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Exploring Communication Patterns in the Discussion of Maternal PKU Syndrome Between Parents and Daughters

Hannah Beth Andrews

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Exploring Communication Patterns in the Discussion of Maternal PKU Syndrome
Between Parents and Daughters

by

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Bachelor of Science
University of California, San Diego, 2013

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Abstract

Maternal PKU syndrome is the collection of features and birth defects that arise from uncontrolled phenylalanine levels in a pregnant woman with phenylalanine hydroxylase (PAH) deficiency, previously known as phenylketonuria (PKU). Currently, the literature is lacking in exploring what young women are being told about maternal PKU syndrome. In this study, communication patterns between parents and their daughters about maternal PKU syndrome were investigated through an online survey completed by parents. The survey assessed parents' level of comfort with this topic, the information they discussed with their daughter and the resources they accessed. Follow-up interviews were conducted with participants to elaborate on survey responses. The majority of participants were very comfortable discussing maternal PKU syndrome (51%); however, 21% reported being very uncomfortable with the discussion. Parents most often discussed health concerns associated with maternal PKU syndrome (94%) and least frequently discussed unplanned pregnancies (58%). The most frequently used resource was a metabolic doctor (73%); however, parents included mothers with PAH deficiency among the most helpful resources. Themes from open-ended responses and interviews emphasized qualities of parents' discussion with their daughters. Parents commented on the timing and how they presented the information to their daughters. They described challenges such as the emotional impact of the conversation as well as their daughter's decision-making and consequences of her actions. Lastly, they discussed advice for treatment compliance, resources, and ways to normalize the topic of maternal

PKU syndrome. These results can help genetic counselors better understand the parent-daughter conversation so that healthcare professionals can better assess and inform families about maternal PKU syndrome.

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Chapter 1. Background

1.1 PAH Deficiency Background

Asbjørn Følling, a Norwegian scientist in 1934, first discovered phenylalanine hydroxylase deficiency (PAH deficiency), traditionally referred to as phenylketonuria (PKU) (as cited by Christ, 2003). PAH deficiency is an inherited metabolic disorder associated with a deficiency in phenylalanine hydroxylase. This enzyme is responsible for metabolizing phenylalanine, an essential amino acid, into tyrosine. Tyrosine is a precursor for a number of hormones and neurotransmitters. The inability to metabolize phenylalanine results in toxic levels of the amino acid, which can lead to intellectual disability, seizures, microcephaly, autistic-like behaviors, characteristic body odor, and eczema-like skin problems (Paine, 1957). Also, since phenylalanine is not converted into tyrosine, affected individuals have decreased tyrosine levels. Both elevated plasma phenylalanine concentrations and its metabolites, along with a deficiency of tyrosine, are the proposed causes of impaired growth and intellectual disability (van Spronsen, van Rijn, Bekhof, Koch, & Smit, 2001).

The primary treatment for PAH deficiency is a phenylalanine or protein-restricted diet combined with specialized medical formulas known as medical foods. The diet is used to maintain low levels of phenylalanine in the blood to prevent adverse clinical outcomes such as irreversible brain damage (Camp et al., 2014). In the past it was thought the PAH deficiency diet could be discontinued once the critical period of brain

development in early childhood was reached (Gentile, Hoedt, & Bosch, 2009), but it is now recommended that this treatment should be continued throughout life (Camp et al., 2014). According to the Phenylketonuria Scientific Review Conference in 2014, asthma, recurrent headaches, eczema, neurological signs, cognitive deficits such as impaired executive function, hyperactivity, lethargy, phobias and depression are symptoms seen throughout life when PAH deficiency is not controlled (Camp et al., 2014). Once the individuals returned their blood phenylalanine levels to the treatment range, the majority of the signs and symptoms resolved (Camp et al., 2014). In a study by de Groot et al. (2013), it was found that synaptic plasticity in the brain occurs lifelong and is dependent on cerebral protein synthesis. Reduced cerebral protein synthesis in adult patients untreated for PKU could contribute to impaired cerebral functioning (de Groot et al., 2013). Therefore, it is recommended that individuals maintain metabolic control as they move into adulthood (Vockley et al., 2014).

1.2 Maternal PKU Syndrome

In the 1950's, there was a new reason for continuing a phenylalanine restricted diet as the first group of individuals treated for PAH deficiency reached childbearing age (Levy, 2003). It was observed that the children of mothers with PAH deficiency had a higher rate of birth defects with certain congenital anomalies and almost all had some form of intellectual disability. Since these women were no longer on a phenylalanine-restricted diet, it was observed that the high levels of phenylalanine in a mother's body were having teratogenic effects on the pregnancy. The phenomenon is currently called maternal PKU syndrome.

Maternal PKU syndrome is associated with a collection of birth defects and intellectual disability in the offspring of women who have untreated PAH deficiency during their pregnancy. Elevated levels of phenylalanine in the mother's blood cross the placenta and can have teratogenic effects on a developing fetus. Higher levels of maternal phenylalanine were found to directly correlate with a higher frequency of birth defects (Rouse et al., 1997). Certain birth defects associated with maternal PKU syndrome include heart defects, microcephaly, intrauterine growth restriction and intellectual disabilities (Rouse et al., 1997). There are conflicting reports regarding a possible increased chance of spontaneous abortion in pregnancies of women with uncontrolled PAH deficiency (Prick & Duvekot, 2012).

Close monitoring of blood phenylalanine levels is especially important during times of increased anabolism such as infancy, childhood and pregnancy (Singh et al., 2014). A study by Alexander (2003) found that the most promising approach to address maternal PKU syndrome was to reinstate a phenylalanine-restricted diet during pregnancy. Rouse et al. (1997) highlighted that a phenylalanine restricted diet prior to conception as well as continued throughout the pregnancy is recommended to reduce the levels of phenylalanine acting on the fetus to reduce the risk for birth defects

The 2014 Phenylalanine Hydroxylase Deficiency Diagnosis and Management Guideline also stated that women who become pregnant while not on a restricted diet will need to lower their blood phenylalanine levels immediately to reduce the risks of maternal PKU syndrome. Women with PAH deficiency are recommended to have phenylalanine levels under control even before conception to reduce the risk of early malformations. For example, the fetal heart develops prior to eight to ten weeks of

gestation so it is crucial for mothers to be in metabolic control before this period to reduce the risk of congenital heart defects. Intensive intervention for dietary control is needed and hospitalization might be required to achieve this. (Vockley et al., 2014).

Healthcare professionals must be aware of this problem to help ensure that all women with PAH deficiency will know their risk of birth defects and what measures to take in order to have healthy children (Alexander, 2003).

1.3 Barriers to Dietary Adherence

A critical time period that is often challenging to maintaining good metabolic control is adolescence and transitioning to adulthood. By adulthood, less than 20% of individuals with PAH deficiency have good metabolic control (Gentile et al., 2010). Vockley et al. (2014) demonstrated the difficulty for an individual to return to metabolic control once they have discontinued the diet, so it is stressed that individuals stay on a restricted diet as they transition into adulthood, especially as the effects of high levels of phenylalanine in adults are now being appreciated. Dietary compliance in PAH deficiency decreases with age, which complicates the matter of maternal PKU syndrome (Walter et al., 2002). This is especially worrisome as those are the childbearing years for women. If women with PAH deficiency do not have good metabolic control, become pregnant, and have difficulty returning to dietary control, the fetus is at a significantly increased risk for birth defects and intellectual disability related to maternal PKU syndrome.

Efforts to document barriers to diet adherence have been reported in the literature. In a study that examined the perspectives of families, the majority of caretakers showed that knowledge about the diet is not a problem, but the majority agreed that dietary

adherence requires a lot of time and effort and many families were dissatisfied with the diet. (Bilginsoy, Waitzman, Leonard, & Ernst, 2005) In the study conducted by Bilginsoy et al. (2005), families noted that finding and preparing the proper food as well as how the diet impacts the family's and individual's social life were the main difficulties in adhering to the phenylalanine restricted diet. In addition, Bilginsoy et al. (2005), found that while all the families recognized that there were negative long-term consequences with being off diet, they apparently did not clearly understand the consequences.

Another article that analyzed the dietary challenges of adhering to treatment in the context of the family found a trend that caregivers who reported using authoritarian practices reported that their strategies were less effective than caregivers who did not use authoritarian practices (Kazak, Reber, Snitzer, & Kazak, 1988). Dietary adherence is an important factor in maternal PKU syndrome and certain parenting styles may influence the effectiveness of a parent-daughter conversation about maternal PKU syndrome.

In a study by Sharman, Mulgrew, & Katsikitis (2013), eight adolescent individuals were interviewed about factors affecting their dietary adherence and the following barriers were identified: feeling different, difficulties in managing social situations, and having to explain their condition multiple times to different people. Positive factors affecting following their diet included support from family and friends. One girl described seeing pictures of untreated individuals with PKU, which encouraged her to follow her diet so she could be healthy or normal. Commenting on the challenges of returning to diet, a female described a lack of caring when her levels are high which impacted her decision-making. Other participants also reported this pattern of inability to

care when their levels are high. Only once their levels stabilize were they able to realize the full impact of their poor dietary choices. (Sharman et al., 2013).

Overall, these articles demonstrated the importance of proper education with families about the consequences that can occur when being off diet, the parenting styles that can promote dietary adherence, and the mindset that the individual has once one has started making poor dietary decisions. This knowledge can provide guidance in communicating about maternal PKU syndrome.

1.4 Factors that Affect Maternal PKU Syndrome Treatment

Reports from the 2014 Phenylketonuria Scientific Review Conference (Camp et al., 2014) it was discussed that although severe intellectual disability is now preventable in treated individuals with PAH deficiency, there are often subtle physical, cognitive and behavioral findings. Cognitive symptoms include reduced: executive function, processing speed, fine motor skills and perception spatial abilities. Increased hyperactivity and impulsivity were seen even in those treated early (Camp et al., 2014). These are unique issues in the PAH deficiency population, which were further discussed by Gentile et al. (2010) in a review of the symptoms of PAH deficiency. Gentile et al. (2010) highlighted that individuals with PAH deficiency do not appear sick and often do not feel the effects of poor metabolic control, yet may still have cognitive effects from the condition. These “hidden disabilities” are similar to women with PAH deficiency who become pregnant, as they may feel healthy and not realize the teratogenic effects of high levels of phenylalanine on their pregnancy (Simon et al., 2008).

Gentile et al. (2010) summarized that the key to better health outcomes in PAH deficiency is to improve adherence to dietary treatment. In individuals with PAH

deficiency, having reduced executive function directly impacts how achievable it is to maintain good metabolic control. Executive function is responsible for goal-directed activities that require planning, organization, attention and impulse control. Each of these skills is necessary for maintaining metabolic control in PAH deficiency. Deficits in executive function can be a barrier to maintaining diet treatment, and reduced adherence to dietary restrictions leads to further impairments in executive functioning (Gentile et al., 2010).

