how useful you perceive each element would be in this site, based on the following scale: 1 = not useful, 2= minimally useful, 3= neutral, 4= somewhat useful, 5= very useful

Site Feature
Common LP Substitutions for HP foods
Tips: School Lunches
Private annotation of recipe/personal recipe box
Common LP substitutions for the picky eater
Tips: Cooking for LP loved oens simultaneously with the rest of your family
Recipes for prep. large amounts in advance
“How-to” tutorial videos (e.g. meal-prepping)
Reading food labels w/ common phe-containing foods
Step-by-step photos of recipe prep.
Grandparents/Extended Family Guide - "dos/don'ts"
Categorization of foods to different life phases
Recipe rating system (e.g. a 5-star scale)
Public annotation of recipe (e.g. what my child said)

Additional example questions are outlined below. Please refer to Appendix A for the comprehensive outline of questions and answer choices included in the survey.

- ❖ What do you think is the biggest barrier preventing you or others from using HowMuchPhe.org? Check all that apply.
- ❖ What is the likelihood the proposed resource would increase your frequency of low-protein cooking?
- ❖ What is the likelihood the proposed resource would help promote lifelong adherence to the diet?

A post with a link to the survey and a message requesting user participation was shared in the following Facebook groups: Cook For Love, How Much Phe, PKU Worldwide Support Group, Parents of PKUers, and PKU News. The survey was posted on 9/26/17 and closed on 10/23/17, yielding 432 responses. The survey results were organized by question into tables (Appendix A). The question containing an option for open-text responses were grouped into categories for each question (Appendix B). Finally, certain questions were identified as relevant

for stratification by age. Responses to these questions were broken down by age group (0-5, 6-11, 12-18, 19-25, 26-50, 50+), to provide more age-specific feedback to survey questions (Appendix C). Please refer to the appendices for the comprehensive results produced by the survey.

When interpreting the survey results, it is important to acknowledge the limitations of survey design and data collection. First, participants were self-selecting, which may have resulted in a selection bias. Selection bias can lead to results different than those that would have been obtained if the entire target population were used (i.e. the entire metabolic community). Because the survey was marketed in online forums, the survey participants were individuals who may be more likely to utilize online resources and thus more likely to take interest in the proposed resource.

Second, this sample of survey respondents was a convenience sample, which is a type of non-probability sample. Non-probability samples are not truly representative of the overall target population, which weakens generalizability. The exact number of all individuals with PKU within the groups sampled on Facebook for survey participation is unknown, so the survey completion rate within each group cannot be determined.

Third, an error in setting up conditional logic on one of the questions may have impacted responses. For the following question, “if you use a different program to look up phe values or track intake, what program do you use and why do you like it?” the conditional logic was set so that “If no, why not?” was prompted by “I don't need to track intake,” and “What do you use to track phe/pro intake?” was prompted by “I just keep track in my head.” Consequently, many of the individuals who indicated they use a different program entered responses indicating that they do not actually use a different program. These responses were grouped into a category “I don't use another program” and should be interpreted with this error in mind.

Finally, within the “Where We’re Headed Next” section of the survey, one of the proposed site features was added after the initial survey launch. The average score produced for this feature, “Insurance networking center to share tips on securing coverage,” should be

interpreted with this context in mind. Please refer to Appendix A for context for these questions.

### ***Chapter VII: Key Recommendations from Survey Results***

Survey administration to the online PKU community provided a wide scope of information across the following topics: demographics, perceived barriers to existing resources, and input to inform development of a new resource for the metabolic community. Please refer to Appendix D for an abbreviated summary of survey design and results, which was provided to the community partners at HMP. Summaries drawn from the data produced several key recommendations for HMP.

The demographic data collected in this survey produced the recommendation for an effort to increase discussion of resources during patient visits in metabolic clinics in order to better reach individuals and families affected with metabolic disorders with HMP and CFL. This may be accomplished through clinic outreach to ensure metabolic clinics across the country are aware of and well-versed in what these resources offer so that families are informed first thing upon diagnosis. Continued advertisement on Facebook is also recommended as this avenue appears to be a primary source of learning of these resources for this population.

Cost appears to be the biggest perceived barrier to using HMP. A recommended strategy is to investigate possibilities to contract with metabolic clinics. Clinics could purchase a block of subscriptions to offer to their patients at reduced cost. Seventeen individuals indicated “lack of knowledge about HMP” as a perceived barrier, which further supports the recommendation for increased partnership with metabolic clinics to increase awareness of and access to HMP.

Within the “other” responses to the question about perceived barriers, 11 out of 113 individuals described cultural barriers to using HMP. This may be an area to consider addressing in the new CFL platform (i.e. Canadian brand equivalents). Also, although only six individuals responded, 100% respondents indicated they would use HMP if it were available in their country. As such, extending availability and advertisement of HMP to other countries may be warranted.

More individuals were interested in a program to pay for foods of their choosing to be tested for protein/Phe content than those who were not interested. The range of amounts individuals indicated they were willing to pay was from \$0 to \$1000, with most individuals suggesting amounts in the \$5 to \$100 range (only one respondent answered “\$1000”). The cost of amino acid analysis of a food depends on the type of food and what type of preparation is required of the lab to perform the analysis. Through its AAAP, HMP sends each food sample to two separate labs. The cost is \$200-\$300 per sample per lab, equating to a total of \$400-\$600 per sample. For protein analysis, the cost is \$20-\$50 per sample per lab. This program should be integrated within HMP. Payment to have a food tested should be set at \$25 as the minimum dollar amount but include the option for individuals to exceed that amount as a donation. Additionally, a breakdown of the cost associated with testing foods for amino acid and protein content should be provided for users’ knowledge.

Survey results suggest that CFL is a highly valued and utilized resource. Individuals value the quality of the recipes, the support provided by the CFL community, and the variety and normalcy it adds to their lives, among other elements. The top perceived barriers to using CFL include time and effort to prepare recipes, lack of confidence in ability to cook LP foods, and barriers related to ingredients, such as cost and “special ingredients.” Identification of these barriers provides an opportunity to further enhance the site to make it more user-friendly and accessible to the metabolic community. The proposed community-driven recipe site is an excellent opportunity to do so.

The survey results from this sample population demonstrate a demand for increased resources for the metabolic community. These results indicate the proposed community-driven recipe site will be a widely utilized resource for this population. Respondents indicated not only likelihood the proposed resource would be utilized but also an indication that it would increase frequency and variety of LP cooking as well as help promote lifelong adherence to the LP diet.

All of the proposed site features, besides “public annotation of recipes (e.g. what my child said about this recipe),” produced results indicating a high-level of perceived usefulness. The top three desired features based on survey results were “Common LP Substitutions for HP Foods,” “Tips: School Lunches,” and “Private Annotation of Recipe/Personal Recipe Box.” Please

refer to Appendix A for the comprehensive list of features included in this question. Inclusion of all features is recommended; however, prioritization based on rankings of perceived usefulness should be exercised in the event that all features cannot be included.

Eight potential “search-by” tools were presented in the survey for possible inclusion in the site. Seven out of eight of the tools produced results indicating a high level of perceived usefulness. Including those seven search-by tools will facilitate optimal user-friendliness of the proposed site.

Description of a program that would allow individuals to pay to have a family recipe adapted to the LP diet solicited positive feedback; however, given the marginal interest as well as the degree of time, resources, and money this process entails, there is not a recommendation to incorporate this program at this time.

