Imagine to Remember: Improving Medication Adherence in Pre- and Type 2 Diabetes
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Complete Research Protocol (HRP-503)

Table of Contents

PROTOCOL TITLE:

Include the full protocol title.

Response:

Imagine to Remember: Improving Medication Adherence in Pre- and Type 2 Diabetes

PRINCIPAL INVESTIGATOR:

Name
Department
Telephone Number
Email Address

Response:

Leonard H. Epstein
Division of Behavioral Medicine, Pediatrics
716-829-3400
lhenet@buffalo.edu

VERSION NUMBER/DATE:

Include the version number and date of this protocol.

Response:

v.8 4/7/2020

REVISION HISTORY

Revision #	Version Date	Summary of Changes	Consent Change?
7	3/7/2020	Due to the ongoing concern in our area regarding COVID-19, we are updating sections 12 and 18 to allow for us to take precautions to ensure the safety of our participants and staff.	
8	4/7/2020	Updates for Covid-19	yes
9	7/22/2020	Updates for CR	no

FUNDING:

Indicate any funding for this proposal. This should match the Funding Sources page in Click IRB.

Response:

This study is funded by the grant "Delay Discounting as a target for self-regulation for prediabetics" funded by NIDDK RFA-RM-14-020, "Science of Behavior Change: Assay Development and Validation for Self-Regulation Targets (UH2)".

GRANT APPLICABILITY:

Indicate whether this protocol is funded by a grant (e.g. NIH, foundation grant). For a grant with multiple aims, indicate which aims are covered by this research proposal.

NOTE: This question does not apply to studies funded by a sponsor contract.

Include a copy of the grant proposal with your submission.

Response:

This study is funded by the grant "Delay Discounting as a target for self-regulation for prediabetics" funded by NIDDK RFA-RM-14-020, "Science of Behavior Change: Assay Development and Validation for Self-Regulation Targets (UH2)". This study was submitted and approved in request to carry forward funds from the UH2, to UH3 phase of this grant; and covers all three specific aims outlined in the application for approval to keep the carryforward funds.

1.0 Study Summary

Study Title	Imagine to Remember: Improving Medication Adherence in Pre- and Type 2 Diabetes
Study Design	Three groups, nonconcurrent multiple baseline experimental design
Primary Objective	Determine if a 4-8 week intervention consisting of future-thinking improves medication adherence
Secondary Objective(s)	Determine if a 4-8 week intervention consisting of future-thinking improves different facets of memory/executive function and/or decision-making.
Research Intervention(s)/ Investigational Agent(s)	The intervention being researched is called episodic future thinking (EFT), which consists of imagining specific instances of one's future. In this study, participants will engage in EFT pertaining to medication use, guided by a research staff member in intervention sessions across a 4-8 week period.
IND/IDE #	N/A
Study Population	Adults with prediabetes or Type 2 diabetes prescribed medication, as well as those who are at risk for developing pre and type 2 diabetes (BMI ≥ 30 and hyperlipidemia or hypertension)
Sample Size	20

Study Duration for individual participants	15 weeks
Study Specific Abbreviations/ Definitions	Episodic future thinking (EFT), prospective memory (PM), working memory (WM), episodic memory (EM), and delay discounting (DD).

2.0 Objectives*

2.1 Describe the purpose, specific aims, or objectives of this research.

Response:

Aim 1: To examine whether EFT improves medication adherence.

Aim 2: To test the influence of EFT on DD (Aim 2A), and PM (Aim 2B).

2.2 State the hypotheses to be tested, if applicable.

NOTE: A hypothesis is a specific, testable prediction about what you expect to happen in your study that corresponds with your above listed objectives.

Response:

Aim 1: We hypothesize that EFT will improve medication adherence.

Aim 2: We hypothesize that EFT will reduce DD and improve PM.

3.0 Scientific Endpoints*

3.1 Describe the scientific endpoint(s), the main result or occurrence under study.

*NOTE: Scientific endpoints are outcomes defined before the study begins to determine whether the objectives of the study have been met and to draw conclusions from the data. Include primary and secondary endpoints. Some example endpoints are: reduction of symptoms, improvement in quality of life, or survival. Your response should **not** be a date.*

Response:

The primary endpoint is the increase in medication adherence and improvements in memory and decision making.

4.0 Background*

4.1 Provide the scientific or scholarly background, rationale, and significance of the research based on the existing literature and how it will contribute to existing knowledge. Describe any gaps in current knowledge. Include relevant preliminary findings or prior research by the investigator.

Response:
Adherence to medications in persons with prediabetes, type 2 diabetes or related comorbidities (e.g., hypertension, hyperlipidemia) can help prevent the development/progression of type 2 diabetes. However, adherence to diabetes medications[1,2] and medications for its comorbidities is relatively low,[3] with a commonly cited reason in those with prediabetes being "forgetting"[1]. The ability to recall and successfully engage in an action at an appropriate time in the future is referred to as prospective memory (PM). Accumulating research shows that poorer prospective memory is related to medication non-adherence among individuals using various types of medications;[4] and as such, improving PM represents a potentially fruitful means of increasing medication adherence.

