Study Protocol Cover page

Title: Adaptation of an Evidence-based Interactive Obesity Treatment Approach (iOTA) for Obesity Prevention in Early Serious Mental Illness: iOTA-eSMI.

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GENERAL INFORMATION:

Title: Adaptation of an Evidence-based Interactive Obesity Treatment Approach (iOTA) for Obesity Prevention in Early Serious Mental Illness: iOTA-eSMI

Short Title: iOTA-eSMI

OBJECTIVES:

The main objectives of this study are:

Study Aims:

I) **Evaluate barriers and facilitators for intervention engagement, effectiveness and implementation, and identify needed adaptations of the prior iOTA for use in obesity attenuation in Early Serious Mental Illness (eSMI).** We will conduct multi-level provider, client, and caregiver focus groups and interviews within two Community Mental Health Centers (CMHC) systems – one in Missouri (MO), and one in Florida (FL) – to characterize qualitative factors relevant to intervention engagement, effectiveness and implementation within diverse care environments. Client and caregiver assessments will specifically characterize client-level determinants of intervention engagement.

II) **Adapt the prior iOTA for use in obesity attenuation in eSMI.** Using the multi-level qualitative data collected in Aim 1, we will adapt health coach visits and SMS messaging to maximize acceptability, engagement, sustainable reach and target engagement for eSMI. Key components of the adapted intervention will be reviewed with participants from Aim 1 to identify any additional needed adaptations.

III) **Conduct a randomized pilot and feasibility study of iOTA-eSMI in a diverse sample of adults with eSMI, comparing iOTA-eSMI to a health education control condition.** iOTA-eSMI will be piloted in a representative sample of 60 adults from MO and FL CMHCs with eSMI, randomizing participants 2:1 to 24 weeks (6 months) of iOTA-eSMI involving daily goal-specific text messaging and self-monitoring prompts, versus monthly health education control condition that includes weekly non-specific supportive text messaging. Both groups will then enter a 12-week continuation phase of text messaging only. We hypothesize favorable differences in weight change from baseline for iOTA-eSMI compared to control. Secondary analyses will assess effects on RDoC domains relevant to psychophysical skills and self-efficacy, exploring the relationship between weight change and target engagement. Feasibility, engagement and implementation challenges will be measured by i) enrollment & retention, ii) intervention acceptability, iii) text response rates, iv) visit adherence v) client expectations, vi) fidelity and vii) CMHC staff-rated acceptability, appropriateness and burden.

BACKGROUND AND RATIONALE:

Most obesity and related complications in serious mental illness (SMI) occur with chronic treatment. Behavioral interventions to reverse obesity in chronic SMI face challenges with long-term effectiveness and/or challenges with implementation and sustainability. There are no FDA-approved pharmacotherapies for obesity in SMI, and off-label treatments have limited effectiveness and/or serious adverse event risks. Using low-cost, simple digital health approaches such as SMS messaging for increased support and accountability during lifestyle interventions has been shown to lead to increased engagement, especially among youth and young adults.

PROCEDURES:

AIM 1

Aim 1 will build on our chronic SMI iOTA pilot data to determine how to best facilitate health behavior change in eSMI patients through interventions at the levels of the CMHC and the individual. Using the I-Corps discovery methods, we will conduct focus groups with CMHC administrators, physicians, nurses, case managers, clients and client family members/caregivers to identify barriers and facilitators to use of an iOTA intervention for

health behavior change and weight loss/obesity prevention in eSMI. Information gained in Aim 1 will drive the intervention adaptation process proposed in Aim 2, by helping to shape simple and actionable individual health behavior change messages, and by identifying feasible changes in the cultural, organizational, and physical CMHC environment that will help workers achieve and sustain healthy weight. Activities in Aim 1 will ensure that health messages and other intervention components are relevant and culturally appropriate.

Study participants will include eight focus groups of five participants each, conducted at each CMHC site, for a total of 16 focus groups. Group composition will reflect the age, racial and ethnic distribution of the population at each site.

Inclusion criteria: 1) focus group participants for CMHC Administrators will include individuals holding leadership roles within the CMHC structure: clinical director, medical director, nursing director, case management supervisor, clinic manager; ii) participants for CMHC prescribers will include advanced practice nurses, physician's assistants and physicians who see patients and prescribe medications within the CMHC setting; iii) participants for CMHC nursing staff will include registered nurses, licensed practical nurses, nurse health coaches and nurse managers who provide care within the CMHC setting; iv) participants for CMHC case managers will include community support workers and case managers; v) participants for CMHC clients will include individuals ages 18-45 with SMI (e.g., depression with psychotic features, bipolar disorder, schizophrenia or schizophreniform disorder) who receive case management and psychiatric and/or medical services within the CMHC setting; vi) participants for CMHC client family/caregivers will be family members or caregivers of client participants; vii) all participants are willing/able to provide written informed consent.

Exclusion criteria: i) not willing/able to provide written informed consent; ii) participants under age 18.

