EVALUATION OF DIET QUALITY IN CHILDREN AND ADOLESCENTS WITH PRADER-WILLI SYNDROME USING THE HEALTHY EATING INDEX-2010

by

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STATEMENT OF THESIS APPROVAL

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ABSTRACT

Nutrition management is crucial to the health of children and adolescents with Prader-Willi syndrome. However, minimal evidenced-based information is available to provide health care professionals with specific nutrient-based recommendations and guidelines for assessing diet quality for individuals in the Prader-Willi syndrome population. With tight control of energy intake and maintenance of a healthy weight, lifespan can be that of a typically developing individual. Therefore, more research is needed on dietary quality in the Prader-Willi syndrome population.

This pilot study analyzed diet quality in children and adolescents aged 10-16 years with Prader-Willi syndrome (N=6). Diet recalls were collected using the Automated Self-administered 24-hour Recall (ASA24) system, developed by the National Cancer Institute. Diet quality was determined from the recalls using the Healthy Eating Index-2010 criteria. Descriptive statistics, including frequencies and means, were computed for demographic and socioeconomic information, food-related behaviors, physical activity levels, and Healthy Eating Index-2010 scores. The independent samples t-test was used to compare Healthy Eating Index-2010 mean total scores between the study participants and the 2007-2008 NHANES reference population.

The Healthy Eating Index-2010 mean score was significantly higher for the study participants with Prader-Willi syndrome, as compared to that of the 2007-2008 NHANES reference population (N=2703) (66.9 vs. 49.8, p<0.001). In summary, this study provides

preliminary data on the dietary quality of children and adolescents with Prader-Willi syndrome. Further research, with larger sample sizes, is needed to understand diet quality and potentially apply the information to optimize evidenced-based nutrition recommendations that promote appropriate growth outcomes for children and adolescents with Prader-Willi syndrome.

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INTRODUCTION

Background and Literature Review

Prader-Willi syndrome is a multifaceted genetic condition. It is the most commonly identified genetic cause of obesity. [1] The disorder results from abnormal methylation or a deletion on chromosome 15. The most common genetic alteration, present in about 70% of individuals with Prader-Willi syndrome, is a noninherited parental chromosome 15. [2] The next most frequent genetic alteration, present in approximately 25% of Prader-Willi syndrome diagnoses, is maternal uniparental disomy in which the child inherits two maternal copies of chromosome 15, and no paternal copies of chromosome 15. [2] The least common genetic alteration, present in less than 5% of individuals with Prader-Willi syndrome, is a result of a mutation during the imprinting process in the chromosome 15q11-q13 region. [2]

Prevalence of the disorder is estimated to range from 1 in 12,000 to 1 in 15,000 individuals. [3] Prader-Willi syndrome can be identified through clinical findings; however, genetic testing is necessary for a definitive diagnosis that rules out other disorders that may present similarly from a clinical perspective. [1] The age of diagnosis is continuing to decrease with greater awareness of the syndrome. Currently, most infants with Prader-Willi syndrome are diagnosed by three months of age. [4]

In infants, Prader-Willi syndrome presents as low muscle tone, or hypotonia, excessive sleepiness, a soft cry, and decreased feeding-related reflexes; these symptoms combined increase the risk for failure to thrive if appropriate intervention does not occur

in a timely manner. [1, 5]

Specifically, failure to thrive may result from an inability to suckle properly on a nipple or bottle to obtain adequate nourishment. [6] Intervention strategies include the use of fortified formulas, so the infants receive a higher concentration of calories per ounce of formula consumed, use of an adapted nipple, or placement of a feeding tube to bypass the issue of suckling difficulties. [6] Corrections for failure to thrive are crucial so the child's linear growth is not stunted.

The period of time when children with Prader-Willi syndrome are unable to obtain adequate nourishment is short-lived, however, and around age two, the same children are predisposed to obesity. [7] In addition to low muscle tone, children with Prader-Willi syndrome tend to be very lethargic and experience frequent fatigue, which combined further decreases energy requirements. [7] Between the age of one and two years, once the children are able to eat independently, they will frequently develop an insatiable appetite, or hyperphagia. [8] The onset of hyperphagia may manifest as an obsession surrounding food, a feeling of always being hungry, and food seeking and sometimes food stealing behaviors. This change in behavior may result in rapid weight gain, if the child's food intake is not closely monitored and controlled by parents, physicians, and dietitians. [5] Generally, all food in the child's environment must be locked up and controlled to prevent dangerous food seeking behaviors and binges by the affected child.[5] Other characteristics that are seen in children with Prader-Willi syndrome include hypogonadism and delayed puberty in males and females, cognitive delays, behavioral issues, short stature, and sleep apnea. [5]

Short-term studies show promising results for the use of growth hormone replacement therapy in patients with Prader-Willi syndrome. [9] For example, Festen et al.

reported a significant increase in height and lean body mass over two years of growth hormone treatment in male and female children aged 3-14 with Prader-Willi syndrome. [10] These results are encouraging because increases in height and lean body mass are generally associated with an increased basal metabolic rate. [11, 12] Furthermore, this association has also been observed in populations with Prader-Willi syndrome. [13] Anecdotally, the correlation between increased lean body mass and increased basal metabolic rate, as indicated by increased caloric needs per centimeter of height, has not always been seen in the Prader-Willi population managed by the Department of Pediatrics' Division of Medical Genetics at the University of Utah (S. Ernst, MPH, RD, oral communication, Oct. 2014). Therefore, nutrition management is crucial to the health of individuals with Prader-Willi syndrome to promote proper weight management through calorie restriction, behavior modification, and encouragement of a nutrient dense and overall high diet quality.

Diet quality is of particular importance in individuals with Prader-Willi syndrome due to the decreased energy requirements of this population. There is little room for empty calories on a calorie-restricted diet since the calories consumed need to provide the necessary nutrients the body requires for growth and maintenance. Individuals with Prader-Willi syndrome have a tendency to eat for purposes other than satisfaction of hunger and nourishment, as well as have difficulty in making independent food choices that are in line with recommended dietary guidelines. As a result, it is important that individuals with Prader-Willi syndrome receive the appropriate level of support necessary to consume a high quality, nutrient dense diet, in addition to assistance in complying with calorie restriction recommendations. [14]

An interdisciplinary approach is recommended for dietary management in Prader-

Willi syndrome.[9] This interdisciplinary collaboration includes the individual with the disorder, family members, the school system, and healthcare providers, including a dietitian. As in many medical conditions, prevention is the best medicine, and assisting these children in maintaining a healthy weight from the start, rather than focusing on weight loss, reduces the burden on the entire support team and the child.[15] Once a child enters school, further challenges can present. In addition to creating an Individualized Education Plan or 504 Accommodation Plan for the child, steps such as not allowing any food in the classroom so that the child is able to concentrate on the lessons and having set meal expectations throughout the day are recommended.[15]

Specifically, the role of the dietitian in the interdisciplinary team is to estimate energy requirements, provide guidelines on environmental control and food access, counsel on a reduced calorie diet, and identify and recommend behavior management techniques.[9] Currently, estimated energy needs for children with Prader-Willi syndrome are set based on whether weight loss or weight maintenance is necessary to promote a healthy weight and decrease the risk of comorbid conditions. If the child's weight indicates a need for weight loss, recommendations are set at eight to nine calories per centimeter of height, while a child aiming for weight maintenance would have calorie recommendations ranging from ten to eleven calories per centimeter of height.[16]

The families and support teams of children with Prader-Willi syndrome receive education on counting calories, making appropriate food choices, maintaining diet records, and weighing their children weekly. These records are then shared with the dietitian, who personalizes the estimated energy needs in regards to the relationship between the calorie count, nutrient analysis, and growth trends. Maintenance of diet records can be further complicated by the cognitive delays and food sneaking behaviors

that are commonly present in Prader-Willi syndrome. [15] These behaviors may create difficulties for families to accurately capture everything a child is eating throughout the day.