Furthermore, executive functioning skills, including planning, organization, attention and impulse control are important when planning a family in any situation. Impairments in these skills may influence family planning or could contribute to unplanned pregnancies. In an individual with PAH deficiency, an unplanned pregnancy could mean that the individual is not on diet when they conceived, putting their pregnancy at risk for the teratogenic effects of maternal PKU syndrome. Also, lacking these skills can impact how individuals comprehend the risks of maternal PKU syndrome, as the symptoms may not be detected until after delivery. Impaired attention and impulse control may affect one's adherence to recommendations for reducing the chance of becoming pregnant as well as the risks of maternal PKU syndrome during pregnancy.

1.5 Methods to Improve on Maternal PKU Syndrome

Guidelines recommend counseling on maternal PKU syndrome and family planning for all women of childbearing age (Koch et al., 2003). As awareness for maternal PKU syndrome has increased, management for individuals with PAH deficiency has also continued to shift. The current American College of Medical Genetics and

Genomics (ACMG) Guidelines recommend treatment for life for individuals with PAH deficiency (Vockley et al., 2014).

A survey of mothers of children with PAH deficiency found that unsatisfactory maternal knowledge could influence long-term blood phenylalanine control in the children. Mothers who scored higher in knowledge levels about PAH deficiency had children with better annual levels of blood phenylalanine (Macdonald et al., 2008). Maternal education on PAH deficiency is important not only for the child's immediate metabolic control, but it also sets a good precedence for the child's future metabolic control (MacDonald et al., 2008). Maternal PKU syndrome does not become an issue until a female child reaches childbearing age, though having metabolic control is critical in preventing the teratogenic effects. Educating parents specifically on the risks of maternal PKU syndrome may have a positive impact on maternal PKU syndrome outcomes. As stated by Bernstein et al. (2013), the clinicians also reported that poor parental involvement is the main reason that nutrition educational tools do not correlate to increased adherence to diet in patients. From the patient perspective, the majority of patients consider their families as the most effective educational tool (Bernstein et al., 2013).

Creating educational, behavioral and social support strategies that can be used by health care professionals could help improve adherence to dietary treatment. When considering social support, healthcare professionals should speak not only with the parents, but should also include the patient's input in order to support the individual's path towards independence (Gentile et al., 2010). For parents of daughters with PAH deficiency, the most appropriate time to address the risks of maternal PKU syndrome

would be when these individuals are entering their childbearing years. Jaccard, Dodge, & Dittus (2002) noted that most strategies to reduce teen pregnancy have been designed to educate the individuals directly; however, another approach was to aim interventions at the parents. Interventions aimed at the parents are thought to help them acquire skills and information that will aid them in effectively communicating with their adolescents about sex, birth control and avoiding unintended pregnancies (Jaccard et al., 2002).

Currently there are no published studies on how parents educate their daughters on the risks of maternal PKU syndrome. Maternal PKU syndrome is a unique topic involving information about PAH deficiency as well as sensitive subjects such as unintended pregnancies and sexual health. There is no formal system in place that specifically addresses and defines the education that parents need when they have a child with a chronic condition such as PAH deficiency (Macdonald et al., 2008). As research on maternal PKU syndrome is limited, trends in parent communication seen in families with other chronic genetic conditions may be similar. Parent-child communication of reproductive risks has been studied in cystic fibrosis, another chronic genetic condition (Koreniewska et al., 2009).

Koreniewska et al. (2009) explored the sexual and reproductive health knowledge in cystic fibrosis female patients and their parents. In this study, 70% of women never had any discussion of these reproductive health issues with their parents. Only 23% of young women asked their parents about sexual and reproductive health. Helpful parenting skills include initiating discussions with their adolescent on topics that parents know to be important to their child. Most women felt that this type of discussion should begin at

an age between 12 and 14 years. Also, 78% of women suggested that the sexual issues should be discussed with mothers. (Korzeniewska et al., 2009).

If these young women with a chronic condition are looking to their mothers for an accurate conversation of their reproductive health, it is imperative that the mothers are being properly educated on the specifics of reproductive health as it pertains to their child.

Educationally, knowledge of disease and its treatment needs to improve by enhancing verbal information with written materials (Gentile et al., 2010). As described by Bernstein et al. (2013), clinicians reported most nutritional education of PAH deficiency is done with one-on-one counseling and handouts. Parents report that educational handouts are an effective tool for learning about PAH deficiency, even though handouts are not reported as an important tool by young patients themselves. Individuals with PAH deficiency are looking toward their families to educate them about PAH deficiency- specific nutrition. (Bernstein et al., 2013). Since nutrition and diet are important factors in preventing maternal PKU syndrome, families should be able to educate their child on this as well. Handouts from health professionals such as geneticists or genetic counselors could be an effective way to help parents educate their child about the risks of being off diet, and especially on how the pregnant mother's diet applies to maternal PKU syndrome.

Chapter 2. Manuscript

Exploring Communication Patterns in the Discussion of Maternal PKU Syndrome between Parents and Daughters¹

2.1 Abstract

Maternal PKU syndrome is the collection of features and birth defects that arise from uncontrolled phenylalanine levels in a pregnant woman with phenylalanine hydroxylase (PAH) deficiency, previously known as phenylketonuria (PKU). Currently, the literature is lacking in exploring what young women are being told about maternal PKU syndrome. In this study, communication patterns between parents and their daughters about maternal PKU syndrome were investigated through an online survey completed by parents. The survey assessed parents' level of comfort with this topic, the information they discussed with their daughter and the resources they accessed. Follow-up interviews were conducted with participants to elaborate on survey responses. The majority of participants were very comfortable discussing maternal PKU syndrome (51%); however, 21% reported being very uncomfortable with the discussion. Parents most often discussed health concerns associated with maternal PKU syndrome (94%) and least frequently discussed unplanned pregnancies (58%). The most frequently used resource was a metabolic doctor (73%); however, parents included mothers with PAH deficiency among the most helpful resources. Themes from open-ended responses and interviews emphasized qualities of parents' discussion with their daughters. Parents

¹ Andrews, H., Jordon, E., Baggett, L., & Singh, R. To be submitted to *Journal of Genetic Counseling*.

commented on the timing and how they presented the information to their daughters. They described challenges such as the emotional impact of the conversation as well as their daughter's decision-making and consequences of her actions. Lastly, they discussed advice for treatment compliance, resources, and ways to normalize the topic of maternal PKU syndrome. These results can help genetic counselors better understand the parent-daughter conversation so that healthcare professionals can better assess and inform families about maternal PKU syndrome.

2.2 Introduction

This study aimed to investigate the current communication patterns between parents and daughters about maternal PKU syndrome. It has the potential to identify areas to improve education and facilitate this discussion about maternal PKU syndrome. Education helps address adherence to PAH deficiency treatment, which in turn can help to reduce avoidable birth defects from maternal PKU syndrome. Although it is recommended that individuals stay on a restricted diet for life, not all individuals do so. Unplanned pregnancies are particularly at risk for effects of maternal PKU syndrome since young women may not have strict control of their diet. The ACMG guidelines state “counseling and education involve teaching individuals and/or their caregivers the importance of the diet in maintaining appropriate... health maintenance” (Singh et al., 2014, p. 128). Appropriate health maintenance for women with PAH deficiency should include education about the risks of maternal PKU syndrome, especially if a future pregnancy may be unplanned. The committee also states, “research into effective education and counseling strategies... are lacking” (Singh et al., 2014, p. 128). Therefore,

this study may aid in the research of identifying effective education strategies for families.

2.2.1 Hypothesis and Study Objectives. Parents of daughters with PAH deficiency will express concerns about discussing the risks of maternal PKU syndrome with their daughters and will identify additional education materials, which may help facilitate this conversation.

The objective of this study was to explore the current attitudes and communication patterns that parents have with their daughters regarding the daughter's sexual health and the risks of maternal PKU syndrome. Assessing the current state of communication and needs of parents will help both healthcare professionals and parents approach this sensitive but important subject with girls with PAH deficiency. Information from this study will be used to create an educational tool to help parents initiate and navigate communication of maternal PKU syndrome with their daughters. The four main objectives of this study are as follows:

- To identify current themes in parental communication of maternal PKU syndrome;
- To identify areas of discomfort for parents in the discussion of maternal PKU syndrome;
- To identify areas of improvement for facilitating the discussion of maternal PKU syndrome for parents; and
- To design an educational handout for parents based on the findings of this study.

2.3 Materials and Methods

2.3.1 Study Design. The primary method of data collection was a survey instrument. An original survey was created in Survey Monkey specifically for this study. It included a short section of demographic questions followed by an assessment of parents' experiences communicating with their daughters about the risks of maternal PKU syndrome. Initial questions assessed if parents have discussed topics of sexual health or maternal PKU syndrome with their daughters. Skip logic was used to direct parents to further questions based on if they had discussed maternal PKU syndrome with their daughter or not. Current communication practices of maternal PKU syndrome were assessed by using multiple choice, Likert scale and free response questions.

At the end of the survey, participants were invited to take part in an optional telephone interview. All contact information was confidential and stored separate from the survey responses. The contact information was used to arrange a time for the optional interview and was destroyed after the interviews were complete. The interview consisted primarily of qualitative questions, which were recorded and transcribed. The interview questions focused on the most challenging aspects of discussing maternal PKU syndrome and what resources would be most helpful. All recordings were destroyed. Records of all the transcriptions were coded for analysis and did not include any participant identifying information.

Compensation was not provided in exchange for participating in the study. Participation was voluntary and participants chose to skip questions or end their participation in the study at any time. All participants remained anonymous for the purposes of data analysis. This research study was approved by the Institutional Review

Board, Office of Research Compliance, of the University of South Carolina, Columbia, SC on December 2014.

2.3.2 Qualitative and Quantitative Research. A mixed methodology of quantitative and qualitative data was used to explore the experiences and attitudes of parents about communication of the risks of maternal PKU syndrome with their daughters. The method of obtaining quantitative research utilized an online survey. Chi Square test and Spearman's Rho analysis were used to evaluate the responses of the participants to identify possible associations between speaking with their daughter about maternal PKU syndrome and their daughter's sexual health, level of comfort with this discussion, and various demographics. For questions concerning resources and the conversation initiator, the frequency of the responses was analyzed.

The qualitative responses were obtained from free response questions in the online survey as well as a semi-structured interview. Major themes from these responses were identified and coded by the primary researcher. The frequency of each theme was calculated to describe the patterns found in the responses. All themes were based solely on the immediate responses of the participants and there was no limit to the number of themes for each participant. Direct quotes from the participants were cited in the results to represent themes from the responses.