Finally, data was collected to determine whether there is a perceived need for future expanded resources for the metabolic community. Over half of survey respondents indicated the presently available online resources are insufficient. When asked whether there is a need for a resource that includes features such as information on latest research, a metabolic community networking component, a calendar of metabolic events, a community question and answer forum, and an “online diet board,” survey respondents indicated strong support and high likelihood of utilizing such a resource. Survey results suggested “Information on Latest Research,” “Networking Component,” and “Calendar of Metabolic Events/Ability to Find Events Near You” as the most sought after components in this type of resource.

Additional recommendations outside of the ideas and tools proposed within the survey include the following: Adding a section to guide finding “specialty” or “hard to find” ingredients (i.e. jackfruit at Trader Joe’s, best place to find certain spices, etc.); including a section providing tips and tricks to help cut back on the time and effort to prepare CFL recipes (i.e. batch cooking, group cooking, etc.); and addition of a section addressing strategies to promote a “healthy” lifestyle while on the LP diet.

## ***Chapter VIII: Summary***

PKU bears significant nutrition consequences for all who are affected by the disorder. The critical need for severe restriction of protein from the diet creates challenging and burdensome lifestyle implications for individuals and their families living with PKU. Included among these challenges are obtaining and financing LP medical foods, tolerating the often unpalatable nature of LP food, tracking Phe-intake throughout the day, cooking multiple dishes to accommodate both LP and non-diet portions, and preparation and consumption of a necessary VM Phe-free supplement multiple times per day.

Considering the many daily obstacles to promoting basic health as well as the threats posed by diet non-adherence for those with PKU, efforts to facilitate lifestyle improvements to this community are important. This capstone project sought to help explore and build upon resources presently available to the PKU community in order to provide improved support and encourage positive outcomes. Through recipe testing, survey development and survey analysis, this project concluded with provision of key recommendations to help guide development of a community-driven recipe site that will help build an online community for individuals affected by PKU, easy daily stressors of PKU management, and promote LP diet adherence.

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## Appendix A: Survey Analysis

### Demographics

**Question:** Where do you live?

Country	% (n= 432, total survey respondents)
United States	86.34
Canada	9.26
Zimbabwe	0.23
Serbia	0.23
New Zealand	0.46
Ireland	1.16
Australia	0.46
Czech Republic	0.23
Denmark	0.23
Vanuatu	0.23
Portugal	0.23
United Kingdom	0.23
Germany	0.23
Belgium	0.23
Belarus	0.23
<i>Total US</i>	86.34
<i>Total outside US</i>	13.66

**Question:** Please identify your relationship to someone with a metabolic disorder. Check all that apply.

	Myself	My child/children	My significant other	My grandchild	Another family member	Friend	Other
<b>% (n=432, total survey respondents)</b>	17.59	78.01	0.69	3.01	2.31	0.69	0.93

\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

**Question:** How old are the individual(s) with a metabolic disorder? Check all that apply.

	0-5	6-11	12-18	19-25	25-49	50+
<b>% (n=432, total survey respondents)</b>	44.44	27.78	12.73	6.25	16.67	2.31

\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

**Question:** Which of the following online resources do you currently use? Check all that apply.

Resource	% (n=432, total survey respondents)
Howmuchphe.org	78.01
CookForLove.org	86.81

HowMuchPhe Facebook group	63.19
Cook For Love Facebook group	78.94
NPKUA.org	50.46
NPKUA Facebook page	42.13
Regional PKU Facebook pages (MACPAD, Intermountain PKU etc)	24.77
PKU.com	24.77
PKU Worldwide Support Group Facebook Group	36.57
PKU Parents Only Facebook Group	25.23
Other	11.81

\*Surveyors may choose more than one answer; thus, percentages will not total to 100%.

**Question:** How did you hear about HowMuchPhe.org?

	Family member	Friend	Hospital	Metabolic Clinic	Other**
<b>% (n=432, total survey respondents)</b>	5.09	10.42	3.01	45.14	41.90

\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

\*\*See Appendix B

**Question:** How did you hear about HowMuchPhe.org?

→ If you heard about How Much Phe from a source other than those listed above, where did you hear about it?

Category	Count	<b>% (n=181, total "other" respondents)</b>
FB	91	50.28
Online/Internet	30	16.57
PKU Organizations	21	11.6
CFL	16	8.84
Conferences	13	7.18
Unclassifiable	9	4.97
Newsletters/Mail	8	4.42
Transition from Book →Online	6	3.33
Listserv	4	2.21
Virginia	3	1.66
PKU Camp	2	1.1

**Question:** Do you currently use HMP to look up phe/protein/exchange content of foods?

Y/N	<b>% (n=432, total survey respondents)</b>
Yes	76.12
No	23.84

**Question:** Do you currently use HMP to look up phe/protein/exchange content of foods?

→ If no, why not?

If no, why not?	% (n=103, total "no" responses)
Other	43.69
I know the phe/pro of most foods consumed	33.98
We use other resource(s) for phe content	22.33
I know the phe/pro of most foods consumed	11.65
HowMuchPhe.org isn't available where I live (outside North America)	5.83

\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

**Question:** Do you currently use HMP to look up phe/protein/exchange content of foods?

→ If no, why not?

→ "We use other resource(s) for phe content."

→ What other resources do you use to find phe/pro content?

Category	Count	% (n=23, total "We use other resource(s) for phe content" responses)
Food Lists/Book	13	56.52173913
Unclassifiable	6	26.08695652
Food Labels	4	17.39130435
DietWell	2	8.695652174
AccuGo	1	4.347826087
Pen and Paper	1	4.347826087

\*Open-text responses for "other" responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** Do you currently use HMP to look up phe/protein/exchange content of foods?

→ If no, why not?

→ "Other"

Category	Count	% (n=45, total "other" responses)
Cost	12	26.66666667
Simplified Diet	4	8.888888889
Count Something Besides Phe	4	8.888888889
Challenges w/ Using Site	5	11.11111111
International Barrier	3	6.666666667
Off Diet/Don't Know Limits	3	6.666666667
Level of Accuracy Not Needed	3	6.666666667

Age of Child	5	11.11111111
Unclassifiable	8	17.77777778

\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** If HowMuchPhe.org were available in your country, do you think the metabolic community would use it?

→ 100% respondents said yes (6 out of 6)

**Question:** Do you use the diet-tracking feature on HMP?

Y/N	% (n=432, total survey respondents)
Yes	55.62
No	44.38

**Question:** Do you use the diet-tracking feature on HMP?

→ If no, why not?

If no, why not?	% Respondents (n=103, total “no” responses)
I use pen & paper	54.79
I just haven't taken the time to set it up	22.60
Other reason	19.18
I use another electronic method/app	10.27
I don't need to track intake	4.11

\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

**Question:** Do you use the diet-tracking feature on HMP?

→ If no, why not?

→ “Other”

Category	Count	% (n=28, total “other reason” responses)
Level of Accuracy Not Needed and/or Not Tracking	6	21.4285714
Age of Child	6	21.4285714
Not Primary Caregiver	4	14.2857143
Pen & Paper/Track in Head is Easier	4	14.2857143
Challenges Related to HMP	4	14.2857143
Unclassifiable	3	10.7142857
Haven't taken time to figure it out yet	2	7.1428571

\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** Do you use the diet-tracking feature on HMP?

→ "No"

→ What do you use to track phe/pro intake?

What do you use to track phe/pro intake?	% Respondents (n=118, total responses to this question)
Pen & Paper	44.92
Spreadsheet or word doc (electronic)	7.63
Another web site or app	7.63
I just keep track in my head	39.83

**Question:** Do you use the diet-tracking feature on HMP?

→ "No"

→ If you use a different program to look up phe values or track intake, what program do you use and why do you like it?