An important facet of behavior that may contribute to medication non-adherence is delay discounting (DD). Delay discounting refers to the extent to which an individual devalues an outcome due to its delay in time. Prior research has shown that greater DD is related to poor glycemic control, and this relationship is partially mediated by medication adherence.[5] Previous research by our group within the experimental medicine framework[6], which serves as the platform for the NIH Science of Behavior Change Initiative[7], has shown that DD is related to HbA1c levels in those with prediabetes, that changes in DD over a year are associated with changes in HbA1c, and that we can manipulate DD with episodic future thinking (or the prospection of one's self in future scenarios; EFT). These findings set the stage for our UH3 grant on using EFT to modify DD and HbA1c levels. Several laboratory studies have shown EFT is a successful approach to improving PM[8–11]. Given that EFT also produces robust effects on DD[12–14], EFT may be an especially efficacious intervention in that it has the potential to improve two different processes related to poorer medication adherence. Current research examining the effects of EFT on PM have been confined to laboratory tasks, and research is needed to assess EFT effects on medication adherence.

We propose an RCT that will assess the effects of EFT on medication adherence, general PM, and DD among those with pre- or type 2 diabetes or related comorbidities who are currently taking at least one oral medication for diabetes or related comorbidities. We will recruit participants who are relatively non-adherent to an oral medication ($\leq$ 80% of prescribed doses taken in the past month; to accommodate over-reporting) for prediabetes or type 2 diabetes or other conditions that commonly co-occur with these conditions (e.g., hypertension, hyperlipidemia). Medication adherence will be monitored using electronic pill bottle caps (MEMS caps, which record bottle openings with date and time stamps), pill counts, and pharmacy records. Medications for glucose control as well as control of hypertension and/or hyperlipidemia will be considered as targets for measurement. Participants self-rated as non-adherent ($\leq$ 80% prescribed doses taken), and report difficulty remembering to take one's medication as a primary reason for non-adherence, will undergo a 6 week, 8 week, or 10 week baseline period. After the staggered baseline periods, all participants will receive EFT intervention. In total, participants will be in baseline and treatment for a total or 15 weeks.

Randomized participants will complete bi-weekly in person sessions plus phone sessions for the weeks in which they do not come to the lab, in which they learn toengage in EFT for medication adherence. Initial EFT for medication adherence will focus on taking the targeted medication on a typical day (e.g., a weekday when the participant usually works), and in subsequent sessions EFT will be used to assist participants in adapting to unusual circumstances that may interrupt adherence or have been reported as contributing to non-adherence.

At an initial baseline session, post-intervention, and follow-up, participants will complete measures of working memory, lab-based PM, and DD. Dependent measures include change in targeted medication adherence (based on MEMS data), change in non-targeted medication adherence (for participants initially reporting non-adherence to multiple medications; based on self-report and pill count measures), DD, and PM. Moderators to be tested include working. The goal of the study will be to collect pilot data to test the feasibility and initial efficacy of the approach, as well as effect sizes for a subsequent R01.

4.2 Include complete citations or references.

Response:

References

1. Walker EA, Molitch M, Kramer MK, et al. Adherence to preventive medications: Predictors and outcomes in the diabetes prevention program. Diabetes Care. 2006;29(9):1997-2002. doi:10.2337/dc06-0454

2. Polonsky WH, Henry RR. Poor medication adherence in type 2 diabetes: Recognizing the scope of the problem and its key contributors. Patient Prefer Adherence. 2016;10:1299-1307. doi:10.2147/PPA.S106821

3. Brown MT, Bussell JK. Medication adherence: WHO cares? Mayo Clin Proc. 2011. doi:10.4065/mcp.2010.0575

4. Zogg JB, Woods SP, Sauceda JA, Wiebe JS, Simoni JM. The role of prospective memory in medication adherence: A review of an emerging literature. J Behav Med. 2012;35(1):47-62. doi:10.1007/s10865-011-9341-9

5. Lebeau G, Consoli SM, Le Bouc R, et al. Delay discounting of gains and losses, glycemic control and therapeutic adherence in type 2 diabetes. Behav Processes. 2016;132:42-48. doi:10.1016/j.beproc.2016.09.006

6. Bernard C. An Introduction to the Study of Experimental Medicine. Oxford, England: MacMillan; 1927.

7. Riddle M. News from the NIH: using an experimental medicine approach to facilitate translational research. Transl Behav Med. 2015:486-488. doi:10.1007/s13142-015-0333-0

8. Kretschmer-Trendowicz A, Schnitzspahn KM, Reuter L, Altgassen M. Episodic future thinking improves children's prospective memory performance in a complex task setting with real life task demands. Psychol Res. 2017:1-12.

9. Altgassen M, Rendell PG, Bernhard A, et al. Future thinking improves prospective memory performance and plan enactment in older adults. Q J Exp Psychol (Hove). 2015;68(1):192-204. doi:10.1080/17470218.2014.956127

10. Altgassen M, Kretschmer A, Schnitzspahn KM. Future thinking instructions improve prospective memory performance in adolescents. Child Neuropsychol. 2016;7049(April):1-18. doi:10.1080/09297049.2016.1158247

11. Neroni MA, Gamboz N, Brandimonte MA. Does episodic future thinking improve prospective remembering? Conscious Cogn. 2014;23:53-62. doi:10.1016/j.concog.2013.12.001

12. Daniel TO, Stanton CM, Epstein LH. The Future Is Now Reducing Impulsivity and Energy Intake Using Episodic Future Thinking. Psychol Sci. 2013;24(11):2339-2342. doi:10.1177/0956797613488780

13. Stein JS, Wilson AG, Koffarnus MN, Daniel TO, Epstein LH, Bickel WK. Unstuck in time: episodic future thinking reduces delay discounting and cigarette smoking. Psychopharmacology (Berl). 2016;233(21-22):3771-3778. doi:10.1007/s00213-016-4410-y

14. Snider SE, LaConte SM, Bickel WK. Episodic future thinking: expansion of the temporal window in individuals with alcohol dependence. Alcohol Clin Exp Res. 2016;40(7):1558-1566. doi:10.1111/acer.13112

15. Group DPPR (2003). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. Obstetrical & Gynecological Survey, 58:182-183.