2.3.3 Participants. Eligible participants included parents of a female diagnosed with PAH deficiency, with their daughter currently between ages 10 and 25. "Parents" are defined as the primary caregivers, including biological parents, step-parents, adoptive parents and grandparents. Participants were recruited through online support groups. Both parents did not have to complete the survey. Participants could complete the survey

in the future tense if they have not yet had a discussion with their daughter about the risks of maternal PKU syndrome, or in the past tense if they have already discussed it. The survey was published only in English.

2.3.4 Measures. A link to the survey was emailed to the PKU Alliance electronic mailing list members and the Emory Maternal PKU Camp electronic mailing list members. The survey was distributed to five support groups on the social media site, Facebook; PKU Friendly, Phenylketonuria (PKU) World Wide Support Group, PKU Family Network International, Support Children with PKU and Raise Awareness for Phenylketonuria (PKU) and posted on the PKU.com Community Board as well as their corresponding Facebook page.

The first page of the survey included a participant letter with instructions. Eligible participants were asked to complete the survey online. The survey took approximately 15 minutes. Participants were able to choose not to answer a question or to end their participation in the study at any time. Ninety-five participants completed the online survey.

All participants who provided contact information at the end of the survey were contacted for the optional 15-minute telephone interview. Of these participants, ten completed telephone interviews. The interview response data was independently coded to look for major themes of the responses by the primary investigator.

2.4 Results

A total of 95 parents or caregivers responded to the first question of the survey. Fifty-two participants were excluded for significantly incomplete surveys or for not meeting survey criteria. Forty-three participants met the criteria of having a daughter with

PAH deficiency currently between the ages of 10 to 25 years old and were included in data analysis. The participants were predominantly female, Caucasian and had some degree of higher education. Demographics of the participants are shown in Table 2.1.

Table 2.1 Demographic Information

	Percent	<i>n</i>	Mean	Range
Parents or Caregivers (<i>N</i> = 43)				
Gender				
Female	93%	40		
Male	5%	2		
Prefer not to say	2%	1		
Participant's Age (in years)				
			44.9	20-63
Ethnicity				
Caucasian	91%	38		
African-American	2%	1		
Asian	2%	1		
Other	5%	2		
Education Level				
Some high school	2%	1		
Graduated high school	7%	3		
Some college	22%	9		
Graduated college	42%	17		
Further graduate studies	22%	9		
Other	5%	2		
Location				
Northeast United States	21%	9		
Southeast United States	14%	6		
Midwest United States	30%	13		
Southwest United States	2%	1		
West United States	2%	1		
Outside of the United States	30%	13		
Daughter's Current Age (in years)			17.2	10-25
Daughter's age at diagnosis (in days)			9.0	0-42
Daughter's status of receiving care at metabolic clinic				
Yes	81%	34		
No	2%	1		
Used to when she was younger	14%	6		
Other	2%	1		

2.4.1 Comfort Level. All participants answered the question “How comfortable do/did you feel discussing the risks of maternal PKU syndrome with your daughter?”

Approximately, two-thirds of the participants responded that they were comfortable or very comfortable with discussing maternal PKU syndrome. A significant number of

participants (21%) responded that they were very uncomfortable discussing this topic with their daughter. See Figure 2.1. There was no significant association between the level of comfort and age of caregiver or education level. There was no significant correlation between level of comfort and the daughter's current age or the age of the daughter when sexual health was discussed.

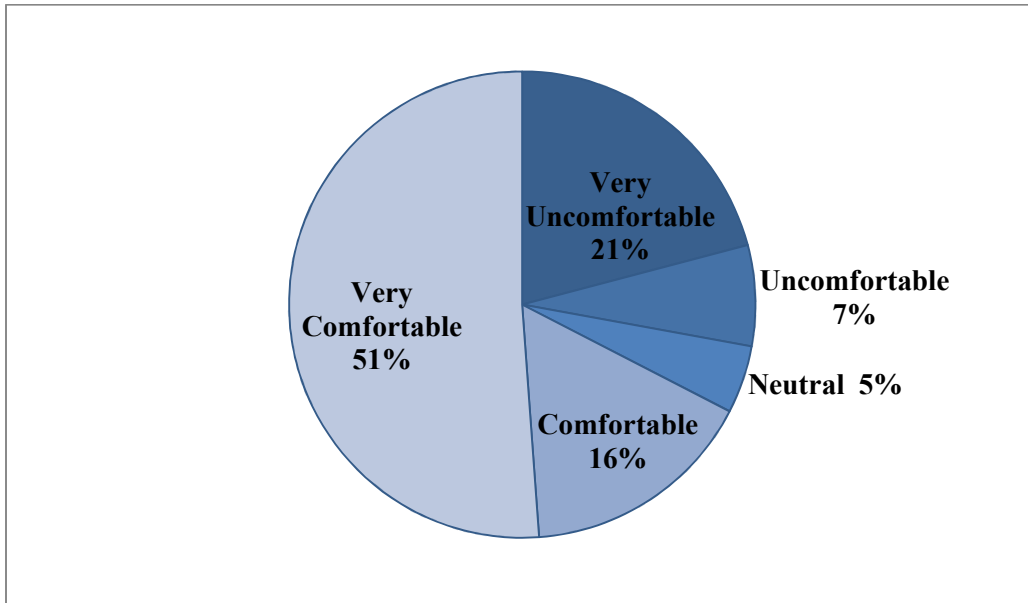


Figure 2.1 Level of Comfort in Discussing Maternal PKU Syndrome

2.4.2 Sexual Health and Maternal PKU Syndrome. The vast majority (91%) of participants have talked to their daughter about sexual health ($n = 43$). On average, parents began to discuss sexual health when their daughter was 13 years of age. The range of ages when sexual health was first discussed was from less than 10 years to 16 years of age. Of the participants who had spoken with their daughter about her sexual health ($n = 39$), 82% had also spoken with their daughter about maternal PKU syndrome. Of those who have spoken with their daughter about her sexual health and maternal PKU syndrome, 24% discussed maternal PKU syndrome before talking about sexual health ($n = 6$), 40% discussed maternal PKU syndrome and sexual health in the same conversation

($n = 10$) and 36% discussed maternal PKU syndrome after talking about sexual health ($n = 9$). Most frequently, parents were the individuals to initiate the conversation of maternal PKU syndrome with their daughters (72%, $n = 33$). See Figure 2.2

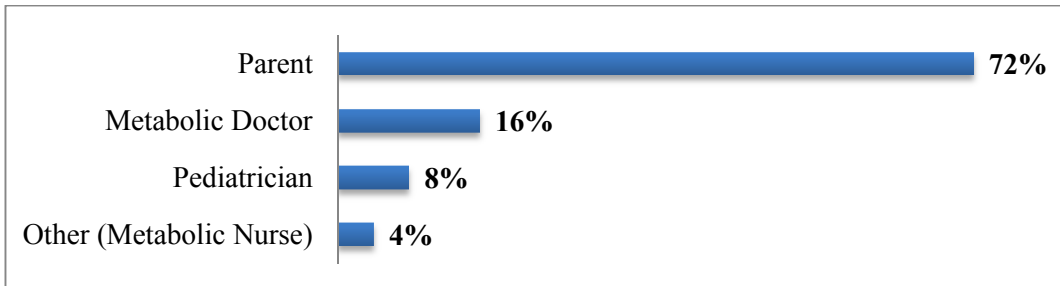


Figure 2.2 Initiators of the maternal PKU syndrome conversation

Of the participants who had discussed sexual health with their daughter but not maternal PKU syndrome (18%) ($n = 7$), the most common reason selected was “my daughter isn’t old enough” (50%). Thirty-three percent cited a lack of knowledge of maternal PKU and 17% reported that a health care professional initiated the conversation with their daughter. All of the participants plan to talk about maternal PKU syndrome with their daughter in the future. The majority of participants (60%) felt that a parent, followed by a metabolic doctor (20%), should be the individual to start the conversation about maternal PKU syndrome. Of the nine percent of participants who had not discussed sexual health with their daughter, one half had discussed maternal PKU syndrome. One parent responded to the follow up questions surrounding the details of the conversation: the conversation happened at age 13 and was started by a healthcare professional and the caregiver will follow up with the conversation of maternal PKU syndrome if her daughter asks about it. The remaining participants ($n = 2$) who have not discussed sexual health or maternal PKU syndrome with their daughter plan to talk about maternal PKU syndrome and all responded that the parents should start the conversation about maternal PKU

syndrome. Overall, 79% of participants have discussed maternal PKU syndrome with their daughter ($n = 42$). See Figure 2.3.