The dietitian and other health professionals also work with families to create an environment that offers healthy cues for the child with Prader-Willi syndrome. A sense of food security can be greatly beneficial to children within this population. Due to the constant sense of hunger, knowing set meal times, as well what foods they will be eating, can help in controlling negative food-related behaviors. Having menus visually displayed can also aid in creating a sense of security and decreasing anxiety for the child.

The selection of the most appropriate method to track growth in the Prader-Willi syndrome population is controversial. [17] Two sets of growth charts are available specifically for children with Prader-Willi syndrome: One set for children aged birth to thirty-six months and the second set for children and adolescents aged three to twenty-four years. However, the growth charts for older children and adolescents were developed using fewer than 100 individuals. [18, 19] Additionally, there is discussion whether comparisons of growth within a population of children with Prader-Willi syndrome is the best indicator of appropriate growth, because the typical growth pattern in a child with Prader-Willi syndrome is not necessarily healthy. [17] The current recommendation is to utilize the Centers for Disease Control and Prevention (CDC) growth charts when plotting the growth of children with Prader-Willi syndrome. [20] This recommendation is in line with the Academy of Nutrition and Dietetics recent position statement to "use evidence-based protocols for typically developing youth…to promote appropriate growth velocity and prevent excessive weight gain." [14]

Individuals with Prader-Willi syndrome are likely to go through a series of phases

in which their nutrition therapy needs will change. New research indicates that children with Prader-Willi syndrome may transition through up to five phases throughout their lifetime in which their nutritional needs change. [8] As described earlier, the two primary nutritional phases include: 1) feeding issues and failure to thrive during infancy and 2) an insatiable appetite, food seeking, and excessive weight gain unless intervention occurs, for the remainder of life. [15]

In 2011, Miller et al. redefined the stages that individuals with Prader-Willi syndrome progress through over the lifespan. [8] Researchers concurred that the first phase of the syndrome is failure to thrive in infancy, but then divided the following years into four distinct nutritional phases, all of which have different implications for clinical management. The second phase identified typically begins around age two, and is associated with an increase in weight correlating with improved eating skills and increased appetite. By age four, a heightened interest in food typically develops and the children tend to become obsessive about food. Body weight can quickly increase if food intake is not carefully managed.

At approximately eight years old, children typically enter phase three. This phase is associated with an insatiable appetite and constant desire to eat large quantities of food. During phase three, food-seeking behaviors can become an issue due to increased food-related restrictions. In food seeking, children may resort to scavenging through the garbage looking for food, eating nonfood items, stealing money to purchase food, and even breaking in and stealing food from neighbors. If not closely supervised, it is very likely that a child will have excessive weight gain leading to obesity during this nutritional phase, and as a result have increased risk of developing comorbidities such as diabetes, sleep apnea, gastroparesis, and cardiovascular disease. All individuals with

Prader-Willi syndrome do not attain phase four described in the research. In this phase, the individuals develop and maintain more independent control of their diet, as well as recognition of satiety after consuming a calorically appropriate amount of food. Since the majority of people with Prader-Willi syndrome will not progress to phase four, it is usually necessary for people with this disorder to have external food restrictions and a strong support system in place for their entire lives to prevent unhealthy weight gain. [8]

Significance of Problem

Minimal evidenced-based information is available to provide health care professionals with specific nutrient-based recommendations for individuals with Prader-Willi syndrome. Miller et al. defined a well-balanced diet as approximately 30% of calories from fat, 45% of calories from carbohydrates and 25% of calories from protein. [21] In an intervention trial, Miller et al. found that a diet of this composition in addition to reduced energy intake resulted in a reduction of fat mass and body mass in children aged two to ten years with Prader-Willi syndrome compared to a group that adhered solely to the reduced energy intake recommendations. [21] The researchers did encourage fiber intake of at least 20 grams per day, but beyond macronutrient distributions, there did not appear to be a significant emphasis on diet quality components, such as quantity and variety of fruits or vegetables. [21] Of note, the participants self-selected their group for the purpose of the study, so the results may have been skewed by factors such as parental motivation, education, and access to nutrition information, that potentially led participants to choose to participate in the well-balanced diet intervention group.

To note, there is no information in the Academy of Nutrition and Dietetics' Evidence Analysis Library on Prader-Willi syndrome. Furthermore, information in publications from the Academy of Nutrition and Dietetics on Prader-Willi syndrome is

limited to small snapshots of estimated energy requirements.[22] Generally, these publications focus on assisting parents with limiting calories; however, diet quality is of particular importance for this population. With tight control of energy intake and maintenance of a healthy weight, lifespan can be that of a typically developing individual.[5] Therefore, more research is needed on appropriate diet assessment and recommendations to assist health care providers in delivering evidenced-based nutrition recommendations in this population.

Purpose of Research

The purpose of this study was to assess diet quality in individuals with Prader-Willi syndrome using the Healthy Eating Index-2010.

The specific aims for the research were:

(1) To analyze two, 24-hour recalls from individuals with Prader-Willi syndrome aged eight to 17 years and calculate corresponding Healthy Eating Index-2010 mean scores to determine if a significant difference in scores exists based on BMI classification.

(2) To evaluate if there is a difference in diet quality as measured by the Healthy Eating Index-2010 mean scores between the sample population of individuals with Prader-Willi syndrome and a reference population aged two to 17 years from the National Health and Nutrition Examination Survey (NHANES) in 2007-2008.[23]

For the first specific aim, we hypothesized that the Healthy Eating Index-2010 mean score would be higher in the sample of participants with a healthy BMI, as compared to participants with a BMI $\geq$85th percentile. This hypothesis was derived from the Healthy Eating Index-2010 inclusion of components from the Dietary Guidelines for

America, which focuses on the maintenance of a healthy body weight. [24, 25] The null hypothesis for this research aim was that there would not be a significant difference in Healthy Eating Index-2010 mean scores between the participants with a healthy BMI and participants with a BMI $\geq 85^{th}$ percentile.

For the second specific aim, we hypothesized that the Healthy Eating Index-2010 mean score would be higher in the sample population with Prader-Willi syndrome, as compared to the NHANES reference population. The null hypothesis for specific aim two was that there would not be a significant difference in Healthy Eating Index-2010 mean scores between the research participants with Prader-Willi syndrome and NHANES reference population.