Aim 1 Study Procedures

I-Corps Approach to Focus Groups and Interviews: The Innovation Corps method uses the Lean Launchpad approach to developing hypotheses, then quickly moving to a continuous customer discovery method with the aim of translating hypotheses into facts. In this study, the process will begin with developing a list of hypotheses about the problem under study with the study team, consisting of faculty and community partners, here specifically regarding barriers or challenges to implementing an iOTA program in a CMHC environment. Then the team identifies individuals who are representative of consumers/customers at multiple levels within the organization who can inform the questions. These are our focus group participants – administrators, clinicians (nurses, case managers, physicians), clients and caregivers. Interviews and focus groups are conversational and discovery-oriented, with the goal of testing hypotheses. Focus group composition will be monitored to balance groups with respect to age, race and gender, taking care to include outlier perspectives. Once facts about the hypotheses have been obtained, the team will review all interview and focus group data, looking for emergent themes. This allows the team to determine the "value proposition" for the customer or key stakeholder, identifying potential "pain" and "gain" areas. The team can then determine actions needed to change or adapt iOTA to best fit the CMHC environment.

Table 1: Focus Group Makeup and Questions

Focus Group	# Groups per Site	Participants	Areas of Interest
CMHC Administrators	1	Medical Director (1), Director of Nursing (1), Clinical Director (1), Case Manager Supervisor (1), Clinic Manager (1)	1) What should the qualifications and characteristics of the health coach be? Is it reasonable for the health coach to be an existing CMHC clinical or other type of staff member? Or should it be someone else? 2) How often should health coaches meet with clients face-to-face? What should the content of the meetings be? 3) How frequent should text messages be? What should the content of the messages be? Is it helpful to have two-way texting capability? 4) How much time could an existing staff member devote to intervention delivery? What would the optimal amount of time be for intervention effectiveness? 5) Are there age-specific modifications needed to make the intervention more feasible/acceptable to adolescents and young adults? 6) Are there modifications needed to address other social determinants of clients and caregivers? (Race/ethnicity, gender, socio-economic status, level of education?)
CMHC Prescribers	1	Psychiatrists (1-2), Advanced Practice Nurses (1), Physician Assistants (1), Primary Care Physicians (1)	
CMHC Case Managers	1	Case Managers (2) and Community Support Workers (2-3) from adolescent and adult teams	
CMHC Nursing Staff	1	Nursing staff (1-2), nurse care managers (1-2), nurse health coaches (1)	
CMHC Clients	2 - Group composition will reflect the racial and ethnic distribution of the population at each site.	Adult clients ages 18-45 (2-3)	
CMHC Client Family/Caregivers	2 - Group composition will reflect the racial and ethnic distribution of the population at each site.	Parents (2-3), adult siblings (1) or other adult family members of client group participants (1-2)	

Focus Group Makeup, Preparation & Topics Purposive sampling methods will be applied to avoid bias in focus group responses, working with community partners to ensure group composition represents a broad range of perspectives. Six focus groups will be conducted at each community site, and will consist of:

1) Administrators (medical director, director of nursing, director of clinical services, case manager supervisor, clinic manager)
2) Prescribers (psychiatrists, advance practice nurses, physician assistants, primary care physicians)
3) Nursing staff (nursing staff, nurse care managers, nurse health coaches)
4) Community clinicians (community support specialists and case managers)
5) Transition-age clients (18-45 years)
6) Client family or caregiver (parents, adult siblings or other adult family members)

Once focus group participants are identified, they will be asked to participate in one in-person or phone visit to set up health goals and related text messages. They will then participate in 1-2 weeks of iOTA text messaging so as to facilitate optimal feedback on intervention adaptations. Focus groups will be scheduled within 1 week of completing the 2-week iOTA trial. Groups will be conducted at the CMHC site during a time that is convenient for participants, and will be facilitated by a research assistant facilitator and CMHC staff member taking additional notes. Groups will be digitally recorded. Focus group areas of interest will include:

1) What should the qualities and characteristics of the health coach/interventionist be?
2) What would be the optimal workload associated with intervention delivery?
3) What are the optimal qualities and content of the in-person iOTA intervention component?
4) What are the optimal qualities and content of the text-messaging intervention component?
5) What age-specific intervention modifications are needed?
6) What other social determinants should be considered in making treatment adaptations?

Data Management and Analytic Plan Recorded groups will be transcribed, and text data will be entered into NVivo, coded by two independent raters. We will use inductive coding methods based on pragmatic-variant grounded theory, to develop a coding tree based on both the focus group question framework and new themes identified in the focus group transcripts. We will use NVivo software for coding and analysis to identify prevalent themes. Pre-coding data exploration using the Word Frequency function will identify the most commonly-used words by focus-group. Commonly occurring words and phrases will be explored for meaning and context using the Word Tree function to create “meaning units.” Content will be further searched using “meaning units” to identify additional text representing relevant themes and. Repeated themes will be identified and coded as “nodes.” Links between themes and subthemes within each node will be explored using line-by-line coding.

AIM 2

Aim 2 will involve adaptation of the iOTA intervention using the Stirman adaptation framework, including modification of contextual, content and training aspects of the treatment based on qualitative data collected using the I-Corps methods. These might include adaptations to the treatment manual, in-person visit structure, and SMS text messaging. Once adaptations have been completed, they will be tested for feasibility by members of the focus groups queried in Aim 1 via semi-structured interview. Final adaptations will be made based on interview data.