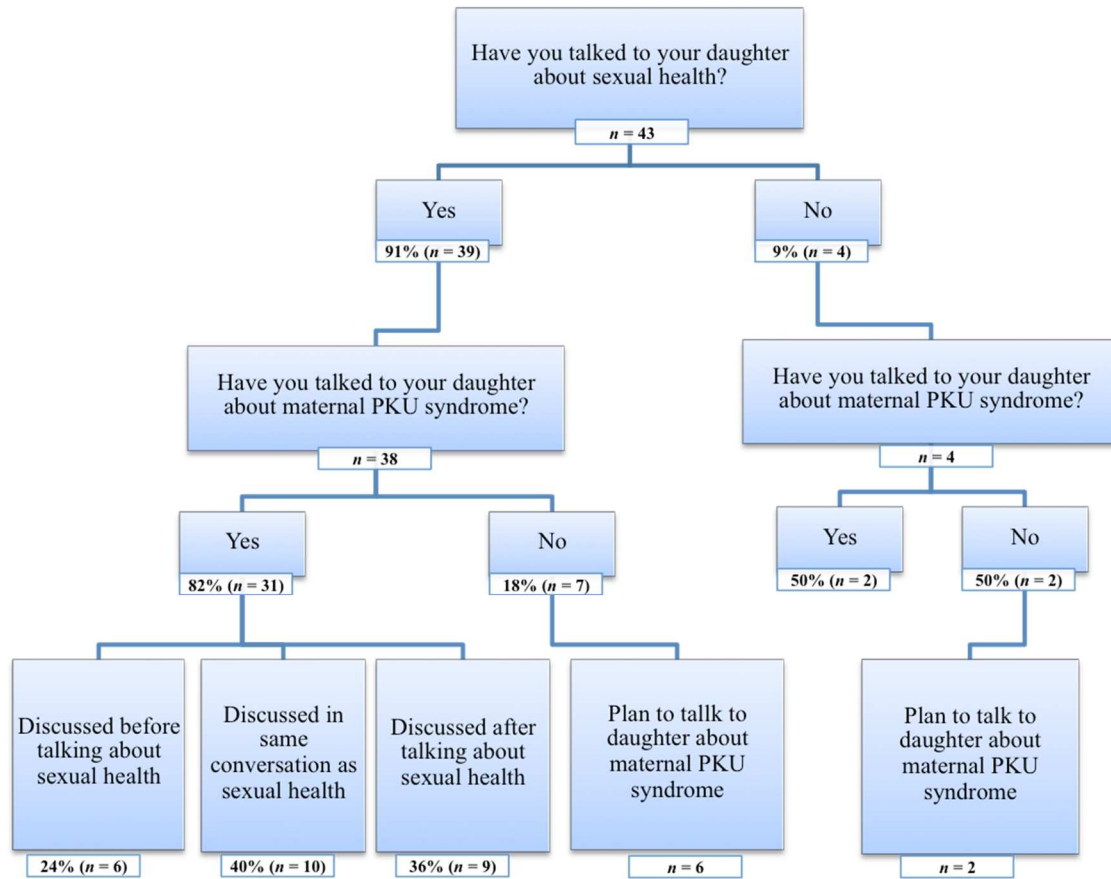


Figure 2.3 Flowchart of sexual health and maternal PKU syndrome responses

2.4.3 Topics Discussed. Participants were asked to select from a list all topics that were discussed or are planned to be discussed in the conversation of maternal PKU syndrome with their daughter. The most frequent topic discussed was health concerns associated with maternal PKU syndrome (94%) and the least frequent topic discussed was unplanned pregnancies (58%). See Figure 2.4. Participants most frequently discussed all six topics with their daughter (33%) and 84% discussed more than three maternal PKU topics in their discussion. There was no association found between the number of topics discussed and the daughter’s current age or between the total number of topics discussed

and the participants' education level. Additionally, no association was found between the region of the participants and if birth control or unplanned pregnancies were discussed.

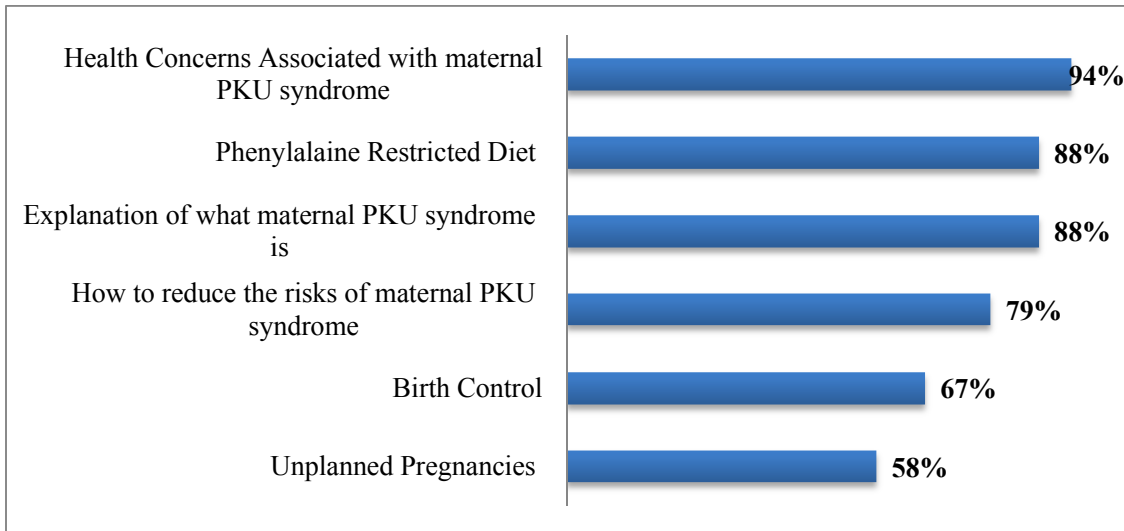


Figure 2.4 Conversation topics relating to maternal PKU syndrome ($n = 33$)

The participants were divided into two age categories based on the average onset of vaginal intercourse in women based on data from the Special Tabulation by the National Center for Health Statistics (2013). The frequency of the topics of birth control and unplanned pregnancies were compared between the participants who had daughters currently 16 years old or younger ($n = 22$) and daughters currently 17 years old or older ($n = 21$). Birth control was selected at a frequency of 53% in the 16 and under age category compared with 81% of participants in the 17 and over group, $t(31) = 1.75, p = .09$. In the 16 and under age category, 47% selected the topic of unplanned pregnancies and in the 17 and over age category 69% of participants selecting the topic of unplanned pregnancies, $t(31) = 1.25, p = .22$. See Figure 2.5.

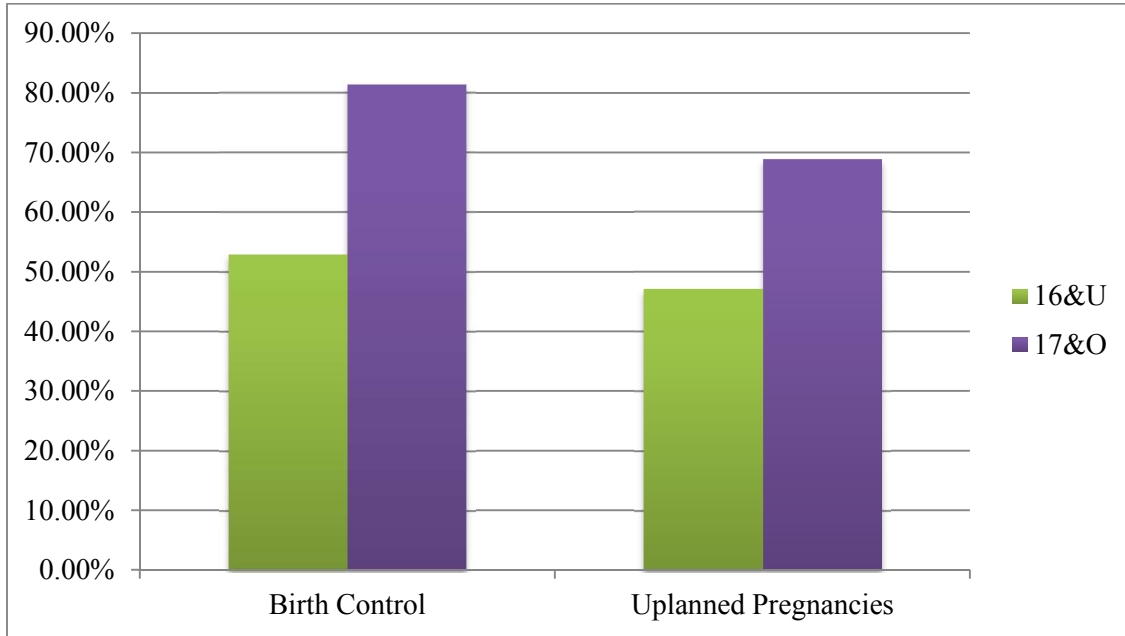


Figure 2.5 Frequency which parents selected birth control and unplanned pregnancies with respect to age

2.4.4 Resources. Participants were asked to select from a list all resources that they used or plan to use for the conversation of maternal PKU syndrome. The four most frequently selected resources were metabolic doctor at 73%, websites at 49%, genetic counselor at 42% and handouts at 33%. The least frequent resource selected was other healthcare professional. See Figure 2.6. The majority of participants would turn to two resources and 57% would use three or more resources.

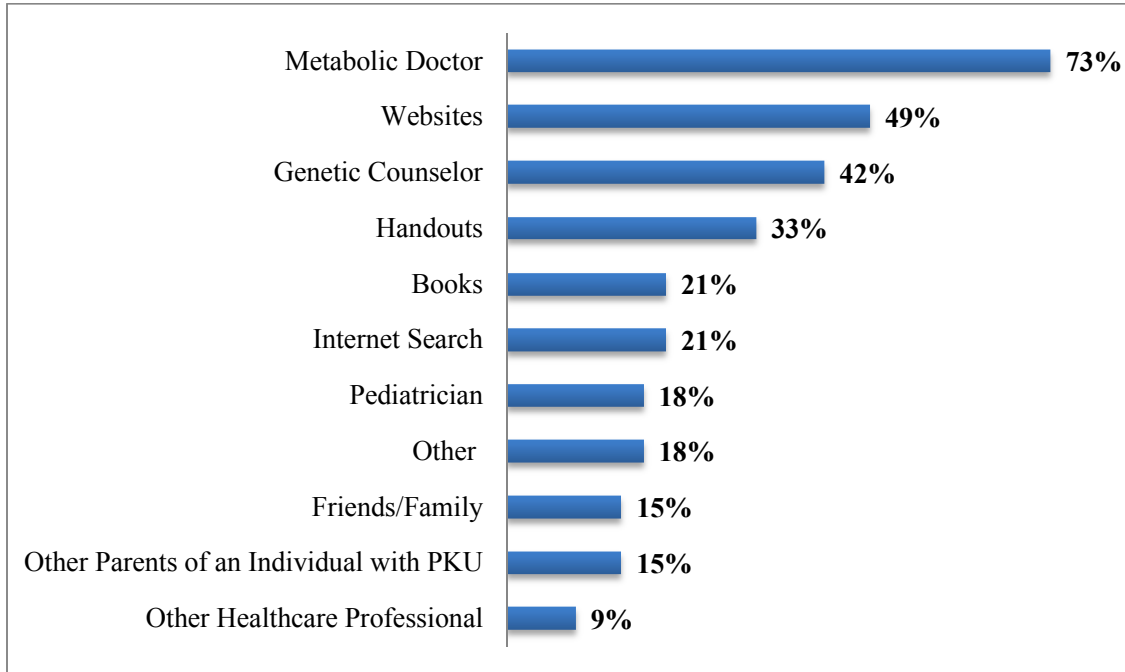


Figure 2.6 Resources ($n = 33$)

2.4.5 Free Response. Free response questions were analyzed for the most frequent themes discussed. Free responses were divided between participants who had already discussed maternal PKU syndrome and participants who have not yet discussed maternal PKU syndrome with their daughter but are planning to.

2.4.5.1 Emphasizing treatment compliance. Participants commonly discussed the importance of treatment compliance as a main topic in their discussion of maternal PKU syndrome ($n = 5$). One parent emphasized, “Diet for life is best.” Another parents described the difficulty of encouraging treatment adherence on an age appropriate level such as, “having her understand the challenges of sticking with her diet and formula at this age.” The sole participant who had not discussed maternal PKU syndrome yet plans to include a discussion of untreated individuals with PAH deficiency ($n = 1$).

2.4.5.2 Most challenging aspect. Several themes emerged as parents commented on the most challenging aspects about discussing maternal PKU syndrome with their daughters.