METHODS

Healthy Eating Index

The Healthy Eating Index-2010 is a dietary assessment tool used to measure diet quality. [26] The tool was developed by the United States Department of Agriculture and the National Cancer Institute to assess the extent to which diets conform to the recommendations set forth in the 2010 Dietary Guidelines for Americans. The Healthy Eating Index-2010 total score is the sum of component scores, with a maximum of 100 points. The Healthy Eating Index-2010 has twelve components: nine that assess nutrient adequacy and three that address moderation. Higher scores indicate greater compliance with the 2010 Dietary Guidelines. [26]

The Healthy Eating Index-2010 was chosen as the analysis tool to measure diet quality in this research study for multiple reasons. First, individuals with Prader-Willi syndrome generally require a low-calorie diet to maintain a healthy weight. Many diet quality analysis tools are based off of number of servings of a food per day, whereas the Healthy Eating Index-2010 analyzes the diet by amounts of food per 1,000 calories. This feature allows a high quality, but low calorie diet to still fall into a high level of quality. Utilizing the Healthy Eating Index-2010 to evaluate the diets of the research participants put the emphasis on nutrient density in the limited amount of calories that a person with Prader-Willi syndrome should consume. Second, the Healthy Eating Index provided an objective, quantitative measure of diet quality, rather than a more subjective alternative. [26]

Research Design

This research is a cross-sectional pilot study assessing diet quality in children and adolescents with Prader-Willi syndrome. It provides an explorative and descriptive comparison of diet quality between the study participants with Prader-Willi syndrome and the 2007-2008 NHANES reference population.

As an overview, diet recalls were collected using the Automated Self-administered 24-hour Recall (ASA24), developed by the National Cancer Institute, Bethesda, MD. [27] Diet quality was determined from the recalls using the Healthy Eating Index-2010 criteria. The Healthy Eating Index-2010 mean score obtained from the research participants was compared to the mean score identified from the 2007-2008 NHANES reference population. [23] The study protocol was approved by The University of Utah Institutional Review Board for Human Subjects.

Participant Selection Criteria

The participant inclusion criteria included a diagnosis of Prader-Willi syndrome and age between eight to 17 years. Medical records were mined for verification of the Prader-Willi syndrome diagnosis via health professional report. Participants were not recruited for the study if a secondary diagnosis of another genetic condition was present. The minimum age of eight for inclusion in the research was based on the findings that by age eight, most children with Prader-Willi syndrome have developed food seeking behaviors and difficulties with appetite regulation, in addition to weight gain. [8] Additionally, the individual completing the diet recalls on behalf of the research participant needed to be literate in English. Individuals with a BMI $<5^{th}$ percentile were excluded from the study due to underweight weight status. For the purpose of this study, the interest was in a comparison between individuals with a BMI in the healthy weight

range to those individuals with a BMI in the overweight or obese category.

Regarding recruitment, a convenience sample of potential participants was identified through the Prader-Willi syndrome interdisciplinary clinic hosted by the Department of Pediatrics' Division of Medical Genetics at the University of Utah. Patients aged 8-17 years in the clinic were invited to participate in this research study. Once identified, the individuals and their parents or legal guardian were mailed a packet that provided the information necessary to participate in the research study, including the consent form. The packets were addressed to the parent or guardian of the participant being recruited. Written and informed consent was obtained from one or both parents and/or legal guardians of participants aged 18 years and younger according to the University of Utah Institutional Review Board (IRB) policy and utilizing the Parental Permission and Authorization Document Template provided by the IRB. A $20 gift card to a movie theater was offered as an incentive for those that completed all parts of the study.

Data Collection

Participant Questionnaire

A questionnaire was included in the initial packet mailed to participants, with a prestamped envelope to return the questionnaire included. It was divided into 8 sections, with a total of 28 questions. The questionnaire was completed by the parent or guardian to obtain participant information on their child's diagnosis, food behaviors commonly associated with Prader-Willi syndrome, and growth hormone therapy treatment, as well as household sociodemographic data (Appendix A).

The diagnosis section was included to give the parent, guardian, or caregiver the opportunity to confirm that the participant has received a diagnosis of Prader-Willi

syndrome. The diagnosis section also inquired about the age that the participant received a diagnosis of Prader-Willi syndrome, as well as what type of chromosome 15 mutation or deletion the child has, if known. Information on historical and present use of growth hormone therapy by the participant was determined via self-report in the participant questionnaire.

Food behavior data for the participant with Prader-Willi syndrome were collected from the parent or guardian in the participant questionnaire. This three-item section gathered information on food-related behaviors commonly seen in individuals with Prader-Willi syndrome, including food foraging, such as food obsessions and hoarding; food sneaking or stealing; and pica-type behavior, or eating nonfood items, such as pet food or items in the garbage, as well as space for the parent or guardian to provide any additional information or explanation they believed was pertinent in this section. [9]

Household information was collected to address potential socioeconomic differences between participants, which may have impacted diet quality. Previous research has established that age, gender, race/ethnicity, household income, and education are determinants of food intake. [28, 29]

Physical Activity Questionnaire

Physical activity data were gathered for participants using the International Physical Activity Questionnaire (Appendix B), which the parents completed. This hardcopy questionnaire was included in the mailing with the consent form and participant questionnaire, and returned in the provided envelope. The questionnaire included items on frequency, duration, and intensity of physical activity over a seven-day period. [30]

Diet Recalls

Parents and guardians were asked to complete two, 24-hour recalls on behalf of their child to include one weekday and one weekend day within the allotted time period. Dietary intake data were collected in entirety using the ASA24 system.[27] ASA24 is a multipass, validated[31, 32] system developed for research participants and patients in a clinical setting to be able to complete a thorough and detailed diet recall. The recall system was designed to be completed by the person the food intake was being collected for, however, due to the cognitive delays in the population of interest, the parent or guardian completed the recalls for the child or adolescent. In addition to the multiple questions it asks the person completing the recall, it also provides over 1,000 pictures to help with identification of serving sizes. Information on supplement intake was not collected in this study.

In the initial packet mailed to participants, information was provided on how to access and use the ASA24 system. Every research participant was provided with a unique username and password to login into the ASA24 system. The username also served as the participant ID throughout the study, so the collected data were not connected with names. Participant dietary intake data were connected to their username, making it possible to link dietary intake from ASA24 to the hardcopy questionnaire data.

To prevent participant selection bias based on Internet access and computer literacy, the parent or guardian had the option to complete the recalls using a local clinic, library or university computer with assistance by the researcher as needed. No one in this study chose this option, but rather completed the recalls on personal computers with assistance from the research team via email as necessary.

A diet record form was also included in the information packet since the study

participants were of school age. The diet record form was accompanied by instructions on how to complete the form. Specifically, the form was designed for teachers or caregivers to record dietary intake when the study participant was not with the parent or guardian, such as at school or daycare. The intended use of the diet record, as communicated to parents and guardians, was to assist in the collection of information related to food intake in their absence, so they had the necessary information to thoroughly complete the diet recall using the ASA24 system.