Study Participants Individuals who participated in Aim 1 focus groups will be queried with individual semi-structured interviews to obtain feedback on treatment adaptations.

Aim 2 Study Procedures

iOTA adaptation Procedures: We will work with the parent WfY study intervention team to make adaptations to the existing intervention manual and text messaging protocol. We will then use a process for message and technology testing that follows the process used for the adaptation of the parent iOTA program, which uses personalized daily and weekly feedback via text messaging. Text message adaptations for the proposed project will be based on those used in previous iOTA studies aimed at low-income people and racial minorities[16,53,54] and those used in the current St. Louis study in the workplace. Before deployment, existing libraries of text messages will be tested for usability and cultural appropriateness among members of our target

population of eSMI patients. We will conduct key informant interviews using the I-Corps methodology following this testing and adapt the messages and risk assessment platform as needed based on this information.

Key Informant Interview Procedures: Using a standardized interview guide developed using I-Corps methods, we will conduct semi-structured, in-person key informant interviews with 1-2 members from each focus group at each study site to obtain impressions about adaptations made based on focus group results. Interviewing will be curtailed when saturation occurs (i.e., when the same themes repeatedly emerge). We will focus in particular on clients, caregivers and case managers, whose buy-in, participation, and ongoing support will be critical for our intervention at the level of the CMHC.

Data Management and Analytic Plan: Interviews will be digitally recorded and transcribed verbatim. Transcripts will be used in conjunction with notes taken during the interview, and will be analyzed using NVivo software. Themes will be grouped into categories informed by the overall aims of the interviews, including attitudes toward the adapted iOTA intervention, feasibility of interventions in specific age/race/ethnic groups, and organizational barriers and facilitators to health promotion in the CMHC setting. Experienced raters will use the tree to code transcripts using NVivo software for coding and analysis. Data will be analyzed using standard content analysis strategies listed in Aim 1.

AIM 3

In this aim we will work with BJC BH and SFBHN to implement and evaluate the adapted iOTA-eSMI intervention that provides support for behavior change to increase physical activity and modify diet, in order to achieve clinically significant weight loss and/or prevent obesity, thereby reducing diabetes and cardiovascular disease risk in eSMI. For the proposed iOTA testing, all otherwise eligible eSMI clients who have experienced ≥7% increase in weight in the past 2 years and/or are currently overweight (BMI 25-29.9) or early class I obesity (BMI 30-32.49) by BMI will be offered participation in the adapted iOTA. Our proposed pilot study aims to assess feasibility, acceptability, tolerability, and target engagement and will explore one primary hypothesis: participants in the intervention group will show favorable change in body weight compared to clients in the Health Education Control group. Secondary analyses will assess iOTA effects BMI and on RDoC domains relevant to needed psychophysical skills and self-efficacy, exploring the relationship between weight change and target engagement. Feasibility, engagement and implementation challenges will be characterized, measured by i) enrollment & retention, ii) obesity intervention acceptability, iii) text response rates, iv) visit adherence v) client expectations, vi) fidelity and vii) CMHC staff-rated acceptability, appropriateness and burden. To achieve these goals, we will conduct a randomized controlled pilot study in 60 eSMI patients ages 18-45. Participants will be randomized 2:1 to 24 weeks in the Psych iOTA Program or in the Health Education Control program. Both intervention groups will have monthly in-person visits with a health coach. The iOTA group will receive daily text messages specific to heath goals set during the in-person visits, and will receive treatment content that incorporates empirically supported approaches to increasing self-efficacy and psychophysical awareness. The Health Education Control group will receive education based on the Stanford health care self-management program developed by Kate Lorig and colleagues and modified to be similar to the iOTA intervention in number and length of visits. We will also obtain acceptability, appropriateness and feasibility feedback from case managers and clients on benefits, barriers, and suggested improvements to the SMS portion of the intervention during monthly in-person health coaching visits.

Study Participants Aim 3 will include a randomized 24-week pilot study of the adapted intervention, followed by 12 weeks of text messaging intervention alone in 60 participants (30 at each study site). Participants will be CMHC clients aged 18-45 with eSMI receiving mental health services at each clinical site, and will be randomized 2:1, iOTA-eSMI intervention: health education control. Groups will be balanced to reflect the age, gender, racial and ethnic distribution of the client-base at each site. Targeted group size for this pilot study will permit exploration of treatment group interactions with age and with racial/ethnic differences. The study manager, under the supervision of the study statistician, will maintain control of the randomization matrix to ensure unbiased group assignment during the randomization process. Although this is not a blinded study, the PI's and health coaches will not be involved in any part of the randomization to further ensure an unbiased process.

Inclusion criteria: i) aged 18-45 years, ii) "at-risk" weight defined as >7% weight gain in the prior 2 years, overweight (BMI 25-29.9) OR class I obesity (BMI 30-32.49) iii) SMI diagnosis with <5 years treatment,

iv) receiving case management services in one of the two CMHC study sites v) University of California, San Diego Brief Assessment of Capacity to Consent (UBACC) score > 14 vi) not taking weight loss medications or participating in another behavioral weight loss intervention, vii) mild to moderate psychiatric symptom severity as measured by the Clinical Global Impression – Severity scale viii) willing and able to provide written informed consent.