5.0 Study Design*

5.1 Describe and explain the study design (e.g. case-control, cross-sectional, ethnographic, experimental, interventional, longitudinal, observational).

Response:

This study is a nonconcurrent multiple baseline design; participants will be randomized to a 6 week, 8 week, or 10 week staggered baseline periods followed by 4-8 weeks of Episodic Future Thinking (EFT).

6.0 Study Intervention/Investigational Agent

6.1 Describe the study intervention and/or investigational agent (e.g., drug, device) that is being evaluated.

Response:

The intervention being researched is called episodic future thinking (EFT), which consists of imagining specific instances of one's future. In this study, participants will engage in EFT focused on imagining taking one's medication, guided by a research staff member in their intervention sessions in addition to bi-weekly

check-in calls across a 4-8 week period. The research staff member will conduct the intervention session using a semi-structured interview format in which the staff member works to identify situations/circumstances in which the participant encounters challenges with taking their medication, and subsequently asking questions to prompt the participant to imagine what successful medication adherence would consist of (and "look" like). Sessions may also involve imagining positive events resulting from successful medication adherence and the details surrounding those events. For example: if the research staff member finds that a participant struggles to take their medication on weekends, the staff member will ask the participant to visualize what successfully doing so might entail (getting the medication bottle and putting it next to the waffle iron, which is frequently used on the weekends) and to imagine the sensory aspects of the experience of doing so (picking up the medication bottle, taking out the waffle iron, placing it on the counter—and noting any typically associated smells, items one sees, etc.).

6.2 Drug/Device Handling: If the research involves drugs or device, describe your plans to store, handle, and administer those drugs or devices so that they will be used only on subjects and be used only by authorized investigators.

- *If the control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference that SOP in this section.*

Response:

N/A

6.3 If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:

- *Identify the holder of the IND/IDE/Abbreviated IDE.*
- *Explain procedures followed to comply with sponsor requirements for FDA regulated research for the following:*

Response:

N/A

7.0 36 Local Number of Subjects

7.1 Indicate the total number of subjects that will be enrolled or records that will be reviewed locally.

Response:

Up to 20 subjects will be enrolled from Buffalo, and the neighboring cities. Subjects will be randomized after completion of the baseline period. The goal will be to randomize at least 10-12 participants.

7.2 If applicable, indicate how many subjects you expect to screen to reach your target sample (i.e. your screen failure rate).

Response:

We expect to initially screen approximately 60 subjects (online or by phone screen survey) and complete about 20 in person and baseline screenings.

7.3 Justify the feasibility of recruiting the proposed number of eligible subjects within the anticipated recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?

Response:

Given that we will be taking advantage of CTSI resources for recruiting based on individuals' diagnosed medical conditions, we anticipate that recruiting this relatively small number of participants for our final sample will be feasible within a 4-month period. The Buffalo Research Registry has 200-some potentially eligible individuals based on a diagnosis of Pre- or Type 2 Diabetes, and TriNetX an additional 15,110 with these diagnoses (with 5,150 of these prescribed an oral blood glucose-regulating medication).

8.0 Inclusion and Exclusion Criteria*

*8.1 Describe the criteria that define who will be **included** in your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

Adults over the age of 18 with prediabetes or Type 2 Diabetes currently prescribed at least one oral medication for blood glucose regulation, or for related comorbidities e.g., hypertension, hyperlipidemia, and are relatively non-adherent to taking them (< 80% of prescribed doses taken), but are motivated and/or have the intent to better comply with their medication regimen, will be studied.

During the Baseline Period, if participants are adherent to their medications (>80%), their participation in the study may be terminated.

Prediabetes and Type 2 Diabetes: Participants must report having have a diagnosis of prediabetes or Type 2 Diabetes within the last 2 years or meet criteria for prediabetes or Type 2 Diabetes. The American Diabetes Association guidelines (Group, 2003) defines prediabetes and Type 2 Diabetes as Fasting Plasma Glucose (FPG) 100mg/dl or greater, 2h glucose 140mg/dl or greater after Oral Glucose Tolerance Test (OGTT), or hemoglobin A1c (HbA1c) of approximately 5.4% or greater. We will also include individuals who have

increased risk for developing prediabetes and type 2 diabetes, which includes individuals who have a BMI of 30 of higher with one or more related comorbidities (e.g., hypertension, hyperlipidemia).

*8.2 Describe the criteria that define who will be **excluded** from your final study sample.*

NOTE: This may be done in bullet point fashion.

Response:

Pregnancy: Women who are pregnant or lactating will be excluded from participation.

Substance use, abuse, or dependence: Individuals that currently have problems with substance dependence, addiction, or problematic substance use that would limit participation (e.g., binge drinkers, alcoholics, daily stimulant/opiate users) will be excluded.

Conditions that affect adherence: Participants should not have a condition that would limit participation which include medical conditions that would affect individuals' ability to use the computer for prolonged period of time; leave the individual unable to ambulate; unmanaged psychiatric disorder (e.g., depression, anxiety, attention deficit hyperactivity disorder, schizophrenia), cognitive impairment that would impact memory (e.g., symptomatic concussion), or an intellectual impairment that would impact study adherence. Additionally, participants should be able to attend to all intervention sessions (Due to Covid-19 all sessions will be completed remotely/virtually) and have reliable access to technology required to complete the measures in this study. If a participant is not able to make most sessions (e.g. participant is out of town during most of the study for work or vacation travel), or does not have reliable access to technology, they may be excluded from the study.