Category	Count	% (n=225, total individuals who offered response for this question)
Pen and paper/Track in head	76	33.77777778
Spreadsheet/Electronic	8	3.555555556
Simplified Diet	5	2.222222222
Track Protein	10	4.444444444
Book/List	22	9.777777778
Age of child	3	1.333333333
Difficulties w/ app or access	4	1.777777778
Miscellaneous	9	4
Dietwell	4	1.777777778
Accugo	12	5.333333333
MyFitnessPal	4	1.777777778
Other	7	3.111111111
I don't use another program	57	25.33333333

**Question:** How likely are you to recommend HowMuchPhe.org to a fellow individual managing a metabolic disorder? (Answers on a 1-5 scale: 1 = not very likely, 5 = very likely)

Average score: 4.427

**Question:** How likely are you to recommend HowMuchPhe.org to a fellow individual managing a metabolic disorder?

→ Why or why not?

→ Responses categorized under “why” reasoning:

Category	Count	% (n=282, total “why” or “why not” response)
Up to date	19	6.737588652
Convenience/Ease of use	74	26.24113475
Looking up phe (w/ accuracy)	44	15.60283688
Tracking	49	17.37588652
Communication/Coordination of Care	15	5.319148936
Determining phe in supermarket/restaurants	14	4.964539007
Completeness of food list	10	3.546099291
Utility of various features	7	2.482269504

\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** How likely are you to recommend HowMuchPhe.org to a fellow individual managing a metabolic disorder?

→ Why or why not?

→ Responses categorized under “why not” reasoning:

Category	Count	% (n=282, total “why” or “why not” response)
Neutral	12	4.255319149
Cost	8	2.836879433
Difficulty w/ site logistics	8	2.836879433
International Barrier	4	1.418439716
Unclassifiable	4	1.418439716

\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** What do you think is the biggest barrier preventing you or others from using HowMuchPhe.org? Check all that apply.

Category	Count	% (n=432, total survey respondents)
Cost	219	50.69
Other	113	26.16
Time	79	18.29
I basically know the phe/protein content of what we eat.	71	16.44
Difficult to use	63	14.58

The level of accuracy for phe/protein that HowMuchPhe.org provides is not needed.	17	3.94
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\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

**Question:** What do you think is the biggest barrier preventing you or others from using HowMuchPhe.org? Check all that apply.

→Open-text responses for “other” grouped into categories

Category	Count	% (n=113, “other” responses)
No barriers	23	20.3539823
Lack of Knowledge about HMP	17	15.04424779
Accustomed to other method or resource/resistance to change	14	12.38938053
Completeness of Database	11	9.734513274
Cultural barriers/barriers to other countries	11	9.734513274
Site Organization	10	8.849557522
Cost	9	7.96460177
General Accessibility	7	6.194690265
Unclassifiable	6	5.309734513
Lack of Need for HMP	4	3.539823009
Internet Access	4	3.539823009
Time	3	2.654867257

\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** National PKU News runs an amino acid analysis program that allows us to determine the exact protein and/or phe content of a food. Would you be interested in a program that allowed you to pay to have foods of your choice tested for phe/protein content?

Y/N	% (n=432, total survey respondents)
Yes	54.12%
No	45.88%

National PKU News runs an amino acid analysis program that allows us to determine the exact protein and/or phe content of a food. Would you be interested in a program that allowed you to pay to have foods of your choice tested for phe/protein content?

→“Yes”

**Question:** What’s the most you would be willing to pay for each food?

→Range: \$0.00 - \$1000

→Average: \$33.60

\$ Amount	# Respondents	% (n=234, total “Yes” respondents)
0	1	0.43
0.1	1	0.43

0.25	1	0.43
1	11	4.70
2	3	1.28
3	3	1.28
5	40	17.09
6	1	0.43
8	3	1.28
10	40	17.09
15	10	4.27
20	41	17.52
25	17	7.26
40	3	1.28
45	2	0.85
50	31	13.25
75	2	0.85
100	17	7.26
150	2	0.85
200	2	0.85
250	2	0.85
1000	1	0.43

**Question:** How did you hear about CookForLove.org?

	Family member	Friend	Hospital	Metabolic Clinic	Other
<b>% (n=432, total survey respondents)</b>	55.56	17.82	2.78	36.57	44.68

\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

**Question:** How did you hear about CookForLove.org?

→"Other"

Category	Count	% (n=193, total "other" responses)
Facebook	87	45.07772021
Online/Internet	71	36.78756477
Brenda	8	4.14507772
PKU Event	8	4.14507772
PKU Organization	6	3.10880829
PKU Listserv	5	2.590673575
Newsletter	4	2.07253886
Don't Remember	4	2.07253886
HMP	3	1.554404145
Never heard of it	2	1.03626943



\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** How often do you use CookForLove.org?

Response	#	% (n=432, total survey respondents)
Never	45	10.42
Sometimes	222	51.39
Often	165	38.19

**Question:** How important is it to you to be able to prepare food for you or your loved one with a metabolic disorder? (1-5 scale; 1=not important at all, 5=very important)

→ Average score: 4.839

**Question:** Why do you use Cook for Love’s recipes? Check all that apply.

Reason	% (n=432, total survey respondents)
The recipes are delicious.	66.20
I know the recipes are tested and reviewed so I am more comfortable putting the effort into preparing them.	49.07
I can ask questions on Facebook about a recipe and receive answers.	47.92
I can share the end results with family and friends, high- and low-protein alike, so I am not making two versions.	47.22
It is cheaper than purchasing ready-made low-protein items.	46.99
I enjoy cooking.	40.51
The person I cook for does not like the taste of ready-made low-protein foods (medical foods).	33.10
It empowers me.	27.78
I have no medical food coverage.	23.15
I don’t use CookForLove	8.80
Other	8.56

\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

**Question:** Why do you use Cook for Love’s recipes?

→ “Other”

Category	Count	% (n=37, total “other” responses)
Health/freshness	10	27.02702703
Unclassifiable	8	21.62162162
More variety	5	13.51351351
Taste	4	10.81081081

Brenda's guidance	3	8.108108108
Inspiration	3	8.108108108
Reliability for the future	2	5.405405405
Affordability	1	2.702702703
Importance of homecooking	1	2.702702703

\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** How likely are you to recommend CookForLove.org to a fellow individual managing a metabolic disorder? (1 to 5 scale; 1=not likely at all, 5=very likely)

Average score: 4.654

**Question:** How likely are you to recommend CookForLove.org to a fellow individual managing a metabolic disorder? (1 to 5 scale; 1=not likely at all, 5=very likely)

→Why or why not?

→Responses categorized under “why” reasoning:

Category	Count	% (n=268, total “why” or “why not” responses)
Quality of Recipes	132	49.25373134
Unclassifiable	37	13.80597015
Ease/Convenience	26	9.701492537
Adds Variety	24	8.955223881
Adds Normalcy	20	7.462686567
Support (FB group, Brenda, site instructions)	18	6.71641791
Phe info. accurate & adaptable to fit tolerance	15	5.597014925
Homemade > Premade	8	2.985074627

\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** How likely are you to recommend CookForLove.org to a fellow individual managing a metabolic disorder? (1 to 5 scale; 1=not likely at all, 5=very likely)

→Why or why not?

→Responses categorized under “why not” reasoning:

Category	Count	% (n=268, total “why” or “why not” responses)
Neutral	32	11.94029851
"Obscure Ingredients"	4	1.492537313
Time	4	1.492537313
Recipe-related	3	1.119402985
Phe too high	3	1.119402985
Site Logistics	2	0.746268657
Prefer ready made foods	1	0.373134328

\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** What do you think is the biggest barrier preventing you or others from using CookForLove.org? Check all that apply.