The most commonly mentioned challenge was the potential emotional component of the conversation ($n = 8$), most notably fear. One mother felt challenged “trying to convey the serious nature of the implications without frightening her”. Another mother shared that her daughter, “was very scared this might happen to her although she has always had her diet under control”. Another theme participants described as challenging were discussing the consequences of one’s actions ($n = 7$). One participant discussed “talking about the consequences of poor choices and the people affected” with her daughter. Similarly, discussing unintended pregnancies was also particularly challenging for parents ($n = 5$). Within the theme of unintended pregnancies, participants mentioned birth control, explaining unplanned pregnancies and considering abortion as challenging topics. The timing of the conversation ($n = 4$), specifically young age of the daughter and finding developmentally appropriate information was challenging for participants.

2.4.5.3 Most helpful resource. When participants were asked what was the most helpful resource, metabolic healthcare professionals, primarily metabolic doctors and dietitians, were most frequently mentioned ($n = 8$). Participants also cited older females, mostly who have PKU and who have had children, as a helpful resource ($n = 6$). One participant answered, “the mother with PKU because she had been through a pregnancy with PKU”. A number of participants did not use any resources ($n = 4$) and other cited the Internet, specifically YouTube, as most helpful ($n = 5$). Lastly, handouts, articles and books ($n = 4$) were helpful in this conversation. The participants who have yet to have this conversation of maternal PKU syndrome voiced a lack of resources ($n = 3$). “I don’t have any information on the subject so any!!” was expressed by one parent.

2.4.5.4 Recommendations for other parents. The most common recommendations parents gave for discussing maternal PKU syndrome revolved around the timing of the conversation ($n = 14$). This theme included sub themes such as start early (participants did not define “early”), to make it an ongoing conversation and keep the information appropriate for the age of the daughter. Secondly, participants most frequently advised other parents to normalize the topic of maternal PKU syndrome ($n = 8$). One parent stated “it [the discussion of maternal PKU syndrome] was not challenging, it is just an extension of the way she lives”. Another parent stated that, “it’s important, but if that are doing diet-for-life then it’s not a huge change in dietary habits.” Participants also frequently recommended transparency ($n = 6$) with the conversation such as being open, non-judgmental, honest, and direct. Discussing treatment compliance ($n = 5$) was a lesser-mentioned theme compared to the previously noted themes. One parent advised others to “talk to parents of grown women with PKU and the women themselves”($n = 1$) and another parent comments that she made sure her daughter “knew about and where family planning clinic and youth health services were” ($n = 1$). See Table 2.2.

2.4.5.5 Recommendations for healthcare professionals. Parents advised healthcare professionals to be transparent with relaying information to their daughters ($n = 8$). Participants want healthcare professionals to “be straight forward and tell it like it is”, to “use common language not scary medical terms”, and to “be sensitive”. Also, participants recommended making resources available for the parents, family and patients ($n = 7$). One parent urged healthcare professionals to “prepare parents for the conversation...not just the science but the social aspects... paths to fulfillment besides childbearing and that if she wants to be pregnant then there may be healthy options for

her and the baby.” Timing, including the subthemes of starting early and have ongoing conversations ($n = 4$), was mentioned less frequently as well as treatment compliance ($n = 2$). See Table 2.2.

Table 2.2 Recommendations for parents and healthcare professionals

Recommendations for Parents		Recommendations for Healthcare Professionals	
Timing of conversation ($n = 14$)	-Start early -Make it an ongoing conversation -Keep the information developmentally appropriate	Transparency ($n = 8$)	-Be straight forward -Use common language -Be sensitive
Normalize the topic of maternal PKU syndrome ($n = 8$)	-Healthy way of life -Not a big change if already doing diet for life	Make resources available ($n = 7$)	-Provide information for immediate and extended family -Pamphlets -Tools for maintaining diet -Stress keeping appointments
Transparency ($n = 6$)	-Be open -Non judgmental -Honest -Direct	Timing ($n = 4$)	-Start early -Have ongoing conversations
Treatment compliance ($n = 5$)	-Importance of diet -Discuss treatment with metabolic team	Treatment compliance ($n = 2$)	-Stress continued diet -Maternal PKU syndrome is avoidable with treatment
Use resources ($n = 2$)	-Other parents with grown daughters with PAH deficiency -Family planning clinics		

2.4.6 Interview Results. Interviews were divided between participants who had already discussed maternal PKU syndrome and participants who have not yet discussed maternal PKU syndrome with their daughter but are planning to. Areas that the participants were asked to elaborate on included the conversation in general, challenges, and helpful information to include in a resource.

2.4.6.1 Participants who have discussed maternal PKU syndrome. All parents interviewed who had already discussed maternal PKU syndrome with their daughter

presented the theme of the timing of the conversation ($n = 7$). One mother summed up her view on the timing of the conversation:

I would say the first talk in combination with when girls are turning 10 to have that initial conversation ... so parents can respond appropriately to the developmental phase that they are in and sort of build on that conversation and introduce maternal PKU as soon as their daughter is really able to understand it.

The next frequent theme was treatment compliance ($n = 6$). One mother explained this very simply; “you shouldn’t get pregnant if you aren’t sticking to your diet, if you aren’t drinking your formula.” Symptoms of maternal PKU syndrome were frequently discussed ($n = 5$). One parent kept the effects simple, “it’s not bad for you but it would be really bad for the baby.” Another parent felt that, “its my job to make sure you have all the information going forward that you have options and levels you can deal with and you know, I told her what things could happen.” Certain parents continued the conversation about maternal PKU syndrome to include their daughter’s significant other ($n = 4$). One mother shared, “you know as an older teenager and young adult as she was in more serious relationships and you know I would always slide that in and say remember... this takes on added responsibilities.” Parents directed their daughters to resources, specifically the Internet, to understand the effects of maternal PKU syndrome ($n = 2$). One mother shared that, “I know that I had mentioned to her different internet sites that I had looked at too and told her that she should look at them as well.”

Decision-making was a theme discussed by parents ($n = 4$). Parents discussed that it was their daughter’s decision to have healthy babies. One mother said:

I told her with her PKU it's nothing I could have prevented and it's nothing that I had even known about and I live with that daily and I couldn't imagine having some control over that and having a child you know with some birth defects that was in my power to change."

Another mother related this decision to more common practices:

I look at the decisions about PKU as being similar to the decisions about alcohol, drugs and smoking. You give the information and whether or not you like your child's choice it is their decision to make as an adult.

Parents emphasized the consequences of one's actions when conversing with their daughters ($n = 4$). These parents described trying to get their daughter to understand how far the consequences extend of having a baby with maternal PKU syndrome. One mother stated:

You know one decision, or one poor decision, or not managing your diet, or not being prepared for a child, that's something that affects you for the rest of your life and not only you but the child too and you know if she has a child with any sort of birth defects that is going to affect me as a grandparent. You know she will need some help with that, you know emotionally and obviously physically and even financially and just trying to stress the importance of that I guess is challenging.

Three parents brought up the theme of unplanned pregnancies ($n = 3$). One mother shared:

She [her daughter] has been on birth control since she was 13-14 years old and mainly for this reason, I mean, I just, you know, I just want to make sure that any child she brings into the world is something that is planned very carefully.

Exposure to the challenges of maternal PKU syndrome was another theme seen ($n = 3$). One parent had her daughter listen to a panel that included a woman who had babies with maternal PKU syndrome and another mother has a family friend with PKU who was able to have four healthy babies. Lastly, a mother shared:

She [her daughter] teaches in a 5th and 6th behavioral challenged classroom and she has a little boy who has maternal PKU and she said even though he is in 5th grade he reached his potential in 2nd grade and she saw it with her own eyes.

When the parents were asked what would be most helpful to include in an educational handout on maternal PKU syndrome for parents, all parents ($n = 7$) agreed that having an explanation about maternal PKU syndrome would be beneficial. One parent suggested, “as parents we wanted information geared for us in clear, easy to understand language. We wanted to know what maternal PKU was and what the risks were for our daughter.” Also, all parents ($n = 7$) wanted balanced information on maternal PKU syndrome. One parent felt that outcomes needed to be outlined because, “a lot of times the clinics want to put you in touch with the positives and that’s not completely realistic you know you need to hear some of those negative stories too.”

Another parent responded:

No matter how unpalatable, the PKU community needs to hear about the bad outcomes and the percentage risks involved of each scenario. As a young woman,

why would you bother with the hassle of staying on diet or going on diet when all you hear are the good outcomes. It implies that there is no risk.

2.4.6.2 Participants who have not discussed maternal PKU syndrome. Three interviewees have not yet discussed maternal PKU syndrome with their daughter. One mother felt that it was not an appropriate topic: “it’s really not appropriate at this time for me to be talking to her about having babies. I mean she understands how all that works but she is not even kissing boys not even holding hands.” Two parents described not knowing what to tell their daughter about maternal PKU syndrome although they were both open to the discussion if initiated by their daughter.

All three parents mentioned most frequently throughout the interviews that they were lacking information on what maternal PKU syndrome was. With respect to maternal PKU, one parent stated, “I don’t really understand a whole lot”. All parents addressed that a perceived challenge of this conversation is bringing up one more thing that makes their daughter different from others because of PKU. Two parents compared PKU to diabetes and plan to use the analogy of keeping sugar levels controlled in maternal diabetes. Two parents also discussed the desire for a healthy baby as possible motivation for their daughters to be controlled during pregnancy. One mother said, “I don’t think it’s any different than having to cut back on caffeine when you’re pregnant or not smoking when you’re pregnant because these are things that you do because you love this unborn child”.

All parents also addressed the phenylalanine-restricted diet, two parents discussed their daughter’s difficulty with the diet and the other parents discussed that her daughter understands her diet is for life.

All parents discussed wanting their daughter to be aware of both positive and negative outcomes of pregnancies. One parents stated that:

Seeing the good and the bad and the certain risks, I think children should be made aware of it so if they want to have children, if they do decide, then they need to know what could happen or could not happen.

When asked about what would be useful to include in a pamphlet geared toward parents, all three parents agreed that an explanation of maternal PKU syndrome would be useful as well as including balanced information on maternal PKU outcomes ($n = 3$).

2.5 Discussion

Most parents surveyed have discussed maternal PKU syndrome with their daughters. The minority that had not discussed maternal PKU syndrome most commonly felt that their daughter was too young, but all of them planned to have the conversation in the future. Most parents broached the subject of maternal PKU syndrome during or after discussing sexual health with their daughters. The vast majority of parents thought they should be the ones to bring up this conversation. This is consistent with the findings from those who had discussed maternal PKU syndrome with their daughter already. Given that parents are the individuals initiating the discussion, they need to be the ones who are informed and equipped to start this conversation. Based on the open-ended responses, feedback from parents who had already had this conversation with their daughter it was frequently expressed by participants to have this conversation early and make it an ongoing conversation. Healthcare professionals need to be aware of this in order to properly prepare parents on initiating the conversation and how to continue it over time.