Statistical Methods, Data Analysis and Interpretation

Descriptive statistics, including frequencies and means, were computed for demographic and socioeconomic information, food-related behaviors, physical activity levels, and Healthy Eating Index-2010 scores. Income data were converted to a percent of the federal poverty line, [24] according to the 2015 Federal Poverty Guidelines. This calculation accounted for household income and family size. [33]

The dietary recalls were analyzed to compute the Healthy Eating Index-2010 score. The ASA24 output was in the form of energy, nutrients, and food groups (MyPyramid Equivalents). Individual scores for each of the twelve components were calculated and then summed for an overall Healthy Eating Index-2010 score. The generation of scores was conducted using the SAS ® software's capabilities (SAS, University Edition for OS X, 2014). The SAS code was provided through ASA24 for calculating HEI–2010 scores per person when multiple days of ASA24 data are available for each individual.

The hypothesis that Healthy Eating Index-2010 mean scores in the participants with Prader-Willi syndrome would be higher in individuals with a BMI in the healthy range than individuals in the BMI $\geq 85^{th}$ percentile was not tested due to the inadequate

sample size to make within-group comparisons.

The hypothesis that there would be a significant difference in Healthy Eating Index-2010 mean scores between the research participants and the NHANES reference population was tested using an independent samples t-test. A mean Healthy Eating Index-2010 score was calculated for the research participants and compared to the mean Healthy Eating Index-2010 score of 49.8 obtained from the 2007-2008 NHANES participants. [23] An independent samples t-test analysis was completed using SPSS (IBM SPSS version 22.0, Armonk, NY, 2013), with significance set as $p < 0.05$. Standard error data were not published for the 2007-2008 NHANES participants. However, standard error would be expected to decrease as sample size increased, so the standard error value for the reference population is likely smaller than in the sample group.

RESULTS

Participant Questionnaire Data

Based on the study inclusion and exclusion criteria, individuals (*N*=23) were mailed information regarding participation in the study using the contact information in their electronic medical records. Of these, four packets were returned due to incorrect addresses, resulting in 19 individuals being recruited for the study. Consent forms were received from parents or guardians of seven of the original 19 individuals. All components of the study, including returning the consent form, participant questionnaire, physical activity questionnaire, and both 24-hour recalls, were completed for six participants. The participant questionnaire and physical activity form were also completed for one other participant, however, this family did not complete the diet recalls due to time constraints. The final study response rate was 37%.

The six participants ranged in age from ten years nine months to 16 years, with an average age of 12 years four months. Four of the participants were female and two were male. All participants identified as Caucasian, non-Hispanic. Regarding parental education level, all parents of the six participants had obtained at least a Bachelor's degree, with five of the 12 parents at the Master's, Professional, or Doctorate degree level. The average household income was $100,333, with household size ranging from five to eight individuals. The average income for the six families was 282.9% of the poverty line, calculated using the federal poverty guidelines. No families recorded incomes below the federal poverty line.

The average age of diagnosis for participants in the study was three months old, with a range in diagnosis age from one month to seven months. Parents or guardians self-identified the chromosome 15 abnormality resulting in Prader-Willi syndrome in the participant questionnaire. Three identified the cause as a deletion on chromosome 15, two identified maternal uniparental disomy as the cause, and one parent was unsure. Regular, long-term use of growth hormone therapy was indicated for all participants.

All of the participants had BMI percentiles in the overweight or obese ranges based on their age, height, and weight information from the electronic medical records. Two individuals had BMIs at the 89th percentile in the overweight range, and the other four participants had BMIs ranging from the 96th percentile to greater than the 99th percentile in the obese range.

On the questions related to food behaviors, parents or guardians were able to mark whether their children engaged in the specified behavior daily, weekly, rarely, or never. Regarding food foraging, five of the six participants typically engaged in food foraging, obsessions, and hoarding daily, while the other participant engaged in food foraging on a weekly basis. There were varied responses regarding the amount of food sneaking or stealing amongst the individuals in the study; half of the parents indicated that their children sneak or steal food daily or weekly, while the other half of respondents indicated that their children rarely sneak or steal food. The last food behavior question addressed the frequency of pica behavior, or eating of nonedible items. One parent responded that their child experiences this daily, specifically eating hair. The other four responses specified that their children rarely or never have pica behaviors. The food behavior data are displayed in Figure 1.

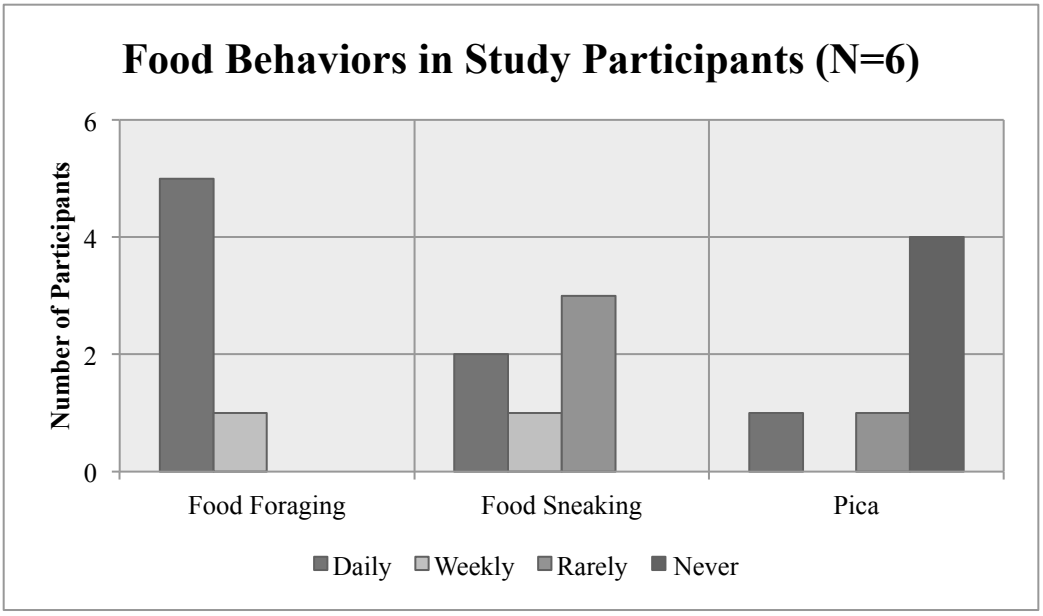

Figure 1. Results from participant questionnaire data related to common food-related behaviors in children and adolescents with Prader-Willi Syndrome.

Physical Activity Data

Physical activity data were assessed using the flow chart algorithm for the analysis of International Physical Activity Questionnaire (IPAQ) short form (Appendix C). Using this protocol, four participants had physical activity recorded in Category 1: Inactive, while two participants had physical activity recorded in Category 2: Minimally active. To be categorized as minimally active, participants had to meet one of the following physical activity criteria during the previous seven days: (1) Three or more days of vigorous activity of at least 20 minutes per day, (2) Five or more days of moderate-intensity activity or walking of at least 30 minutes per day, or (3) Five or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of at least 600 MET-min/week. The four individuals categorized as inactive did not have a combination of the frequency, duration, and intensity of physical activity to meet the minimal activity requirements. No participant in this study met the activity requirements for the Health-Enhancing Physical Activity (HEPA) category.