<b>Barrier</b>	<b>% (n=432, total survey respondents)</b>
Time to prepare recipes	65.04
Effort to prepare recipes	49.77
Not confident in ability to cook low-protein foods.	34.03
Cost of ingredients	19.21
The person I cook for doesn't eat the food I prepare so it's not worth the time and effort.	15.97
The recipes are too high for the person I cook for.	15.51
Other	14.81
The recipes are too low for the person I cook for.	1.85

\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

**Question:** What do you think is the biggest barrier preventing you or others from using CookForLove.org? Check all that apply.

→ “Other” responses:

<b>Category</b>	<b>Count</b>	<b>% (n=64, total “other” responses)</b>
Special Ingredients	22	34.38
Recipes overwhelming/time-consuming	10	15.63
Lack of Knowledge/Forget about / Haven't tried CFL	8	12.5
Recipes not/not yet suitable to my eater	6	9.38
Challenges w/ phe tolerance/counting phe	5	7.81
No barriers	5	7.81
Site structure/functionality	4	6.25
Not enough recipes	1	1.56
Preference for other method	1	1.56

\*Open-text responses for “other” responses were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.

**Question:** How can those individuals and families affected by metabolic disorders who are not using these resources better be reached?

<b>Method</b>	<b>% (n=432, total survey respondents)</b>
Increased discussion of resources during patient visits in metabolic clinics	86.34
Word of Mouth	41.67
Targeted marketing	38.19
Other	6.25

\*Surveyors could choose more than one answer; thus, percentages will not total to 100%.

**Question:** How can those individuals and families affected by metabolic disorders who are not using these resources better be reached?

→ "Other" responses

Category	Count	% (n=27, total "other" responses)
Clinicians	12	44.44
Social Media	6	22.22
In Person Workshops/Cooking Demos	6	22.22
Group Cooking	4	14.81
Discount Opportunities	1	3.70
Collaboration with Other Organizations (e.g. Cambrooke)	3	11.11
Handouts at PKU Events	2	7.40

*For the following 4 questions, the following scale was used: 1 to 5 scale; 1 = not likely at all, 2 = not likely, 3 = neutral, 4 = likely, and 5 = very likely (n=432 respondents)*

**Question:** How likely are you to utilize an online, community-driven recipe site?

Average score: 4.586

**Question:** What is the likelihood a resource such as this would increase your frequency of low-protein cooking?

Average score: 4.218

**Question:** What is the likelihood a resource such as this would help promote lifelong adherence to the diet?

Average score: 4.291

**Question:** What is the likelihood such a website would increase the variety of your low-pro cooking?

Average score: 4.502

**Question:** The following are potential elements of a community-driven recipe site. Please indicate how useful you perceive each element would be in this site, based on the following scale: 1 = not useful, 2= minimally useful, 3= neutral, 4= somewhat useful, 5= very useful (n=432 respondents)

Ranking	Site Feature	Average Score
1	Common LP Substitutions for HP foods	4.637

2	Tips: School Lunches	4.559
3	Private annotation of recipe/personal recipe box	4.5
4	Common LP substitutions for the picky eater	4.478
5	Tips: Cooking for LP loved oens simultaneously with the rest of your family	4.469
6	Recipes for prep. large amounts in advance	4.381
7	“How-to” tutorial videos (e.g. meal-prepping)	4.366
8	Reading food labels w/ common phe-containing foods	4.337
9	Step-by-step photos of recipe prep.	4.282
10	Grandparents/Extended Family Guide - "dos/don'ts"	4.264
11	Categorization of foods to different life phases	4.247
12	Recipe rating system (e.g. a 5-star scale)	4.244
13	Public annotation of reci. (e.g. what my child said)	3.863

**Question:** Please indicate how useful you perceive each of the following “search by” tools would be in this site, using the following scale: 1 = not useful, 2 = minimally useful, 3 = neutral, 4 = somewhat useful, 5 = very useful  
(n=432 respondents)

Ranking	Site Feature	Score
1	Phe per serving	4.619
2	Meal category	4.467
3	Recipe requiring specialty products vs. recipes requiring only grocery store foods	4.465
4	School lunch foods	4.421
5	Time to Prepare	4.275
6	Category (e.g. “pizza night” - guide low-protein options/accommodate a theme)	4.227
7	Recipes containing specific specialty low-protein products	4.225
8	Number of Ingredients	3.892

**Question:** Would you be interested in a program that allowed you to pay to have a family recipe adapted to the low-protein diet (e.g. Mom’s famous pumpkin-mousse pie?)

Y/N	% (n=432, total survey respondents)
Yes	46.76
No	53.24

**Question:** Would you be interested in a program that allowed you to pay to have a family recipe adapted to the low-protein diet (e.g. Mom’s famous pumpkin-mousse pie?)

→If yes, how much would you be willing to pay?

\$ Amount	# Responses (n = 202,

	total "yes" responses)
0	2
1	4
2	2
3	4
4	1
5	24
8	2
10	33
15	13
20	38
25	20
30	8
40	3
45	1
50	30
60	1
100	12
150	1
250	2
500	1

→Range: \$0.00 - \$500

→Average: \$30.99

Where We're Headed Next

**Question:** Do you think the current online resources for the metabolic community (both the web sites and Facebook) are sufficient?

Y/N	% (n=432, total survey respondents)
Yes	46.69
No	52.31

**Question:** National PKU News, How Much Phe, and Cook For Love hope to eventually develop an online resource with some of the following features. Please let us know which would be most useful to you: (n = 432, total survey respondents)

Ranking	Site Feature	Average Score
1	Info. on latest research	4.542
2	Networking component	4.427
3	Calendar of metabolic events/ability to find events near you	4.383

4	Forum: Question & community answers to be filtered by age/stage of life, topic, etc.	4.306
5	"Online diet board"	4.256
6	"Insurance networking center to share tips on securing coverage"	3.196

**Question:** As a member of the metabolic community, do you perceive a need for this type of resource? (1 to 5 scale; 1 = not at all, 2 = not really, 3 = neutral, 4 = possibly, 5 = absolutely)

Average score: 4.72

**Question:** How likely are you to utilize this type of resource? (1 to 5 scale; 1 = not likely at all, 2 = not likely, 3 = neutral, 4 = likely, and 5 = very likely)

Average score: 4.621

**Question:** Based on the description of the proposed resources are there any additional ideas or tools you feel were not mentioned in this survey? Please offer your input below.

Category	Count	% (n = 136, total individuals who offered a response)
No, what you've proposed sounds excellent.	50	36.76470588
Unclassifiable	16	11.76470588
HMP Related	11	8.088235294
Cost	8	5.882352941
Grocery store guide	8	5.882352941
App	6	4.411764706
Recipe-related ideas	6	4.411764706
Simplified Diet	5	3.676470588
Considerations for other metabolic disorders	5	3.676470588
Protein/calorie Info	5	3.676470588
Advocacy	5	3.676470588
Teens/Young adults	5	3.676470588
Reservations about resource	5	3.676470588
Kitchen hacks	4	2.941176471
Young kids	4	2.941176471
Insurance	3	2.205882353
PKU Adults	3	2.205882353
Travel/on-the-go	3	2.205882353
Section addressing comorbidities (celiac, diabetes, allergies, special needs, etc.)	3	2.205882353
Recipe/new food inspiration	2	1.470588235

Mentor program	2	1.470588235
Other country	2	1.470588235
At-home blood testing	2	1.470588235
Eating "Healthy" w/ PKU	1	0.735294118
Friends/Family guide	1	0.735294118

\*Open-text responses for this question were grouped into categories. Some responses fit into multiple categories, so percentages will not total to 100%.



