GROUP EDUCATION FOR CHILDREN WITH PHENYLKETONURIA

By

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ABBREVIATIONS

PKU	phenylketonuria
FFQ	food frequency questionnaire
Phe	phenylalanine
PAH	phenylalanine hydroxylase
BH_4	tetrahydrobiopterin
mg	milligram
kg	kilogram
NHANES	National Health and Nutrition Examination Survey
CHD	Congenital Heart Defects
DM	type 1 diabetes mellitus
Hb A1C	hemoglobin A1C
EATS	Eating at America's Table
CDRC	Child Development and Rehabilitation Center
OHSU	Oregon Health & Science University
BMI	body mass index
NDSR	Nutrition Data System for Research
SPSS	Statistical Package for Social Science

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ABSTRACT

Limited research exists to determine whether education for children with phenylketonuria (PKU) can help improve children's knowledge of their disorder and increase variety in the diet within the confines of a severe phenylalanine (phe) restriction. The planning, preparation and administration of foods provided to children with PKU is parent driven from birth through early childhood. As children enter school age, parents have less control over the child's diet, and once a child reaches adolescence parents may have little to no control due to the adolescent's desire for independence. Because of social pressures and little understanding of the disease many adolescents may have a difficult time choosing appropriate foods to manage their disorder. Poor management of PKU can cause inhibited growth (1, 2), decreased intelligence (3, 4), and difficulty in school (3, 5, 6).

The objective was to determine whether group education for children with PKU could improve knowledge of the disorder and diet recommendations immediately following and three months after the education intervention. Researchers investigated whether group education was effective in increasing the amount of fruit and vegetables consumed by children and/or improving metabolic control as measured by blood phe concentrations. Finally, we used a Food Frequency Questionnaire (FFQ) and 24 – hour recall as a means to document protein intake from foods in patients with PKU. Food frequency questionnaires were used to measure usual intake and blood phe concentrations were used to assess metabolic control.

This quasi-experimental design assessed change in knowledge, protein intake, fruit and vegetables consumption, and blood phe concentrations in four girls and four boys with PKU. There was no significant change in knowledge score ($p = 0.086$), protein intake ($p = 0.105$), fruit ($p = 0.414$) and vegetable ($p = 0.317$) consumption, or phenylalanine concentrations ($p = 0.499$) for girls between baseline measures and three months following education day. Knowledge score ($p = 0.667$), protein intake ($p = 0.105$), fruit ($p = 0.317$) and vegetable ($p = 0.317$) consumption, and phe concentrations ($p = 0.267$) for boys were not different from baseline at three months. When comparing boys and girls, change in knowledge score ($p = 0.543$), protein intake ($p = 0.241$), fruit ($p = 0.207$) and vegetable ($p = 0.780$) consumption, and phe concentrations ($p = 0.147$) were not significantly different. The FFQ compared to the 24-hour recalls was not significantly different in estimating protein needs before ($p = 0.108$) or after ($p = 0.506$) education day.

We conclude that a short one-time nutrition education intervention is not effective at improving knowledge, increasing fruit and vegetable consumption, or improving metabolic control as measured by blood phenylalanine levels. The FFQ may be an appropriate tool for estimating protein intake in the PKU population but due to small sample size (n=4) further research is needed in this area.

CHAPTER 1

HYPOTHESIS AND SPECIFIC AIMS

Hypothesis

We hypothesized that group education for children with PKU would improve general knowledge of PKU and the PKU dietary recommendations, increase the servings of fruits and vegetables consumed, and improve metabolic control. We also hypothesized that the FFQ would be a appropriate instrument for assessing usual protein intake in children with PKU.

Specific Aims

The primary aim of the study was to determine if group education for children with PKU improves the child's knowledge of the disorder and dietary recommendations. The second aim was to investigate whether group education for children with PKU improves metabolic control. The third aim was to determine whether group education for children with PKU increases the number of servings of fruit and vegetables consumed in the diet. The fourth aim was to investigate whether the FFQ was comparable to 24-hour recalls for assessing usual dietary protein intake of children with PKU.

CHAPTER 2

BACKGROUND & SIGNIFICANCE

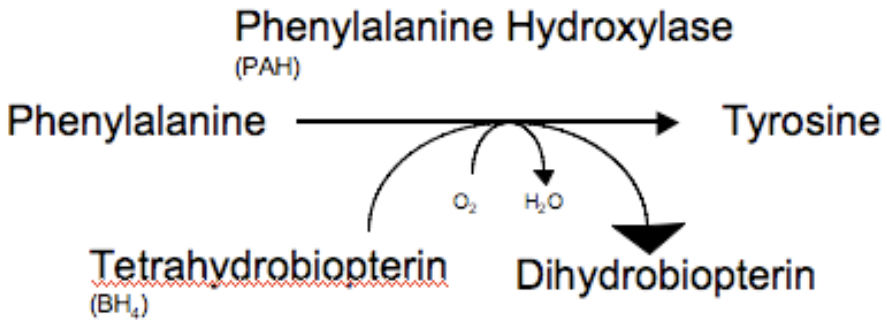
Phenylketonuria

Phenylketonuria (PKU) is an autosomal recessive genetic disorder in which individuals are unable to metabolize phenylalanine to tyrosine. The disease was first discovered in 1934 by Norwegian physician, Dr. Ivar Asbjørn Følling after he observed mentally retarded children that had elevated phenylpyruvic acid in their urine. After it was discovered in the early 1950's that severe mental retardation could be prevented in these patients by following a phenylalanine-restricted diet, the United States began mandating newborn screening. By 1967 newborn screening had become law in 37 states. Screening has provided infants with an opportunity to start treatment early and allows individuals with PKU to achieve normal intelligence and growth patterns (7-10).

Phenylalanine, an essential amino acid, cannot be synthesized in the body and therefore must be ingested in the diet. When phenylalanine (phe) is ingested and absorbed, it is transported through portal circulation to the liver. Once in the liver, some of the phe is converted to tyrosine by the enzyme phenylalanine hydroxylase (PAH). PAH hydroxylates phe at carbon 4 of the aromatic ring to form tyrosine. The reaction is irreversible and regulated by the phosphorylation state of PAH, which is phosphorylated by cyclic adenosine monophosphate when high concentrations of phe are circulating in the serum. This phosphorylated PAH has a higher affinity for phe, driving the reaction equilibrium toward tyrosine. The reaction cannot occur in the absence of

tetrohydrobiopterin (BH_4), an essential cofactor that is converted to dihydrobiopterin during the reaction. Dihydrobiopterin must then be enzymatically converted back to BH_4 to perpetuate the PAH reaction of converting phenylalanine to tyrosine. This reaction is described pictorially in Figure 1.

Figure 1 Phenylalanine Metabolism



Tyrosine is a non-essential amino acid and one of its roles in the body is to generate neurotransmitters such as dopamine. Dopamine is an important regulator of mood, learning ability, attention, memory, motivation, and cognition.

In patients with classic PKU, a genetic defect in the PAH gene results in a decrease in the activity of the PAH enzyme activity. Many genetic mutations have been found in the gene coding for PAH, causing a significant range of functionality in the enzyme between individuals with PKU. Low or absent PAH activity causes plasma phe to rise and plasma tyrosine to become depleted. Thus, tyrosine becomes a conditionally essential amino acid.

Approximately one percent of patients diagnosed with PKU have a defect in the BH_4 synthesis pathway. Due to the fact that BH_4 is required for other

enzymes in addition to PAH, this deficiency is much more severe, requires a different form of treatment, and usually has a poor outcome even if treated early (11).

If phe is unable to be converted to tyrosine, an alternative transamination reaction will convert phe to other metabolites such as phenylpyruvic acid and phenyl acetate. If PKU is not treated at birth, affected individuals will suffer from mental retardation (12). Although the exact mechanism is not known, it is thought that when phe is in high concentrations in the blood, it crosses the blood brain barrier in high amounts causing disruptions in the brain. Even patients treated at birth who later in life have poor dietary control as indicated by high plasma phe concentrations can experience inhibited growth (1, 2), decreased intelligence (3, 4) and difficulty in school (3, 5, 6).

Treatment

Since 1963, individuals have been diagnosed by newborn screening and started on a phe restricted diet, eliminating dairy, eggs, meat, beans, nuts and others protein sources, within weeks of birth. Most institutions in the United States recommend this strict diet for life. Patients are also limited in the amount of normal breads, pasta, and starchy vegetables they consume, but can include the specially developed low phe products that are now available. Because of these severe limitations patients are prescribed a medical formula that is ingested throughout the day to provide 70 – 80% of protein needs which includes all of the amino acids besides phe. Taking formula throughout the day prevents the body from breaking down muscle proteins, which can contribute to high phe

concentrations. The medical formula is supplemented with vitamins and minerals and is typically supplemented with carbohydrate and fat.

In 2003, Acosta et al found that individuals with PKU who were treated with medical formula experienced normal growth and ingested 100% or greater of the recommended dietary intake for protein; however, energy intakes were less than recommended for age. Body mass index (BMI) was compared to z-scores and many children were overweight despite reported low energy intakes. Researchers believe that low energy intake despite trends in overweight was due to underreporting of nutrient intakes (7).

Currently, patients in the United States are prescribed an amount of phenylalanine or protein that can be eaten each day, which is based on each individuals' perceived phe tolerance. Fruits and vegetables are low phe and one research article has shown that eating vegetables and fruits freely, regardless if they contain phe, does not significantly raise blood phe concentrations. A more liberal diet in regards to fruit and vegetable consumption may be possible for individuals with PKU but due to limited research in this area, liberalization of the diet is not standard practice in the United States (13).

Variability of the Diet

Growth and development of children with PKU following a phe-restricted diet was insufficient and malnourishment was common in this population in the 1960's (14-16). Beginning in the early 1980's the prevalence of underweight and malnourishment in children with PKU decreased, possibly due to improved medical formulas and new low phe, high calorie, high fat foods developed

specifically for the PKU population. As advances in treatment continue to be made there is potential for the nutritional status of children with PKU to improve although no research has evaluated food choices of children allowed a more liberal diet.

In December of 2007, the Food and Drug Administration approved the use of Kuvan (sapropterin) for pharmacological use in responsive patients with PKU. Sapropterin dihydrochloride is the stable form of BH_4. In a small subgroup of the population taking doses between 10-20 milligrams per kilogram per day (mg/kg/day) has shown significant improvements in blood phenylalanine concentrations and increases in the amount of protein that can be consumed through food while still maintaining phe concentrations within normal limits (17-20).

In 2009 Trefz et al published a randomized double blind placebo-controlled study that evaluated the effect of sapropterin on phe tolerance in children. Part I of the study screened patients for responsiveness using a 20 mg/kg/day dose for 8 days. Of the 90 patients screened 46 were responsive (reduction in plasma phe > 30%), with a mean decrease in plasma phe concentrations of 65% from day 1 to day 8. In part II, 21 responders between the ages of 4 to 12 currently under dietary control were given 20 mg/kg/day of sapropterin for 10 weeks. Twelve responders were given placebo and considered the control group. During week three, phe supplements were given to both treatment and control groups based on plasma phe concentrations from the previous week. Researchers found that tolerance of phe in the treatment group

nearly doubled, with no significant increase in phe tolerance in the control group (18). No research to date has investigated the dietary choices of children with PKU allowed a more liberalized diet due to sapropterin use.

Variability in the diet has also improved as new food products are developed specifically for this population. While these foods have contributed to the adequate growth of children with PKU, they may also put children at risk of overweight or obesity due to their high fat, high calorie nutrition profile. It is important that clinic visits focus on both dietary management of the disease and overall healthy eating with an emphasis on fruit and vegetable consumption, not only for weight management, but also for overall health.

Fruit and Vegetable Consumption

Using the National Health and Nutrition Examination Survey (NHANES), Kimmons et al discovered that only 0.9% of adolescents consume fruits and vegetables in compliance with the 2005 Dietary Guidelines using the MyPyramid calorie specific recommendations for fruits and vegetables (21, 22). The 2010 Dietary Guidelines currently recommend increasing vegetable and fruit intake and eating a variety of vegetables and specifically recommends consuming 2.5 servings of vegetables and 2 servings of fruits per day (23). Low fruit and vegetable consumption has been associated with overweight and obesity in the general population (24). Since most fruit and vegetables are low in phe and likely do not raise blood phe concentrations (13) it may be beneficial to educate patients on the importance of fruit and vegetable consumption for weight and disease management.

Dietary Compliance

Although patients are advised to stay on diet for life, many choose to go off or become more liberal with their diet. Research done by Walter et al showed that about 27% of children ages 0 to 9 have phe concentrations above the maximum accepted blood phe levels as reported by the National Society for PKU (UK). Once children reached ages 10 to 14 the percentage of children above the recommended range increased to 50% and in the 15 to 19 year old age group 78% of children had phe concentrations above the recommended range (25). There are a number of reasons patients don't fully comply with their diet including the social burden of the diet, problems with formula such as taste and timely preparation, and difficulties associated with diet management such as recipe development, difficulty preparing multiple meals for family members, and having little enjoyment from the diet (26-28).

A study conducted by Vegni et al (28) studied 40 participants between the ages of 8 to 31 years old. All patients had been diagnosed with PKU within the first 3 years of life, were cognitively able to participate and had no other pathologies. The participants were asked open-ended questions related to their experience of their illness and how it impacted their daily life socially and in their relationships. The participants, ages 8 to 12, had difficulty accepting their illness and were trying to gain an understanding of where they fit in with peers and in social situations. Children in this age group had difficulty deciding whether to tell friends about their disease or keep that information confidential, and parents still played a role in informing teachers and other adults. The 13 to 18 year old age

group was able to realize that the disease was a part of them but still had difficulty deciding whether to tell their peers about their disease. Reasons for not telling peers included the fear of being teased or not wanting to explain a complex disease. This age group was also finding a sense of autonomy and took more control over their diet. They started choosing between eating their restrictive foods and eating the same way as their peers. Because of their desire for autonomy this age group particularly experienced complex relationships with parents in relation to their disease. Some patients wanted parent support while others wanted to have control of their own health. Adolescents in this study discussed the ease of going off diet due to pressure from peers and the desire to "fit in". Patients in all groups expressed interest in having more education related to their disease and wanted more support from other individuals with the same disease. All age groups expressed difficulty in social situations. They reported choosing between being with friends and being teased for not eating the same things, or staying home and being isolated (28).

Ievers-Landis et al used a survey to understand the dietary challenges for children and adolescents with PKU, as well as their caregivers. Caregivers (n = 19) and patients over the age of 6 (n = 11) completed the survey. Of caregivers, 53% expressed problems related to the formula such as patient rebellion, social pressures, feeling of sickness, and not enough time to consume the prescribed amount of formula while at school. Other problems related to diet such as difficulty planning meals, poor knowledge of diet, and children not adhering to diet when away from the home were expressed in 83% of caregivers. Children of

caregivers that expressed more challenges with dietary management such as difficulty planning meals or poor understanding of the diet, had elevated phe concentrations compared to those caregivers that had less difficulty with the dietary management of PKU. Similar to caregivers, children also expressed many challenges related to formula consumption and diet. These included dislike of formula, not wanting friends to see them drink formula, side effects to drinking formula, standing out when eating differently, and lack of knowledge about the diet. As with caregivers, children who listed more problems with the diet had significantly higher phe concentrations (26). We are unable to conclude whether higher phe concentrations were related to the child's or the parent's challenges with diet, or a combination of both.

To summarize, children with PKU feel social pressure from peers, particularly during adolescence, which contributes to poor metabolic control. Because adolescents take more responsibility for their diet and make decisions based on peer support, many adolescents do not follow diet as strictly as they should, and could benefit from nutrition education, psychosocial support, and peer support from others with the disease.