Overall, the majority of participants were comfortable or very comfortable with discussing maternal PKU syndrome. Notably, most participants identified with either end of the extreme, either very comfortable or very uncomfortable. This type of identification was also seen with the free response answers. Some parents tried to normalize the conversation of maternal PKU syndrome with explaining it as just an extension of the way she lives or comparing maternal PKU syndrome to maternal diabetes. Other parents expressed extreme concerns of frightening or upsetting their daughter in their quest to make sure she understood why it was so important for her to plan her pregnancies. This is important information for healthcare professionals, as they need to understand that parents can be planning this conversation of maternal PKU syndrome in different ways and be able to provide adequate support for parents depending on their approach.

The two least frequent topics selected were birth control and unplanned pregnancies. This is worrisome as the effects of maternal PKU syndrome are seen when pregnancies in women with PAH deficiency are not fully planned with respect to treatment and diet. According to a special tabulation by the National Center for Health Statistics in 2013 the average age when teenagers first have vaginal intercourse is 17.1 years. Based on this, the participants were also split into a 17 and over category and a 16 and under category. These two groups were compared to see if the frequency of the selection of the topics of birth control and unplanned pregnancies changed. In the 16 and under group 53% discussed birth control and 47% discussed unplanned pregnancies. In the 17 and over group, these topics were included in 81% and 69% of parent-daughter discussions, respectively. This showed a marked increase in the selection of birth control and unplanned pregnancies; however, these increases are not statistically significant.

Generally, 17 years of age may be a milestone which parents are more likely to discuss birth control and unplanned pregnancies. This also coincides with the average age that teenage females have vaginal intercourse. Our study did not assess if parents were aware of when their daughter began or would begin to have sexual intercourse. However, this is an area where further research is needed. Parents might not always be aware at what age their daughter is having sexual intercourse, therefore this leads to the concern that teenage girls may not have discussed how birth control and pregnancy planning could reduce the risks of maternal PKU syndrome. There is still a portion of parents who have not discussed contraception or unplanned pregnancy with their daughters with respect to maternal PKU. This may be because birth control and unplanned pregnancies was often a challenging aspect of parents discussing maternal PKU syndrome with their daughters. Also, it is possible for young women to become pregnant after the onset of menarche. Age of menarche was not discussed in this study but could be an area for future research to assess associations between age of onset and birth control and unplanned pregnancy discussion.

The most commonly selected resources were the metabolic doctor, websites, genetic counselor, and handouts. Quantitatively, parents who have a child with PKU were not a commonly used resource, however, several free responses and interviewees expressed that speaking with other parents who have daughters with PKU or older women with PKU has been the most helpful resource. There may be a discrepancy between the resources most frequently used and the resources that are most helpful. One possibility for this discrepancy is that there is limited access to other parents or individuals who have had experience with maternal PKU syndrome. Recognizing this

area of discrepancy can guide healthcare professionals in the creation of resources and improve existing resources that might be more helpful for parents in facilitating this conversation. One area for future study may be to assess the helpfulness of the resources. Some participants, who had already discussed maternal PKU syndrome with their daughter, shared that they did not use any resources. Also, certain participants in both interviews and free response, especially those who have not discussed maternal PKU syndrome with their daughter, expressed not having enough resources. This reinforces the need for healthcare providers to assess parents' access to resources to help equip them for discussing maternal PKU syndrome. This is another place that further study would be useful to investigate why this is so.

The separate themes seen across all free response questions and interviews could fit into three main overarching categories. The first relates to how to have the conversation of maternal PKU syndrome. This includes the themes seen such as timing, transparency and giving information that is developmentally appropriate. The second category relates to the challenges of the conversation such as unintended pregnancies, consequences of one's actions, the daughter's decision making and the emotional component of the conversation, specifically fear. The third category includes parents' advice about the conversation such as tips for emphasizing treatment compliance, resource utilization and normalizing the conversation of maternal PKU syndrome. Parents' advice about treatment compliance especially "diet for life" is consistent with the 2014 ACMG Guidelines recommending maintaining a restricted diet as an ideal way to reduce the effects of maternal PKU syndrome (Vockely et al., 2014). Of note, the fact that parents are finding the discussion of their daughter's decision making and

consequences of her actions with respect to maternal PKU syndrome challenging may correspond with impaired decision making abilities when blood phenylalanine levels are elevated (Sharman et al., 2013). Phenylalanine levels tend to be increased during the adolescent years (Gentile et al., 2010), the same life stage when parents discuss maternal PKU syndrome, therefore it might be even more difficult for the daughters to fully comprehend the complexities of their actions. Impaired decision making may affect the ability for a young woman to adhere to her restricted phenylalanine diet or consider the consequences of unprotected sexual intercourse. This is why it is critical that preventative measures such as birth control are discussed and implemented with daughters during this transitional time period.

Overall, it was discovered that parents are talking to their daughters about maternal PKU syndrome. Parents are trying to let their daughter's make their own decisions and understand the consequences of their actions, while still encouraging them to remain compliant with their treatment. As discussed in the ACMG Practice Guidelines (Vockley et al., 2014), achievement of controlled maternal phenylalanine levels should occur before conception. Parents are discussing maternal PKU syndrome early in order to normalize staying on treatment for the health of the baby. Parents report discussing the general effects of maternal PKU syndrome, however, in the interviews, all parents wanted balanced information on maternal PKU in an educational handout. Overall, the responses from this study emphasize the need for more education and resources on maternal PKU syndrome. A study by MacDonald et al. (2008) found poor maternal education on PAH deficiency directly correlated with elevated phenylalanine levels in their affected children. Incidentally, a parent had to clarify what maternal PKU syndrome

was in a follow up interview which could mean that the explanation of maternal PKU syndrome included in the survey was not clear. This leads to the idea that parents might not be fully educated on maternal PKU syndrome. Parental level of knowledge of maternal PKU syndrome was not assessed in our study and this is an area where further research is indicated.

MacDonald et al. (2008) also noted that no system is in place to address the educational needs of parents when they have a child with PAH deficiency. An educational handout focused on the needs of the parents, i.e. a clear definition of maternal PKU syndrome and what the effects are, has the potential to improve the parent-daughter maternal PKU syndrome conversation. Participants listed handouts as the fourth most frequently used resource and handouts were mentioned as being the most helpful resource as well which corresponds to a study by Bernstein et al. (2013) where handouts were found to be an effective tool to educate parents.

The 2014 ACMG guidelines state, “during transition, there should be emphasis on pregnancy related issues for females. This should be discussed prior to adolescence and revisited annually” (Vockely et al., 2014, p. 10). While the majority of parents are initiating this discussion, it is ultimately the healthcare provider’s responsibility to ensure that their female patients discuss maternal PKU before adolescence and that the conversation continues. Ultimately, healthcare providers and parents can collaborate to ensure that developmentally appropriate education continues throughout adolescence. The suggestions given by parents along with written handouts can help ensure that the ACMG guidelines are being appropriately addressed. One avenue for future research is to

assess the frequency and preferred methods of revisiting maternal PKU with the participants' daughters.

Little has been known about the conversation of maternal PKU syndrome between parents and daughters. However, based on the surveys completed by 43 parents of females with PAH deficiency, this study was able to identify current patterns in the parent-daughter conversation about maternal PKU syndrome. Resources, topics discussed, and comfort level with the topic of maternal PKU syndrome were assessed. Challenging aspects of having this conversation and recommendations for other parents and healthcare professionals were gathered. Exploring these areas opened the way for a deeper understanding of the needs of the parent and how healthcare professionals can better assist in the journey to reduce the prevalence of the avoidable condition of maternal PKU syndrome.

2.5.1. Study Limitations. There are several limitations to this study that need to be considered. This study had a small sample size of only 43 participants. Participants self-selected into the study from social media support groups, a metabolic camp for females electronic emailing list and National PKU Alliance electronic emailing list. Therefore, the study may be biased towards those who are more aware of maternal PKU syndrome or those more likely to seek outside support and resources. Participants were predominately female, Caucasian and reported high levels of education, so these findings may not be applicable to other demographics. Survey responses were based only on participant report and may be subject to recall bias. While the survey included definitions of maternal PKU syndrome and sexual health it did not assess the participant's knowledge of these topics. It is possible that a participant could have misconceptions of

maternal PKU syndrome features and prevention, which were not assessed, in this survey. Finally, while abstinence is a form of birth control, it was not explicitly stated as a form of birth control in the survey. It is possible that a parent could be discussing abstinence with their daughter but not have selected “birth control” as a discussion point with their daughter.

2.5.2 Future Research. This study aimed to get a general overview on the parent-daughter conversation of maternal PKU syndrome. In light of certain findings further areas for research in this topic were noted. The assessment of parental level of knowledge of maternal PKU syndrome could provide valuable insight as well as determining the helpfulness of resources. Investigating the topic of birth control and unplanned pregnancies with respect to maternal PKU syndrome would be very important as we try to reduce the prevalence of maternal PKU syndrome. Assessing adolescent female’s understanding of maternal PKU syndrome features, treatment, and helpful resources may also help parents and healthcare providers address this topic with this specific population.

2.6 Conclusion

Overall, the majority of parents were comfortable discussing maternal PKU syndrome and most parents are initiating the conversation. There is a significant portion of parents who are uncomfortable discussing maternal PKU syndrome and frequently reference a lack information as a barrier to this discussion. Overall, parents expressed discomfort addressing birth control and unplanned pregnancies with their daughters. They are covering a variety of topics and addressing the management and avoidance of maternal PKU syndrome by treatment compliance. Recommendations for both parents

and healthcare providers are summarized to help address maternal PKU syndrome for young women with PAH deficiency.

These findings are important to health professionals in the metabolic field specifically metabolic physicians and genetic counselors so they can better prepare families to discuss maternal PKU syndrome. Parents are most frequently turning to metabolic physicians and genetic counselors as a resource about maternal PKU syndrome. It is imperative that health professionals understand parent' challenges and concerns in this conversation. Parents prefer to be the individuals that broach this subject with their daughters; therefore, this can be an opportunity for the healthcare professional to empower the parent with developmentally appropriate information and resources. The areas that are lacking in the conversation of maternal PKU syndrome, such as a discussion of birth control and unplanned pregnancies, are areas that can be focused on when guiding the parents through the discussion of maternal PKU syndrome. Being able to aptly educate those leading the discussion of maternal PKU syndrome, the parents, would improve overall education with the hope of reducing the prevalence of maternal PKU syndrome.