Exclusion criteria: i) taking weight loss medications or participating in another behavioral weight loss intervention, ii) documented diagnosis of diabetes and/or treatment with an antidiabetes agent (diagnoses of hypertension and hyperlipidemia acceptable), iii) UBACC score $\leq$ 14, iv) acute suicidality at time of screening, v) unwilling or unable to provide written informed consent.

Randomization of participants:
Participants will be randomized 2:1 to 24 weeks in the Psych iOTA Program or in the Health Education Control program. Both intervention groups will have monthly in-person, zoom, or telephone visits (lasting approximately 1 hour (Baseline and final visit lasting ~ 2 hours) with a health coach. Documentation of the screening and monthly visit assessments will be directly entered into a secure REDcap database by the Health Coaches at each site. Each site will have weight scales for documenting of weight changes.

The iOTA group will receive daily text messages specific to heath goals set during the in-person visits, and will receive treatment content that incorporates empirically supported approaches to increasing self-efficacy and psychophysical awareness.

The Health Education Control group will receive education based on the Stanford health care self-management program developed by Kate Lorig and colleagues and modified to be similar to the iOTA intervention in number and length of visits. We will also obtain acceptability, appropriateness and feasibility feedback from case managers and clients on benefits, barriers, and suggested improvements to the SMS portion of the intervention during monthly sessions with PIs and staff at the Healthy Mind Lab located in the Taylor Avenue Building on the Washington University Medical Campus and at the South Florida Behavioral Health Network facilitates at our associated two Florida study sites (Fellowship House and Guidance Care Center) and at the Independence Center Organization in St. Louis, MO.

Participants unable to attend visits in person will have the option of attending study visits remotely by phone or by using a Washington University-approved video conferencing platform (Skype or Zoom) and digital links to study assessments in REDCap. For potential participants who have computer access and capability, study visits may be conducted via video conferencing. The health coach will use a secure, web-based, HIPAA-compliant, conferencing platform that employs encryption of video and audio content. Potential participants would receive an email or text message with a unique and secure link to join the video session by computer or mobile device.

Participant Enrollment:
We will recruit 60 adult probands from MO and FL CMHCs with SMI.

Recruitment and Screening Procedures:
Fliers will be distributed to community mental health centers and local medical professionals in order to recruit participants. These handouts list the inclusion criteria, benefits of being in the study, and contact information for questions or to enroll. In addition to referrals from providers, study staff will review EPIC patient lists to identify potential participants. Potential participants will then be contacted to introduce them to the study and complete an initial screening for eligibility.

During the initial screening phase, a member of the research team will obtain verbal consent to conduct an IRB approved phone screen with individuals who express interest in participating. There will be questions about a person's medical and mental health history. After completion, a member of the research team will examine and determine whether inclusion criteria are met and contact the individual. No study procedures will begin prior to obtaining informed consent.

Informed Consent Process:
The research team will obtain informed consent from all subjects who participate in the study. The study procedures will be explained in writing and/or orally to the subject by a member of the research team. After all questions have been answered and the risks and benefits of participation in the study have been described, informed consent will be obtained on an informed consent form approved by the WUSM IRB and Human Research Protection Office. The research team will confirm that the subject verbalizes understanding of the study and study-related procedures and be given the opportunity to ask questions prior to obtaining the research participant's signature. The objectives of the project, all of the requirements for participation, the efforts made to protect the private health information and confidentiality of the participant, and any possible discomforts and risks will be clearly explained to the subjects orally and in writing in lay terms which they are able to comprehend.

A member of the research team will witness the subject sign and date the informed consent form as part of the informed consent process and signs as the person obtaining informed consent. Adult participants will be asked to provide informed consent for their own participation. Potential adult participants that have limited decision making capacity will be included in this study, and their legal guardians or legally authorized representatives will be consented and will provide written informed consent for them to participate in the study. Informed consent is an ongoing process. All study related procedures will be explained at each visit and participants will be reminded that participation in research is voluntary and they may refuse to participate or withdraw from the study at any time without penalty or loss of benefits to which they would otherwise be entitled. Should a change be made to the consent document at any time during the subject's participation, the subject and/or legally authorized representatives will be re-consented.

The consent process may take place by phone for participants who have barriers to in-person participation. For potential participants who have computer access and capability, the formal study consent process will be conducted using a REDCap-based electronic consent form. The consent form has been developed in REDCap, a secure, web-based, HIPAA-compliant, data collection platform with a user management system allowing the principal investigator to grant and control varying levels of access to study staff. Potential participants will receive an encrypted email with a unique link to review the informed consent form online. After the research team explains the study and answers any question, the potential participants can electronically fill in an "Agree" button, followed by their electronic signature. Upon completion of the consent, participants are presented with the option to download a copy of the executed form. The research team will also send a [secure] e-mail copy of the executed form to the participant. E-consent versioning will be managed using the e-consent Framework in Redcap. Within the e-consent survey options, we have designated the e-consent version number in this application as e-consent version 1. The PDF's of completed responses will have the timestamp, participant name, and e-consent version number inserted in the footer. Future versions of the e-consent will be created by making a copy of the Redcap form and revising it. The old version would be de-activated upon receiving IRB approval for the new version.