## Appendix B: Open-Text Responses

**Question:** How did you hear about HMP.org?

Categorized open text responses for “other”

Category	Count
FB	91
Online/Internet	30
PKU Organizations	21
CFL	16
Conferences	13
Unclassifiable	9
Newsletters/Mail	8
Transition from Book→Online	6
Listservs	4
Virginia	3
PKU Camp	2

**Question:** Do you currently use HMP to look up phe/protein/exchange content of foods?

→If no, why? →We use other resource(s) for phe content

→Categorization of “other resources”

Category	Count
Food Lists/Book	13
Unclassifiable	6
Food Labels	4
DietWell	2
Pen and Paper	1
AccuGo	1

**Question:** Do you currently use HMP to look up phe/protein/exchange content of foods?

→If no, why? →“other reason”

→Categorization of “other reasons”

Category	Count
Cost	12
Misc.	8
Challenges w/ Using Site	5
Age of Child	5
Simplified Diet	4

<b>Count Something Besides Phe</b>	4
<b>International Barrier</b>	3
<b>Off Diet/Don't Know Limits</b>	3
<b>Level of Accuracy Not Needed</b>	3

**Question:** Do you use the diet-tracking features on HowMuchPhe.org? If no, why?

→ If no, why?

→ Categorization of “other” responses

<b>Category</b>	<b>Count</b>
<b>Level of Accuracy Not Needed and/or Not Tracking</b>	6
<b>Age of Child</b>	6
<b>Not Primary Caregiver</b>	5
<b>Pen &amp; Paper/Track in Head is Easier</b>	4
<b>Challenges Related to HMP</b>	4
<b>Unclassifiable</b>	3
<b>Haven't taken time to figure it out yet</b>	2

**Question:** Do you use the diet-tracking features on HowMuchPhe.org? If no, why?

→ No → If you use a different program to look up phe values or track intake, what program do you use and why do you like it?

→ Categorization of other programs:

<b>Category</b>	<b>Count</b>
<b>Pen and paper/Track in head</b>	76
<b>Don't use other program</b>	57
<b>Book/List</b>	22
<b>Track Protein</b>	10
<b>Unclassifiable</b>	9
<b>Spreadsheet/Electronic</b>	8
<b>Simplified Diet</b>	5
<b>Difficulties w/ app or access</b>	4
<b>Age of child</b>	3
<b>Accugo</b>	12
<b>Other</b>	7

Dietwell	4
MyFitnessPal	4

**Question:** How likely are you to recommend HowMuchPhe.org to a fellow individual managing a metabolic disorder?

→ Categorization of “why” responses:

Category	Count
Unclassifiable	84
Convenience/ Ease of use	74
Tracking	49
Looking up phe (w/ accuracy)	44
Up to date	19
Communication/Coordination of Care	15
Determining phe in supermarket/restaurants	14
Completeness of food list	10
Utility of various features	7

**Question:** How likely are you to recommend HowMuchPhe.org to a fellow individual managing a metabolic disorder?

→ Categorization of “why not” responses:

Category	Count
Neutral	12
Cost	8
Difficulty w/ site logistics	8
International Barrier	4
Miscellaneous	4

**Question:** What do you think is the biggest barrier preventing you or others from using HowMuchPhe.org? Check all that apply.

→ Categorization of “other” responses:

Category	Count
No barriers	23
Lack of Knowledge about HMP	17
Accustomed to other method or resource/resistance to change	14

<b>Completeness of Database</b>	11
<b>Cultural barriers/barriers to other countries</b>	11
<b>Site Organization/Functionality</b>	10
<b>Cost</b>	9
<b>General Accessibility</b>	7
<b>Unclassifiable</b>	6
<b>Internet Access</b>	4
<b>Lack of Need for HMP</b>	3
<b>Time</b>	3

**Question:** How did you hear about CookForLove.org?

→ Categorization of “other” responses

<b>Category</b>	<b>Count</b>
<b>Facebook</b>	87
<b>Online/Internet</b>	71
<b>Brenda</b>	8
<b>PKU Event</b>	8
<b>PKU Organizations</b>	6
<b>PKU Listserv</b>	5
<b>Newsletter</b>	4
<b>Don't Remember</b>	4
<b>HMP</b>	3
<b>Never heard of it</b>	2

**Question:** Why do you use Cook for Love’s recipes?

→ Categorization of “other reasons:”

<b>Category</b>	<b>Count</b>
<b>Health/freshness</b>	10
<b>Unclassifiable</b>	8
<b>More variety</b>	5
<b>Taste</b>	4
<b>Brenda's guidance</b>	3
<b>Inspiration</b>	3
<b>Reliability for the future</b>	2

<b>Normalcy</b>	1
<b>Affordability</b>	1

**Question:** How likely are you to recommend CookForLove.org to a fellow individual managing a metabolic disorder?

→Categorization of “why” responses:

<b>Category</b>	<b>Count</b>
<b>Quality of Recipes</b>	133
<b>Miscellaneous positive feedback</b>	37
<b>Ease/Convenience</b>	26
<b>Adds Variety</b>	24
<b>Neutral</b>	23
<b>Adds Normalcy</b>	20
<b>Support (FB group, Brenda, site instructions)</b>	18
<b>Homemade is Superior to Premade</b>	18
<b>Phe info. accurate &amp; adaptable to fit tolerance</b>	15

**Question:** How likely are you to recommend CookForLove.org to a fellow individual managing a metabolic disorder?

→Categorization of “why not” responses:

<b>Category</b>	<b>Count</b>
<b>Time</b>	4
<b>Obscure Ingredients</b>	4
<b>Recipe-related</b>	3
<b>Phe too high</b>	3
<b>Site Logistics</b>	2
<b>Prefer ready-made foods</b>	1

**Question:** What do you think is the biggest barrier preventing you or others from using CookForLove.org? Check all that apply.

→Categorization of “other” responses:

<b>Category</b>	<b>Count</b>
-----------------	--------------

Special Ingredients	22
Recipes overwhelming/time-consuming	10
Lack of Knowledge / Forget about / Haven't tried CFL	8
Recipes not/not yet suitable to my eater	6
Challenges w/ phe tolerance/counting phe	5
No barriers	5
Site structure/functionality	4
Recipe related barriers	2

**Question:** How can those individuals and families affected by metabolic disorders who are not using these resources better be reached?

→Categorization of “other” responses:

Category	Count
Coordination with Metabolic Clinicians	12
In Person Workshops/Cooking Demos	6
Group Cooking	4
Collaboration with Other Organizations (e.g. Cambrooke)	3
Handouts at PKU Events	2
Discount Opportunities	1

**Question:** Based on the description of the proposed resources are there any additional ideas or tools you feel were not mentioned in this survey? Please offer your input below.

Category	Count
No, what you've proposed sounds excellent.	50
Unclassifiable	16
HMP Related	11
Cost	8
Grocery store tools	8

<b>App</b>	6
<b>Recipe-related ideas</b>	6
<b>Considerations for other metabolic disorders</b>	5
<b>Protein/calorie Info</b>	5
<b>Simplified Diet</b>	5
<b>Advocacy</b>	5
<b>Teens/Young adults</b>	5
<b>Reservations about resource</b>	5
<b>Young kids</b>	4
<b>Kitchen hacks</b>	4
<b>Section addressing comorbidities (celiac, diabetes, allergies, special needs, etc.)</b>	3
<b>Insurance</b>	3
<b>PKU Adults</b>	3
<b>Travel/on-the-go</b>	3
<b>Recipe/new food inspiration</b>	2
<b>At-home blood testing</b>	2
<b>Other country</b>	2
<b>Recipe/new food inspiration</b>	2
<b>Friends/Family guide</b>	1
<b>Eating "Healthy" w/ PKU</b>	1

### Appendix C: Stratified by Age Group

Survey respondents indicated the age of the individual with the metabolic disorder, on behalf of whom they were taking the survey. The following charts provide a breakdown of survey responses by age group, for the questions that were deemed relevant.