Diet Recall Data

Two, 24-hour diet recalls were completed for each of the six participants for a total of 12, 24-hour recalls. The average daily caloric intake for all study participants was 1947 ± 409 kilocalories. The average Healthy Eating Index-2010 score was 66.9 ± 11.8. The individual Healthy Eating Index-2010 scores ranged from 51.2 to 79.5. All of the participant scores were higher than the average Healthy Eating Index-2010 score for the 2007-2008 NHANES reference population of 49.8. [23] Using the standard error found for the current study participants (*N*=6) as the standard error value for the reference population (*N*=2703) as well, a significant difference was found in diet quality between the two groups. The difference between average Healthy Eating Index-2010 scores for

the study group (N =6) and the reference population (N =2703) was significant (p<0.001), with power >80%.

The twelve individual components of the Healthy Eating Index-2010 were compared between the study participants and the reference population. A higher score in each of these categories indicates greater compliance with the 2010 Dietary Guidelines. Figure 2 illustrates the between group comparisons for the nine adequacy components of the Healthy Eating Index-2010. The sample population had higher scores in five of the categories, comparable scores in three categories, and a lower average score in one category.

Standard error data were also not published for the individual component scores for the NHANES reference population. However, using the standard error found for the current study participants (N =6) as the standard error value for the reference population (N =2703) in corresponding categories, a significant difference was found between groups for the total vegetables category (p=0.001), the whole grains category (p=0.006), the seafood and plant protein category (p=0.0145), the fatty acids category (p=0.003), the refined grains category (p=0.0001), and the empty calories category (p=0.0185). In all of these categories, the current study group had higher scores than the reference population.

Figure 3 depicts the comparison between the average Healthy Eating Index-2010 scores of the study participants and the reference population for the three moderation components of the index. For these three areas, there is an inverse relationship between scores and intake, where a higher score indicates lower intake. The study participants had higher scores in all three of these categories, with the most notable differences in the refined grains and empty calories categories, where the participants obtained an average

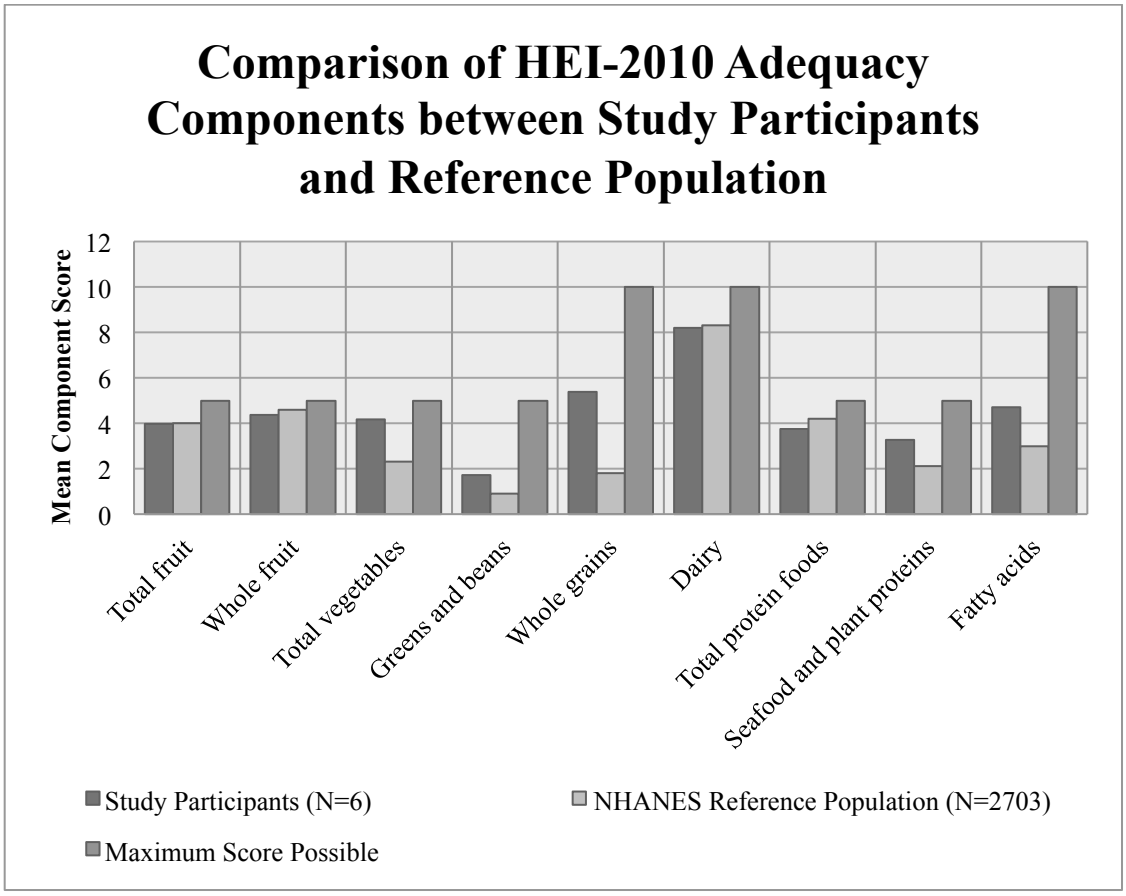

Figure 2. Data represent a comparison of mean scores between the study participants and the 2007-2008 NHANES reference population for the adequacy components from the Healthy Eating Index-2010. Data source. [23]