Consequences of Poor Dietary Control

While it is important to continue to stay on diet throughout life, it is equally important if not more important to start the diet as soon as possible. Research has shown that individuals that are started on a low phe diet 4 and 6 years after birth compared to children started on a low phe diet within 1 month of birth have lower IQ scores by a mean score of 33 points (29). As previously mentioned,

despite recommendations to stay on diet for life, many children, particularly adolescents, choose to go off diet for a variety of reasons (25). Consequences such as attention deficit, required tutoring, decreased intelligence scores, less cognitive flexibility and poor problem solving skills (3, 6, 29, 30) can occur in children that have poor dietary control.

Gassio et al. conducted a study with 26 PKU patients and 26 controls between the ages of 6 to 18 years and measured intelligence and cognitive function. Ten PKU patients compared to 5 controls required special tutoring or repeated classes (3). Bosch et al also showed increased need for tutoring for children with PKU compared to children without PKU (21.9% vs. 4.7%)(6). Gassio et al showed that within the PKU population students that had difficulty in school had poorer dietary control in the 6 months leading up to the study compared with students that had no difficulty in school. Intelligence scores also differed between PKU patients with and without problems in school. Lower intelligence scores and poorer dietary control were seen in children that experienced difficulty in school compared to those with no difficulty (3).

Another study conducted by VanZutphen et al. evaluated the executive function of children with PKU by measuring scales of intelligence, vocabulary skills, and reasoning in 15 participants at a mean age of 13.8 years. Eleven participants were on diet (controls), and four were no longer on dietary treatment. Compared to controls, patients not on diet had difficulty with problem solving, reasoning, and had a harder time with cognitive tests and cognitive flexibility. Both cognitive ability and flexibility with visual-motor sequencing decreased with

increased phe concentrations. The patients that were off diet had significant difficulty with task performance, distraction, short attention span, and multi-tasking compared to patients that remained on the diet (29). Patients that had good dietary compliance throughout life, but had decreased compliance within the 6 months prior to the study showed a decreased ability to problem solve, concentrate, multi - task, and reason indicating that going off diet, even for short periods of time, can be detrimental (29). Similar results were also seen in a study conducted by Huijbregts et al in which patients that had higher phe concentrations had poor attention spans and difficulty with problem solving (30).

It is especially important for women of childbearing age to keep their phe concentrations within the normal range. High phe concentrations during pregnancy have been shown to cause Maternal Phenylketonuria Syndrome, which encompasses congenital heart defects (CHD), microcephaly, and poor developmental outcomes alone or in combination with one another (31-33). As phe concentrations increase the fetus is at increased risk of developing CHD and microcephaly together (32). Rouse et al showed significant impacts to the baby in women with uncontrolled phe concentrations of greater than 360 µmol/L. High phe concentrations between 0 – 8 weeks of pregnancy were most likely to lead to CHD where as high phe levels between 9-12 weeks of pregnancy were most likely to lead to brain, fetal, and post natal growth abnormalities. Phe concentrations above 900 µmol/L were most likely to cause these abnormalities (31). Because of the detrimental effects that can occur in the fetus due to high

phe concentrations during pregnancy, it is important to start educating young women with PKU before their child bearing years.

Education for Children with PKU

The planning, preparation and administration of foods provided to children with PKU is parent driven from birth through early childhood. As children enter school age, parents have less control over the child's diet, and once children reach adolescence parents may have little to no control due to the adolescent's desire for independence. Because of social pressures and little understanding of the disease and dietary treatment, many adolescents may have a difficult time choosing appropriate foods to manage their disorder. Research and educational efforts have been directed towards improving the knowledge of diet and disease in adolescents so they can make better food choices during their teen years.

In one study with 32 PKU patients (22 in the intervention group, 10 in the control group) researchers sent the intervention group an education resource in the mail and asked them to read through the information. Knowledge was assessed using a 20 question true/false questionnaire and compliance was measured based on self-reported data related to consumption of medical formula, intake of natural protein and low protein foods compared to that prescribed, and Guthrie blood tests. At one month, patients in the intervention group had increased knowledge compared to those in the control group, based on their baseline knowledge. Increased knowledge in the intervention group was not sustained at 6 months and despite increased knowledge initially, no improvement in compliance was observed at either time point (34).

A study done by Singh et al showed similar results. This study was conducted with 13 girls between the ages of 11 to 18. Dr. Singh hosts a week long camp experience each year in which she collects data. Participants in this study were enrolled in camp in 1995 and 10 of the 13 girls returned to camp in 1996. During this experience, the patients were assessed on a variety of measures including knowledge of diet and disease, attitudes toward the disease, and health beliefs. Following camp, girls felt that there were fewer barriers to overcome in order to comply with the diet and felt less isolated. At 4, 8, and 12 months these parameters gradually increased back to baseline. Knowledge score increased following camp and this increase in knowledge score was maintained at 4, 8, and 12 months. Plasma phe concentrations were significantly reduced following camp but increased back to baseline by 4 months. From this one small study, improvements in knowledge were not indicative of improved dietary control. The researchers were concerned with the limited knowledge of diet and disease that was reflected in the initial assessment scores. From this information they concluded that current individual counseling with patients is not effective and new, more productive methods of teaching, such as group education, should continue to be explored (35).

There is limited research related to group education and its effects on disease management in patients with PKU. There has been more research involving group education for children that have Type I Diabetes Mellitus (DM) (36-40). DM is comparable to PKU in that it requires strict dietary compliance to prevent adverse acute outcomes such as hyperglycemia or hypoglycemia as well

as long-term outcomes such as neuropathy, retinopathy, and nephropathy. Because of limited research assessing the effectiveness of group education in the PKU population and PKUs similarities to DM, it is helpful to review the literature related to group education for children with DM.

In individuals with diabetes, similar results have been seen in relation to dietary control (hemoglobin A1C concentrations) and education (36, 41-43). One study published in 2010 found that an educational summer camp for children with Type I DM increased knowledge but did not decrease hemoglobin A1C (Hb A1C) concentrations. Subjects participating in camp reported feeling more able to adapt to the school environment when compared to controls not attending camp (44). Viklund et al reported similar conclusions, concluding that a group education intervention increased positive attitudes toward self - care and DM but no changes in Hb A1c were observed (45).

Santiprobhob et al evaluated sixty participants attended a 5-day camp where they learned about their disease and diabetes self - management. Three months following the camp experience, participants improved management of disease and increased knowledge; however, 6 months following the camp experience management of disease returned to baseline while the increased knowledge was maintained (39).

Wang et al. showed different results in a study comparing diabetes control in patients that attended a 20-day camp versus those that did not attend camp. The patients that attended camp had improved control initially and 7 months following camp. Those that did not attend camp had no significant

improvements. This study suggests that longer interventions may have a more significant impact on dietary adherence and control (40).

With increased autonomy in adolescence and the need for strict adherence to diet in patients with PKU, it is important that these patients have a good understanding of their diet and the potential adverse health outcomes that exist if the diet is not followed. Education may increase knowledge but it has not yet been proven whether it can improve dietary control in adolescents. More research is needed in this area.

Educational Resources for PKU

Laurie Bernstein, M.S., R.D. and colleagues at The Children's Hospital of Aurora and the University of Colorado developed the Eat Right Stay Bright curriculum. The program delineates the different life stages – early childhood, childhood, adolescents, and maternal PKU - and was developed using the theory of anticipatory guidance. The group education model has been used for educating patients starting as early as three years of age. At this time, there is no research indicating whether the program has been effective. The University of Washington has also developed activities for children with PKU for different age groups – preschool, school age, and adolescents. This curriculum also has not been researched to determine its effectiveness.

The PKU curriculum developed by Bernstein and colleagues was used as a template to develop our education program. Health care providers at the Child Development and Rehabilitation Center (CDRC) Metabolic Clinic had observed

their group education process and felt that the available detailed lesson plans could be adapted to the patients at CDRC.

Comparison of a Food Frequency Questionnaire

Currently, Biomarin, Inc. is investigating the validity of their newly developed FFQ and no other FFQ's are developed or validated specifically for children with PKU. It has long been known that food frequency questionnaires have significant measurement error that leads to bias and decreased statistical power (46, 47). Carroll et al evaluated data from the Eating at America's Table Study (EATS) and used a variety of statistical methods to evaluate the impact on measurement error when dietary assessment methods are combined. They compared R-squared values between true intakes (24-hour recalls were assumed unbiased and true) in an FFQ only design, a 24-hour recall only design, and a 24-hour recall plus FFQ design. Results indicated that an FFQ plus 2, 4, or six 24 hour recalls were most effective at increasing power, decreasing sample size, and improving the R squared value of the FFQ alone from 0.47 for women and 0.63 for men to 0.74 for both men and women when combined with four 24-hour recalls. The researchers concluded that there are limited returns in relation to R squared and power when more than six 24-hour recalls are used in combination with an FFQ and the use of four to six 24-hour recalls plus a FFQ showed the most promising results (48). In a small sub-sample of our population we will be collecting four 24-hour recalls to compare dietary protein intake to the FFQ.

CHAPTER 3

SUBJECTS AND METHODS

Methods

The main goal of the study was to provide group education for boys and girls, ages 9 to 16, and diagnosed with PKU and to evaluate its effectiveness toward improving knowledge of the disorder and diet recommendations. The second and third aims were to evaluate whether group education improves metabolic control and increases the consumption of fruits and vegetables in the diet. A final aim of the study was to investigate whether the FFQ developed by Biomarin is comparable to 24-hour recalls for assessing usual dietary protein intake in children with PKU. The study was conducted using a quasi-experimental design to evaluate the impact of group education on the previously described parameters. Quasi-experimental design is a research design in which extraneous variables are not controlled for such as random assignment of an intervention or inclusion of a control group. Participants were recruited from the CDRC metabolic clinic at Oregon Health and Science University (OHSU). Subjects participated in a two-hour education session held at the CDRC.

Study Subjects

Study subjects were boys and girls between the ages of 9 and 16 that had been diagnosed with PKU at birth via newborn screening and treated with a low phe diet since diagnosis. Inclusion and exclusion criteria are detailed in Table 1.

Table 1 Inclusion and Exclusion Criteria

Inclusion	Exclusion
• Ages 9 – 16 • Diagnosis of PKU by newborn screening	• Physical or mental limitation that prevents them from participating in the education session

Children between the ages of 9 and 16 were included because a large number of patients within this age range are treated and followed at the CDRC metabolic clinic. All potential study subjects were sent an invitation, consent and assent form by mail prior to the education day.

Screening

All children with PKU between the ages of 9 and16 that are managed by the CDRC metabolic clinic were sent a formal invitation and consent and assent form (Appendix A and B) to participate in the study. Both the parents/guardians and the child were asked to read and sign the consent and assent prior to the education day.

Measurements

Medical Records

The subject's age, height, weight, BMI, and BMI for age percentile were obtained from the OHSU electronic charting system, EPIC. Whole blood phe concentrations from dried filter paper blood spot tests recorded in EPIC were also retrieved. Collection of blood for filter paper testing of phe levels is commonly done at home in children with PKU. The children make a small finger

prick, place a drop of blood on the filter paper, and within 24 hours of getting the blood sample mail the paper into the Oregon State Public Health Laboratory (Hillsboro, OR) where the concentrations are measured. All available phe values taken from 6 months prior to education day to three months following the education intervention were collected for analysis.

Diet Variability

Diet variability was measured using a FFQ (Biomarin Pharmaceutical Company) on education day and 3 months following education day. This FFQ was developed specifically for the PKU population to assess protein intake. A FFQ is our dietary intake measure of choice because it assesses usual food intake over the previous month. The FFQ was completed in person prior to education day and via telephone interview between researcher and subject at three months following the education date. Protein intake in the diet was estimated using the Food Frequency Questionnaire Protein Scoring Worksheet (BioMarin Pharmaceutical Company). The FFQ was further evaluated for consumption of fruits and vegetables in the diet expressed as number of servings per day. The FFQ is located in Appendix C.

Twenty-four Hour Recalls

The protein intake reported on the FFQ was compared with true intake as assessed by four 24-hour recalls administered to a sub-sample (females) of our research participants. Females were chosen as a sub-sample. I completed these recalls over the phone one, two, and three months following education day on 2 weekdays and 1 weekend. One 24-hour recall was completed in person

immediately prior to the education session. I used a multi-pass method when administering the recalls and protein intake was assessed using the software Metabolic Pro (Genetic Metabolic Dietitians International). If a food was not found in Metabolic Pro, Nutrition Data System for Research (NDSR) (University of Minnesota) was used. If a food could not be found in either database, a food with a similar nutritional profile was used. Protein intake recorded from the 24-hour recalls was compared to the FFQ. The 24-hour recall protocol can be found in Appendix D.

Knowledge of PKU and Low Phenylalanine Diet

For boys, knowledge of both the PKU diet and disease was measured using an eleven question multiple choice knowledge assessment modified from a previously published knowledge assessment survey for adolescent girls with PKU (Singh, Emory University). The assessment was given immediately prior to the education session at the CDRC. The assessment was also mailed to participants 3 months following the education session for follow up testing. When research participants were called for the FFQ interview they were reminded to mail the assessment back in the stamped, addressed envelope. The boys' knowledge questionnaire can be found in Appendix E.

For girls, knowledge of the PKU diet, disease and the importance of dietary control during childbearing years was measured using a fourteen question multiple choice knowledge assessment that was modified from a previously published knowledge assessment survey for adolescent girls with PKU (Singh, Emory University). This assessment was given immediately prior to

the education session at the CDRC. The assessment was also mailed to participants 3 months following the education session for follow up testing. When research participants were called for the FFQ interview at three months, they were reminded to mail the assessment back in the stamped, addressed envelope. The girls' knowledge quiz can be found in Appendix F.

Outcome Variables

Table 2 Outcome Variables

Diet Variables:	**Blood Values:**	**Anthropometric Measures**	**Knowledge:**
• Protein consumption • Fruit and vegetable intake	• Phenylalanine concentrations	• Height • Weight • Age • BMI • BMI for Age	• Knowledge assessment score

Education Day and Initial Assessment

Due to differing educational needs of boys and girls with PKU one education curriculum was developed specifically for boys and another developed specifically for girls. For the boys, subjects reported to the CDRC at 0900. Each child and his parents/guardians were taken one at a time by a researcher to collect and review the consent form. A FFQ and knowledge assessment was completed with each participant at this time. Once the FFQ and knowledge questionnaire were completed, children had an opportunity to play PKU Jeopardy (Appendix G) with the group or complete a PKU word find or maze (Eat Right Stay Bright, University of Colorado) individually until all participants had completed the initial paperwork.

At 0945, the group came together and parents/guardians were asked to leave the room. A researcher facilitated a discussion about genes and DNA. Subjects isolated DNA using wheat germ and warm water in a hands on experiment. Following the DNA discussion participants learned how DNA relates to the development of PKU and the amino acids and enzymes involved in PKU. Next, subjects learned about different foods and the level of phe in those foods. Finally, subjects prepared a phe friendly snack. Following the snack preparation, research participants were asked to retake the knowledge questionnaire prior to congregating with parents. A more detailed description of the curriculum is included in Appendix G.

For the girls, subjects arrive at 0900 at the CDRC at OHSU. Each child and her parents/guardians reviewed the consent forms with a researcher. A FFQ was reviewed with each participant. Each participant was asked to complete the knowledge questionnaire at this time. Girls also completed one 24-hour recall to compare to the FFQ. Once the FFQ, 24-hour recall, and knowledge quiz were completed, children had an opportunity to play PKU Jeopardy with the group or complete a PKU word find or maze individually until all participants had completed the initial paperwork.