Prior participation in similar studies: Individuals who have recently participated in a laboratory study using similar methods may also be excluded.

Use of medication adherence aids: individuals who currently use aids to assist with medication adherence (e.g., pill organizers, reminder apps)may be excluded.

8.3 Indicate specifically whether you will include any of the following special populations in your study using the checkboxes below.

NOTE: Members of special populations may not be targeted for enrollment in your study unless you indicate this in your inclusion criteria.

Response:

☐ Adults unable to consent

☐ Individuals who are not yet adults (infants, children, teenagers)

☐ Pregnant women

☐ Prisoners

8.4 Indicate whether you will include non-English speaking individuals in your study. ***Provide justification if you will exclude non-English speaking individuals.***

In order to meet one of the primary ethical principles of equitable selection of subjects, non-English speaking individuals may ***not*** *be routinely excluded from research as a matter of convenience.*

In cases where the research is of therapeutic intent or is designed to investigate areas that would necessarily require certain populations who may not speak English, the researcher is required to make efforts to recruit and include non-English speaking individuals. However, there are studies in which it would be reasonable to limit subjects to those who speak English. Some examples include pilot studies, small unfunded studies with validated instruments not available in other languages, studies with numerous questionnaires, and some non-therapeutic studies which offer no direct benefit.

Response:

This study will not include non-English speaking participants. Since all the materials in this study will be in English, and the validated measurements are not provided in other languages, we will be excluding individuals who do not speak English.

9.0 Vulnerable Populations*

If the research involves special populations that are considered vulnerable, ***describe the safeguards included to protect their rights and welfare.***

NOTE: You should refer to the appropriate checklists, referenced below, to ensure you have provided adequate detail regarding safeguards and protections. You do not, however, need to provide these checklists to the IRB.

9.1 For research that involves ***pregnant women,*** *safeguards include:*
NOTE CHECKLIST: Pregnant Women (HRP-412)

Response:

☒ **N/A**: This research does not involve pregnant women.

9.2 For research that involves ***neonates of uncertain viability or non-viable neonates,*** *safeguards include:*
NOTE CHECKLISTS: Non-Viable Neonates (HRP-413), or Neonates of Uncertain Viability (HRP-414)

Response:

☒ **N/A:** This research does not involve non-viable neonates or neonates of uncertain viability.

*9.3 For research that involves **prisoners**, safeguards include:*
NOTE CHECKLIST: Prisoners (HRP-415)

Response:

☒ **N/A:** This research does not involve prisoners.

*9.4 For research that involves **persons who have not attained the legal age for consent to treatments or procedures involved in the research ("children")**, safeguards include:*
NOTE CHECKLIST: Children (HRP-416)

Response:

☒ **N/A:** This research does not involve persons who have not attained the legal age for consent to treatments or procedures ("children").

*9.5 For research that involves **cognitively impaired adults**, safeguards include:*
NOTE CHECKLIST: Cognitively Impaired Adults (HRP-417)

Response:

☒ **N/A:** This research does not involve cognitively impaired adults.

*9.6 Consider if other specifically targeted populations such as students, employees of a specific firm, or educationally or economically disadvantaged persons are vulnerable. **Provide information regarding their safeguards and protections, including safeguards to eliminate coercion or undue influence.***

Response:

10.0 Eligibility Screening*

*10.1 Describe **screening procedures** for determining subjects' eligibility. Screening refers to determining if prospective participants meet inclusion and exclusion criteria.*

📎 *Include all relevant screening documents with your submission (e.g. screening protocol, script, questionnaire).*

Response:

Interested participants will have the opportunity to complete an initial screening by phone, online, or paper upon their preference to determine if they meet the inclusion criteria. If the participant meets inclusion criteria as assessed in the online screen, they will then be invited to an in-lab or virtual screening appointment and baseline session screening appointment and baseline session. See the Measures.docx document for questions that appear in the online screen assessment, as well as the "I2R – Phone Screening Script" document for the script for the phone administered version.

Information about the study will be provided and consent will be obtained to prescreen for eligibility purposes, and the same will occur in the in-lab or virtual screen/baseline session.

☐ **N/A:** There is no screening as part of this protocol.

11.0 Recruitment Methods

☐ **N/A:** This is a records review only, and subjects will not be recruited. NOTE: If you select this option, please make sure that all records review procedures and inclusion/exclusion screening are adequately described in other sections.

11.1 Describe when, where, and how potential subjects will be recruited.

NOTE: Recruitment refers to how you are identifying potential participants and introducing them to the study. Include specific methods you will use (e.g. searching charts for specific ICD code numbers, Research Participant Groups, posted advertisements, etc.).