If a participant does not have access to a computer at the time of consent potential participants will be provided with a copy of the informed consent form (via mail or email). Once the potential participant has had time to look over the consent form, a study team member will talk with the participant by phone to review the study information and answer any questions. If they choose to continue their participation, they will be asked to sign the consent and return to us either by mail or scanned and emailed or faxed or to verbally agree to take part in the study, which will be recorded in the study record. For any consent document returned, we will instruct participants to keep a copy for themselves.

Detailed Study Procedures:
Literacy & facility with mobile technology: Each participant will be administered the Rapid Estimate of Adult Literacy in Medicine-Short Form or REALM-SF to estimate literacy and the University of California, San Diego Brief Assessment of Capacity to Consent or UBACC to establish understanding of the study and active treatment. The accessibility of and ability to use mobile devices is necessary for participation in this study.

Thus, prior to randomization, all participants will undergo one week of text messaging to ensure that they are able to receive and appropriately respond to text messages.

Rationale for study length of 24 weeks: In the MEAC study, the PI's demonstrated rapid onset weight gain within 12 weeks of initial antipsychotic exposure. Although weight gain, particularly that associated with medications, can be rapid, it is generally well accepted that meaningful weight loss efforts may take longer than 12 weeks. We plan for a fully powered future study with an active treatment phase that is 6 months in duration, similar to currently running Phase 3 clinical trials (cite Alkermes). Published weight loss intervention studies in mentally ill youth and adults of 4 months in duration show separation from control groups. For the proposed study, our primary goal is to establish feasibility, tolerability and target engagement during active treatment, as well as to evaluate engagement and outcomes following a text-only 12-week extension.

iOTA intervention: The individual-level interactive obesity treatment approach (iOTA) intervention is based on assessment of individual behavior risks, collaborative goal-setting with a health coach, and use of an interactive text system to provide ongoing support and self-monitoring of behavior change goals. The SMS intervention is programed to "touch" participants an average of five days per week. The SMS system prompts participants to report their weight and their progress on achieving their goals on a "check-in" day each week, and sends immediate, tailored feedback about their progress. If a participant is making progress on their goal, the SMS system suggests a change to the participant's goal in between health coaching sessions. In addition, the system sends weekly and monthly tips customized to the goals the participant selected. The iOTA intervention has been adapted for use in mentally ill populations, including monthly in-person visits and weekly telephone check-ins as needed depending on level of engagement with the SMS messaging, monitored by the health coaches remotely via a web portal. Monthly in-person visits consist of assessing current health behaviors, working collaboratively with the client to identify desired behavior changes, then using a list of 19 goals including stepped level of difficulty based on participant's current behaviors, the client and health coach collaboratively select up to three goals for the next month. These goals have prescribed SMS messaging tailored to level of difficulty to support the participant on a daily basis with health behavior change.

Health Education Control: A control condition that matches for group setting, time, and attention is necessary to minimize the chance that study findings might be attributable to non-specific differences in conditions rather than the active ingredients of the adapted iOTA intervention. Health Education is based on the Stanford health care self-management program developed by Kate Lorig and colleagues. Health Education improves chronic disease management, but it does not teach self-efficacy or psychophysical awareness, and does not involve specific empirically supported psychotherapeutic techniques to help with weight management. It matches iOTA in time and number of sessions. Participants randomized to the control condition will receive monthly in-person health coaching visits and a weekly SMS general "Health Tip" message. Visits will be structured according to current US Preventive Services Task Force recommendations to counsel participants on energy balance, physical activity and nutrition. The Health Coach will use educational materials developed for the iOTA-SMI adaptation for health education groups, which includes information from www.MyPlate.gov and from the Be Fit Be Well program. Health education control group participants will not be engaged in formal goal setting.

Ensuring Rigor & Reproducibility: Behavioral intervention treatment fidelity is determined by structured, direct observation of individuals carrying out the behavioral intervention, evaluating for evidence of 1) adherence to the treatment protocol and 2) competence in the treatment delivery. The demonstration of treatment fidelity is critical to the development of a valid behavioral intervention, such that the intervention cannot be tested for efficacy in a randomized clinical trial, nor can said intervention be considered evidence-based until this critical step is accomplished. Therefore, a primary goal of the proposed project is to demonstrate treatment fidelity of the iOTA and Health Education Control in-person health coaching visits. This will be accomplished by audio-recording monthly in-person sessions, which will be reviewed by the PIs and discussed during weekly study teleconferences. Health Coaches will self-monitor treatment fidelity at each visit using an established Treatment Fidelity and Competence Rating Scale.

Study Assessments Completed at Baseline Only

UC San Diego Brief Assessment of Capacity to Consent (UBACC): This is a 10-item scale developed to determine whether potential research participants are capable of providing informed consent. Questions focus on understanding the purpose of the research protocol, safety and ability to withdraw consent.

Credibility and Expectations for Improvement (CEI): Participants will be asked to rank their expectations about the intervention and how much they believe it is reasonable and will be useful on a likert scale. Both case managers and clients will be asked to complete this questionnaire prior to study initiation.