At 0945, parents/guardians were asked to leave the room. Subjects learned about dietary control during adolescence and the effects a poor diet can have on fetal development during pregnancy. Subjects also learned about DNA, amino acids and the enzyme deficiency responsible for the development of PKU by making bracelets and role-playing. Finally, a snack was provided which

encouraged discussion of foods low in phe. Following the snack participants were asked to fill out the knowledge questionnaire before being dismissed. A more detailed description of the curriculum is included in Appendix H.

Follow-up Assessment

At three months male subjects were sent the knowledge questionnaire by mail. A researcher called each participant at this time to do a follow up FFQ. The researcher reminded the subject to complete the knowledge assessment and return it in the stamped, addressed envelope.

Female subjects were called, unannounced, at one, two, and three months following education day to complete the 24-hour recalls over the phone. Recalls were done on 2 weekdays and 1 weekend. On the third month, female subjects also completed their final FFQ over the phone. The knowledge assessment survey was mailed and subjects were reminded to return the survey in the addressed, stamped envelope.

Statistic Analysis

All statistical analyses were run in Statistical Package for Social Science (SPSS) statistical software. Change in knowledge score, dietary protein intake, and blood phe concentrations for boys and girls between education day and three months following education day were evaluated using one sample T-tests. Change in number of servings of fruits and vegetables from education day to three months following education day were evaluated by a Wilcoxon-Rank Sum test.

Comparisons between boys and girls were also made. For change in protein, knowledge, and blood phe concentrations an independent T-test was used. A comparison between boys and girls for change in servings of fruit and vegetables was done using a Mann-Whitney Test.

To compare protein intake recorded from the FFQ versus the 24-hour recall, an independent t-test was run. A correlation test was run between protein intake and blood phe concentrations, blood phe concentrations and knowledge score, and age and blood phe concentrations. Finally, a test of variance was done using a Pitman's test for all outcome variables for boys and girls.

CHAPTER 4

RESULTS

Descriptive Analysis

Thirteen boys and ten girls were invited to participate in the study. Nine subjects, four girls and five boys, with PKU were consented to participate. One boy could not be reached for follow up for a total of eight subjects included in the study. Nine subjects completed knowledge questionnaires prior to education day, eight were received immediately after education day, and eight were received three months following education day. Statistical analysis for knowledge questionnaires included 7 subjects. FFQ's were obtained from all subjects before education day and at three months. Twenty-four hour recalls were collected from all girls before education day and one, two, and three months following education day. Subject characteristics are presented in Table 3.

Table 3 Demographics

Demographics	
	Mean ± Standard Deviation
Boys (n=4)	
Age (years)	11.25 ± 1.25
Height (cm)	145.4 ± 13.69
Weight (kg)	44.77 ± 21.66
BMI for Age (%)	67.54 ± 31.89
Phe Before (µmol/L)	186.29 ± 43.63
Girls (n=4)	
Age (years)	12.5 ± 1.29
Height (cm)	129.2 ± 44.52
Weight (kg)	48.85 ± 16.6
BMI for Age (%)	50.52 ± 40.55
Phe Before (µmol/L)	380.13 ± 230.78

Age, height, weight, BMI, and BMI for age percentile obtained closest to education day, and blood phe concentrations for the six months prior to the intervention were used for analysis. One boy did not have any phe concentrations prior to education day and his data was not included in the statistical analysis for phe. All phe concentrations for the 3 months following education day were also gathered. Two girls did not have any phe measurements after education day and were not included in the statistical analysis for phe concentrations. There was no significant difference between boys and girls in mean age, weight, height, weight for age percentile, or phe concentrations prior to education day.

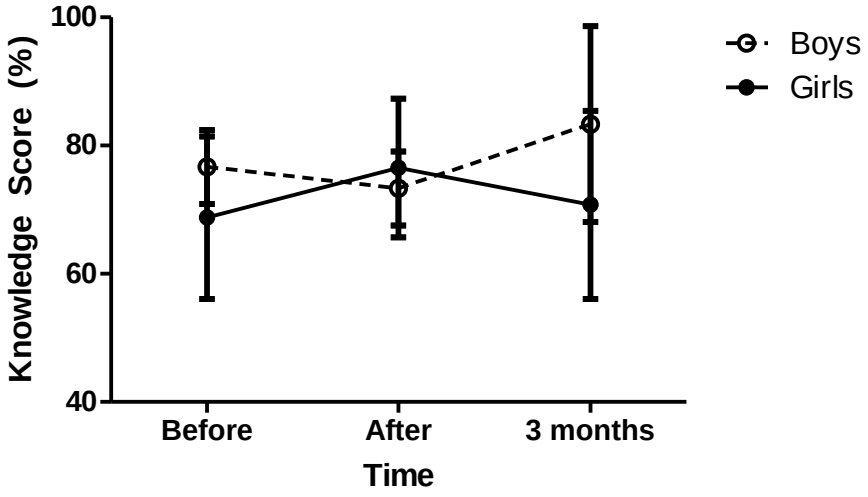
Knowledge Scores

Girls' knowledge scores increased slightly immediately following education day ($p = 0.086$) but were back to baseline at three months. There was no significant difference in knowledge score before and after education day for boys ($p = 0.667$). At three months knowledge score for boys increased slightly, but was not statistically significant ($p = 0.423$). When comparing knowledge scores to phe concentrations for all participants prior to education day, a negative correlation indicated that as knowledge decreased phe concentrations increased ($p = 0.077$) but this was not statistically significant. The trend was less apparent 3 months following education day ($p = 0.602$), however, it is difficult to compare this result due to fewer phe measurements available for use in the analysis.

Knowledge scores were also compared between boys and girls. Boys' knowledge scores before education day were higher than girls (mean 76.6% vs.

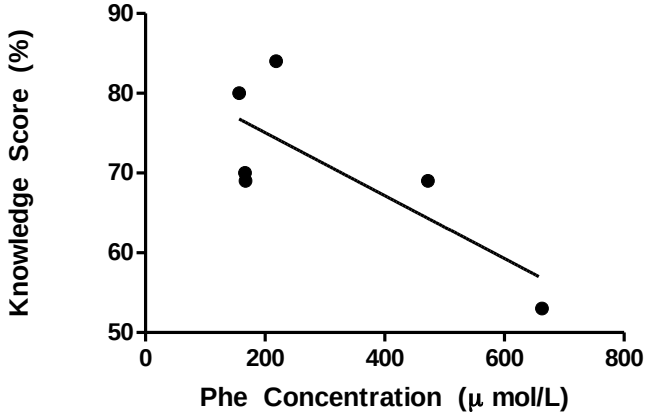
68.7%), however, not statistically significant. Girls had a greater increase in knowledge immediately following education day compared to boys but the difference was not statistically significant (p = 0.157). Change in knowledge score before education day and at three months (p = 0.543) and immediately following education day and at three months (p = 0.243) were not different between boys and girls. Mean knowledge score over time for boys and girls is presented in Figure 2. Knowledge scores versus phe concentrations for all participants are shown in Figures 3 and 4.

Figure 2 Knowledge Score Over Time



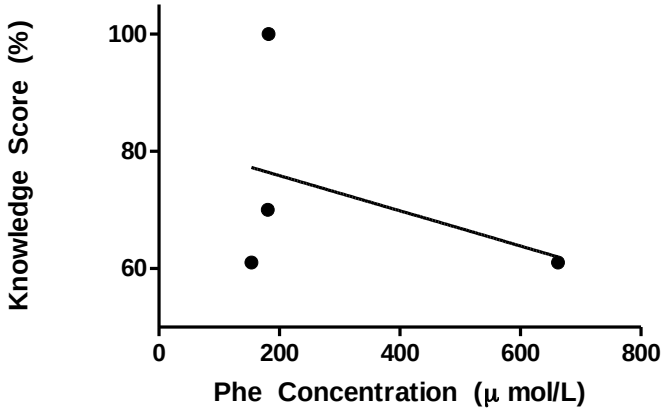
Knowledge score over time for boys and girls.Data is presented as the mean and standard deviation. No significant change in knowledge score was observed for girls (p = 0.086) or boys (p = 0.667). Change in knowledge between boys and girls (p = 0.157) was not significant. p, significance.

Figure 3 Correlation Between Knowledge Score and Phenylalanine Concentrations Before Education



Knowledge score and phenylalanine concentration correlation for girls and boys before education day. No correlation was observed between knowledge score and phenylalanine concentration (p = 0.077) (n = 6). p, significance; phe, blood phenylalanine concentration.

Figure 4 Correlation Between Knowledge Score and Phenylalanine Concentration 3 Months After Education



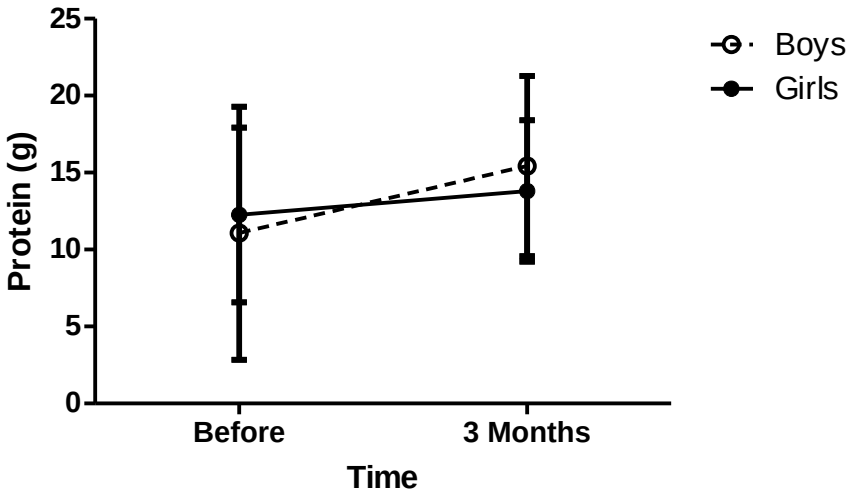
Knowledge score and phenylalanine concentration correlation for boys and girls 3 months after education day. No correlation (p = 0.602) was observed between knowledge score and phenylalanine concentrations 3 months after education day (n = 4). p, significance; phe, blood phenylalanine concentrations.

Protein Intake

Total protein intake is defined as protein from natural sources, low protein medical foods, and the phenylalanine free medical formula. For simplicity throughout the remainder of the discussion, protein from food includes all naturally occurring foods plus low protein medical foods. Change in protein intake was compared before education day and three months following intervention. Boys and girls both had a slight increase in protein intake from foods but this increase was not statistically significant ($p = 0.105$, $p = 0.224$). Total protein intake for girls was 1.00 g/kg of body weight with 27% coming from food. There was not a significant change in total protein intake between time points for girls ($p = 0.173$). On education day boys had a total protein intake of 1.3 g/kg of body weight with 20% coming from food and changes in total protein intake between time points was not significant ($p = 0.105$).

Change in protein intake from food was compared between boys and girls. No difference was seen in protein intake from food between boys and girls ($p = 0.241$). No difference was seen in total protein intake measured in grams per kilogram of body weight between boys and girls ($p = 0.757$). Protein intake was not correlated with phe concentrations at either time point, before education day or 3 months following education day. Protein consumption from foods is presented in Figure 5.

Figure 5 Line Graph of Protein Intake Before and Three Month After Education Day

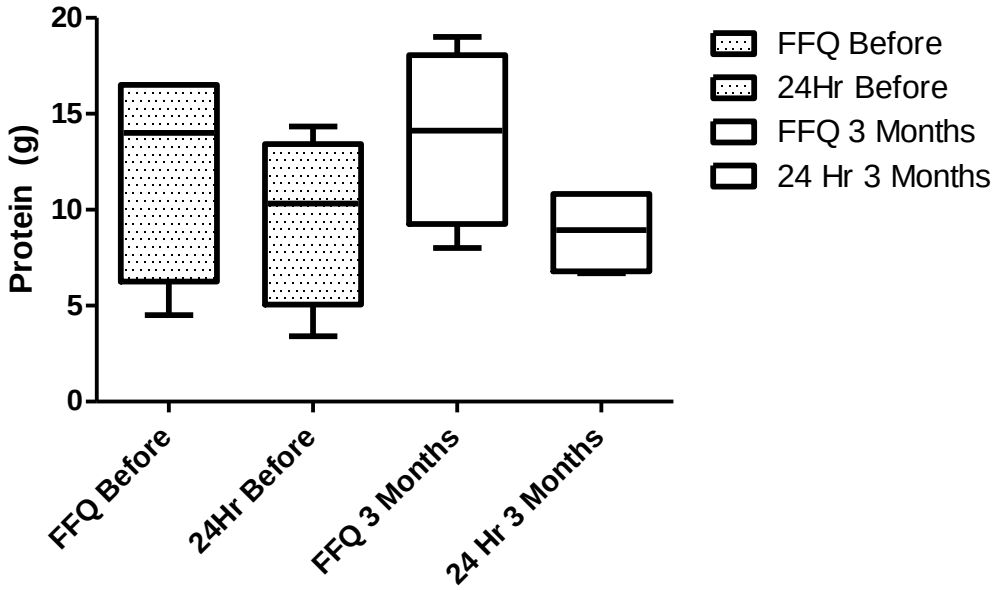


Protein intake from natural sources and medical foods over time for boys and girls. Data is presented as the mean and standard deviation. No significant change in protein intake for girls (p = 0.224) or boys (p = 0.105) was observed. Change in protein intake between boys and girls (p = 0.241) was not signficantly different. p, significance.

Protein Intake: 24-Hour Recall Compared to the FFQ

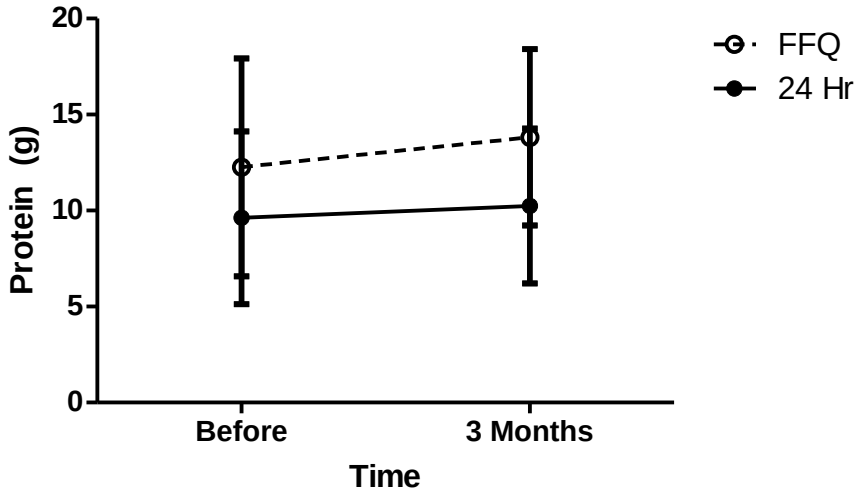
In girls, we observed protein intake from foods as recorded with an FFQ compared to 24-hour recalls. The FFQ tended to report a higher protein intake compared to the 24-hour recalls at both times points but this observation was not statistically significant (before: p = 0.108, after: p = 0.506). A comparison of protein intake over time for girls' FFQ and 24-hour recalls are presented in Figures 6 and 7.

Figure 6 Box Plot of Protein Intake: 24 Hour Recall Compared to the Food Frequency Questionnaire



Protein intake from natural foods and low protein medical foods for the FFQ compared to 24-hour recall over time. The box represents 90% of values, the line represents mean protein intake, and error bars are the standard deviation.There was no significant difference in reporting of protein intake between the FFQ and 24-hour recall before (p = 0.108) and after (p = 0.506) the education session. p, significance; FFQ, food frequency questionnaire.