Response:

The different types of recruitment methods to be used are the following:

1. We will post and/or disseminate recruitment materials (e.g., flyers, letters, and handouts/postcards) both in the community (e.g., health clinics, stores, public spaces, community and organizational events) and online (e.g., craigslist, social media websites/apps, division website).
2. We will use the i2b2 and TriNetX database through UB's Institute for Healthcare Informatics (IHI) to recruit participants from the UBMD medical data base.
3. The study team may also utilize the University at Buffalo's Clinical and Translational Science Institute (CTSI) for recruitment assistance and consultation. The CTSI's Recruitment Team provides resources, guidance on appropriate recruitment strategies, and assistance in linking out study team with partners to effectively reach recruitment goals and target populations. We may also work with CTSI Community Engagement Team (CET) to create awareness of the study through their professional and community contacts. The tools they have available may include the Buffalo Research Registry (BRR, IRB Approved STUDY00000806), the Patients Voices Network (PVN), the Conventus CTSI/PVN Research Table, and conducting outreach at various community events. The BRR is a voluntary registry which can connect us to community members who have completed a health profile and are interested in participating in research. These community members have agreed to be contacted about potential research opportunities based on their self-reported information. These tools are method by which the CET distributes IRB-approved recruitment information to community members. As described in the BRR's IRB Approved Protocol (STUDY00000806), the BRR's Community Recruitment Liaison (CRL) will complete the process of sorting BRR data to reflect the inclusion and exclusion criteria for this study if

it is appropriate to utilize the BRR for this study. The CRL may reach out to potentially eligible participants in the BRR to provide information about our research study. After receiving proof that IRB has approved BRR's use in this study, the CRL can then provide our study team with name and contact information for potentially eligible participants for the purpose of following up with them after they have been informed of the study by the CRL. No recorded health information will be shared from BRR data. Our research team will proceed to reach out to interested potential participants regarding eligibility and moving forward in the study.

The CET also tables at many events in the community throughout the year and may display the IRB approved flyer for this project at their table at community events. Examples of events the CET attends include Good for the Neighborhood hosted by Independent Health Foundation, UB on the Green, Juneteenth, Elmwood Arts Festival and many others.

The CET also hosts a standing table at the Conventus Building on the 4th floor of UBMD where the IRB approved flyer and other handouts can be made available to community members and patients. This will occur only after agreement between the CRL and UBMD Conventus partners that the study is appropriate for the Conventus space.

4. A database of participants that have been involved in previous studies at the University at Buffalo Behavioral Medicine laboratory that expressed interest in future studies will be used. Participants who have indicated interest in contact for future studies will be contacted by email or phone with the study advertisement and survey link. The database is used by all approved members of the Division of Behavioral Medicine and has been approved by previous IRB Committees, for phone/email contact (385420, 389912, 385442). No data or identifying information is collected prior to a potential participant's expression of interest in the research study. In addition, there are several similar but smaller databases maintained by individual labs within our department. These labs also conduct studies with type II diabetic and/or prediabetic patients, and maintain a list of individuals who were interested in participating, but did not meet the eligibility criteria for the given study. We plan to collaborate with these labs, sharing information about our study with these potential participants who indicated an interest in hearing about other study opportunities, and also sharing information about these colleagues' studies with individuals who were interested in, but not eligible for, the present study. These interested individuals' contact information will be shared to us by the other labs. Following this, these potential participants will be contacted by our study team.

5. Urban Family Practice: Used in previous IRB approved studies (030-796526, STUDY 00000936), the physicians from Urban Family Practice have provided us with a list of patient names, addresses, contact information, and brief medical history (e.g., diagnosis of hypertension, diagnosis of hyperlipidemia, previous HbA1c measurements, BMI) for recruitment purposes of the MINDD Grant. We plan to use this same recruitment method

with Urban Family Practice. These patients may be mailed a letter that has been jointly signed from the study team and their physician. Included in the mailing are postcards with return address and that have been pre-stamped, so that these potential participants have the option to send back a reply regarding their interest in the study via postal mail Interested patients may contact the research team. Potential participants who were mailed a letter jointly signed by the study team and patient's physician at Urban Family Practice may also be contacted by the study team by phone to assess interest if the study team has not received a response from the individual after one week. Since this is the first time we will be using Urban Family Practice to recruit from, we will follow their recruitment protocol, which allows us to contact and follow up with potential participants in this manner.

6. Trialfacts: A recruitment service that creates advertisements and information on landing page. Potential participants will then complete an online prescreening questionnaire (which is identical to the prescreen used by the study) to determine if eligible to continue to a phone screening. Potential participants chose an appointment time for their phone screening to connect with the study staff. Potential participants also have the option to either email us or phone us for further information. All information collected through this service will be made available to the research team using google spreadsheets on Trialfacts protected servers.

11.2 Describe how you will protect the privacy interests of prospective subjects during the recruitment process.

NOTE: Privacy refers to an individual's right to control access to him or herself.

Response:

Individuals who contact the research team after viewing the above recruitment materials disseminated at local sites control their own privacy interests.

Individuals from our Division's database and other databases as described in section 11.1 that have previously indicated interest and willingness to be contacted for participating in future studies will be contacted and thus can control their own participation. All individuals will be informed that participation is voluntary and they can withdraw from participation at any time. The study team will cease contact with any individuals that they have learned are not interested.

The privacy of patients recruited using the i2b2/TriNetX and Urban Family Practice data will be protected by following the UB IRB-approved procedure. A letter will be sent to the eligible patient's physician (see attached). After a minimum of one week, if the physician doesn't contact the research team to refuse, a recruitment letter will be sent to participants via mail (see attached). If we don't hear from the patients within a minimum of one week, one follow-up call will be made (see attached phone script). If at any point the physician or the patient declines, the patient will be removed from the contact list.

The privacy of patients recruited through Trialfacts: Trialfacts adheres to the Principles of Good Clinical Practice (GCP) in all of its recruitment activity. All recruitment materials are provided to the research staff to ensure accuracy and seek relevant independent review board (IRB) or human research ethics committee (HREC) approval. Trialfacts will pass referrals to the research team using Google spreadsheets, for which they have a BAA in place to ensure HIPAA compliance.