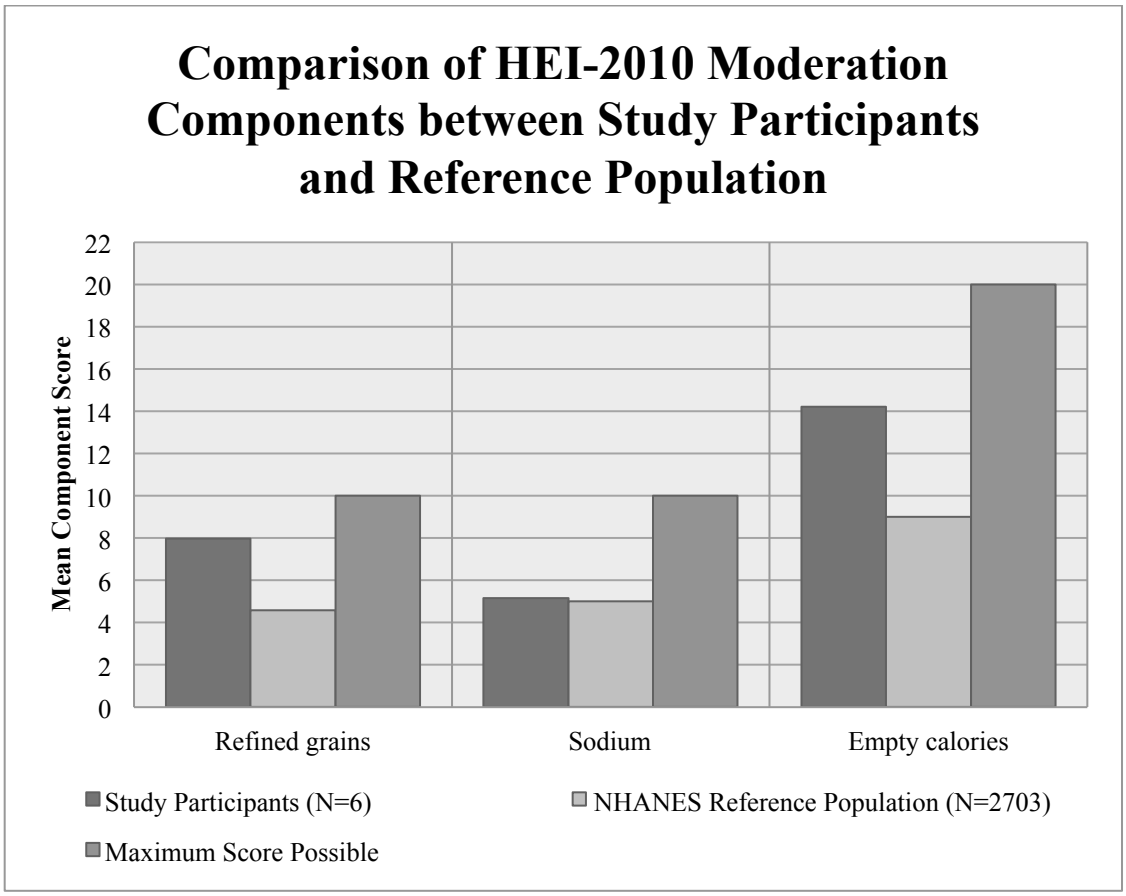

Figure 3. Data represent a comparison of mean scores between the study participants and the 2007-2008 NHANES reference population for the moderation components from the Healthy Eating Index-2010. Data source. [23]

of 80% and 71% of the maximum possible points, respectively.

The participant data were also compared to the macronutrient distribution ranges recommended by Miller et al. that were found to improve body composition in children and adolescents with Prader-Willi syndrome.[21] The specific recommendations are 25% of calories from protein, 30% of calories from fat, and the remaining 45% of calories from carbohydrates, as well as a minimum of 20 grams of fiber per day.[21] The comparison of the study participants' macronutrient distributions is shown in Figure 4. The average fat percentage from study participants of 28% of calories from fat was in line with the recommendations; however, carbohydrate intake was much higher than the recommendation with an average of 59% of calories from carbohydrates, and the protein intake was much lower with only 15% of calories coming from protein. The study participants had an average daily fiber intake of 20 grams, which meets the minimum recommendation for fiber intake set in the comparison research study.

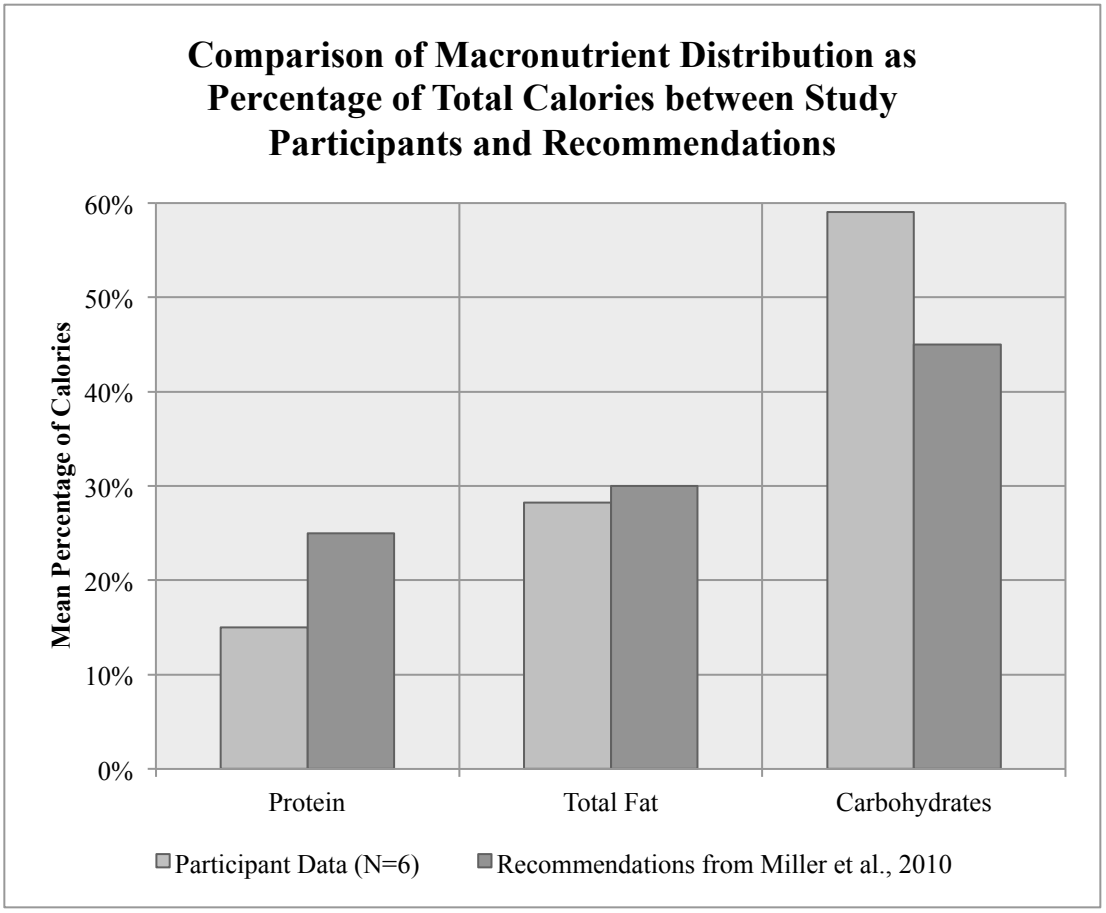

Figure 4. A comparison of the macronutrient distribution for the calories consumed in the study group compared to recommendations in the literature. Data source. [21]

DISCUSSION

Overall, the study participants were a relatively homogenous group, with similar racial/ethnic background, age, socioeconomic status, age of Prader-Willi syndrome diagnosis, and history of growth hormone therapy. Additionally, all of the parents reported that their child with Prader-Willi syndrome frequently experienced food foraging, obsessions, and hoarding. However, there was considerable variation in reports of food sneaking and stealing amongst participants. Other research identified that 87% of children with Prader-Willi syndrome (N =31) had a strong tendency toward food obsessions. [34] This same study also found variation in the frequency of food sneaking and stealing. Interestingly, the researchers reported that children with a deletion on chromosome 15 were more likely to steal and sneak food than children with maternal uniparental disomy. [34] For the current study, there was minimal pica behavior reported among the participants. This finding corresponds to other reports that the prevalence of pica in individuals with Prader-Willi syndrome ranges from 9%-25%. [35]

Regarding physical activity, study participants were all inactive or minimally active throughout the week, with much of the physical activity time occurring during recess at school. Also, many of the parents indicated that their child was sedentary for the majority of the day. The current findings are in congruence with previous research that children with Prader-Willi syndrome have a tendency toward an inactive lifestyle. [36] Furthermore, the low physical activity levels observed are likely due to the frequent fatigue experienced by this population, as well as the low muscle tone, which both make

physical activity challenging. [36]

Due to the similarities between participants, as well as the small sample size, the information collected from the participant questionnaire and physical activity form were not controlled for in the diet analysis. Additionally, the small sample size did not allow for within group comparisons of anthropometric outcomes related to diet quality for the study participants.