Figure 7 Protein Intake: 24 Hour Recall versus Food Frequency Questionnaire



Protein intake from natural foods and low protein medical foods for the FFQ compared to 24-hour recall over time. Data is presented as the mean and standard devation. There was no significant difference in reporting of protein intake between the FFQ and 24-hour recall before (p = 0.108) and after (p = 0.506) the education session. p, significance; FFQ, food frequency questionnaire.

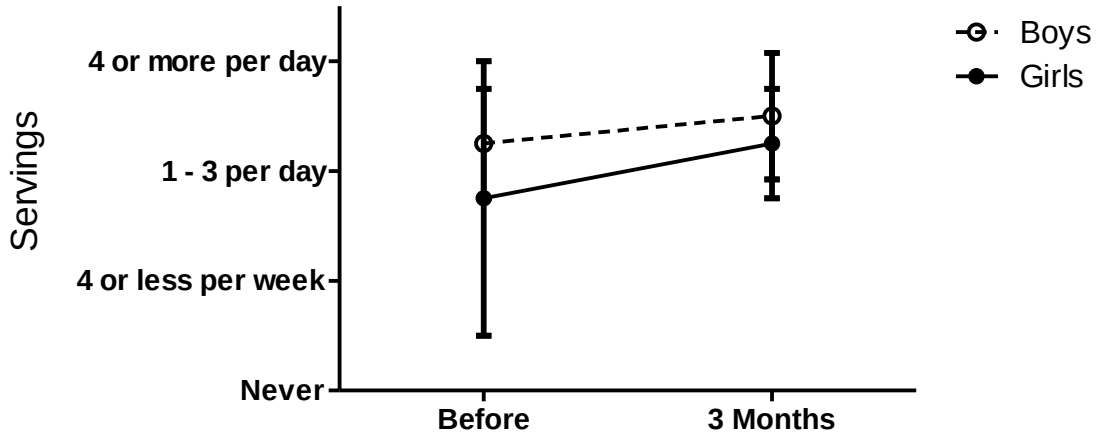
Fruit and Vegetable Consumption

Change in fruit and vegetable consumption was compared before education and three months after education day. There was no difference in fruit consumption (p = 0.317) or vegetable consumption (p = 0.317) at three months following education day for boys. Girls had a slight increase in vegetable consumption (p = 0.317) and a slight decrease in fruit consumption (p = 0.414) but neither of these results were statistically significant.

Change in fruit and vegetable consumption was also compared between boys and girls. There was no difference in fruit consumption (p = 0.207) or vegetable consumption (p = 0.780) between boys and girls. Vegetable

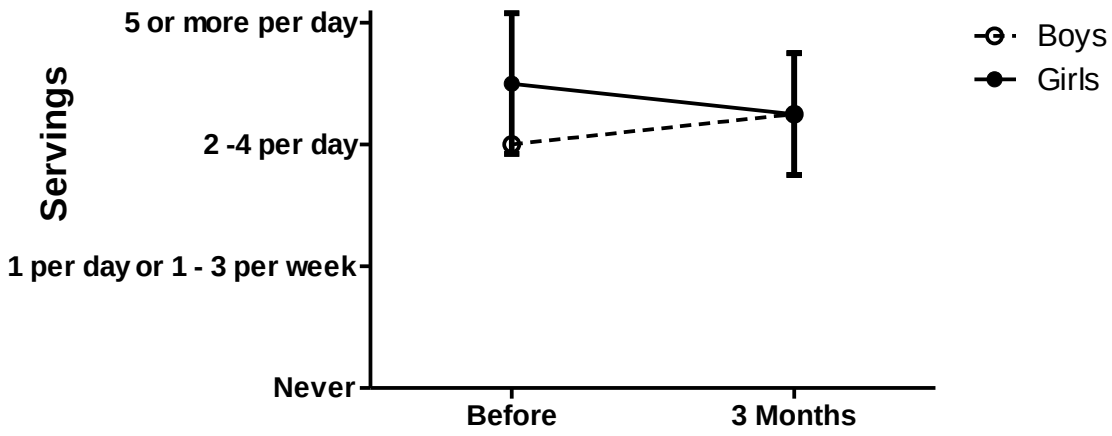
consumption over time for boys and girls is presented in Figure 8 and fruit consumption over time for boys and girls is presented in Figure 9.

Figure 8 Vegetable Consumption Over Time



Vegetable consumption over time for boys and girls. Data is presented as the mean and standard deviation. Change in vegetable consumption for girls (p = 0.317) and boys (p = 0.317) was not signficantly different. Change in vegetable consumption between boys and girls (p = 0.780) was not different. p, significance.

Figure 9 Fruit Consumption Over Time



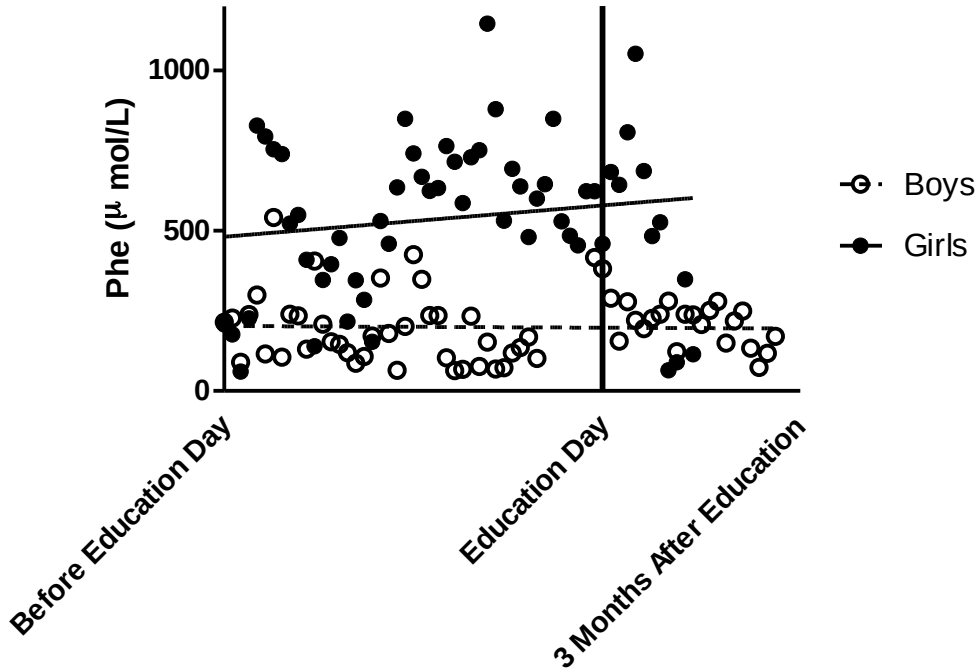
Fruit consumption over time for boys and girls. Data is presented as the mean and standard deviation. No significant change in fruit consumption for girls (p = 0.414) or boys (p = 0.317) was observed. Change in fruit consumption between boys and girls (p = 0.207) was not statistically different. p, significance.

Phenylalanine Concentrations

Mean phe concentrations during the 6 months prior to intervention and three months after intervention were compared. Only two girls had phe concentrations at three months following intervention and although for girls there was a decrease compared to before education day, it was not statistically significant (p = 0.499). There was also no significant difference in change in phe concentrations following education day for boys (p = 0.267).

Change in phe concentrations was not different between boys and girls (p = 0.221). Phenylalanine concentrations over time for boys and girls are presented in Figure 10.

Figure 10 Phenylalanine Concentrations Over Time



Phenylalanine levels over time for boys and girls. No significant change in phenylalanine levels for girls (p=0.449) or boys (p = 0.267) was seen over time. Change in phe levels between boys and girls was not significantly different (p = 0.221). p, significance; phe, blood phenylalanine concentration.

CHAPTER 5

DISCUSSION

Summary and Conclusions

Researchers recruited nine children who had PKU but were otherwise healthy. One participant was lost to follow up. The primary objective of the study was to evaluate group education's effectiveness of improving knowledge of diet and disease. The second aim was to determine if group education improved blood concentrations of phe. The third aim was to determine whether education in a group setting increased fruit and vegetable consumption. The final aim was to compare protein intake from foods gathered on a FFQ to protein intake from foods gathered from 24-hour recalls. Knowledge scores, fruit and vegetable consumption, and blood phe concentrations did not change following a single two-hour group education session and therefore the primary, secondary, third, and final hypotheses were rejected.

As children with PKU approach adolescence, they have a more difficult time treating their disease as evidenced by uncontrolled phe concentrations (25). There are many reasons that PKU may be less controlled as children age including isolation, the social burden of the diet, and lack of knowledge (26).

The traditional treatment style currently in use involves an exchange between the parent and members of the medical team, and has not been as effective at managing phe concentrations as practitioners would like. Limited research exists evaluating whether group education for children with PKU can

improve the child's knowledge of the disorder and its treatment, and increase variety in the diet within the confines of a severe phe restriction.

In this research study a group education model was used for children to provide social support and prevent isolation in hopes of improving knowledge of diet and disease as well as improve dietary control (28). Our research showed no significant improvements in dietary control as interpreted by blood phe concentrations. This outcome was previously seen in a study using a single education intervention model (34). A study done in a week long camp experience by Singh et al showed significant improvements in plasma phe concentrations ($p = 0.0001$) post camp but these improvements in plasma phe concentrations were not observed long term.

In our research study, girls showed a slight increase in knowledge immediately following education day but this result was not statistically significant. These results differ from previous reports (34, 35). Singh et al showed improved knowledge of diet ($p < 0.0288$) and disease ($p<0.0013$) post camp and one year following camp ($p<0.008$ and $p <0.0001$ respectively) (35). Durham-Shearer et al also showed improvements in knowledge scores one month following intervention, however, this improvement was not sustained at 6 months. One potential reason for this difference is that the study done by Singh et al was done in a camp environment for one week while our study participants attended only one 2-hour education session. It is possible that a one-time education experience may not be as effective as a longer camp experience at improving knowledge and metabolic control.

Researchers have shown that children with PKU that perceive more barriers to treating their disease, such as lack of knowledge, difficulty planning meals, social pressures, and disliking the formula, also have elevated phe concentrations compared to children that perceive less barriers (26), but no research has evaluated a correlation between knowledge and phe levels. While not statistically significant, our results did show a trend that indicated that children that had a better understanding of their disease and diet had phe concentrations that were better controlled. It is important to note that mean phe ranges for boys and girls were within or near normal ranges at baseline making it more difficult to show significant improvements in phe concentration levels.

It was also observed that girls seemed to have a better understanding of what they were eating on a day-to-day basis but had less of an understanding of what PKU is and how it affects them, as reflected in the lower knowledge scores prior to education day. Although not significant, the girls also had higher plasma phe concentrations than the boys. Both decreased knowledge and increased phe concentrations compared to boys may be an indication of different parenting behaviors or educational strategies in clinic between boys and girls with PKU, which elicits further research.

We also saw no significant improvement in diet variability as measured through increased fruit and vegetable consumption. There is currently no research looking at fruit and vegetable intake in children with PKU. From a study published in 2009, only 0.9% of adolescents consume the recommended dietary guidelines for fruit and vegetables (21). In our research, most kids (80%)

reported eating 1-3 servings of vegetables per day and 2-4 servings of fruit per day. Because of the ranges used in the FFQ it is difficult to tell what percentage of our research participants were meeting the dietary guidelines for fruit and vegetable consumption but it appears that children with PKU in our study consume more fruits and vegetables than reported in the general population. With the advent of specialty low protein foods for children with PKU, a population that was often thought to be at risk for malnourishment, they are now at risk for overweight or obesity. Because of this finding, it is important to find an educational model that is effective at encouraging kids with PKU to increase their consumption of nutrient dense fruit and vegetables as the diet continues to become more variable.

Protein intake in synthetic form from formula and in its natural form from food sources is an important part of the PKU diet, especially in children. Although there was a slight increase in protein intake from foods following education day for boys and girls the result was not statistically significant, and there was no difference in protein intake between boys and girls. The slight increase in protein intake was not reflected in increases in phenylalanine levels. Based on the mean weight for age and phe concentrations of our study participants, we would assume that our study participants are getting adequate protein to support growth while maintaining metabolic control. Adequate protein intake to support growth and maintain phe concentrations within the normal range is not uncommon in children with PKU who consume formula on a regular basis (7); however, girls, on average were consuming less than the

recommended > 50 g/day as stated in the Ross Guidelines (49). Boys, on average, were consuming adequate amounts of protein per Ross Guidelines (49). The Ross Guidelines are developed by Ross Products Division in the Division of Abbott Laboratories in Columbus, Ohio and is commonly in used as a tool for clinicians working with patients with metabolic disorders

As dietary research for individuals with PKU continues to progress it is important that we have a tool that can accurately measure dietary protein intake. Biomarin Inc. has developed a FFQ for this reason. From our results it seems that the FFQ may overestimate protein intake slightly, however, the result was not statistically significant. Because of our limited population size, it is difficult to conclude whether this tool would be appropriate for a larger sample and further research is needed in this area.

While there were no statistically significant findings in our research, there were many observed benefits to group education and the potential use of group education sessions as a clinic model. Following education day children had established relationships with other children. Children were more prone to try the snack when they saw their peers trying snacks and during follow up parents often asked if there would be another session as they perceived that their child had benefited in some way from the group education model.

In conclusion, providing a single two-hour education session is not effective at improving dietary control, increasing fruit and vegetable consumption or increasing knowledge regarding PKU in boys and girls between the ages of 9 and 16. However, the potential benefits that were not measured here such as

increased support and perceived benefits from the parents perspective make this model an enticing one. While one group education session may not be effective, further research is needed to determine if repeat interventions will have more definitive outcomes.

Limitations

There were many limitations to this research. Recruitment of participants in a specific age range with a rare genetic disorder in a single clinic is challenging and therefore resulted in a small sample size. Some children that are followed at the CDRC metabolic clinic for management of PKU live far away, while others could not miss school mid-week or were involved in extra-curricular activities. Busy schedules made it difficult to plan an education day that all study participants could attend and therefore multiple education days with smaller numbers of children were used to increase the number of participants. Due to the small number of participants after the first recruitment that was limited to boys, girls were included in the study. Due to the importance of educating young women about maternal PKU, a new curriculum and quiz was developed specifically for the girls. A different curriculum and quiz for boys and girls makes it difficult to conclude differences in knowledge between boys and girls.

Involvement of study subjects in extra-curricular activities and busy schedules also made it difficult to collect FFQ's and 24-hour recall data. Often the FFQ and 24-hour recalls were a combination of child and parent input rather than just the child or just the parent which may have skewed our results.

Challenges with recruitment and lack of flexibility in clinic schedules made it difficult to get children in for a clinic appointment on education day. This prevented us from getting heights, weights, and plasma phe concentrations on the day of education. Instead we used medical record data to obtain these concentrations, which were from varying time periods relative to education day and a different number of data points for each participant. While phe concentrations are currently the best way to measure dietary control, it is a measure that is highly influenced by what the participant ate prior to the test. Because phe concentrations can vary based on prior dietary intake, it makes it difficult to conclude much about dietary control looking at these concentrations retrospectively, especially when participants had limited blood spot tests. The inability to have clinic visits on education day could have also been a barrier to participation due to increased participant burden.

Advantages

While there were many limitations to this study there has been no previous research evaluating the impacts of group education for children with PKU as a clinic model. This research is an integral starting point to understanding the best way to empower children and adolescents to manage their diet as well as improve their quality of life.

Future Directions

Further research is needed to assess whether multiple exposures versus one-time interventions for nutrition and disease education are more effective at improving phe concentrations and knowledge of diet and disease in children with

PKU. Additional measures of perceived benefits such as social support and quality of relationships between parents, children, friends and health care providers should also be included. As more metabolic clinics begin to develop a group education model for health care, understanding the benefits and limitations of this alternative approach is key to developing evidence based practice models for patients with PKU.