Study Assessments Completed at Baseline and Endpoint

The Health Status/Knowledge/Behaviors/Attitudes Questionnaire will be completed at Baseline and Endpoint, and includes:

Rapid Eating Assessment for Patients -Short Form (REAPS): This a is a very quick assessment of daily diet quality and eating behaviors that the health coach will use to assess for any eating areas in need of dietary counseling and education.

International Physical Activity Questionnaire - Short Form (IPAQ-SF): This is a 7-item questionnaire that measures intensity of physical activity in the last 7 days, including time spent sitting.

Ten Item Personality Inventory (TIPI): This is a brief, 10-item measure of the Big-Five personality dimensions.

Questionnaire on Eating and Weight Patterns-DSM 5 (QEWP-5): The Questionnaire on Eating and Weight Patterns (QEWP) is a 26-question self-report screening tool that has been developed for use in research and clinical settings to identify persons who may have binge eating disorder or bulimia nervosa, and has been updated to conform to DSM-5 diagnostic criteria for BED (QEWP-5).

Activity Tracking: Participants will be given a Fitbit Flex to be worn for 1 week prior to study visit 1 and endpoint visits. Data will be downloaded by the health coach upon return of the device.

Digital Behavioral Assessment Completed by the Participant at Each Study Visit

At each visit, participants will fill out a digital assessment battery that self-scores and provides recommendations for treatment focus in the visit.

Patient Health Questionnaire (PHQ-9). This 9-item scale measures symptoms of depression on a scale of 0 (not at all) to 3 (nearly every day). Scores >10 is consistent with moderate depressive symptoms and will prompt the health coach to consider use of emotion regulation techniques to promote emotion regulation.

Self-Efficacy for Mental Health. This is a 6-item visual analogue scale from 1-10 (1 = not at all confident, 10 = very confident) that assesses perceived control over emotional states and ability to cope with stress. A mean score >15 will prompt consideration of emotion regulation or distress tolerance materials.

Loss of Control over Eating Scales (LOCES). The LOCES is a 7-item scale that measures behavioral, cognitive/dissociative, and positive/euphoric aspects of loss-of-control eating on a scale of 1 (never) to 5 (very often). Scores > 25 will prompt the health coach to consider use of dialectic behavior therapy strategies to promote self-regulation to prevent binge and loss of control eating (mindfulness, distress tolerance).

Psychophysical Awareness & Skills Scale (PASS). This composite measure draws from RDoC (NIH Research Domain Criteria) domains of cognitive systems and social processes, and includes 10 items that assess cognitive control, self-determination and interoceptive awareness on a likert scale. A mean score <4 will prompt the health coach to utilize materials related to improving awareness of hunger and satiety cues.

Self-Efficacy (Diet and Exercise). This scale consists of 32 items (20 nutrition-based, 12 activity-based) and assesses a participant's current eating and exercise behaviors and knowledge on a likert scale. A mean score < 4 on either subscale will prompt the health coach to access energy balance and self-efficacy treatment content.

UCLA Loneliness Scale (Version 3). A 20-item scale designed to measure one's subjective feelings of loneliness as well as feelings of social isolation. Participants rate each item on a scale from 1 (Never) to 4 (Often). Higher scores are correlated with poorer social functioning in friendships and romantic relationships. Scores >40 will prompt use of interpersonal effectiveness materials in coaching sessions.

Multidimensional Scale of Perceived Social Support. This 12-item scale is designed to measure perceived social support from three sources: Family, Friends, and a Significant Other. Scores < 3 will prompt use of interpersonal effectiveness materials in coaching sessions (identifying relationships that support health behavior change, shoring up interpersonal effectiveness skills).

Clinical Global Impression Scale. The CGI was developed for use in NIMH-sponsored clinical trials to provide a brief, stand-alone clinical assessment of the patient's global functioning, taking into account the patient's history, psychosocial circumstances, symptoms, behavior, and the impact of the symptoms on ability to function.

Medication Reconciliation & Compliance: Our group has developed a medication log and reconciliation form to track medication compliance and changes during study participation. Participants will be asked at each in-person health coaching visit to update their medication list, which will then be reconciled with the case manager, physician and pharmacy.

Completed by the Health Coach at Each Study Visit

Treatment Adherence: Participant compliance with in-person health coaching visits will be measured as attendance; compliance with SMS messaging will be monitored by the health coach in real-time via a web portal. The study team will evaluate compliance with in-person visits and weekly SMS messaging by measuring attendance and % response rate to SMS prompts.

Treatment Fidelity Monitoring: In addition to audio recording each in-person health coaching visit and reviewing audio-recordings during weekly study team teleconferences with the PI's, Health Coaches will also be required to rate their performance and competence in delivering prescribed intervention content at each visit using an established Treatment Fidelity and Competence Rating Scale used by the PIs in previous NIH-funded lifestyle intervention trials.

Response to Intervention Form: The health coach will assess the participant's level of engagement, motivation and understanding of materials with five questions at the end of each monthly visit. This form has been used by our team in previous behavioral weight management studies.

Body Mass Index (BMI): BMI is correlated with direct measures of body fat like skinfold thickness measurements, bioelectrical impedance, densitometry (underwater weighing) and dual energy x-ray absorptiometry (DEXA), and is strongly correlated with various metabolic and disease outcomes, similar to more direct measures of body fatness. Because calculation requires only height and weight, it is inexpensive, easy to reproduce and relevant to public health guidelines. BMI will be assessed at each study visit using calibrated scales and stadiometers.