Chapter 3. Conclusions

Overall, the majority of parents were comfortable discussing maternal PKU syndrome and most parents are initiating the conversation. There is a significant portion of parents who are uncomfortable discussing maternal PKU syndrome and frequently reference a lack information as a barrier to this discussion. Overall, parents expressed discomfort addressing birth control and unplanned pregnancies with their daughters. They are covering a variety of topics and addressing the management and avoidance of maternal PKU syndrome by treatment compliance. Recommendations for both parents and healthcare providers are summarized to help address maternal PKU syndrome for young women with PAH deficiency.

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Appendix A Interview Questions

Introduction: Hello, my name is Hannah Andrews. I am a genetic counseling graduate student at the University of South Carolina. You are being contacted because you responded to an online survey about communication patterns between parents and daughters about the discussion of maternal PKU syndrome and gave your information to be contacted for a follow-up interview. The purpose of this follow-up interview is go more in depth about some of your answers to the online survey. This interview will be recorded and the recording will be destroyed after the information is collected. All identifying information will be kept confidential. If you feel uncomfortable at any point during the interview with the question being asked you can skip the question. At any time you can end the interview if you wish.

Have you discussed maternal PKU syndrome with your daughter?

If the participant has already discussed maternal PKU syndrome with their daughter:

Please elaborate on what you think is most challenging when discussing maternal PKU syndrome with your daughter. What do you think would help make that part of the discussion less challenging?

Did your daughter ask questions about maternal PKU syndrome or family planning?
What types of questions did she ask you?

What do you think was most helpful when you were discussing maternal PKU syndrome with our daughter?

If you could design your ideal educational tool to help with this discussion of maternal PKU syndrome what would it include?

If the participant has not discussed maternal PKU syndrome with their daughter:

Please elaborate on what you think will be most challenging when discussing maternal PKU syndrome with your daughter. What do you think would help make that part of the discussion less challenging?

What do you think would be most helpful in preparing for this discussion?

If you could design your ideal educational tool to help with this discussion of maternal PKU syndrome what would it include?

Conclusion: Do you have any other comments or specific questions you would like answered? Thank you for participating in this interview!

Appendix B Survey Questions

Communication Patterns of Parents in Discussion of Maternal PKU

Dear Potential Participant,

You are invited to participate in a graduate research study focusing on the communication between parents/care-givers and daughters about maternal phenylketonuria syndrome, traditionally referred to as maternal phenylketonuria (PKU). I am a genetic counseling graduate student at the University of South Carolina School of Medicine. My research investigates the communication patterns about maternal PKU syndrome between parents and their daughters who have phenylalanine hydroxylase (PAH) deficiency. The research involves completing an online survey about communication patterns. It should take approximately 20 minutes.

All responses gathered from the survey will be kept confidential. If you do not wish to answer a certain question, please skip that question and move on to the next. There is a section to provide your name and phone number if you are interested in being contacted for a short optional interview at a later date. The contact information will be used only for an optional telephone interview and not for any other purpose. It is not necessary that you provide this information.

Your participation in this research study is voluntary. By completing the survey, you are consenting that you have read and understand this information. At any time, you may withdraw from the study by not completing the survey. The results of the study may be published or presented at academic meetings; however, participants will not be identified.

Thank you for your time and consideration to participate in this survey. Your response may help health care professionals such as genetic counselors in the future, as well as parents of daughter with PAH deficiency in the future with information to better aid and support parents about effective communication styles when they discuss the risks of maternal PKU syndrome with their daughters. If you have any questions regarding this research, you may contact my thesis advisor, Emily Jordon, MS, CGC, or myself by using the contact information below. If you have any questions about your rights as a research participant, you may contact the Office of Research Compliance at the University of South Carolina at (803) 777-7095.

Emily Jordon, MS, CGC
Thesis Advisor
Emily.jordon@uscmed.sc.edu

Hannah Andrews, B.S.
Principal Investigator
handrews@email.sc.edu

Communication Patterns of Parents in Discussion of Maternal PKU

Demographic Information

1. What is your age?

2. What is your gender?

- Male
- Female
- I would prefer not to say

3. What is your ethnicity?

- Caucasian
- African American
- Hispanic
- Native American
- Pacific Islander
- Asian
- Other (please specify)

4. What is your education level?

- some high school
- graduated high school
- some college
- graduated college
- further graduate studies
- Other (please specify)

Communication Patterns of Parents in Discussion of Maternal PKU

5. Where do you live?

- United States: Northeast (ME, MA, RI, CT, NH, VT, NY, NJ, PA, DE, MD)
- United States: Southeast (WV, VA, KY, TN, NC, SC, GA, AL, MS, AR, LA, FL)
- United States: Midwest (OH, IN, MI, IL, MO, WI, MN, IA, KS, NE, SD, ND)
- United States: Southwest (TX, OK, NM, AZ)
- United States: West (CO, WY, MT, ID, WA, OR, UT, NV, CA, AK, HI)

Other (please specify)

Communication Patterns of Parents in Discussion of Maternal PKU

The purpose of this survey is to better understand how parents talk with their daughters about maternal PKU syndrome. Maternal PKU syndrome is a pattern of birth defects that can occur in the baby during a pregnancy when the mother has phenylketonuria (PKU), also known as phenylalanine hydroxylase deficiency (PAH deficiency).

In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

6. What is your daughter's current age?

7. How old was your daughter when she was diagnosed with PKU (PAH deficiency)?

8. Does your daughter receive care at a metabolic clinic?

- Yes
- No
- Used to when she was younger
- Other (please specify)

9. How comfortable do/did you feel discussing the risks of maternal PKU syndrome with your daughter?

- very uncomfortable
- uncomfortable
- neutral
- comfortable
- very comfortable

10. Have you talked with your daughter about her sexual health?

- Yes
- No

Communication Patterns of Parents in Discussion of Maternal PKU

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In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

11. How old was your daughter when you discussed sexual health?

12. Have you talked with your daughter about maternal PKU syndrome?

- Yes
- No

Communication Patterns of Parents in Discussion of Maternal PKU

The purpose of this survey is to better understand how parents talk with their daughters about maternal PKU syndrome. Maternal PKU syndrome is a pattern of birth defects that can occur in the baby during a pregnancy when the mother has phenylketonuria (PKU), also known as phenylalanine hydroxylase deficiency (PAH deficiency).

In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

13. When did you talk with your daughter about maternal PKU syndrome?

- before talking to her about her sexual health
- within the same conversation as her sexual health
- after talking to her about her sexual health
- Other (please specify)

14. Who started the conversation about maternal PKU syndrome?

- daughter
- parent/caregiver
- pediatrician
- metabolic doctor
- other healthcare professional
- Other (please specify)

15. Please check all the topics that you discussed with your daughter during your conversation about maternal PKU syndrome.

- phenylalanine-restricted diet
- explanation of what maternal PKU syndrome is
- how to reduce the risks of maternal PKU syndrome
- health concerns associated with maternal PKU syndrome
- birth control
- unplanned pregnancies
- Other (please specify)

Communication Patterns of Parents in Discussion of Maternal PKU

16. What other details do you remember about this conversation with your daughter about maternal PKU syndrome?

17. What was the most challenging part of talking with your daughter about maternal PKU syndrome?

18. Did you have any follow-up conversations about maternal PKU syndrome with your daughter?

- Yes
 No
 We will if she brings it up

19. Please check all the resources you used for help in the conversation of maternal PKU syndrome with your daughter.

- books
 handouts or pamphlets
 your daughter's pediatrician
 your daughter's metabolic doctor
 genetic counselor
 other healthcare professional
 friends or family
 other parents of children with PKU
 websites associated with PKU
 internet search
 Other (please specify)

20. Please explain the resources you found most helpful for the conversation about maternal PKU syndrome and why.

Communication Patterns of Parents in Discussion of Maternal PKU

21. What advice would you give to other parents about speaking with their daughter about maternal PKU syndrome?

22. What advice would you give to healthcare providers who speak to girls about maternal PKU syndrome?

Communication Patterns of Parents in Discussion of Maternal PKU

The purpose of this survey is to better understand how parents talk with their daughters about maternal PKU syndrome. Maternal PKU syndrome is a pattern of birth defects that can occur in the baby during a pregnancy when the mother has phenylketonuria (PKU), also known as phenylalanine hydroxylase deficiency (PAH deficiency).

In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

23. What are your reasons for not discussing maternal PKU syndrome with your daughter?

- My daughter isn't old enough
- Her doctor already talked to her about it
- I wasn't prepared
- She didn't ask about maternal PKU syndrome
- I was waiting for her doctor to talk about it
- I don't know enough about maternal PKU syndrome
- I don't think maternal PKU syndrome needs to be talked about
- Other (please specify)

24. Do you plan to discuss maternal PKU syndrome with your daughter?

- Yes
- No

Communication Patterns of Parents in Discussion of Maternal PKU

The purpose of this survey is to better understand how parents talk with their daughters about maternal PKU syndrome. Maternal PKU syndrome is a pattern of birth defects that can occur in the baby during a pregnancy when the mother has phenylketonuria (PKU), also known as phenylalanine hydroxylase deficiency (PAH deficiency).

In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

25. When do you plan to talk with your daughter about maternal PKU syndrome?

26. Please check all the topics that you plan to discuss with your daughter during your conversation about maternal PKU syndrome.

- phenylalanine-restricted diet
- explanation of what maternal PKU syndrome is
- how to reduce the risks of maternal PKU syndrome
- health concerns associated with maternal PKU syndrome
- birth control
- unplanned pregnancies
- Other (please specify)

27. What else do you plan to tell your daughter about maternal PKU syndrome?

28. Who do you think should be the person to start the conversation about maternal PKU syndrome?

- daughter
- parent/caregiver
- pediatrician
- metabolic doctor
- other healthcare professional
- Other (please specify)

Communication Patterns of Parents in Discussion of Maternal PKU

29. Please check all the resources you plan to use for help in the conversation of maternal PKU syndrome with your daughter.

- books
- handouts or pamphlets
- your daughter's pediatrician
- your daughter's metabolic doctor
- genetic counselor
- other healthcare professional
- friends or family
- other parents of children with PKU
- websites associated with PKU
- internet search
- Other (please specify)

30. What additional information would you like to have to help talk with your daughter about maternal PKU syndrome?

Communication Patterns of Parents in Discussion of Maternal PKU

The purpose of this survey is to better understand how parents talk with their daughters about maternal PKU syndrome. Maternal PKU syndrome is a pattern of birth defects that can occur in the baby during a pregnancy when the mother has phenylketonuria (PKU), also known as phenylalanine hydroxylase deficiency (PAH deficiency).