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APPENDIX A

CONSENT FORM AND ASSENT FORMS – BOYS

OREGON HEALTH & SCIENCE UNIVERSITY
Consent and Authorization Form

TITLE: Group Education for Children with Phenylketonuria

PRINCIPAL INVESTIGATOR: Melanie B Gillingham, PhD, RD (503) 494-1682

CO-INVESTIGATORS: Jessi Peretti, B.S. (406) 490-7561
Susan Filkins, RD (503) 494-418-2213
Becky J. Whittemore, MN, MPH, FNP (503) 494-2776
David Koeller , MD (503) 494-2604

SPONSOR: Oregon Health and Science University – Child Development and Rehabilitation Center

PURPOSE:

You have been invited to participate in this research study because your child has phenylketonuria (PKU). The purpose of this study is to determine if group education for children with PKU can improve their understanding of PKU, increase their fruit and vegetable intake, and lower blood phenylalanine levels.

This study will involve a visit to the Child Development and Rehabilitation Center for an initial assessment and group education session. Your child will then be followed up three months following education day via telephone. Your child will be asked to return to the Child Development and Rehabilitation Center six months following the initial visit for a final assessment.

PROCEDURES:

Full participation in this study will include your child attending an optional 3.5 hour education session with children with PKU and filling out a 11 question

multiple choice questionnaire and a Food Frequency Questionnaire at three separate time periods over 6 months. The questionnaire will first be filled out on education day. The second and third questionnaires will be filled out three months following the education day via mail and telephone call with the investigator. The final questionnaires will be filled out during your child's routine follow up appointment at the CDRC six months following the education day. A detailed outline of the events for education day is included.

The 11 question multiple choice questionnaire will assess how much your child knows about PKU and the dietary treatment prescribed for PKU. The Food Frequency Questionnaire shows how often your child consumes certain foods over a given time period. The multiple choice questionnaire and food frequency questionnaire will take approximately 30 minutes to complete.

Your child may choose not to participate in the education day and continue with their routine, individual follow up appointments at the CDRC. Your child will be asked to fill out the multiple choice questionnaire and Food Frequency Questionnaire during their routine, individual follow up appointments at two separate appointments.

We will obtain your child's weight, height, and blood phenylalanine levels from your child's medical records. In order to release your child's medical records for this study you must sign this consent form, complete and signed a medical record release form, and return these forms to study personnel in the enclosed self-addressed stamped envelope.

If you have any questions regarding this study now or in the future, contact Jessi Peretti at (406) 490-7561 or Dr. Melanie Gillingham at (503) 494-1682 during business hours.

RISKS AND DISCOMFORTS:

Although we have made every effort to protect your identity, there is a minimal risk of loss of confidentiality.

BENEFITS:

Your child may or may not personally benefit from being in this study. However, by serving as a subject, your child may help us learn how to benefit patients in the future.

ALTERNATIVES:

1. You may choose for your child not to participate in the education day and only fill out the questionnaires.

2. You may choose for your child not to participate in education day and not fill out the questionnaires and your child can continue to receive his or her routine medical care at the CDRC.

CONFIDENTIALITY AND PRIVACY OF YOUR PROTECTED HEALTH INFORMATION:

We will not use your name or your identity for publication or publicity purposes.

If you sign this form, you are agreeing that OHSU may use and disclose protected health information collected and created in this research study. The specific health information and purpose of each use and disclosure are described in the following table:

Health Information	Purpose(s)
☐ Your complete existing health record **	_____
☒ Limited information from your existing health record** (specify): weight, height, body mass index, blood phenylalanine levels	a, c, d
** If we are requesting existing health records that are located outside of OHSU, you will need to complete an additional authorization to release	
THE FOLLOWING CHECKED ITEM(S) WILL BE GENERATED/COLLECTED DURING THE COURSE OF THIS STUDY:	
☐ History and physical examinations	_____
Reports: ☐ Laboratory ☐ Operative ☐ Discharge	
☐ Progress	_____
☐ Photographs, videotapes, or digital or other images	_____
☐ Diagnostic Images/X-ray/MRI/CT	_____
☐ Bioelectric Output (e.g., EEG, EKG)	_____
☒ Questionnaires, interview results, focus group survey, psychology survey, behavioral performance tests (e.g., memory & attention)	a, c, d
☐ Tissue and/or blood specimens	_____
☐ Other: _____	_____
Purpose Categories a. To learn more about the condition/disease being studied b. To facilitate treatment, payment, and operations related to the study c. To comply with federal or other governmental agency regulations d. For teaching purposes e. Other _____	

The persons who are authorized to use and disclose this information are all investigators listed on page one of this Consent and Authorization Form and the OHSU Institutional Review Board.

The persons who are authorized to receive this information are the Office for Human Research Protections.

We may continue to use and disclose protected health information that we collect from you in this study until study is completed***.***

While this study is still in progress, you may not be given access to medical information about you that is related to the study. After the study is completed and the results have been analyzed, you will be permitted access to any medical information collected about you in the study.

You have the right to revoke this authorization and can withdraw your permission for us to use your information for this research by sending a written request to the Principal Investigator listed on page one of the research consent form. If you do send a letter to the Principal Investigator, the use and disclosure of your protected health information will stop as of the date she receives your request. However, the Principal Investigator is allowed to use and disclose information collected before the date of the letter or collected in good faith before your letter arrives. Revoking this authorization will not affect your health care or your relationship with OHSU.

The information about you that is used or disclosed in this study may be re-disclosed and no longer protected under federal law.

Under Oregon Law, suspected child or elder abuse must be reported to appropriate authorities.

COSTS:

It will not cost you anything to participate in this study. You will not be compensated for your participation.

LIABILITY:

If you believe you have been injured or harmed while participating in this research and require immediate treatment, contact the research investigators - Jessi Peretti at (406) 490-7561 or Dr. Melanie Gillingham at (503)-494-1682

You have not waived your legal rights by signing this form. If you are harmed by the study procedures, you will be treated. Oregon Health & Science University does not offer to pay for the cost of the treatment. Any claim you make against Oregon Health & Science University may be limited by the Oregon Tort Claims Act (ORS 30.260 through 30.300). If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

PARTICIPATION:

If you have any questions regarding your rights as a research subject, you may contact the OHSU Research Integrity Office at (503) 494-7887.

You do not have to join this or any research study. If you do join, and later change your mind, you may quit at any time. If you refuse to join or withdraw early from the study, there will be no penalty or loss of any benefits to which you are otherwise entitled.

Your health care provider may be one of the investigators of this research study, and as an investigator is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

You may be removed from the study if the investigator stops the study or if the sponsor stops the study.

If you choose to withdraw from this study no further action will be needed on your part.

We will give you a copy of this form now.

A Child Assent Form is attached to the consent form and should be filled out by your child if he or she is between the ages of 7 and 17.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

OREGON HEALTH & SCIENCE UNIVERSITY

INSTITUTIONAL REVIEW BOARD

PHONE NUMBER (503) 494-7887

CONSENT/AUTHORIZATION FORM APPROVAL DATE

Jun. 20, 2011

Do not sign this form after the Expiration date of: 06-19-2012

_____ _____

Subject signature Date

OR

_____ _____ _____

Parent/Guardian Signature Relationship to subject Date

_____ _____

IRB# : 7573

Protocol Approval Date: 06.20.2011

OREGON HEALTH & SCIENCE UNIVERSITY
Child Assent Form

TITLE: Group Education for Children with Phenylketonuria

PRINCIPAL INVESTIGATOR: Melanie B. Gillingham, PhD (503) 494-3880

CO-INVESTIGATORS:

Jessi Peretti, B.S. (406) 490-7561
Susan Filkins, RD (503) 494-418-2213
Becky J. Whittemore, MN, MPH, FNP (503) 494-2776
David Koeller , MD (503) 494-2604

Part I

A researcher has explained this research study to me. I know how it may or may not help me. I also know that this study will help doctors know more about obesity.

1. The investigator will ask me to explain what I will do and what will happen in this study to be sure I understand the study.

2. The investigator will ask me if I have any questions or want to know anything else about this study or obesity.

3. The investigator will ask me to explain some of the good and bad things that might happen to me if I enter this study.

Part II

I have thought about being a part of this study. I have asked and received answers to my questions. I agree to be in this study. I know that I don't have to agree to be in the study. Even though I agree to be in it now, I know I may feel differently later on and can ask to stop being in the study. I know that I may talk with my parents and/or doctor about not being in this study at any time.

OREGON HEALTH & SCIENCE UNIVERSITY

INSTITUTIONAL REVIEW BOARD

PHONE NUMBER (503) 494-7887

CONSENT/AUTHORIZATION FORM APPROVAL DATE

Jun. 20, 2011

Do not sign this form after the Expiration date of: 06-19-2012

Name/signature:_____ Date:_____

_____ _____ _____

Study coordinator/PI Signature Study coordinator/PI Printed Name Date

APPENDIX B

CONSENT AND ASSENT FORM – GIRLS

OREGON HEALTH & SCIENCE UNIVERSITY
Consent and Authorization Form

TITLE: Group Education for Children with Phenylketonuria

PRINCIPAL INVESTIGATOR: Melanie B Gillingham, PhD, RD (503) 494-1682

CO-INVESTIGATORS: Jessi Peretti, B.S. (406) 490-7561
Susan Filkins, RD (503) 494-418-2213
Becky J. Whittemore, MN, MPH, FNP (503) 494-2776
David Koeller , MD (503) 494-2604

SPONSOR: Oregon Health and Science University – Child Development and Rehabilitation Center

PURPOSE:

You have been invited to participate in this research study because your child has phenylketonuria (PKU). The purpose of this study is to determine if group education for children with PKU can improve their understanding of PKU, increase their fruit and vegetable intake, and lower blood phenylalanine levels.

This study will involve a visit to the Child Development and Rehabilitation Center for an initial assessment and group education session. Your child will then be followed up three months following education day via telephone. Your child will be asked to return to the Child Development and Rehabilitation Center six months following the initial visit for a final assessment.

PROCEDURES:

Full participation in this study will include your child attending an optional 3.5 hour education session with children with PKU and filling out a 14 question

multiple choice questionnaire, a Food Frequency Questionnaire at two separate time periods over 3 months, and four 24-hour recalls at 4 separate time periods over 3 months. The questionnaires will first be filled out on education day. The second food frequency questionnaire will be filled out three months following the education day via mail and telephone call with the investigator. The three additional 24 hour recalls will be completed over the telephone one, two, and three months following education day. A detailed outline of the events for education day is included.

The 14 question multiple choice questionnaire will assess how much your child knows about PKU and the dietary treatment prescribed for PKU. The Food Frequency Questionnaire shows how often your child consumes certain foods over a given time period. The 24-hour recall shows what your child ate and drank over the previous 24 hours. The multiple choice questionnaire, food frequency questionnaire, and 24-hour recall will take approximately 45 minutes to complete.

Your child may choose not to participate in the education day and continue with their routine, individual follow up appointments at the CDRC.

We will obtain your child's weight, height, and blood phenylalanine levels from your child's medical records. In order to release your child's medical records for this study you must sign this consent form, complete and signed a medical record release form, and return these forms to study personnel in the enclosed self-addressed stamped envelope.

If you have any questions regarding this study now or in the future, contact Jessi Peretti at (406) 490-7561 or Dr. Melanie Gillingham at (503) 494-1682 during business hours.

RISKS AND DISCOMFORTS:

Although we have made every effort to protect your identity, there is a minimal risk of loss of confidentiality.

BENEFITS:

Your child may or may not personally benefit from being in this study. However, by serving as a subject, your child may help us learn how to benefit patients in the future.

ALTERNATIVES:

1. You may choose for your child not to participate in the education day and only fill out the questionnaires.

2. You may choose for your child not to participate in education day and not fill out the questionnaires and your child can continue to receive his or her routine medical care at the CDRC.

CONFIDENTIALITY AND PRIVACY OF YOUR PROTECTED HEALTH INFORMATION:

We will not use your name or your identity for publication or publicity purposes.

If you sign this form, you are agreeing that OHSU may use and disclose protected health information collected and created in this research study. The specific health information and purpose of each use and disclosure are described in the following table:

Health Information	Purpose(s)
☐ Your complete existing health record **	_____
☒ Limited information from your existing health record** (specify): weight, height, body mass index, blood phenylalanine levels	a, c, d
** If we are requesting existing health records that are located outside of OHSU, you will need to complete an additional authorization to release	
THE FOLLOWING CHECKED ITEM(S) WILL BE GENERATED/COLLECTED DURING THE COURSE OF THIS STUDY:	
☐ History and physical examinations	_____
Reports: ☐ Laboratory ☐ Operative ☐ Discharge ☐ Progress	_____
☐ Photographs, videotapes, or digital or other images	_____
☐ Diagnostic Images/X-ray/MRI/CT	_____
☐ Bioelectric Output (e.g., EEG, EKG)	_____
☒ Questionnaires, interview results, focus group survey, psychology survey, behavioral performance tests (e.g., memory & attention)	a, c, d
☐ Tissue and/or blood specimens	_____
☐ Other: _____	_____

Purpose Categories

f. To learn more about the condition/disease being studied
g. To facilitate treatment, payment, and operations related to the study
h. To comply with federal or other governmental agency regulations
i. For teaching purposes
j. Other _____

The persons who are authorized to use and disclose this information are all investigators listed on page one of this Consent and Authorization Form and the OHSU Institutional Review Board.

The persons who are authorized to receive this information are the Office for Human Research Protections.

We may continue to use and disclose protected health information that we collect from you in this study until study is completed*.*

While this study is still in progress, you may not be given access to medical information about you that is related to the study. After the study is completed and the results have been analyzed, you will be permitted access to any medical information collected about you in the study.

You have the right to revoke this authorization and can withdraw your permission for us to use your information for this research by sending a written request to the Principal Investigator listed on page one of the research consent form. If you do send a letter to the Principal Investigator, the use and disclosure of your protected health information will stop as of the date she receives your request. However, the Principal Investigator is allowed to use and disclose information collected before the date of the letter or collected in good faith before your letter arrives. Revoking this authorization will not affect your health care or your relationship with OHSU.

The information about you that is used or disclosed in this study may be re-disclosed and no longer protected under federal law.

Under Oregon Law, suspected child or elder abuse must be reported to appropriate authorities.

COSTS:

It will not cost you anything to participate in this study. You will not be compensated for your participation.

LIABILITY:

If you believe you have been injured or harmed while participating in this research
and require immediate treatment, contact the research investigators - Jessi Peretti at (406) 490-7561 or Dr. Melanie Gillingham at (503)-494-1682

You have not waived your legal rights by signing this form. If you are harmed by the study procedures, you will be treated. Oregon Health & Science University does not offer to pay for the cost of the treatment. Any claim you make against Oregon Health & Science University may be limited by the Oregon Tort Claims Act (ORS 30.260 through 30.300). If you have questions on this subject, please call the OHSU Research Integrity Office at (503) 494-7887.

PARTICIPATION:

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You do not have to join this or any research study. If you do join, and later change your mind, you may quit at any time. If you refuse to join or withdraw early from the study, there will be no penalty or loss of any benefits to which you are otherwise entitled.

Your health care provider may be one of the investigators of this research study, and as an investigator is interested in both your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may ask for a second opinion about your care from another doctor who is in no way involved in this project. You do not have to be in any research study offered by your physician.

You may be removed from the study if the investigator stops the study or if the sponsor stops the study.

If you choose to withdraw from this study no further action will be needed on your part.

We will give you a copy of this form now.

A Child Assent Form is attached to the consent form and should be filled out by your child if he or she is between the ages of 7 and 17.

SIGNATURES:

Your signature below indicates that you have read this entire form and that you agree to be in this study.