Completed by Participant and Community Support Worker at Study Midpoint and Endpoint

Feasibility, Appropriateness & Acceptability Questionnaire: At every health coaching visit, both clients and case managers will be asked specifically to rank the feasibility of intervention implementation, appropriateness of the intervention and acceptability/usability of the intervention from their respective perspectives.

Treatment/Program Satisfaction Questionnaire: This satisfaction questionnaire has been used in NIH-funded weight loss studies, and has been modified for use in prior iOTA adaptations completed by our group. Clients and case managers will be asked to complete the satisfaction survey at 16 weeks and at the wrap-up visit; if a participant drops out prior to study completion, the team will ask for final satisfaction surveys of both case manager and client before study termination.

Participant Compensation:

Participants will be compensated with a gift-card in the amount of $25 for every completed study visit.

Participant Withdrawal:

- Participants may withdraw at any point during or after the completion of the study with no penalty by contacting the study team.
- Investigators may choose to withdraw a participant from the study if it is unsafe to continue participation.
- If a subject withdraws from the study, the research team may only use and share information already collected for the study. Subject information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.

Data Management Procedures and Confidentiality:

All data will be entered into the electronic database REDCap via a secure WUSM web portal and stored on secure WUSM servers, which can be accessed securely through the WU or FAU networks. The database management is built with multiple layers of security and follows best practices and WUSM requirements for securing sensitive data. The iOTA program will be monitored through a secure web-portal via the WU network. All automatic system generated messages in the iOTA program will be sent directly to subjects' mobile phones

through an online application developed and supported by technology vendor, Integrity, who has existing WU IRB and Information Security office approval for involvement with the parent iOTA program. The research team will use the iOTA online web portal from WU computers on the WU network. Integrity captures/stores all text messaging data (data sent to participants and received back from participants) and transmits the data to the WU research team using the REDCap API via a secure WUSM web portal stored on secure WUSM servers.

Data Analysis/ Statistical Considerations:

Planned primary and secondary analysis: In addition to the use of change in body weight from baseline as the primary outcome for this pilot study, secondary outcomes will include change in BMI, psychophysical skills and related self-efficacy. Weight/BMI will be measured at each visit (up to 10 visits over 9 months); we will use a repeated-measures mixed model to look at trajectory over study course with a time x treatment interaction estimating the treatment effect. Increase in self-efficacy for diet and exercise is the proposed mechanism of action for the active iOTA intervention. Measures of Psychophysical Awareness will be measured at every visit (total of 5 time points). Trajectory of self-efficacy scores will be compared between treatment groups. Finally, we will use structural equation growth models to estimate the correlation between the trajectory of psychophysical skills and related self-efficacy and that of weight/BMI.

Exploratory analyses: will focus on characterizing feasibility, engagement and implementation challenges as measured by i) enrollment, retention and visit adherence, ii) obesity intervention acceptability, iii) text response rates, iv) client expectations, v) fidelity and vi) client and staff-rated feasibility, appropriateness, acceptability, and vii) staff burden, including evaluation of how these variables impact effectiveness with respect to BMI and self-efficacy. Exploratory analyses will also evaluate how mental health self-efficacy and psychotropic medication compliance impact iOTA treatment compliance/engagement.

Safety and Adverse Events:

Safety and Compliance Monitoring

- The Principal Investigator at each site will provide overall monitoring of the data collection, and data safety throughout the study process. The Project Coordinator will also assist in the monitoring and supervision of data collection and will report any concerns to the PI at their site. All PI's and Project coordinators will attend monthly meetings where any concerns regarding subject safety or data security will be communicated promptly to the 3 lead sites and handled accordingly.
- University and NICHD guidelines will be followed for reporting should an adverse event occur. Monitoring will include checking to see that data files are appropriately stored and bi-weekly group supervision of field interview staff to discuss the process, answer questions and provide assistance when needed. The project will also undergo review and approval by our Institutional Review Board with monitoring as required by annual reports and recertification of human subjects approval. The Data Safety Monitoring Board will meet at least annually and sooner if any needs arise to consult regarding any concerns about the ongoing safety and well- being of participants. These members are expertise in areas of administrative data and child welfare reporting, both key issues pertinent to study implementation.

Medical Monitoring

- Independent Data and Safety Monitoring Board – The Principal Investigator will provide overall monitoring of the data collection, participants, and data safety throughout the study process. Washington University and NICHD guidelines will be followed for reporting should an adverse event occur. Monitoring will include checking to see that data files are appropriately stored and regular supervision of study staff involved in data collection to discuss the process, answer questions and provide assistance when needed. The project will also undergo review and approval by our Institutional Review Board with monitoring as required by annual reports and recertification of human subjects approval. The Investigators will meet monthly, and should any concerns arise regarding the ongoing safety and well-being of participants they will be addressed accordingly. Additional oversight will be provided by the National Center for Translational Science program officer who attends the monthly PI meetings.