11.3 Identify any materials that will be used to recruit subjects.

NOTE: Examples include scripts for telephone calls, in person announcements / presentations, email invitations.

For advertisements, include the final copy of printed advertisements with your submission. When advertisements are taped for broadcast, attach the final audio/video tape. NOTE: You may submit the wording of the advertisement prior to taping to ensure there will be no IRB-required revisions, provided the IRB also reviews and approves the final version.

Response:

Web-based advertisements, emails, flyers, handouts, telephone calls, using the approved text, and mailed letters and postcards, will be used to recruit subjects.

See supporting documents "I2R - Recruitment Materials ALL", "I2R – Phone Screening Script", "I2R – Recruitment – Patient Letter on UB" and "I2R – Recruitment – Physician Permission Letter" , "I2R-Recruitment Letter-Urban Family Practice_Niagara Street", "I2R-Recruitment Letter-Urban Family Practice_Jefferson Ave"

12.0 Procedures Involved*

*12.1 Provide a description of **all research procedures or activities** being performed and when they are performed once a subject is screened and determined to be eligible. Provide as much detail as possible.*

NOTE: This should serve as a blueprint for your study and include enough detail so that another investigator could pick up your protocol and replicate the research. For studies that have multiple or complex visits or procedures, consider the addition of a schedule of events table in in your response.

Response:

Individuals who pass the initial inclusion/exclusion screen and wish to enroll in the study will be invited to complete the in-lab or virtual screen/initial assessment. Participants invited to this session will be asked to share a copy of their medication refill history*. This can be shared either through email or fax.

*Participants will be able to request these from their local pharmacist. Refill records may also be obtained through web or app accounts for their current pharmacy. We may also

ask participants to fill out a pharmacy release form to receive the information directly from their pharmacy/ pharmacist.

In-Lab Screen/Initial Assessment Session:

Upon arrival to the Division of Behavioral Medicine (G56 Farber Hall), participants will be greeted and escorted to a private interview room where they will be given a more in-depth explanation about the study and provide documented consent if they agree to participate. Two copies of the consent form will be signed by all parties involved (person obtaining consent and the participant). One copy will be obtained by study personnel and one copy will be given to participants for their records.

Covid-19 Alternative Procedure: Participants will complete this session virtually over the video call and remote computing program Zoom. This program allows for research staff and participants to communicate, as well as for participants to access study measures remotely. Firstly, research staff will provide participants with a more in-depth explanation about the study. A consent form will be provided on the screen, and participants will have a chance to read through and provide an e-signature indicating their consent. A copy of the completed consent form will be emailed to participants for their records.

After the consent process, participants will provide their prescription refill history and target prescription medication as well as complete measures of decision making and questionnaires including demographics, medical history, alcohol, tobacco, and other substance use, participation and medication adherence motivation, and schedule availability for study participation.

Covid-19 Alternative Procedure: After the consent process, participants will complete measures of decision making and questionnaires including demographics, medical history, alcohol, tobacco, and other substance use, participation and medication adherence motivation, and schedule availability for study participation.

In order to confirm that participants are non-adherent, we may request that participants conduct a pill count of relevant medications. This may be done through sharing a short survey with participants in which they count the remaining quantity of relevant medications or sending research staff a photo of their medications, so that pill counts may be done remotely. Non-adherence will also be confirmed through pharmacy records and self-report.

The research staff will conduct pill counts to calculate adherence measures from pill counts and refill records to verify concordance with those provided in the initial screening survey, and that they meet eligibility criteria. The research staff will also provide the participant with up to 4 MEMS bottles for the medications they are non-adherent to. Measures and questionnaires may be completed on either the computer or paper/pencil labelled only with the participant's ID number and date. In addition, participants may sign forms for release of their relevant medical records to confirm their eligibility (e.g., diagnosis with prediabetes or Type 2 Diabetes, prescription drug use, refill history).). Participants may sign a release form for relevant pharmaceutical records (e.g. refill history of medications

used to treat pre-diabetes, diabetes, and comorbid disorders such as hyperlipidemia and hypertension) from their current pharmacy. Participants may also complete a urine drug screen to confirm non-substance abuse and female participants may complete a urine pregnancy test to ensure eligibility. If throughout the study there is reason to believe a participant has become pregnant (i.e. the participant expresses that is their belief), we will provide pregnancy testing. If the pregnancy results are positive, the participant will be informed and they will not be eligible to continue with the study. If in-lab measures of adherence and substance use indicate that the participant does not meet study criteria, the research staff may choose to end the In-Lab Screen/Initial Assessment session early and compensation will be pro-rated (see compensation section below in protocol for details).

If participants still meet eligibility criteria and have availability for sessions, they will complete the assessments described below in the *Assessment Sessions* description. Then, the research staff will give the participant a pharmaceutical medication vial and a MEMS track-cap (an electronic medication vial cap that records and time-stamps medication vial openings). The research staff will instruct the participant to transfer their medication into the study bottle and adhere the copy of the prescription label onto the study bottle. The staff member will then review appropriate use of the study bottle and MEMS cap; and schedule the participant's intervention sessions. Participants will also have their height and weight measured.