OREGON HEALTH & SCIENCE UNIVERSITY

INSTITUTIONAL REVIEW BOARD

PHONE NUMBER (503) 494-7887

CONSENT/AUTHORIZATION FORM APPROVAL DATE

Jun. 20, 2011

Do not sign this form after the Expiration date of: 06-19-2012

_____ _____
Subject signature Date

OR

_____ _____ _____
Parent/Guardian Signature Relationship to subject Date

_____ _____

IRB# : 7573
Protocol Approval Date: 06.20.2011

OREGON HEALTH & SCIENCE UNIVERSITY
Child Assent Form

TITLE: Group Education for Children with Phenylketonuria

PRINCIPAL INVESTIGATOR: Melanie B. Gillingham, PhD (503) 494-3880

CO-INVESTIGATORS:

Jessi Peretti, B.S. (406) 490-7561
Susan Filkins, RD (503) 494-418-2213
Becky J. Whittemore, MN, MPH, FNP (503) 494-2776
David Koeller , MD (503) 494-2604

Part I

A researcher has explained this research study to me. I know how it may or may not help me. I also know that this study will help doctors know more about obesity.

1. The investigator will ask me to explain what I will do and what will happen in this study to be sure I understand the study.

2. The investigator will ask me if I have any questions or want to know anything else about this study or obesity.

3. The investigator will ask me to explain some of the good and bad things that might happen to me if I enter this study.

Part II

I have thought about being a part of this study. I have asked and received answers to my questions. I agree to be in this study. I know that I don't have to agree to be in the study. Even though I agree to be in it now, I know I may feel differently later on and can ask to stop being in the study. I know that I may talk with my parents and/or doctor about not being in this study at any time.

OREGON HEALTH & SCIENCE UNIVERSITY

INSTITUTIONAL REVIEW BOARD

PHONE NUMBER (503) 494-7887

CONSENT/AUTHORIZATION FORM APPROVAL DATE

Jun. 20, 2011

Do not sign this form after the Expiration date of: 06-19-2012

Name/signature:_____ Date:_____

_____ _____ _____

Study coordinator/PI Signature Study coordinator/PI Printed Name Date

APPENDIX C

FOOD FREQUENCY QUESTIONNAIRE

Name:_____ Clinic Visit #:_____ Date:_____

Food Frequency Questionnaire

1. Before beginning, take a moment to think about the way you usually eat. For each item, select the box that best represents how you have been eating **since your last clinic appointment**.
2. For each food item, put a check mark in column I, II, III or IV in row "a" to indicate how often and in row "b" to indicate how much. If you do not eat a particular food item, do not complete row "b" for that particular food.
3. Please refer to the attached portion size sheet to best estimate the amount that you typically eat.
4. If the available responses do not include a portion size that is how much you usually eat, please use column V and write in the amount under "comments."
5. You can select more than one box within a particular food group (e.g. if you eat high protein breads half of the time and moderate protein breads the other half of the time, check both boxes). If you select more than one box, make a note in column V under "comments" to indicate how often you eat each of the different types of foods, ie. 25% of the time, 50% of the time, etc.
6. When you are not sure how to categorize a food, just write this in the comments column for your dietitian to help you.
7. You can use the portion guidelines sheet and food grouping handout included in this packet to help with making your selections.
8. Once you have completed the food frequency questionnaire, please record your food intake for the day prior to your clinic appointment on the attached form.
9. Your dietitian will review the completed questionnaire with you during your clinic appointment.

Please note that "usually" means that you do this most of the time and "rarely" means that you do this no more than once a month.

Food Item	I	II	III	IV	V
1. Medical Protein Products/Formula (phenylalanine-free)					
a. How often?	□ Never or rarely □ Other, please explain… _____ _____	□ Usually take: <50% of amount prescribed	□ Usually take: 50-75% of amount prescribed	□ Usually take: full amount prescribed	Comments: _____ _____ _____ _____
b. How much?	□ Usually eat/drink: 1 time a day	□ Usually eat/drink: 2 times a day	□ Usually eat/drink: 3 times a day	□ Usually eat/drink: 4 times a day or more	Comments: _____ _____ _____
2. Special Low Protein Foods (specially modified to provide significantly less protein then similar "regular" foods)					
a. How often?	□ Never eat special low-protein foods	□ Usually eat: at least 1 serving per day	□ Usually eat: 2-3 servings per day	□ Usually eat: >3 servings per day	Comments: _____ _____ _____ _____

Food Item	I	II	III	IV	V
b. How much?	□ **Usually eat: low protein cheese and drink rice milk found in grocery store**	□ **Usually eat: special low protein foods and/or low protein products found at health food stores or Trader Joe's**	□ **Usually substitute special low protein foods for: "regular" bread, pasta, cereal, rice, grains, and snack foods**	□ **Usually substitute special low protein foods for: "regular" meat and meat products, *and* "regular" cheese, milk, eggs, bread, cereal, rice, grains, and snack foods**	**Comments:** _____ _____ _____ _____ _____
3. Vegetables					
a. How often?	□ **Never or rarely** □ **Other, please explain…** _____ _____	□ **Usually eat: 4 servings a week or less**	□ **Usually eat: 1-3 servings a day**	□ **Usually eat: 4 or more servings a day**	**Comments:** _____ _____ _____ _____ _____
b. How much?	□ **Usually eat: higher protein vegetables** such as peas, corn, potatoes (>2 grams of protein per 1/2 cup serving)	□ **Usually eat: moderately high protein vegetables** such as bean sprouts, beets, okra, *cooked* mushrooms (<2 grams of protein per 1/2 cup serving)	□ **Usually eat: Moderately low protein vegetables** such as broccoli, green beans, asparagus (1 gram of protein per 1/2 cup serving)	□ **Usually eat: lower protein vegetables** such as lettuce, carrots, cucumbers, celery (<1 gram of protein per 1/2 cup serving)	**Comments:** _____ _____ _____ _____ _____
4. Fruit & Fruit Juices					
a. How often?	□ **Never or rarely** □ **Other, please explain…** _____ _____	**Usually eat/drink:** □ **1 serving a day** □ **1-3 servings a week**	□ **Usually eat/drink: 2-4 servings a day**	□ **Usually eat/drink: 5 or more servings a day**	**Comments:** _____ _____ _____ _____
b. How much?	□ **Usually eat/drink: higher protein fruits** such as bananas, raisins, dates, orange juice (>1 gram protein per 1/2 cup)	□ **Usually eat/drink: fruits/juice with a moderate amount of protein** such as oranges, kiwi, cantaloupe (1 gram protein per 1/2 cup)	□ **Usually eat/drink: lower protein fruits** such as blueberries, pears, peaches, mango, grapes (<1 gram protein per 1/2 cup)	□ **Usually eat/drink: very low protein fruits or fruit juices** such as apples, apple juice, cherries, pineapple, strawberries (<0.5 grams protein per ½ cup)	**Comments:** _____ _____ _____ _____ _____

Food Item	I	II	III	IV	V
5. Regular Bread, Cereal, Starches & Grains					
a. How often?	□ **Usually eat: 3 or more servings per day**	□ **Usually eat: 1-2 servings per day**	□ **Usually eat: one serving about every other day**	□ **Never or rarely** □ **Other, please explain…** _____	**Comments:** _____ _____ _____
b. How much?	□ **Usually eat: higher protein foods** such as bagels, regular pasta, granola (≥5 grams of protein per serving)	□ **Usually eat: moderately high protein foods** such as oatmeal, whole wheat bread, Cheerios®, Lucky Charms®, Raisin Bran® (3-4 grams of protein per serving)	□ **Usually eat: lower protein foods** such as flour tortillas, white rice, Nutri- Grain™ bars, white bread (2 grams of protein per serving)	□ **Usually eat: very low protein foods** such as Trader Joe's Wheat Free Waffles, rice cakes, corn tortillas (≤ 1 gram of protein per serving)	**Comments:** _____ _____ _____ _____ _____
6. Snacks (e.g. packaged cookies, crackers, candies, chips, pretzels, etc.)					
a. How often?	□ **Usually eat: 4 or more servings a day**	□ **Usually eat: 2-3 servings a day**	□ **Usually eat: 1 serving a day**	□ **Usually eat: 4 times a week or less**	**Comments:** _____ _____ _____ _____
b. How much?	□ **Usually eat: high protein snacks** such as Power Bar®, Luna™ Bar, Cliff® Bar (≥5 grams of protein per serving)	□ **Usually eat: moderately high protein snacks** such as Goldfish® crackers, Cheese Nips®, Ritz® Crackers Real Cheese or Peanut Butter (3-4 grams of protein per serving)	□ **Usually eat: moderately low protein snacks** such as graham crackers, cookies, pretzels, tortilla chips, granola bars (2 grams of protein per serving)	□ **Usually eat: *only* very low-protein snacks** such as veggie sticks, potato chips, sugar wafer cookies (≤1 gram of protein serving)	**Comments:** _____ _____ _____ _____
7. Beans (e.g. lentils, refried beans, black beans)					
a. How often?	□ **Usually eat: daily**	□ **Usually eat: about every other day**	□ **Usually eat: once or twice a week**	□ **Never or rarely** □ **Other, please explain…** _____ _____	**Comments:** _____ _____ _____ _____
b. How much?	□ **Usually eat: large portions** (≥½ cup beans)	□ **Usually eat: medium portions** (¼ cup beans)	□ **Usually eat: small portions** (*only* the juice of the beans)	□ **Never or rarely**	**Comments:** _____ _____ _____ _____

Food Item	I	II	III	IV	V
8. Nuts, including nut butters (e.g. peanut butter, almond butter, etc.) or candy and/or trail mixes containing nuts or peanut butter					
a. How often?	□ **Usually eat: daily**	□ **Usually eat: about every other day**	□ **Usually eat: once or twice a week**	□ **Never or rarely** □ **Other, please explain…** _____ _____	**Comments:** _____ _____ _____ _____ _____
b. How much?	□ **Usually eat: large portions** (≥2 Tablespoons nuts or nut butter)	□ **Usually eat: medium portions** (<2 Tablespoons nuts or nut butter)	□ **Usually eat: small portions** (<1 Tablespoon nuts or nut butter)	□ **Never or rarely**	**Comments:** _____ _____ _____ _____ _____
9. Milk & Yogurt					
a. How often?	□ **Usually drink/eat: daily** **Servings per day:** □ **1-2** □ **3-4**	□ **Usually drink/eat: about every other day**	□ **Usually drink/eat: once or twice a week**	□ **Never or rarely** □ **Other, please explain…** _____ _____	**Comments:** _____ _____ _____ _____ _____
b. How much?	□ **Usually drink/eat: regular portion size** (8 fl. oz. milk or 1 cup yogurt. If eat more than this, count as more than one serving)	□ **Usually drink/eat: half portion size** (4 fl. oz. milk, or ½ cup yogurt)	□ **Usually drink/eat: small portion size** (2 fl. oz. milk, or ¼ cup yogurt)	□ **Usually drink/eat: very small portion size** (1 fl. oz. milk, or 2 tbsp. yogurt)	**Comments:** _____ _____ _____ _____ _____
10. Cheese, include only regular cheese (*NOT* low protein cheese)					
a. How often?	□ **Usually eat: daily**	□ **Usually eat: about every other day**	□ **Usually eat: once or twice a week**	□ **Never or rarely** □ **Other, please explain…** _____ _____	**Comments:** _____ _____ _____ _____ _____
b. How much?	□ **Usually eat: large portions** (4 oz. or more) *or* eat regular pizza with cheese	□ **Usually eat: medium portions** (2-3 oz.)	□ **Usually eat: small portions** (1 oz.)	□ **Usually eat: very small portions or mixed in other foods.** (1/2 oz. or less)	**Comments:** _____ _____ _____ _____ _____

Food Item	I	II	III	IV	V
11. Eggs					
a. How often?	□ Usually eat: daily	□ Usually eat: about every other day	□ Usually eat: once or twice a week	□ Never or rarely □ Other, please explain… _____ _____	Comments: _____ _____ _____ _____ _____
b. How much?	□ Usually eat: three eggs or more per serving	□ Usually eat: two eggs per serving	□ Usually eat: one egg per serving	□ Usually eat: *only* egg mixed in other dishes	Comments: _____ _____ _____ _____ _____
12. Meat (e.g. beef, pork, lamb), Poultry (e.g. chicken, turkey), & Fish					
a. How often?	□ Usually eat: daily	□ Usually eat: about every other day	□ Usually eat: once or twice a week	□ Never or rarely □ Other, please explain… _____ _____	Comments: _____ _____ _____ _____ _____
b. How much?	□ Usually eat: large portions (7 oz. or more)	□ Usually eat: medium portions (4-6 oz.)	□ Usually eat: small portions (2-3 oz.)	□ Usually eat: very small portions (1 oz. or less)	Comments: _____ _____ _____ _____ _____
13. Fast Food & Restaurants					
a. How often?	Usually eat out: □ 2-3 times a day	Usually eat out: □ 1 time a day	Usually eat out: □ 2-4 times a week	Usually eat out: □ less than one time a week	Comments: _____ _____ _____ _____ _____
b. How much?	□ Usually eat: meat or other high protein foods	□ Usually eat: regular pizza with cheese or regular pasta	□ Usually eat: pizza without cheese or vegetarian sushi	□ Usually eat: fries and salad	Comments: _____ _____ _____ _____ _____

Who completed this form? □ **Patient** □ **Parent/Caregiver** □ **Dietitian** □ **Other: _____**

How much time was spent completing this form? □ **<5 minutes** □ **10-15 minutes**

□ **5-10 minutes** □ **>15 minutes…** **How much time? _____**

24-Hour Diet Recall Record

Medical Food/Formula Prescription:

Please include all medical food and/or formula you are taking. Write the name and amount of each ingredient used to make you formula. Include any flavorings you add! For example, Phenex™-2, 150 grams powder per day, mixed with 20 fl. oz. water.

_____

_____

_____

Please circle below the amount of medical food/formula you consumed yesterday:

25% 50% 60% 75% 90% 100%

Vitamins, Minerals, and Medications:

Please list all vitamin and mineral supplements (name + brand), and any medications, along with the amount taken per day.

_____

_____

_____

Food/Beverage Intake:

Please write the name and amount of each food and beverage item you consumed during the past 24-hours. Include a description of how the item was prepared (e.g. potatoes, fried) and all foods that were included in mixed dishes (e.g. green beans, mushrooms, carrots, margarine). Remember to include condiments (e.g. ketchup, margarine, salad dressing, etc.). Please refer to the attached portion size pictures when determining how much you ate.