Previous research reported that parents of children with Prader-Willi syndrome might over restrict their child's diet, leading to inadequate intake of fat. [37] Our finding of the low protein intake of participants, as shown by the Healthy Eating Index-2010 total protein component and macronutrient distribution, may have a similar foundation. Increasing the protein in the diet would result in a higher Healthy Eating Index-2010 mean score for this group. These study findings are in congruence with previous recommendations that evaluation of dietary intake by a dietitian is an important factor in ensuring diet quality in individuals with Prader-Willi syndrome. [37]

While protein intake for the study participants was low in comparison to the Miller et al. recommendations [21], as well as an average total protein score of less than 80% of the maximum for the Healthy Eating Index-2010, the participants' protein intake did meet the Dietary Reference Intake (DRI) for protein. [38] All participants met the grams per day DRI based on individual age and gender. [38] The average group protein intake was also within the Acceptable Macronutrient Distribution Range of 10% to 30% for protein listed in the DRIs. [38] This information furthers the point that more research is necessary to determine the most appropriate nutrient recommendations in children and adolescents with Prader-Willi syndrome.

Overall, study participants with Prader-Willi syndrome had a significantly higher

average Healthy Eating Index-2010 score than the NHANES reference population. This outcome corresponds with the initial hypothesis. There are many factors that could potentially explain the higher diet quality for the study participants than the reference population. From infancy, families of children with Prader-Willi syndrome typically meet regularly with a dietitian and receive nutrition education as part of recommended interventions with healthcare providers.[9] It is unlikely that the majority of children and adolescents in the reference population have had as frequent of contact with nutrition professionals. Additionally, there was a marked difference between groups in the component scores related to empty calorie consumption. Due to tight calorie restriction recommendations, there is simply not as much room for empty calories within the diet of a child with Prader-Willi syndrome, while still maintaining energy balance. Another possible contributing factor to the difference in scores between groups is the increased supervision and controlled food environment that are necessary for children with Prader-Willi syndrome.[9]

An additional consideration is the average household income of $100,333 for study participants. In an analysis of Healthy Eating Index-2010 scores for the adults in the 2007-2010 NHANES samples, there was a significant interaction between food costs and diet quality.[39] Lower energy-adjusted diet costs were associated with lower Healthy Eating Index-2010 scores, due to the insufficient intake of foods in the adequacy categories and higher consumption of foods contributing to the moderation components.[39] Therefore, the high mean household income observed in the current study group could have contributed to the higher diet quality observed.

The sample size of six is a study limitation. Due to the small number of participants, it was not possible to calculate Healthy Eating Index-2010 mean scores for

age, gender, or BMI subgroups.[40] Additionally, the homogeneity of the participants in terms of household income, parental education levels, race and ethnicity, and age limit the ability to generalize the study findings. Another factor that potentially impacts our findings is that all of the participants were recruited from the Prader-Willi syndrome interdisciplinary clinic at the University of Utah. As a result, all of the study participants resided in the Rocky Mountain region. Furthermore, diet recall data in the study were self-reported, which frequently results in an underestimation of usual intake.[37] Moreover, the use of two, 24-hour recalls likely does not capture the usual, long-term dietary intake for the study participants.[37] While this is a limitation, it is an improvement over many studies that use a single 24-hour recall to calculate Healthy Eating-2010 scores.[40] Given that this is a pilot study, the information gathered from this research can potentially be used to guide future research using larger sample sizes.

The current study provides preliminary data for evaluating diet quality in children and adolescents with Prader-Willi syndrome, with the prospect that future research in this area may enhance the current limited evidenced-based nutrition recommendations in this population. In particular, future research in this area may inform dietitians and other health care providers on ways to improve diet quality while adhering to the necessary caloric restrictions in this population. For instance, fruit, vegetable, and whole grain intakes were adequate on average amongst study participants, while total protein intake was considerably lower in comparison to the reference population, as well as the macronutrient recommendations set by Miller et al.[21] These data could be used to guide dietitians in providing increased nutrition education on protein sources that fit well into the calorie restricted diet, while still maintaining the other aspects of diet quality.

Further research assessing diet quality could include an intervention study in

which a pre- and postanalysis of Healthy Eating Index-2010 scores are obtained for children and adolescents with Prader-Willi syndrome. The intervention could provide further emphasis stressing the importance of diet quality and appropriate macronutrient distributions, while maintaining the required calorie restrictions during the nutritional phases where overeating is likely to occur. An experimental study of this design could also assess for potential changes in BMI and body composition following the intervention. Body composition could be assessed using a variety of methods including dual-energy X-ray absorptiometry (DXA) scans and bioelectrical impedance analysis. Furthermore, it would be beneficial to see the impact of diet quality on bone mineral density through the use of DXA in the Prader-Willi syndrome population since growth hormone therapy can result in decreased bone mineral density. [5]

Future clinical trials may benefit from including the Healthy Eating Index-2010 as the dietary analysis tool in a clinical setting for groups of individuals with Prader-Willi syndrome. The Healthy Eating Index-2010 score could be calculated from ASA24 data or from diet records to assess the effectiveness of a dietary intervention in the Prader-Willi syndrome population. Then, the score could serve as an informative tool to health care professionals to determine the effectiveness of an intervention that was offered to a group of patients. This approach could translate into more research-based and effective interventions being offered to patients with Prader-Willi syndrome in hopes of improving dietary management and overall health. In summary, the Healthy Eating Index-2010 shows promise as a tool for monitoring dietary quality in the Prader-Willi syndrome population.

CONCLUSION

In this pilot study, the Healthy Eating Index-2010 mean score was significantly higher for the study participants with Prader-Willi syndrome, as compared to that of the 2007-2008 NHANES reference population. More research is necessary to understand the reason for this difference, as well as the use of these data in exploring diet quality in children and adolescents with Prader-Willi syndrome. Diet quality is an important factor as families address the calorie-restriction necessary for their child with Prader-Willi syndrome. Evidenced-based information is still needed for health professionals to be able to provide these families with the most appropriate information to promote healthy weight outcomes and reduce the risks of comorbidities.

APPENDIX A

PARTICIPANT QUESTIONNAIRE

Participant Questionnaire

Contact Information

Participant Name:

_____

_

Parent/Guardian/Caregiver's Name:

_____

Address:

_____

Diet Recall Submission

☐ I will submit diet recalls for 2 days online using the Automated Self-Administered 24-hour Recall tool. My login information is:

Username:

Password:

OR

☐ I would like to be contacted by the researchers to complete the diet recalls on a local clinic, library or university computer. I understand that the researchers will initially call me, and then we will discuss the schedule for the completion of the diet recalls.

General Information

Date of Birth: _____ Age: _____

Gender: ☐ Male ☐ Female ☐ Other

Diagnosis

Has the research participant been diagnosed with Prader-Willi Syndrome?