Covid-19 Alternative Procedure: If participants still meet eligibility criteria and have availability for sessions, they will complete the assessments described below in the Assessment Sessions description. Then, the research staff will give the participant a pharmaceutical medication vial and a MEMS track-cap (an electronic medication vial cap that records and time-stamps medication vial openings). This will be given to participants via mail. The research staff will instruct the participant to transfer their medication into the study bottle and adhere the copy of the prescription label onto the study bottle. The staff member will then review appropriate use of the study bottle and MEMS cap via Zoom or telephone; and schedule the participant's intervention sessions.

Baseline Sessions:

All participants complete a 6-week baseline in which they will use the MEMS bottles. At week 6, all participants will attend an in-person lab session to assess their adherence levels through looking at data from the MEMS bottles and pill counts.

Covid-19 Alternative Procedure: All participants will complete a 6-week baseline in which they will use the MEMS bottles. At week 6, data from the MEMS bottle will be obtained. In order to reduce participant and staff interaction due to COVID-19, this procedure will involve participants placing the cap from the MEMS bottle in a small bag placed in their mailbox. Research staff will conduct mobile data collection, and simply pick up the MEMS cap, and using sanitation

procedures, remotely download the data from the MEMS cap.The cap will then be returned to the participants mailbox.

Participants will then be randomly assigned to either the 6-week, 8- week or 10-week baseline. If a participant's medication adherence is not below 80%, they will be asked to come in at week 8 to reassess their adherence level (similarly, if their adherence is not below 80% at week 8, they will be asked to come back at week 10. If their adherence is not below 80% at this point, they will be dismissed from the study). If a participant is below 80% adherence within this 6-week period and their adherence is stable, meaning that there is no increasing trend in their adherence level, they will be randomly assigned to either a 6-week, 8- week or 10-week baseline. Participants who were assigned 6- week baseline, will now be eligible to start the intervention, those in the 8-week will complete two more weeks of baseline prior to the intervention, and those in the 10-week will complete four more weeks of baseline prior to the intervention *.

*Participants must be considered stable based on their pill counts to continue to the intervention period. For this study stability will be defined as no increasing trend (3 data points) in their adherence level. If a participant was assigned to a group but is not stable during that time period, they will be assigned to the next group (if disqualified for 6-week they will go to the 8-week and so on).

Assessment Sessions:

Participants will complete the major life events assessment and a variety of assessments pertaining to executive function/memory. Similar to the screening/baseline session, these measures will all be administered via Zoom. Some of these tasks may only be administered in certain assessment sessions (e.g., the initial and/or final).

The types of tasks participants may complete are:

- Prospective memory tasks
- A working memory task
- An impulsive choice task

Participants will also have their height/weight taken, and the research staff will obtain self-report and objective measures of medication adherence (e.g., information such as data from MEMS caps, pill counts, reasons for non-adherence, and reasons for opening medication bottles).

Intervention Sessions:

During the Covid-19 Quarantine All intervention sessions will be conducted via zoom.

During each intervention meeting, the research staff will obtain self-report and objective measures of medication adherence, and participants will either complete EFT or IC activities, dependent on group assignment. Pill counts and MEMS data may be obtained by a staff member that is not acting as the interventionist for EFT/IC activities, so as to reduce the total time the participant must be in the lab.

Participants assigned to EFT will be asked to generate episodic cues, similar to the tasks used in our previous studies on EFT's effect (Daniel et al., 2013); unlike in prior studies, however, cues will be specific to instances of taking one's medication and/or positive events resulting from successful medication adherence. The episodic component of the thinking task occurs while the participants are asked to describe the perceptual details of the medication-taking (e.g., taking medication at home on a typical day, or while out of town on vacation) or medication-outcome event (feeling better and more energetic after medication, etc.). Participants will be asked open-ended questions to prompt more detail (such as what they are seeing, hearing, smelling, feeling), and to identify what successful adherence may look like if the initial event description does not go as planned (e.g., if you normally take your medication when you make coffee, what would successfully taking your medication look like on a day when you run out of time to make it?). Participants may record their EFT events into audio cues, so that they can practice using EFT using different modalities at home.

Participants assigned to IC will be asked to generate cues about newly-learned health information. For this activity, the research staff will provide participants with a weekly learning module that will consist of presenting information on relevant health-related topics (e.g., information about diagnosed conditions that made them eligible for participation), which may include brief quizzes, informational videos, and other learning-oriented activities that may help with information retention (e.g., playing a memory game incorporating information about glucose metabolism). Participants will be asked to generate cues about the course content which may include imagining different ways the information could be useful, how it could be applied in different contexts, with different people, etc. As in EFT, participants will be asked open-ended questions as needed to prompt more details, and IC participants may also audio record their cues.

Participants will be asked to rate their cues on different dimensions (e.g., vividness, usefulness, valence, salience), which will be used to calculate a richness score (average of dimension ratings).

EFT participants may be provided the same information that IC participants are provided, to ensure both groups are equally knowledgeable on the topics; this information may be provided in a different format for ease of use/reference outside of the laboratory (e.g., on a study website, pamphlet, or booklet).

Participants will be trained to use EFT/IC outside of the lab using the ecological momentary intervention (EMI) computer based program that we have developed: the Mobile Audio Management and Response Tracker (MAMRT). This program, which is part of the study website, can be accessed by smartphone, tablet or computer. This application stores participants' EFT/IC cues, prompts their use (e.g., reminder text message, reminder email), asks questions about use of their cues, and records their use. Participants will be instructed to practice using EFT/IC daily. The MAMRT software was previously approved in STUDY00000936, and appears in Sze, Daniel, Kilanowski, Collins, and Epstein, 2015. In addition to the above, the MAMRT website may also be used to provide health information (i.e., that provided to the IC group), and other activities such as

completing quizzes to assess mastery of educational materials, with multiple versions of quizzes on each module available to account for those who need or desire additional practice. The website will also contain password protected sections that are for internal use by study personnel. The website will not contain protected health information.