Definitions of Adverse Events

The most serious risk in the proposed research is any adverse outcome that may jeopardize the welfare of participants or caregivers. Possible adverse events that are anticipated include an unintentional disclosure of personal health information to an unauthorized individual. Additionally, it is possible that during the tele-health mediated assessment phase of this project, the individual or their caregiver could conceivably experience an acute medical event requiring immediate medical attention. In the unlikely event that this were to occur, the study staff would assist the participant or their caregiver in alerting local EMS, or alternatively would contact local EMS on their behalf.

Relationship

- Parents or caregivers of participants must have permanent custody (i.e., not a foster parent) and will be excluded if they have severe mental health disorders (e.g., psychotic disorders) or severe cognitive delay that diminishes their capacity to consent or effectively participate in the study.
- Child subjects will include only those with a variant in a suspected brain gene. Should there be more than two children in the family with the same genetic variant will enroll them as individual participants.
- Special classes of subjects: The participants may be considered vulnerable due to developmental delays, intellectual disability or other medical conditions caused by their genetic variant. It is impossible to assess the outcomes of the study without their inclusion. Several aspects of the study reduce concerns in this area: (1) we are drawing from a population receiving services as usual from Intellectual Disabilities Research Centers with expert clinicians doing the initial screening and judgment about inclusion and exclusion, (2) the team has extensive research and clinical experience with children and families impacted by developmental delays and other genetic disorders, (3) the study procedures are brief and designed to take place within a typical clinic visit, and are designed to be implemented in a fully remote format.

Severity

- The most serious risk in the proposed research is any adverse outcome that may jeopardize the welfare of participants or caregivers. Possible adverse events that are anticipated include an unintentional disclosure of personal health information to an unauthorized individual. Additionally, it is possible that during the tele-health mediated assessment phase of this project, the individual or their caregiver could conceivably experience an acute medical event requiring immediate medical attention. In the unlikely event that this were to occur, the study staff would assist the participant or their caregiver in alerting local EMS, or alternatively would contact local EMS on their behalf.

Expectedness

- AEs that are unanticipated will be reported immediately to the Washington University in St. Louis IRB by the PI. The IRB will determine whether it is appropriate to stop the study protocol temporarily or will provide suggestions/modifications to the study procedures. Possible modifications include adding these possible adverse events to the consent form and re-consenting all study participants. The PI will be responsible for monitoring participant safety on a monthly basis at regularly scheduled research meetings. The PI will keep a written log of all adverse events and ensure that the IRB is contacted immediately. The PI will also keep a log of the outcome of IRB decisions regarding adverse events and enforce any changes that need to occur as a result of the IRB decisions. If the preliminary outcome data indicates harmful impact of the program to caregivers or their families, the Washington University in St. Louis committee will be notified and it is possible that the study will be discontinued.

Data Collection Procedures for Adverse Events

- The PI will be responsible for monitoring participant safety on a monthly basis at regularly scheduled research meetings. The PI will keep a written log of all adverse events and ensure that the IRB is contacted immediately and will also keep a log of the outcome of IRB decisions regarding adverse events and enforce any changes that need to occur as a result of the IRB decisions. If the preliminary outcome data indicates harmful impact of the program to caregivers or their families, the Washington University in St. Louis committee will be notified and it is possible that the study will be discontinued.

Reporting Procedures

- The PI will be responsible for monitoring participant safety on a weekly basis. He will be informed of any adverse events (AE) as soon as they occur, and he will report them to the Washington University in St. Louis IRB within 24 hours of becoming aware of the event. The IRB will determine whether it is appropriate to stop the study protocol temporarily or will provide suggestions/modifications to the study procedures. Possible modifications include adding these possible adverse events to the consent form and re-consenting all study participants. Because this study takes place at 13 sites, the PI will also be responsible for notifying all other site's PI's.
- Additionally, in accordance with NIH policy, the PI will notify the study's NIH program officer within 10 business days of the study team becoming aware of an unexpected serious adverse event (SAE). For all AEs or serious adverse events (SAE) that are either expected or unrelated to the study, the PI will provide a summary to the study's NICDH program officer with the annual progress report.

Adverse Event Reporting Period

AE reporting to the Washington University in St. Louis IRB will occur within 24 hours of becoming aware of the event. Additionally, in accordance with NICHD policy, the PI will notify the study's NICHD program officer within 10 business days of the study team becoming aware of an unexpected serious adverse event (SAE).

Post-study Adverse Event

There are no anticipated post-study adverse events that would accrue from cross-referencing or analysis of research data since this information will not be returned to the family.

EXPECTED RISKS/ BENEFITS:

Potential Risks

- There is always a risk of loss of privacy and loss of confidentiality, however the study team will do the following to make sure risk remains minimal:
- Data will be maintained on password-protected secure networks at each site.
- Only investigators and approved study staff will have access to identified data.
- Any unplanned events or breaches in data security will be reported to the WU HRPO office.
- In the unlikely event of a breach of genetic data, the data are protected under the Genetic Information Nondiscrimination Act of 2008 (GINA), which makes it illegal for health insurance companies, group health plans, and most employers to discriminate based on genetic information.
- There is the risk that a participant or caregiver may feel uncomfortable answering study questions. Participants may leave blank any questions they prefer not to answer.

Benefits

The societal benefit of this study this text-based intervention can be translated to other clinical or community-based settings to reduce obesity and diabetes risk among patients with a psychiatric condition.

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