In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

31. Have you talked to your daughter about maternal PKU syndrome?

- Yes
 No

Communication Patterns of Parents in Discussion of Maternal PKU

The purpose of this survey is to better understand how parents talk with their daughters about maternal PKU syndrome. Maternal PKU syndrome is a pattern of birth defects that can occur in the baby during a pregnancy when the mother has phenylketonuria (PKU), also known as phenylalanine hydroxylase deficiency (PAH deficiency).

In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

32. How old was your daughter when you discussed maternal PKU syndrome?

33. Who started the conversation about maternal PKU syndrome?

- daughter
- parent/caregiver
- pediatrician
- metabolic doctor
- other healthcare professional
- Other (please specify)

34. Please check all the topics that you discussed with your daughter during your conversation about maternal PKU syndrome.

- phenylalanine-restricted diet
- explanation of what maternal PKU syndrome is
- how to reduce the risks of maternal PKU syndrome
- health concerns associated with maternal PKU syndrome
- birth control
- unplanned pregnancies
- Other (please specify)

35. What other details do you remember about this conversation with your daughter about maternal PKU syndrome?

Communication Patterns of Parents in Discussion of Maternal PKU

36. What was the most challenging part of talking with your daughter about maternal PKU?

37. Did you have any follow-up conversations about maternal PKU syndrome with your daughter?

- Yes
 No
 We will if she brings it up

38. Please check all the resources you used for help in the conversation of maternal PKU syndrome with your daughter.

- books
 handouts or pamphlets
 your daughter's pediatrician
 your daughter's metabolic doctor
 genetic counselor
 other healthcare professional
 friends or family
 other parents of children with PKU
 websites associated with PKU
 internet search
 Other (please specify)

39. Please explain the resources you found most helpful in the conversation about maternal PKU syndrome and why.

40. What advice would you give to other parents about speaking with their daughter about maternal PKU syndrome?

Communication Patterns of Parents in Discussion of Maternal PKU

41. What advice would you give to healthcare providers who speak to girls about maternal PKU syndrome?

Communication Patterns of Parents in Discussion of Maternal PKU

The purpose of this survey is to better understand how parents talk with their daughters about maternal PKU syndrome. Maternal PKU syndrome is a pattern of birth defects that can occur in the baby during a pregnancy when the mother has phenylketonuria (PKU), also known as phenylalanine hydroxylase deficiency (PAH deficiency).

In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

42. Do you plan to discuss maternal PKU syndrome with your daughter?

- Yes
 No

Communication Patterns of Parents in Discussion of Maternal PKU

The purpose of this survey is to better understand how parents talk with their daughters about maternal PKU syndrome. Maternal PKU syndrome is a pattern of birth defects that can occur in the baby during a pregnancy when the mother has phenylketonuria (PKU), also known as phenylalanine hydroxylase deficiency (PAH deficiency).

In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

43. When do you plan to talk with your daughter about maternal PKU syndrome?

44. Please check all the topics that you plan to discuss with your daughter during your conversation about maternal PKU syndrome.

- phenylalanine-restricted diet
- explanation of what maternal PKU syndrome is
- how to reduce the risks of maternal PKU syndrome
- health concerns associated with maternal PKU syndrome
- birth control
- unplanned pregnancies
- Other (please specify)

45. What else do you plan to tell your daughter about maternal PKU syndrome?

46. Who do you think should be the person to start the conversation about maternal PKU syndrome?

- daughter
- parent/caregiver
- pediatrician
- metabolic doctor
- other healthcare professional
- Other (please specify)

Communication Patterns of Parents in Discussion of Maternal PKU

47. Please check all the resources you plan to use for help in the conversation of maternal PKU syndrome with your daughter.

- books
- handouts or pamphlets
- your daughter's pediatrician
- your daughter's metabolic doctor
- genetic counselor
- other healthcare professional
- friends or family
- other parents of children with PKU
- websites associated with PKU
- internet search
- Other (please specify)

48. What additional information would you like to have for help in speaking with your daughter about maternal PKU syndrome?

Communication Patterns of Parents in Discussion of Maternal PKU

The purpose of this survey is to better understand how parents talk with their daughters about maternal PKU syndrome. Maternal PKU syndrome is a pattern of birth defects that can occur in the baby during a pregnancy when the mother has phenylketonuria (PKU), also known as phenylalanine hydroxylase deficiency (PAH deficiency).

In this survey, the term "sexual health" includes topics of puberty, pregnancy, sexual reproduction, family planning and health concerns specific to young women who are in their adolescent to teenage years.

49. What are your reasons for not planning to discuss maternal PKU syndrome with your daughter?

50. Are there any circumstances that you might discuss maternal PKU syndrome with your daughter?

51. Who do you think should be the person to talk to your daughter about maternal PKU syndrome?

- metabolic doctor
- pediatrician
- other healthcare professional
- counselors at metabolic camp
- I do not think it needs to be talked about
- Other (please specify)

52. Would having resources to help in the conversation about maternal PKU syndrome change your plan? Please explain.

Communication Patterns of Parents in Discussion of Maternal PKU

Contact Information For Optional Telephone Interview

If you are interested in participating in a short telephone interview relating to the topics covered in this survey, please leave your full name and email address. You will be contacted by email to arrange a time and date for a 15 minute interview over the phone. The questions in the interview invite you to elaborate on your discussion of maternal PKU syndrome as well as your daughter's reaction. This is optional.

53. Full Name

54. Email Address

55. Telephone Number

Communication Patterns of Parents in Discussion of Maternal PKU

Thank you for your participation!

Appendix C
Maternal PKU Syndrome Handout

Let's Talk About Maternal PKU Syndrome!

What is Maternal PKU Syndrome?

Maternal PKU syndrome refers to the toxic effects of high levels of phenylalanine on a developing fetus. When a woman with PAH deficiency (previously known as PKU) is not controlling her phenylalanine levels and becomes pregnant, the elevated levels of phenylalanine can cause serious problems for the unborn baby. Usually these babies do not have PAH deficiency themselves, but they can have birth defects such as **microcephaly, poor fetal growth, congenital heart defects and intellectual disability.** ¹ **Maternal PKU syndrome can be avoided with proper treatment!**

Effects of Maternal PKU Syndrome

Microcephaly: This is when the baby's head is smaller than normal usually because the brain is not developing. This most often happens during the early months of fetal development. Effects of microcephaly can include developmental delay, such as delayed speech and motor functions, intellectual disability, seizures, hyperactivity, balance and coordination problems and other brain abnormalities. Some children with microcephaly will have normal intelligence. There is no treatment for microcephaly that can return a child's head to a normal size. Children with microcephaly are usually evaluated by a pediatric neurologist and followed by a medical management team that can include therapists and early interventionists.²

Poor Fetal Growth: This is when baby is measuring smaller than normal for its

gestational age. This can also be called intrauterine growth restriction (IUGR). This can happen at any time during the pregnancy. Poor fetal growth increases the chance that the baby will need a C-section delivery and the chance for complications at birth such as a lack of oxygen or the baby swallowing some of its own feces. Babies with poor fetal growth also have an increased chance for motor and neurological disabilities and there is even a chance that the baby will die inside the womb before birth.³



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Congenital Heart Defect: This is a problem with the structure of the heart that is present at birth. The normal flow of blood through the heart can be slowed down, go in the wrong direction or wrong place or be blocked completely. Treatment for congenital heart defects can include monitoring, medicines, surgery and heart transplants. Serious heart defects usually are seen soon after birth or within the first few months of life. Less serious heart defects may not be seen until later in childhood. The heart starts to develop during the first 6 weeks of pregnancy, so a congenital heart defect can occur very early on in pregnancy. The long-term effects of a congenital heart defect include congestive heart failure, slower growth and development, heart rhythm problems, and strokes. Most children with congenital heart defects need lifelong follow up from a cardiologist.⁴

¹ Vockley, J., Anderson, H. C., Antshel, K. M., Braverman, N. E., Burton, B. K., Frazer, D. M., ... Berry, S. a. (2014). Phenylalanine hydroxylase deficiency: diagnosis and management guideline. *Genetics in Medicine: Official Journal of the American College of Medical Genetics*, 16(2), 188-200.

² Davis, Charles Patrick. (2014, Mar 31). Microcephaly Facts. In *Microcephaly*. Retrieved from <http://www.medicinenet.com/microcephaly/article.htm>

³ Intrauterine growth restriction. (2014, Nov 16). In *MedlinePlus online*. Retrieved from <http://www.nlm.nih.gov/medlineplus/ency/article/001500.htm>

⁴ Mayo Clinic Staff. (2015, Feb 28). Congenital Heart Defects in Children. In *Diseases and Conditions*. Retrieved from

Intellectual disability: This is when a child has below average intellectual function and a lack of skills needed for daily living. The baby's brain is continuously developing throughout the pregnancy and this can occur at anytime. Intellectual disability, which used to be called mental retardation, can range from mild to severe. Children with intellectual disability may have slow or no development of motor, language or self-help skills, problems keeping up in school, difficulty understanding and following social rules and failure to adapt. Children with intellectual disability have services such as early intervention therapies and special education in public schools available to help them reach their potential.⁵



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Summary: These birth defects can occur right at the beginning of pregnancy. Some women don't even know they are pregnant and the baby's heart has already developed! This means it is really important that mom has control of her phenylalanine levels even before she gets pregnant. These effects that can be seen in maternal PKU syndrome can happen on a spectrum. Some babies can be severely affected and others can have more mild effects. Any

<http://www.mayoclinic.org/diseases-conditions/congenital-heart-defects/basics/definition/con-20034017>

⁵ Intellectual disability. (2013, May 10). In *MedlinePlus online*. Retrieved from <http://www.nlm.nih.gov/medlineplus/ency/article/001523.htm>

effect, mild or severe, will have long-term consequences for the child. Women with PAH deficiency can have healthy babies by keeping their phenylalanine levels in the recommended range! **Maternal PKU syndrome is preventable!**

Advice from Parents

Explain that maternal PKU is just that they have PKU and they have to monitor their levels very closely and make an analogy of someone who has to be very careful about what they eat

It is just an extension of a healthy way of life

I look at the decisions about PKU as being similar to the decisions about alcohol, drugs and smoking. You give the information and whether or not you like your child's choice it is their decision to make as an adult

Teach her early about the importance of diet compliance and healthy pregnancies

Be open and non judgmental

Be positive about their chance for success

Just keep at it! The more you bring it up at different times they are going to hear you

Do it! Don't be afraid, the sooner the better!

Resources for Parents

- ✓ **The National Society for Phenylketonuria:** www.nspku.org
- ✓ **National PKU Alliance:** www.npkua.org
- ✓ **Mother to Baby:** <http://www.mothersobaby.org>
- ✓ **Maternal PKU Support:** maternalpku.weebly.com
- ✓ **PKU.com:** www.pku.com