Today's Date:		
Time	**Food/Beverage Item**	**How much did you eat?**

Today's Date:		
Time	**Food/Beverage Item**	**How much did you eat?**

Dietitian's Calculations	**Protein (grams)**	**PHE (mg)**	**Calories**
TOTAL from Medical Food/Formula:			
TOTAL from other foods/beverages:			
TOTAL per day:			

Dietitian's Name: _____


½ cup
of fruit juice
= size of a 4 oz
juice box
orange
juice
1 small apple = 1 cup
= size of a baseball
½ cup of sliced fruit
= size of a small computer mouse
½ cup of carrots or other vegetables
= size of a small computer mouse
10 medium fries
counts as ½ cup
= size of a deck of cards
1 cup of raw
vegetables
= size of a baseball
1 cup of milk
= an 8 oz
carton of milk
LOWFAT
MILK
1 cup
of yogurt
= size of a baseball
Lowfat
Yogurt
1½ oz. of
low-fat natural
cheese*
= size of two
9-volt batteries
9 volt
*Counts as one cup
2-3 oz. of meat,
poultry or fish
= size of a deck
of cards
1 tablespoon of
peanut butter
counts as 1 oz
= size of one 9-volt
battery
9 volt
½ cup of beans counts as 2 oz
= size of a small computer mouse
½ cup of cooked pasta = 1 oz
= size of a small computer mouse
1 cup of dry cereal = 1 oz
= size of a baseball
1 slice of bread counts as 1 oz
= size of a CD*
*About the thickness of 10 CDs (½ inch)

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Listing of Low, Moderately Low, Moderately High, and High Protein Foods:

(Use this listing only when protein per serving not available for that food item)

Fruits & Fruit Juice

Very Low < 0.5 gm per ½ cup serving	**Low** < 1 gm per ½ cup serving	**Moderate** 1 gm per ½ cup serving	**High** > 1 gm per ½ cup serving
apples, apple juice, apple chips, applesauce, cherries *canned*, cranberries, cranberry sauce, cranberry juice, crabapples, figs, fruit cocktail, fruit juice, fruit punch, fruit snacks, grapefruit juice, gooseberries, honeydew melon, lemonade, pineapple, strawberries	apricots, *fresh, canned and dried*, Asian pear, banana chips, boysenberries, blueberries, crenshaw melon, grapefruit, grapes, grape juice, guava, guava nectar, mango, papaya, pears, peaches, pineapple, pineapple juice, plums, pomegranate, watermelon	blackberries, cantaloupe, casaba melon, cherries fresh, kiwi, lemon, lime, mandarin orange, nectarine, orange, persimmon, plantains, rhubarb, tangerines, tangelo, tomato juice	bananas, dates, coconut *dried*, currants, prunes, orange juice, raisins, raspberries, star fruit,

Vegetables

Low < 0.5 gm per ½ cup serving	**Moderately Low** 1 gm per ½ cup serving	**Moderately High** < 2 gm per ½ cup serving	**High** ≥ 2 gm per ½ cup serving
arugula, lettuce, cabbage, cabbage *red*, carrots, chayote, cucumbers, celery, jicama, radishes, radicchio, watercress	asparagus, basil fresh, beets, bok choy, broccoli, Chinese cabbage, cauliflower, chard *Swiss*, chickory greens, chilies, chives, cilantro, collard greens, eggplant, endive, green beans, ketchup, leaks, mushrooms *raw*, parsley, parsnips, peppers, sauerkraut, squash *summer or winter*, taro, tomatillo, turnips, water chestnuts	alfalfa sprouts, bamboo shoots, bean sprouts, beets, broccoflower, kelp, chilli peppers raw, mushrooms *cooked*, mustard greens, okra, onion, pumpkin, rutabaga, shallots, spinach *raw*, sorrel, sweet potato, tomato sauce, tomato, tomato cooked, wakami seaweed	artichoke, corn, French fried potatoes, kale, kohlrabi, peas, potatoes, onion rings, snow peas, peas & carrots, spinach *cooked*, mixed vegetables, soy sauce

Breads, Cereals, Starches, & Grains

Very Low < 1 gm per serving	**Low** 2 gm per serving	**Moderately High** 3 – 4 gm per serving	**High** ≥ 5 gm per serving
rice cakes, rice noodles, cellophane noodles, corn tortillas, Trader Joes Wheat free waffles, taco shell, croutons, veggie sticks, popcorn, puffed rice or wheat cereal, corn flakes cereal, rice krispies cereal	flour tortillas, white bread, raisin bread, Italian or French bread, oatmeal bread, dinner roll, bread stick, crescent roll, biscuit, cinnamon roll, Chow Mein noodles *fried type*, pearl barley, white rice, white rice Basmati, white rice instant, white rice long or short grain, stuffing, potato chips, animal crackers, saltine crackers, cheerios cereal, raisin bran cereal, bran flakes cereal, Malt-O-Meal cereal, cream of wheat cereal, cream of rice cereal, corn grits, pancake, waffle, donut, pop tart	oatmeal, macaroni noodles, egg noodles, spaghetti noodles, Chow Mein noodles, Japanese Soba noodles, macaroni and cheese, whole wheat bread, corn bread, multigrain bread, rye bread, brown rice, fried rice, bulgur, couscous, wild rice, English muffin, blueberry muffin, corn muffin, pizza crust, tortilla chips, pretzels, oatmeal cereal,	bagels, regular pasta, granola, pita bread, hamburger or hotdog bun, croissant, soft pretzel, French toast, English muffin mixed grain, Ramen noodles

* Per ½ cup serving size, and prepared

Food Frequency Questionnaire Protein Scoring Worksheet

Instructions to Calculate Total Daily Protein Intake:
Identify the column the patient has selected in row "a" for each food group 1-12. Choose the number next to either I, II, II, or IV under the selected column based on the number of servings selected in row "b" of the same food group. This represents the grams of protein provided by that food group. Record this number in column V. Repeat this process for each food item and then add together rows 1-12 of column V to determine the total amount of natural protein consumed from food. If protein intake from fast food and restaurants is not captured in a previous category, determine the average daily protein contribution and add this to the total of column V. To calculate total daily protein intake from all sources, calculate the amount of protein provided by medical protein products/formula and add to the total of column V.

Food Item	I	II	III	IV	V
1. Medical Protein Products/Formula	All: 0 grams	All: 0 grams	All: 0 grams	All: 0 grams	
2. Special Low Protein Foods	All: 0 grams	All: 1 gram	All: 3 grams	All: 5 grams	
3. Vegetables	All: 0 grams	I: 2 / II: 2 / III: 1 / IV: 0.5	I: 6 / II: 4 / III: 2 / IV: 1	I: 14 / II: 9 / III: 5 / IV: 2	
4. Fruit & Fruit Juices	All: 0 grams	**1 serving a day** I: 2 / II: 1 / III: 0.5 / IV: 0 **1-3 servings a week** I: 1 / II: 0.5 / III: 0 / IV: 0	I: 6 / II: 3 / III: 2 / IV: 0	I: II / II: 6 / III: 3 / IV: 0	
5. Regular Bread, Cereal, Starches, and Grains	I: 21 / II: 14 / III: 7 / IV: 4	I: 9 / II: 6 / III: 3 / IV: 2	I: 3 / II:2 / III: 1 / IV: 0.5	All: 0 grams	
6. Snacks	I: 27 / II: 18 / III: 9 / IV: 5	I: 15 / II: 10 / III: 5 / IV: 3	I: 6 / II: 4 / III: 2 / IV: 1	I: 3 / II: 2 / III: 1 / IV: 0.5	
7. Beans	I: 7 / II: 4 / III: 2 / IV: 0	I: 4 / II: 2 / III: 1 / IV: 0	I: 2 / II: 1 / III: 0.5 / IV: 0	All: 0 grams	
8. Nuts	I: 6 / II: 3 / III: 2 / IV: 0	I: 3 / II: 2 / III: 1 / IV: 0	I: 2 / II: 1 / III: 0.5 / IV: 0	All: 0 grams	
9. Milk & Yogurt	**1-2 servings a day** I: 12 / II: 6 / III: 3 / IV: 2 **3-4 servings a day** I: 28 / II: 14 / III: 7 / IV: 4	I: 4 / II: 2 / III: 1 / IV: 0.5	I: 2 / II: 1 / III: 0.5 / IV: 0	All: 0 grams	
10. Cheese	I: 28 / II: 18 / III: 4 / IV: 2	I: 14 / II: 9 / III: 2 / IV: 1	I: 6 / II: 4 / III: 1 / IV: 0.5	All: 0 grams	
11. Eggs	I: 18 / II: 12 / III: 6 / IV: 2	I: 12 / II: 9 / III: 3 / IV: 1	I: 4 / II: 3 / III: 1 / IV: 0.5	All: 0 grams	
12. Meat, Poultry, & Fish	I: 49 / II: 35 / III: 18 / IV: 7	I: 25 / II: 18 / III: 9 / IV: 4	I: 11 / II: 8 / III: 4 / IV: 2	All: 0 grams	
13. Fast Food & Restaurants					
				TOTAL Protein from Food:	
				TOTAL Protein from Medical Protein Products/Formula:	
				TOTAL Daily Protein Intake:	

APPENDIX D

24-HOUR RECALL SCRIPT

Overview of the 24-Hour Dietary Recall Interview

A trained interviewer will call the parent/caregiver to conduct a 24–hour dietary recall interview. A standardized multiple-pass approach is used by the interviewer to administer the 24-hour dietary recalls. The interviews are unannounced but take place during late afternoon and early evening hours on weekdays and late morning, afternoon, and early evening hours on weekend days. Each interview should take no more than 30 minutes to complete.

General Guidelines for Conducting the 24-hour Dietary Recall Interviews

Creating Rapport

Because the parent or primary caregiver of the participant is the primary respondent for the 24-hour dietary recall, it is important for the interviewer to be able to motivate him/her to provide complete and accurate information. The interviewer will always remain neutral and not let anything in words or manner express criticism, surprise, approval, or disapproval related to the respondent or his/her responses during the dietary interview. Interviewers will adapt their style and approach to make the respondent comfortable.

Every effort will be made to keep 24-hour dietary recall collection as objective and non-judgmental as possible. The interviewer will avoid congratulating the respondent for providing certain foods or reacting with dismay to reports of other foods. The interviewer can stress that he/she wants to know what the participant really ate and that honesty is appreciated. Interviewers must maintain a demeanor of neutrality to all respondents. The interviewer should look for both verbal and non-verbal responses, be a good listener, and thank the respondent for the information provided.

Confidentiality

The interviewer will gain trust by assuring the respondent before the recall begins that everything the respondent says is all right. Any necessary discussion between the interviewers and coordinator of the study about a specific 24-hour dietary recall will be conducted in private and not in the presence of others. Furthermore, the participant's personal information (such as contact information) is kept in a secure location.

Using a script

A standard script is used to introduce the 24-hour dietary recall interview and start the recall process. The script provides continuity between interviews. The remainder of the dietary recall will be guided by interview prompts and is ad hoc in nature due to the variability of respondent comments.

Probing is the technique used by the interviewer to stimulate discussion and obtain more information. Interviewers probe when a respondent's response is not meaningful or is incomplete, i.e., when it does not adequately answer the question. Probing can be used to gather information about additional meals and snacks as well as additions to reported foods. The quality of the interview depends a great deal on the interviewer's ability to probe meaningfully and successfully.

Conducting the Interview using the Multiple-Pass Approach

PASS 1: Using the Quick List

The Quick List will be used to collect an outline of the previous day's intake. It is designed to get the respondent to begin to think about what the participant ate and when they ate. Foods and beverages as reported by the respondent are recorded along with time eaten and meal name if provided by the respondent at this time. Quick List is the first pass in the multiple-pass approach. If the respondent does not volunteer the time of the meal or give a specific meal name during the Quick List, the interviewer need not interrupt to ask for this information. The interviewer will prompt for this information during the third pass.

PASS 2: Reviewing the Quick List

A review of the Quick List permits the interviewer to obtain an overview of the day's intake to note if there are large gaps in time, missed meals or missing beverages, and to insert the meals and or foods recalled during this pass. This review is the second pass of the multiple-pass approach.

PASS 3: Collecting complete meal, food, and amount detail

Complete descriptive detail for foods and beverages is obtained during the third pass of the multiple-pass approach. The respondent is asked about additions to foods and beverages entered on the Quick List. The interviewer asks probing questions based on the information previously recorded and probes to obtain complete detail for food descriptions, preparation methods, and variable ingredients.

(a) After specifying the food, an open-ended question "How much did your child eat (drink)?" is asked to obtain the amount eaten.

(b) After entering the amount specified the interviewer needs to be able to visualize the amount reported and subsequently confirm with the respondent any questionable amounts (e.g., 1 FO of juice or 4 cups of ice cream).

PASS 4: Reviewing the recall

(c) The fourth and final pass of the multiple-pass approach occurs after recording all of the food detail. During this review, the interviewer probes

for missed meals, beverages, and snacks and any other information that was earlier omitted. Edits are made as needed and notes are provided.

(d) After the final review, the respondent may ask the participant to provide additional information about the foods and beverages that the respondent was unable to provide during the recall. This is used mainly to confirm amounts identified as very small or very large, large gaps in eating occasions, and missed meals.

The Scripted 24 hour Dietary Recall Interview

The interviewer begins by introducing himself or herself to the identified respondent. He/she should be friendly and relaxed. The interviewer should always give neutral responses to whatever the participant tells them.

- The interviewer will say:

*"**Hi** (insert respondent's name). **My name is** (insert your name). **How are things going today?**"*

  - Pause, wait for their response, spend a minute or so to establish rapport, and proceed:

"I'm talking to you today as part of Group Education for Children with PKU study to learn about what you ate and drank yesterday. I'll record the information that we need. This is easy because it's just about what you ate. There are no right or wrong answers. Whatever he/she ate is okay. Do you have any questions for me? Are you ready? I'm sure you'll do a great job of helping me!"

Entering the Quick List

- The interviewer proceeds by asking the respondent to make a list of all the foods and beverages their child ate or drank yesterday. Say:

"First, we'll make a list of what you ate yesterday starting with when you got up. Then I will ask you some more questions and we'll figure out how much you had to eat. Do you have any questions?"

  - Pause, wait for and respond to questions, and proceed:

"**What was the first time you had something to eat or drink?"**

  - Enter the response then as needed say:

"What did you have at that time?"

- The interviewer records the information reported by the respondent, not requiring the respondent to give time, meal name, or meal location. The interviewer will use a slash to mark each eating occasion and will prompt later for the time and meal name. Above all, the interviewer should let the respondent think and say what ever comes to mind about the previous day's intake, avoiding interruptions that may be distracting to the participant.

Reviewing the Quick List

- The interviewer verifies all of the entries on the Quick List and probes for missed items by reading the list back to the respondent and asking:

"I am going to read back what you have told me. Let me know if you want to add or change anything. Can you think of anything else you ate or drank yesterday that we haven't put on the list? Did you get up during the night (after midnight) and have anything to eat or drink? Did you have any snacks after school or before bed?"

- Any errors should be corrected, and any additional foods the respondent may report are added at this time.

Collecting Meal Information Detail

- The interviewer begins by saying:

"Next we'll go over our list and I will ask you some questions about each food."

- The interviewer will use this opportunity to ask questions about meal time, meal name, and meal location if this information was not provided earlier during the Quick List.

Asking About Additions

- The interviewer will ask about additions to every food. An on-line prompt will remind you to say:

"The first thing on your list is *(inserts the name of each food)."*

- Then, reading from the list the interviewer will say**:**

"Did you add anything to the *(inserts the name of the food)**?"***

- Ask the additional questions until you receive a "no" response.

Collecting Complete Food and Amount Detail

- Begin by saying:

*"**What type of** (insert name of food**) was it?"***

- The interviewer continues to define the food. Remember to ask:

*"**How much did (you) eat (drink)?"***

- After recording the amount provided by the respondent, the interviewer must be able to visualize the amount reported and confirm as needed any questionable amounts by making reference to other familiar items or recognizable standards. For example, 1/16 of a hamburger should have a note saying, "ate only one bite" or 8 cups of popcorn should have a note saying, "ate entire box at the movies".
- The interviewer should ask if the complete amount described was eaten:

*"**Were you able to finish that?** or **the** (insert name of food)**?"***

  - As the interviewer conducts the 24-hour dietary recall, he/she will provide positive reinforcement by stating:

***"You are doing a good job, working hard, a big help"** as appropriate.*

The interviewer should maintain a pleasant tone of voice and avoid responding to the respondent in any negative ways. If it is necessary to ask the respondent to repeat what he/she said, the interviewer should ask him/her to do so in a gentle way and take ownership by saying:

*"**Sometimes it's hard for me to hear things. Could you please tell me that again?"***

Reviewing the Recall

- During the fourth and final pass of the multiple-pass approach, the interviewer will probe for missed meals, beverages, and snacks, making sure no information was inadvertently omitted. The interviewer will try to get a mental picture of the day, looking especially for time gaps of more than four hours between eating. The interviewer should look at the most likely snack times for the participant, for example, after school or work, before bed, etc. Notes should be made to indicate skipped meals or not consuming a beverage or condiments with food. During the review, the interviewer reads back each food and amount, asking for confirmation from the respondent. For example:

*"**Now we'll go over what I've recorded one last time. The first thing that I have is at** (insert meal name and time) **when you had** (insert food name).*

- When the interviewer notices a large time gap he/she should asks:

*"**Did you have anything to eat or drink after school? Anything before your** (insert time e.g., evening meal) **and** (before bed)**?"***

- Additional foods and meals are recorded. If the respondent hesitates and can't remember whether any food was eaten for a long period of time, the interviewer may say:

*"**Can you think what you were doing** (after school, at dinner/supper time, etc.)**? Sometimes if we think about where you were or whom you were with, it helps to remember what was eaten."***

- The process continues until each food has been reviewed.