☐ Yes ☐ No

How old was the participant at diagnosis: _____

Type of Mutation/Deletion, if known:

Household Information

Highest Degree Received by Mother:

☐ Less than High School ☐ High School Diploma ☐ Bachelor's Degree

☐ Master's, Professional, or Doctorate Degree ☐ Unknown

Highest Degree Received by Father:

☐ Less than High School ☐ High School Diploma ☐ Bachelor's Degree

☐ Master's, Professional, or Doctorate Degree ☐ Unknown

Annual Household Income (to the nearest $1000):

_____

Number of People in Household (Please Circle):

2 3 4 5 6 7 8 Other (Specify): _____

Race/Ethnicity

Race: ☐ Caucasian ☐ African American ☐ Asian ☐ American Indian

☐ Other (specify)_____

Ethnicity: ☐ Hispanic ☐ Non-Hispanic

Food Behaviors

For this section, please report any food behaviors that your child experiences and the frequency to which they occur.

Food Foraging (food hoarding, food obsessions, etc.):

☐ Daily ☐ Weekly ☐ Rarely ☐ Never

Food Sneaking or Stealing: ☐ Daily ☐ Weekly ☐ Rarely ☐ Never

Pica (eating of non-edible items): ☐ Daily ☐ Weekly ☐ Rarely ☐ Never

Other pertinent information regarding food behaviors:

_____

_____

_____

_____

Growth Hormone Therapy

For this section, please report the research participant's growth hormone therapy:

Has the participant ever received growth hormone therapy? ☐ Yes ☐ No

If yes, what are/were the dates of use:

_____

Is the participant currently receiving growth hormone therapy?

☐ Yes ☐ No

If yes, what type: _____

Dose:_____

Length of current treatment:

_____

Other pertinent information regarding growth hormone use:

_____

APPENDIX B

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

SHORT FORM

Physical Activity Questionnaire

We are interested in finding out about the kinds of physical activities that your child does as part of their everyday lives. The questions will ask you about the time your child spent being physically active in the **last 7 days**. Please answer each question even if you do not consider your child to be an active person. Please think about the activities they do at school or work, as part of your house and yard work, to get from place to place, and in their spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that your child did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that your child did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did your child do **vigorous** physical activities like heavy lifting, running, aerobics, or fast bicycling?

   _____ **days per week**

   ☐ No vigorous physical activities → ***Skip to question 3***

2. How much time did your child usually spend doing **vigorous** physical activities on one of those days?

   _____ **hours per day** _____ **minutes per day**

   ☐ Don't know/Not sure

Think about all the **moderate** activities that your child did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that your child did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did your child do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

   _____ **days per week**

   ☐ No moderate physical activities → ***Skip to question 5***

4. How much time did your child usually spend doing **moderate** physical activities on one of those days?

   _____ **hours per day** _____ **minutes per day**

   ☐ Don't know/Not sure

Think about the time your child spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that your child

might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did your child **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking → ***Skip to question 7***

6. How much time did your child usually spend **walking** on one of those days?

_____ **hours per day** _____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time your child spent **sitting** on weekdays during the **last 7 days**. Include time spent at school, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did your child spend **sitting** on a **week day**?

_____ **hours per day** _____ **minutes per day**

☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

APPENDIX C

FLOW CHART ALGORITHM FOR THE ANALYSIS OF IPAQ

SHORT FORM

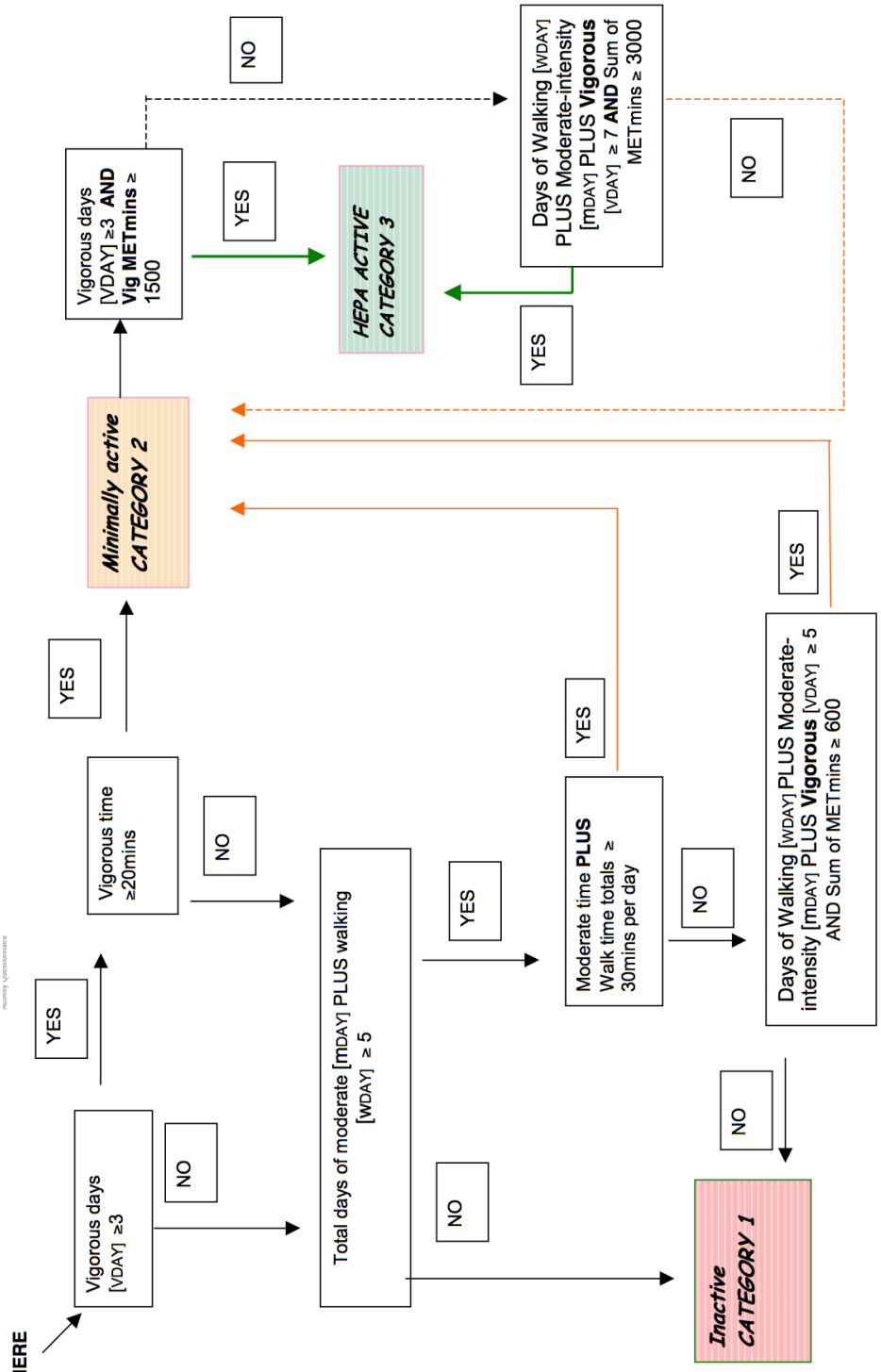

Figure 5. The flow chart algorithm for the analysis of IPAQ short form. Reprinted. [42] This flow chart was used to categorize the participants' physical activity into one of three categories based on the responses provided in the Physical Activity Questionnaire.

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