**Question:** How often do you use CookForLove.org?

Age Group	Count (n)	Average Score out of 3
0-5	192	2.32
6-11	120	2.48
12-18	55	2.38
19-25	27	2.19
26-50	72	2.03
50+	10	2.2
Never = 1 Sometimes = 2 Often = 3		

**Question:** How important is it to you to be able to prepare food for you or your loved one with a metabolic disorder?

Age Group	Count (n)	Average Score out of 5
0-5	192	4.93
6-11	120	4.91
12-18	55	4.87
19-25	27	4.93
26-50	72	4.65
50+	10	4.6
Not important at all = 1 Not that important = 2 Neutral = 3 Important = 4 Very important = 5		



**Question:** What do you think is the biggest barrier preventing you or others from using CookForLove.org? Check all that apply.

Barrier	Age Group	Count (n)	% (of total "n" for each age group)
Time to prepare recipes	0-5	192	67.19
	6-11	120	60
	12-18	55	65.45
	19-25	27	33.33
	26-50	72	70.83
	50+	10	60
Effort to prepare recipes	0-5	192	50.52
	6-11	120	48.33
	12-18	55	49.09
	19-25	27	51.85
	26-50	72	51.39
	50+	10	10
Cost of ingredients	0-5	192	19.79
	6-11	120	14.17
	12-18	55	14.55
	19-25	27	18.52
	26-50	72	26.39
	50+	10	40
Not confident in ability to cook low-protein foods.	0-5	192	35.42
	6-11	120	35
	12-18	55	34.55
	19-25	27	33.33
	26-50	72	27.78
	50+	10	10
The person I cook for doesn't eat the food I prepare so it's not worth the time and effort.	0-5	192	20.31
	6-11	120	19.17
	12-18	55	16.36
	19-25	27	14.81

	26-50	72	0
	50+	10	0
The recipes are too high for the person I cook for.	0-5	192	14.06
	6-11	120	9.17
	12-18	55	20
	19-25	27	18.52
	26-50	72	23.61
	50+	10	10
	The recipes are too low for the person I cook for.	0-5	192
6-11		120	0.83
12-18		55	18.18
19-25		27	0
26-50		72	2.78
50+		10	0
Other		0-5	192
	6-11	120	15
	12-18	55	12.73
	19-25	27	29.63
	26-50	72	11.11
	50+	10	60

**Question:** The following are potential elements of a community-driven recipe site. Please indicate how useful you perceive each element would be in this site, based on the following scale: 1 = not useful, 2 = minimally useful, 3 = neutral, 4 = somewhat useful, 5 = very useful

Element	Age Group	Count (n)	Average Score out of 5
Tips: Cooking for low-protein loved ones simultaneously w/ the rest of your family	0-5	192	4.67
	6-11	120	4.4
	12-18	55	4.25
	19-25	27	4.48
	26-50	72	4.38
	50+	10	4.5
	Tips: School lunch section (e.g. how to make your loved one feel like everybody else, how to add variety to lunches, etc.)	0-5	192

	6-11	120	4.68
	12-18	55	4.47
	19-25	27	4.44
	26-50	72	4.04
	50+	10	4.1
Common low-protein substitutions for high-protein foods (e.g. cauliflower for chicken)	0-5	192	4.77
	6-11	120	4.6
	12-18	55	4.53
	19-25	27	4.67
	26-50	72	4.56
	50+	10	4.2
Common low-protein substitutions to accommodate foods that your low-protein child or loved one may not like (e.g. cauliflower for mushrooms)	0-5	192	4.63
	6-11	120	4.44
	12-18	55	4.22
	19-25	27	4.26
	26-50	72	4.36
	50+	10	4.3
Guide to recipes well-suited for preparing large amounts in advance	0-5	192	4.49
	6-11	120	4.34
	12-18	55	4.27
	19-25	27	4.48
	26-50	72	4.32
	50+	10	4.4
Step-by-step photos of recipe preparation	0-5	192	4.31
	6-11	120	4.18
	12-18	55	4.25
	19-25	27	4.48
	26-50	72	4.4
	50+	10	3.8
Ability to publicly annotate recipes with items such as “what my child said about this recipe”	0-5	192	3.97
	6-11	120	3.89

	12-18	55	3.65
	19-25	27	3.96
	26-50	72	3.81
	50+	10	3.7
Ability to privately annotate and/or modify a recipe and save to personal recipe box	0-5	192	4.65
	6-11	120	4.33
	12-18	55	4.4
	19-25	27	4.63
	26-50	72	4.44
	50+	10	4.1
“How-to” tutorial videos (e.g. meal-prepping, making pizza dough, etc.)	0-5	192	4.47
	6-11	120	4.26
	12-18	55	4.27
	19-25	27	4.52
	26-50	72	4.44
	50+	10	4
Recipe rating system (e.g. a 5-star scale)	0-5	192	4.26
	6-11	120	4.24
	12-18	55	4.24
	19-25	27	4.24
	26-50	72	4.24
	50+	10	4.2
“Grandparents/Extended Family Guide” – quick “dos and don’ts” related to the diet for when grandparents or friends are supervising your loved one	0-5	192	4.52
	6-11	120	4.27
	12-18	55	3.98
	19-25	27	4.22
	26-50	72	3.97
	50+	10	3.8
Guide to reading a food label with list of common phe-containing foods	0-5	192	4.51
	6-11	120	4.24
	12-18	55	4.24

	19-25	27	4.3
	26-50	72	4.19
	50+	10	4
Categorization of recipes best-suited to different life phases (introducing solids, toddler, primary school, teen years, college)	0-5	192	4.51
	6-11	120	4.22
	12-18	55	4.15
	19-25	27	4.04
	26-50	72	3.86
	50+	10	4
	Not At All Useful = 1 Not Useful = 2 Neutral = 3 Useful = 4 Very Useful = 5		

**Question:** Please indicate how useful each of the following “search by” tools would be to you (1 to 5 scale; 1 = not at all useful, 2 = not useful, 3 = neutral, 4 = somewhat useful, 5 = very useful)

Element	Age Group	Count (n)	Average Score out of 5
Time to Prepare	0-5	192	4.27
	6-11	120	4.29
	12-18	55	4.24
	19-25	27	4.56
	26-50	72	4.46
	50+	10	4.2
	Number of Ingredients	0-5	192
6-11		120	3.78
12-18		55	3.76
19-25		27	4.22
26-50		72	4.01
50+		10	3.9
Meal category (breakfast, lunch, dinner, snack, dessert, holiday, etc.)		0-5	192
	6-11	120	4.44
	12-18	55	4.53

	19-25	27	4.63
	26-50	72	4.38
	50+	10	4.2
Recipes containing specific specialty low-protein products	0-5	192	4.29
	6-11	120	4.25
	12-18	55	4.07
	19-25	27	4.48
	26-50	72	4.35
	50+	10	4.2
Category (e.g. "pizza night" or "taco night" to help guide low-protein options to accommodate a certain theme)	0-5	192	4.32
	6-11	120	4.19
	12-18	55	4.25
	19-25	27	4.33
	26-50	72	4.28
	50+	10	3.7
School lunch foods	0-5	192	4.64
	6-11	120	4.58
	12-18	55	4.35
	19-25	27	4.07
	26-50	72	4
	50+	10	3.5
Phe per serving	0-5	192	4.69
	6-11	120	4.56
	12-18	55	4.62
	19-25	27	4.7
	26-50	72	4.42
	50+	10	4.3
Recipe requiring specialty products vs. recipes requiring only grocery store foods	0-5	192	4.52
	6-11	120	4.44
	12-18	55	4.22
	19-25	27	4.78
	26-50	72	4.58

	50+	10	4.2
Not At All Useful = 1			
Not Useful = 2			
Neutral = 3			
Useful = 4			
Very Useful = 5			

**Question:** Do you think the current online resources for the metabolic community (both the web sites and Facebook) are sufficient?