Completing the Recall

- The interviewer ends the recall saying:

"In terms of the amount of food you ate, would you say this was close to the amount that you usually eat, a lot more than you usually eat, or a lot less than you usually eat?"

- This question refers to the overall amount of food for the day, not the type of food. The interviewer records the respondents response to the last question. If needed the interviewer can say:

*"**What makes you say it's** (a lot more or a lot less than usual)**?"***

- The interviewer will determine the reliability of the data. If the dietary recall is unreliable because the respondent was unable to recall one or more meals or for some other reason question the reliability, he/she will add a note. The interviewer does not ask the participant this question, nor share their opinion with them.

Thank the Participant

- The interviewer thanks the participant and ends the recall:

*"**Thanks so much for your help. Do you have any questions?"***

- Pause, wait for and response to questions, and proceed:

"You did a great job and I really enjoyed talking with you."

"Thanks. Bye."

APPENDIX E

KNOWLEDGE QUIZ – BOYS

KNOWLEDGE OF PHENYLKETONURIA (PKU) QUESTIONNAIRE

NAME:_____

DATE:_____

Please circle the best answer.

1. PKU is _____
    a. A blood disease.
    b. An enzyme deficiency.
    c. A kidney disorder.
    d. A protein deficiency.

2. PKU Is inherited from:
    a. Mom.
    b. Dad.
    c. Mom and Dad.

3. If a child has PKU they are unable to break down an amino acid called_____
    a. Glutamine.
    b. Purine.
    c. Phenylalanine.
    d. Arginine.

4. High phenylalanine levels can be caused by_____
    a. Not exercising.
    b. Being sick.
    c. Eating too much fruit.
    d. Not drinking enough juice.

5. High phenylalanine levels for several months _____
    a. Is not a problem.
    b. Can effect the way you think and feel
    c. Can cause high blood sugar.
    d. Can cause kidney problems.

6. The low phenylalanine diet for PKU is made up of _____
    a. A special formula.
    b. Low protein foods.
    c. Fruits and vegetables.
    d. All of the above.

7. Which of the following snacks has the least amount of phenylalanine?
    a. Chocolate chip cookies
    b. Apple
    c. A cheeseburger on a regular bun
    d. Potato chips

8. Which of the following meals has the most amount of phenylalanine?
    a. Low phenylalanine spaghetti and vegetarian tomato sauce
    b. Vegetable soup
    c. Pizza on regular crust with tomato sauce and cheese
    d. Fruit salad

9. Which of the following sweeteners contains phenylalanine?
    a. Maple syrup
    b. Honey
    c. Saccharin (Sweet N Low)
    d. Aspartame (Nutrasweet)

10. Have you ever attended a group meeting or camp about PKU?
    NO_____ YES_____

APPENDIX F

KNOWLEDGE QUIZ – GIRLS

KNOWLEDGE OF PHENYLKETONURIA (PKU) QUESTIONNAIRE

NAME:_____

DATE:_____

Please circle the best answer.

1. PKU is _____
    a. A blood disease.
    b. An enzyme deficiency.
    c. A kidney disorder.
    d. A protein deficiency.

2. PKU Is inherited from:
    a. Mom.
    b. Dad.
    c. Mom and Dad.

3. If a child has PKU they are unable to break down an amino acid called_____
    a. Glutamine.
    b. Purine.
    c. Phenylalanine.
    d. Arginine.

4. High phenylalanine levels can be caused by_____
    a. Not exercising.
    b. Being sick
    c. Eating too much fruit.
    d. Not drinking enough juice

5. High phenylalanine levels for several months _____
    a. is not a problem.
    b. can effect the way you think and feel
    c. can cause high blood sugar.
    d. can cause kidney problems.

6. The low phenylalanine diet for PKU is made up of _____
    a. A special formula.
    b. Low protein foods.
    c. Fruits and vegetables.
    d. All of the above.

7. Which of the following snacks has the least amount of phenylalanine?
    a. Chocolate chip cookies
    b. Apple
    c. A cheeseburger on a regular bun
    d. Potato chips

8. Which of the following meals has the most amount of phenylalanine?
    a. Low pro spaghetti and vegetarian tomato sauce
    b. Vegetable soup
    c. Pizza on regular crust with tomato sauce and cheese
    d. Fruit salad

9. Which of the following sweeteners contains phenylalanine?
    a. Maple syrup
    b. Honey
    c. Saccharin (Sweet N Low)
    d. Aspartame (Nutrasweet)

10. It is best if I drink my medical formula
    a. All at one time
    b. At breakfast and dinner
    c. Three or four times throughout the day
    d. Anytime as long as I drink all the formula for the day

11. In addition to mental retardation, other problems that have been seen in mothers with PKU and uncontrolled blood phenylalanine levels include:
    a. low birth weight
    b. heart problems
    c. small head size
    d. all of the above

12. The best known treatment for maternal PKU to prevent damage to the baby is
    a. following a well-balanced diet
    b. following a vegetarian diet
    c. following a high protein diet during pregnancy
    d. following a low phenylalanine diet before conception and throughout pregnancy

13. On the low phenylalanine diet, most of the nourishment for you and the baby is provided by:

a. the special formula
b. fruits and vegetables
c. free foods
d. low protein foods
e. a vitamin supplement.

14. Have you ever attended a group meeting or camp about PKU?
NO_____ YES_____

APPENDIX G

EDUCATION CURRICULUM - BOYS

Education Curriculum
Oregon Health and Science University
Child Development and Rehabilitation Center
Summer 2011

9:00 a.m. Parents and children gather

As children arrive they will be taken one at a time to go through the Food Frequency Questionnaire (see appendix) and Initial Assessment Questionnaire (see appendix). Children that have finished their food frequency questionnaire and initial assessment or are waiting to complete it will participate in PKU Jeopardy with their parents and peers or can do a PKU word find or maze individually.

9:45 a.m. Welcome

- Introduce Staff
- Hand out schedule for the day
- Dismiss parents to their own session

9:50 a.m. Ice Breaker

Equipment
Soft rubber ball with questions written around it.

Ball Game

1. Everyone stands in a circle.
2. The instructor will start by stating her name, where she is from, and answer the question that her left thumb landed one.
3. The instructor will then toss the ball to someone across the circle.
4. The ball will continue to be passed until everyone in the circle has introduced themselves.

Ball Questions:

- What is your favorite color and why?
- If you could be any animal what would you be and why?
- What is your favorite sport and why?
- What do you like to do in your free time?
- What is your favorite type of music and why?
- What is your favorite way to be active?
- What is your favorite holiday and why?
- What is your favorite season of the year and why?
- What is your favorite subject in school and why?
- If you could meet anyone in the world who would you meet and why?
- If you could travel anywhere in the world where would you travel and why?

10:00 a.m. Let's Talk About Genes

Discussion

Use a Venn Diagram as a visual aid to the follow questions:

1. From our introduction, can someone tell me some ways that we are all alike?
2. What are ways that we are all different?
    - You can see that we all have different pieces of us that make us alike and make us different.
    - You all share the trait of having PKU in the room. When you are at school with your friends that do not have PKU, the PKU trait makes you unique and special from others.

A double helix of some kind will be used as a visual aid for the following questions.

3. Some traits we have are genetic. Genetic means that they are something you inherit from your parents. Parents do not have control over which genes they give to their kid's. Can anyone give me an example of a genetic trait?
    a. The trait for blond hair comes from a code of something we call genes.
4. Other traits we pick up from people and things around us. Can anyone give me an example of a trait that we get from other people or things?
5. What type of trait is PKU?
6. Each gene you receive from your parents codes for something that makes you uniquely you. These genes are strung into a code called DNA. Each living thing – food, trees, animals – have their own sets of DNA that make them unique.

10:15 a.m. Isolating DNA Experiment

Groups of 3-5

Ingredients:
Warm water
Raw wheat germ
Liquid detergent
Rubbing alcohol (70 or 91%)
Baking soda
Meat tenderizer

Equipment:
Plastic cups
Measuring cups
Measuring spoons
Spoon
Small Strainer
Funnel

Test tube
Toothpick/unbent paperclip

1. Measuring ½ cup warm water and pour into a plastic cup.
2. Add ½ tablespoon raw wheat germ and stir well.
3. Add ½ tsp detergent and stir for one minute.
4. Add ¼ teaspoon meat tenderizer and ½ teaspoon baking soda.
5. Stir slowly for 1 minute, let the solution settle and cool for a few minutes.
6. Pour the top half of the liquid through a strainer into another cup.
7. Pour a little of the thick liquid into test tubes so that there are enough test tubes for each person in your group.
8. Gently add ice cold alcohol to each tube and let sit for several minutes. Try not to mix the two layers.
9. Take a toothpick or bent paperclip and stir it just below the bottom of the alcohol layer. Turn it in ten very slow circles. You should see globs attaching. Pull out your paperclip and observe the DNA.

Courtesy of Wesleyan University Women in Science, the Wesleyan Hughes Program, and The Science Mom's (Laurel F. Appel)

11:15 a.m. – 11:25 a.m. Bathroom break/set up for next activity

11:30 a.m. PKU and Diet

Use an easel to write out answers to the following questions as a visual aid.

1. What does it mean to have PKU?
    - Briefly describe the inability to break down phe.

Use beads and string as visual aid to explain proteins and amino acids

2. What foods contain phenylalanine?
    - Briefly describe what happens in the body after eating phe containing food
    - Explain/demonstrate how some phe foods have more phe in them than others.

11:40 a.m. Low, Medium, High Phe Foods

Equipment
Variety of different foods
Popsicle sticks with green, yellow, and red construction paper

Instructions

1. Hold up one food at a time.

2. As each food is held up, have students hold up the red sign for high phe foods, the yellow sign for medium phe foods, and the green sign for low phe foods.
3. Continue until a variety of foods have been discussed and continue to discuss what happens when low, medium, and high phe foods once they enter the body.

12:00 p.m. Snack Development

Equipment
Toothpicks/kabob sticks
Variety of Fruits and Vegetables

- Kiwi
- Grapes
- Banana
- Apple Slices
- Yellow Pepper
- Grape tomato
- Cucumbers
- Olives

Low Phe fruit dip
Low phe vegetable dip

Instructions:

1. Wash hands
2. Students will develop different kabob combinations and figures to dip and share with parents.

12:15 p.m. Parents and students regroup and share snack

- Wrap up and allow students to share with parents what they learned.

12:30 p.m. Dismissed

Curriculum Adapted from:
"Eat Right Stay Bright - "Guide for Hyperphenalalaninemia"
Laurie Bernstein and Cindy Freehauf
The Children's Hospital at Aurora, University of Colorado

Protein Jeopardy Questions
From University of Washington PKU Clinic
1. Does your body use protein for energy?
Yes
2. What do we call the "building blocks" of protein?
Amino acids
3. From what drink do kids with PKU get most of their protein?
Formula
4. True or False: We don't need protein to be healthy.
False
5. True or False: Kids with PKU should eat lots of high protein foods like meat.
False
6. Is meat a "yes" or a "no" food?
It is a "no" food
7. Are all foods that are high in protein also high in phe?
Yes, except for formula
8. What parts of our bodies are made of protein as a primary component?
Hair, nails, tissues, cells, everything
9. Do kids with PKU need protein?
Yes
10. Is cheese a "yes" or a "no" food?
It is a "no" food
11. Why is cheese a "no" food?
Because it is high in protein and high in phe
12. Does protein help you grow?
Yes
13. What is the difference between kids with PKU and kids without PKU?
Kids with PKU need to eat protein without phe
14. Which food is higher in phe—an apple or a banana?
Banana
15. If you're at a birthday party and everyone is eating hot dogs, what do you do?
--Ask for some fruit or vegetables instead
--Go play a game until they're done eating
--Drink your formula
--Other ideas?
16. Name two foods that are high in phe.
17. How long do you need to stay on a diet low in phe?
All through life
18. Name two foods that are low in phe.
19. Name one reason your body needs protein.
20. **Can kids with PKU eat foods (or pop) with Nutrasweet?**
No, because they have phe in them.
21. True or False: People who do not eat meat are not in good health.
False, it is quite possible for a person to eat no meat and still be healthy. You

can meet your protein requirement by drinking your formula and eating different types of foods.

22. Do athletes or very active people need more protein than people who are not active?

No, athletes need more *energy* for *fuel* (like a car). Consuming extra protein will not make people stronger or healthier. Extra protein will be used for energy or stored as fat. However, insufficient amounts of protein can cause physical fatigue and poor growth.

23. True or False: Protein deficiencies can cause problems with growth.

True. All body cells have protein. In periods of undernutrition, the number of cells is decreased. If cells do not have enough protein, problems with growth and development can occur. Not enough protein can also cause problems with thinking and with doing well in school. This is why it is very important to drink your formula—to get enough of the kind of protein that is good for you.

University of Washington PKU Clinic
CHDD - Box 357920, Seattle, WA 98195
(206) 685-3015, Toll Free in Washington State 877-685-3015
http://depts.washington.edu/pku

APPENDIX H

EDUCATION CURRICULUM - GIRLS

PKU EDUCATION CURRICULUM
Oregon Health and Science University
Child Development and Rehabilitation Center
January 20th, 2012

9:00-9:45 a.m.

- Participants arrive.
  - Complete consent forms
  - Complete FFQ
  - Complete Knowledge Questionnaire
  - Complete 24 hr recall

10:00 a.m.

- Welcome – Ice Breaker: Famous couples
  - Gather a list of famous couples
  - Tape the name of different people on each persons back
  - Have the girls walk around asking yes or no questions about themselves to determine who they are and then find their partner
  - Following the activity have each girl introduce her "partner"

10:15 a.m.

- PKU twister
  - Pg 41 – Eat Right Stay Bright the Adolescent Years
  - Will include questions about maternal PKU in this portion.

10:45 a.m.

- PKU Bracelets (30 minutes)
  - Demonstrates how sequencing of amino acids can affect PAH activity
  - Discussion – What happens in the body when someone has PKU? What is phenylalanine converted to in someone without PKU? What is not working correctly during the break down of PHE with an individual with PKU.

11:15 a.m.

- Role playing
  - Provide girls with a scenario. Have one person be a girl with PKU. Have the other be a friend that does not have PKU and "act" out how each individual would react in the situation.
  - If not comfortable with role playing could have a group discussion about different challenging scenarios, increasing the tools in their "toolbox" when dealing with challenging situations.

11:45 a.m.

* Snack and discussion about healthy eating.

12:15 p.m.

* Retake Quiz

12:30 dismissed.

Curriculum Adapted from:
“Eat Right Stay Bright - “Guide for Hyperphenalalaninemia”
Laurie Bernstein and Cindy Freehauf
The Children’s Hospital at Aurora, University of Colorado