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Protocol Title **A study to assess change in weight over six months in Prader-Willi Syndrome**

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I. Objectives

The primary objectives of the study are:

1. Perform a real-world study of weight changes over 6 months in PWS children and adults aged 12 and over.
2. Study factors that could directly or indirectly affect weight change such as diet, medication, food access and environment.
3. Collect data on participant height change over 6 months to calculate body mass index (BMI)

II. Background and Introduction

Prader-Willi syndrome (PWS) is a complex neurodevelopmental disorder resulting from disruption of an imprinted region of chromosome 15 (15q11.2-q13). PWS has an estimated incidence of 1:15,000-1:30,000 births worldwide, and equally affects males and females of all ethnicities. PWS

is characteristically associated with feeding difficulties and failure to thrive in infancy and early childhood, followed by the development of excessive eating (hyperphagia), intense food seeking behavior, and morbid obesity. Additional features of PWS include poor muscle tone and strength (hypotonia), hypogonadism, osteoporosis, scoliosis, infertility, delayed motor and language development, impaired cognition, sleep abnormalities, behavioral challenges including tantrums, obsessive compulsiveness and skin picking, and psychiatric illness in adulthood. The phenotype exhibits a broad spectrum of severity.

The incidence and natural history of several PWS symptoms are poorly defined. Gathering data on these is essential not only to understand the development and severity of each symptom without relying on anecdotal evidence, but also to appropriately direct therapeutic efforts and clinical trials.

For this study, we will gather and analyze data on changes in body weight over a 6-month interval, roughly the time frame for a clinical trial, for individuals aged 12 and over to focus on age groups that are likely be recruited in hyperphagia trials. It has previously been shown that weight changes in PWS may depend on age-and nutritional stages (Miller et al 2011), however, larger datasets across different age groups, with frequent measurements, are required to fully understand real world data regarding weight gain and obesity in PWS.

Weight may also be influenced by living situation, diet, medication and access to food. Therefore, we will also survey participants on diet and medication changes and food access, and study the extent to which these may play a role in any observed weight change.

Participants will be recruited from the U.S. and Canada through patient advocacy websites, Facebook and email. Interested participants will sign an informed consent prior to enrolling in the study.

III. Study Design

- We will utilize a commercially available text messaging based clinical app called Mosio (HIPAA and CFR Part 11 compliant) to collect data. (www.mosio.com)
- We will recruit up to n=300 participants. We expect to be able to recruit this number over 1-2 months prior to data collection (6 months).
- The study is expected to last 9 months, with 2 months for recruitment and start up, and 7 months for data collection.
- Mosio will create “Storylines”- a series of questions/surveys, that will be sent at pre-scheduled intervals, as and when participants sign-up.

  Data to be collected:

1. **Initial Survey** at baseline only
   - Was PWS diagnosis made by blood test.
   - Gender
   - Age
   - Does the person receive growth hormone (GH) therapy? If yes, what age was therapy initiated? If no, were they ever on GH therapy? Age at initiation and how long were they on it.

- In the past 6 months, approximately how often did you weigh your child with PWS? daily, weekly, monthly, less than monthly, only at doctor visits.

2. **Weight**- Once a week, every week, for 6 months. Participants will be sent a pre-scheduled text message reminder to weigh in and send a text response with the participant's weight.
3. **Survey**-At 3 months and 6 months participants will answer a survey-

    1. Has there been any change in the living situation for the person with PWS in the last 3 months (example: moved, change in primary caregiver, illness in the family etc.? Y/N

    2. To your knowledge has access to food at home or outside the home increased/decreased/stayed the same for the person with PWS?

    3. Has the activity level in the last 3 months increased/decreased/stayed the same for the person with PWS?

    4. Has there been medication change in the last 3 months for the person with PWS? Y/N
    If yes-
    Please list drug- and select start/stop/increased dose/decreased dose. Will provide option to list more than one drug.

    5. Please record participant's height.

Data will be stored in a secure database. Researcher will be given a log-in and have access to patient data throughout the course of the study.

IV. Duration of study

Study is expected to last 9 months with 3 months for recruitment followed by 6 months of data collection.

V. Eligibility and Recruitment of Participants

a. Inclusion Criteria

Male and female individuals diagnosed with PWS, 12 years and older.

b. Exclusion Criteria
- younger than 12
- non-PWS

c. Sample Size
Target sample size is 300 participants for this study

d. Recruitment of Participants

Participants will be informed of the study via website and social media outlets. These include patient advocacy websites, email, and the Global PWS Registry.

VI. Process of Obtaining Consent

Submission of information by participant or their representative: Participants will be provided details about the study, which will be posted on patient advocacy websites, Facebook, email and other social media outlets. They will be provided contact information and given every opportunity to read, understand and ask questions about the study via electronic means or phone. A consent form will be created on SurveyMonkey and a link to the consent form will be included with recruitment materials.

If they wish to participate in the study, participants or their parent/representative will be directed to an electronic informed consent form where they will be asked to review and sign an informed consent. Individuals providing consent will be asked to confirm that s/he is the participant or legally authorized representative of the participant. Consent from a legally authorized representative is required for participants who are minors or who are over the age of 18 but unable to provide informed consent. Because individuals with PWS have some degree of intellectual disability, the ability to provide consent will depend on the cognitive ability of the individual.

A copy of the completed consent form will be made available to all participants.

VII. Data Analysis and Reporting

The following analyses are planned

1. Trends in weight and BMI change over 6 months.
2. Description of factors that could affect weight and BMI in this group, including food access, change in living situation, physical activity and medication.

VIII. Facilities and Performance Sites

This study will use mobile health technology. Interested participants will sign an informed consent and provide a mobile phone number on which they are able to send and receive text messages. FPWR will assign each participant a unique, random, study-related ID, not linked to any identifying information (eg. fpwr2018_001). Only this unique ID will be used on the Mosio platform. The key to the IDs will only be available to researchers associated with this study. Once registered, participants will receive text messages and surveys at pre-determined intervals on their mobile phones (discussed above) and will respond directly via text. Mosio will store all data on a secure server and provide investigators a login to the site. Only study personnel will be able to access the data.

IX. Potential Benefits

There is no direct benefit to the patient from participating in the study. As mentioned above, real-world studies are essential in PWS to understand the natural progression of the disease. At the end of the study, participants will receive a personalized chart detailing their weight progression over the course of the study.

X. Potential Risks, Discomforts, Inconveniences, and Precautions

Participation in the study presents minimal risks to its participants. The greatest risk is loss of confidentiality of personal health information.

XI. Risk/Benefit Analysis:

This is a minimal risk study without direct benefits to the individual. There are no risks of physical harm associated with participation in the study. While every effort will be made to keep data confidential there is a potential risk of a breach of confidentiality of medical information and associated privacy of the participants. This risk will be minimized by storing data on a secure server. Only authorized study personnel will have access to the data.

XII. Privacy and Confidentiality:

Participants' privacy and confidentiality will be safeguarded by using modern database management techniques and informed consent. Only authorized study personnel will have access to the data.
Data will be stored for up to one year after completion of the study. Deidentified data will be stored indefinitely.
Only de-identified information will be used for potential publications or sharing with the community.

XIII. Cost of Participation

There is no cost to participating in the study. Participants will be informed that they are responsible for any charges related to sending/receiving text messages on their mobile phones.

XIV. Payment for Participation

There will be no reimbursements made to participants.