Response	Age Group	Count (n)	% (of total "n" for each age group)
Yes	0-5	192	49
	6-11	120	56
	12-18	55	45
	19-25	27	19
	26-50	72	35
	50+	10	70
No	0-5	192	51
	6-11	120	44
	12-18	55	55
	19-25	27	81
	26-50	72	65
	50+	10	30

**Question:** National PKU News, How Much Phe, and Cook For Love hope to eventually develop an online resource with some of the following features. Please let us know which would be most useful to you (1 to 5 scale; 1 = not at all useful, 2 = not useful, 3 = neutral, 4 = useful, 5 = very useful):

Feature	Age Group	Count (n)	Average Score out of 5
Information on the latest research (both related to finding a cure and to dietary practices)	0-5	192	4.52
	6-11	120	4.58
	12-18	55	4.65
	19-25	27	4.59
	26-50	72	4.51

	50+	10	4.3
A calendar of metabolic events and the ability to find events near you	0-5	192	4.47
	6-11	120	4.28
	12-18	55	4.36
	19-25	27	4.41
	26-50	72	4.22
	50+	10	4.1
A networking component that would allow you to find members of the community near you, connect with them, and encourage networking through events such as batch cooking get-togethers and support groups.	0-5	192	4.58
	6-11	120	4.34
	12-18	55	4.38
	19-25	27	4.56
	26-50	72	4.31
	50+	10	4
A forum with questions & community answers you could filter by age/stage of life, topic, tolerance, and other filters	0-5	192	4.42
	6-11	120	4.23
	12-18	55	4.35
	19-25	27	4.33
	26-50	72	4.13
	50+	10	4
An "online diet board" to help children learn to manage the diet.	0-5	192	4.47
	6-11	120	4.48
	12-18	55	4.27
	19-25	27	4
	26-50	72	3.69
	50+	10	3.7
An insurance networking center to share tips on securing coverage from different carriers & plans	0-5	192	4.27
	6-11	120	4.24
	12-18	55	4.11
	19-25	27	4.45
	26-50	72	4.31



	50+	10	3.5
Not At All Useful = 1 Not Useful = 2 Neutral = 3 Useful = 4 Very Useful = 5			

**Question:** As a member of the metabolic community, do you perceive a need for this type of resource?

Age Group	Count (n)	Score out of 5
0-5	192	4.79
6-11	120	4.68
12-18	55	4.67
19-25	27	4.67
26-50	72	4.67
50+	10	4.7
Not At All = 1 Not Really = 2 Indifferent = 3 Possibly = 4 Absolutely = 5		

## **Appendix D – Summary of Survey Findings**

### *Background*

The intent of the present survey was to inform the development of a new and improved CookForLove.org (CFL), by soliciting feedback from the PKU community. The new platform will be a community-driven recipe site, containing all of the previous elements of CFL in addition to an expanded set of resources, thanks to the institutional muscle provided by HowMuchPhe.org. A message requesting users participate in the survey along with the link to the survey was posted in the following Facebook groups: Cook For Love, How Much Phe, PKU Worldwide Support Group, Parents of PKUers, and PKU News.

The survey was posted on 9/26/17 and closed on 10/23/17, yielding 432 responses. The survey results were organized by question into tables (Appendix A). Several questions contained an option for open-text responses to obtain more detailed information about individuals' responses (i.e. "why," "why not," etc.) These open-text responses were grouped into categories for each question (Appendix B). Finally, certain questions were identified as relevant for stratification by age. Responses to these questions were broken down by age group (0-5, 6-11, 12-18, 19-25, 26-50, 50+), to provide more age-specific feedback to survey questions (Appendix C). Please refer to these appendices for the comprehensive results produced by the survey.

### *Demographics*

86.34% of the 432 survey respondents reside in the United States, 9.26% reside in Canada, and the remaining 4.4% are from other countries. Please refer to Appendix A for the exhaustive list of countries.

The majority of survey participants reported to be parents of a child or children with a metabolic disorder (78.01%). 17.57% of total respondents indicated they were the individual with a metabolic disorder, and the remaining respondents fell into the categories "my significant other," "my grandchild," "other family member," "friend," or "other." Survey respondents were asked to indicate the age of the individual with a metabolic disorder on

behalf of whom they took the survey. The breakdown by age, in order of prevalence, is as follows: 44.44% 0-5 year olds, 27.78% 6-11 year olds, 16.67 25-49 year olds, 12.73% 12-18 year olds, 6.25% 19-25 year olds, and 2.31% 50 years old and above.

#### *HowMuchPhe.org and CookForLove.org Utilization*

Most survey participants report using CFL (86.81% of total respondents) and HMP (78.01% of total respondents), as well as their respective Facebook group pages (CFL: 78.94% and HMP: 63.19%). Please refer to Appendices A and B for the comprehensive list of online resources utilized, as reported by this population of survey participants.

86.34% of total survey respondents suggested “increased discussion of resources during patient visits in metabolic clinics” as the best method for reaching individuals and families affected by metabolic disorders to increase usage of HMP and CFL. 41.67% suggested word of mouth, and 38.19% believed targeted marketing would be effective. 6.25% of respondents suggested “other” methods, which are listed in Appendices A and B.

#### *HowMuchPhe.org Utilization*

Participants were asked to indicate how they heard about HowMuchPhe.org. The majority of respondents reported hearing about the resource at their metabolic clinic or from “other” sources (45.14% and 41.90%, respectively). Facebook, CFL, and “online” were among the “other” sources reported. Please refer to appendices A and B for the comprehensive list.

When asked whether participants use HMP to look up phe/protein/exchange content, 76.12% of total respondents reported “yes,” and 23.84% reported “no.” Among the 103 individuals who reported “no,” the following responses were the most common responses as to why they don’t use this resource within HMP: “Other,” “I know the phe/protein of most foods consumed,” and “We use other resource(s) for phe content.” The “other” resources indicated were DietWell, AccuGo, food lists, food labels, pen and paper, and a variety of other miscellaneous resources. The most common “other” reasons indicated for *not* using HMP to look up phe/protein/exchange content included cost, age of the child, and challenges with using the site. The exhaustive list of reasons can be viewed in Appendix A.

100% of respondents said “yes” when asked whether the metabolic community would use HMP if it were available in their country; however, it should be noted that there were only six respondents to this question. Response to this question may have been low given that only 4.4% of survey respondents live in countries where HMP is not offered (all other countries besides US and Canada).

55.62% of total survey respondents report using the diet-tracking feature on HMP. Of the 44.38% respondents (n=103) who reported they do not use this feature, the most popular reason was that they use pen and paper instead (54.79% of 103 “no” respondents). The next most common response was “I just haven’t taken the time to set it up.” Please refer to Appendix A for a list of the other reasons participants do not use the diet-tracking feature on HMP as well as a list of alternative programs participants use to look up phe values and/or track intake.

A Likert scale was used for several of the questions in the survey. On a 1 to 5 scale, with 1 = not very likely, 2 = not likely, 3 = neutral, 4 = likely, and 5 = very likely, participants were asked to indicate how likely they were to recommend HMP to an individual managing a metabolic disorder. The results produced an average score of 4.427, indicating respondents fall somewhere between likely and very likely to recommend HMP. When prompted to indicate why or why not individuals would recommend this resource, “up to date,” “convenience/ease of use,” and “looking up phe (w/ accuracy)” were the most common reasons “why” and “neutral,” “cost,” and “difficulty with site logistics” were the most common reasons “why not.” It should be noted that many of the open-text responses within the “neutral” category were related to having never used CFL. It is also important to note that the “why or why not?” portion of this question was optional, so the number of responses impact the power of the results. Further, there were only 36 total responses that fell into categories explaining “why not.” Please refer to Appendix A for the comprehensive list of “why” or “why not” rationales in addition to the counts for each rationale.

National PKU News runs an amino acid analysis program that allows exact protein and/or phe content of a food to be determined. Survey participants were asked whether they would be interested in a program that allowed them to pay to have foods of their choosing

tested for phe/protein content. 54.12% of total survey respondents said “yes,” while 45.88% said “no.” If participants responded “yes,” they were asked to indicate the maximum amount they would be willing to pay for this service. Dollar amounts ranged from \$1 to \$1000, with an average of \$33.60. The most common listed dollar amounts, in order, were \$20 (n=38), \$10 (n=33), and \$5 (n=24).

#### *HMP: Barriers to Use*

Cost, “other,” and time were reported as the three most common categories of perceived barriers preventing survey respondent or others from using HMP. Other barriers and the comprehensive list of open-text responses offered within the “other” category can be viewed in Appendices A and B.

#### *CookForLove.org Utilization*

Participants were asked to indicate how they heard about CFL. The majority of respondents reported hearing about it from a family member, at their metabolic clinic, or from another source (55.56%, 36.57%, and 44.68% respectively, with n=432 total survey respondents). “Facebook,” “online/internet,” and “Brenda” (founder of CFL) were among the “other” sources reported. Please refer to appendices A and B for the comprehensive list.

Most individuals (51.39% total survey respondents) indicate using CFL “sometimes,” while 38.19% reported using CFL often and 10.42% reported “never” using CFL.

Using a 1 to 5 Likert scale, with 1 = not important at all, 2 = not important, 3 = neutral, 4 = important, and 5 = very important, respondents were asked to indicate the level of importance when it comes to preparing food for their loved one with a metabolic disorder. The average score was 4.839, indicating food preparation to be of high importance for this population sample.

When asked why participants use CFL, the following reasons were most common (individuals were able to select multiple responses): “the recipes are delicious,” “I know the recipes are tested and reviewed so I am more comfortable putting the effort into preparing them,” and “I can ask questions on Facebook about a recipe and receive answers.” Please refer

to Appendices A and B for the comprehensive list of reasons, including those indicated via open-text response within the “other” category.

On a 1 to 5 Likert scale, with 1 = not very likely, 2 = not likely, 3 = neutral, 4 = likely, and 5 = very likely, participants were asked to indicate how likely they were to recommend CFL to an individual managing a metabolic disorder. The results produced an average score of 4.654, indicating respondents fall somewhere between likely and very likely to recommend CFL. When prompted to indicate why or why not individuals would recommend this resource, the most common responses for “why” were grouped into the following categories: “quality of recipes,” “miscellaneous positive feedback,” and “ease/convenience of use.” The most common reasons behind “why not” were related to: “neutral,” “obscure ingredients,” and “time.” It is important to note that the “why or why not?” portion of this question was optional, so the number of responses impact the power of the results; there were only 49 total responses that fell into categories explaining “why not.” Please refer to Appendix A for the comprehensive list of “why” or “why not” rationales in addition to the counts for each rationale.

#### *CFL: Barriers to Use*

“Time to prepare recipes,” “Effort to prepare recipes,” and “Not confident in ability to cook low-protein foods” were selected as the top three perceived barriers preventing individuals from using CFL. Other barriers and the comprehensive list of open-text responses offered within the “other” responses can be viewed in Appendices A and B.

#### *Community-Driven Recipe Site*

Likert scales were used for a host of questions to gather consumer insight as to how to best design the new CFL platform. First, questions were asked to solicit whether the sample population perceives the site as useful and the likelihood it might enhance their lifestyle with respect to managing a metabolic disorder (1 to 5 scale; 1 = not likely at all, 2 = not likely, 3 = neutral, 4 = likely, and 5 = very likely). Based on averages from the responses of all 432 survey respondents, the sample population indicated high likelihood they would use the tool (4.586),

and strong likelihood this resource would increase both frequency (4.218) and variety (4.502) of low-protein cooking.

To poll the participants on perceived “usefulness” of a variety of potential elements for the site, Likert scales were used (1 = not useful, 2= minimally useful, 3= neutral, 4= somewhat useful, 5= very useful). The following potential site features scored highest on perceived usefulness: “Common Low-Protein Substitutions for High-Protein Foods” (4.637), “Tips: School Lunches” (4.559), and “Private Annotation of Recipe/Personal Recipe Box” (4.5). Please refer to Appendix A for the comprehensive list of features and their respective “usefulness” scores.

Using the same scale as in the question prior, survey respondents were asked to indicate how useful a variety of “search-by” tools would be in the site. The following scored highest on perceived usefulness: “Phe per serving,” “Meal category,” and “Recipe requiring specialty products vs. recipes requiring only grocery store foods.”

When asked whether participants would be interested in a program involving payment for having a family-recipe adapted to LP, 46.76% of total respondents said “yes,” and 53.24% said “no.” Of the 202 individuals who responded “yes,” \$31 was the average amount individuals reported they would be willing to pay for a recipe adaptation.

### *Future Projects*

National PKU News, How Much Phe, and Cook For Love hope to eventually develop an additional online resource with even further expanded resources. This survey provided a description of potential future resources and contained questions to assess the degree of interest from the metabolic community. Participants were asked whether the current available online resources for the metabolic community (HMP, CFL, and Facebook) are sufficient. 46.69% of total survey respondents indicated “yes,” and 52.31% indicated “no.” A variety of site features were listed, and a 1-5 Likert scale was used to assess perceived usefulness (1 = not useful, 2= minimally useful, 3= neutral, 4= somewhat useful, 5= very useful). “Information on latest research” (4.542), “networking component” (4.427), and “calendar of metabolic events/ability to find events near you” (4.383) were the features indicated as most useful, based on average participant scores.

When asked whether there is a need for this type of resource, the survey respondents (n=432) produced an average score of 4.72, based on a 1-5 Likert scale (1 to 5 scale; 1 = not at all, 2 = not really, 3 = neutral, 4 = possibly, 5 = absolutely). A score of 4.621 suggested strong likelihood this population would use such a resource (based on the following scale: 1 = not likely at all, 2 = not likely, 3 = neutral, 4 = likely, and 5 = very likely). Finally, survey participants were asked to provide any additional ideas or tools not mentioned in the survey in an open-text format. Responses were grouped into categories, and the following categories contained the greatest number of responses: “no, what you’ve proposed sounds excellent,” “unclassifiable,” and “HMP-related.” Unclassifiable refers to open-text responses that were generic in nature and did not fit into another category. Please refer to Appendices A and B for the exhaustive list of suggestions, which are grouped into categories.