Because use of the EMI is not incentivized in any way, staff will conduct walk-throughs by phone with the participant to ensure that the participant is using the intervention outside of the lab. These walk-through calls will consist of guiding the participant through the use of their EFT/IC cues; calls will last about 15 mins, and will be scheduled with participant. Check-ins (practice and reminders) may occur both during the intervention weeks and during the study follow-up period prior to the final assessment. Participants may also receive reminder texts/email/or phone calls to use their EFT/IC cues.

During CDC recommended travel restrictions due to flu, respiratory illness or coronavirus, we are enacting preventative measures to ensure both participants and employees limit exposure.

(1) Participants will be asked during reminder calls/emails/text messages/scheduling contacts questions regarding their health and their child's health before in-person meetings. This language can be used in any contact of scheduling participants such as, in-person or phone, email, text, letter,etc

Example of .."With the current situation involving the flu, respiratory illnesses, and the coronavirus, the Imagine to Remember Study team are enacting some preventive measures to keep everyone healthy. The Imagine to Remember Study Team wants to ensure the safety of all staff and our participants. While we understand that there are areas with confirmed cases of the virus and your area may or may not be affected, we would like to help prevent the possible spread by asking a few questions prior to your appointment."

1. -"Have you or your child traveled in the last 14 days? If so, where? (effected confirmed areas are changing daily)

2. -Are you or your child experiencing or showing any symptoms related to the flu, or other respiratory illnesses such as the coronavirus, including fever, cough or shortness of breath?

If new information about symptoms is found, we will follow CDC guidelines/recommends

https://www.cdc.gov/coronavirus/2019-ncov/about/symptoms.html

3. -Have you had any potential contact with someone who has tested positive for any of the above illnesses?

This information is not data but can be used to determine if an in-person meeting can be scheduled or if an alternative should be scheduled at least 14 days from the date of incident (or the current CDC/health department time recommendations).

If necessary, attempts will be made to administer study materials and measures remotely. This may include administering surveys that are already used in current study materials online, as well as conducting phone calls in lieu of face to face meetings as needed.

In the event a participant/staff member tests positive for coronavirus, we will work with Erie County Health department to provide any information they need; including names, address and phone numbers, of potential contacts as per the Health department policies. NYS law indicates that it is mandatory to provide this information in the case of an identified infectious disease:

INFORMATION FOUND HERE:

https://regs.health.ny.gov/content/section-210-reporting-cases-or-suspected-cases-or-outbreaks-communicable-disease-physicians

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For all session types above, the tasks and procedures may be completed in an order different from that outlined as feasibility and efficiency warrants.

12.2 Describe what data will be collected.

NOTE: For studies with multiple data collection points or long-term follow up, consider the addition of a schedule or table in your response.

Response:

Data consists of audio recordings of participants cues; recordings of the sessions, demographic measures; delay discounting; prospective, and working memory; substance use/consumption; pregnancy status; medication adherence (pill counts, pharmacy refill records, MEMS-provided medication adherence, self-report measures); and participants' heights and weights recorded during the experimental sessions, in addition to medical history and details about past medication use.

12.3 List any instruments or measurement tools used to collect data (e.g. questionnaire, interview guide, validated instrument, data collection form).

Include copies of these documents with your submission.

Response:

Please see the attachment labeled, "Measures.docx". Additional questionnaires may be added a later time via modification.

Recordings: Intervention sessions will be recorded for to review EFT/IC fidelity and provide feedback to Interventionists/research staff.

Demographics and Health Behavior: Race/ethnicity, household income, and educational level will be assessed using a survey-based questionnaire. Participants will also be asked about their health behavior, including substance use, mental health, and medical history.

Medication Use and Adherence: We will obtain pill counts, reasons for non-adherence, intent to take medication, and motivation to adhere to medications, as well as medication adherence data as recorded by the MEMS caps and prescription refill history.

Major Life Events: Individuals will be asked to complete the major life events questionnaire which measures major life events that may have been experienced during their involvement, or just prior to involvement in the study. Individuals who are undergoing major life events such as a move, new baby or a new job may influence their performance on study measures and tasks.

Height, Weight, BMI: Participants' height will be assessed using a digital stadiometer. Participants' weight will be assessed using a digital scale. Based on the height and weight data, Body Mass Index (BMI) will be calculated according to the following formula: BMI = kg/m^2. These are the current standards set forth by the Centers for Disease Control and Prevention (Kuczmarski et al., 2002).

Cue Measures: Rating scales assessing dimensions of the cues (e.g., vividness of imagining, or recalling the info, attentiveness to cues) and cue use (e.g., vividness, usefulness) will be administered at cue generation and when cues are accessed via our software program. Cues will be rated on numerical and/or ordinal scales; e.g., on a scale of 1 to 5, where 1 indicates "not at all" and 5 indicates "very much".

Delay Discounting (DD): An operational definition of impulsivity is delay discounting, the degree to which a person will discount the value of a larger delayed reward in favor of a smaller immediate reward. Computerized/ experimenter administered assessments will provide participants with choices between a smaller amount of hypothetical money available immediately or a larger amount of hypothetical money available later.

Du, W., Green, L., & Myerson, J. (2002). Cross-cultural comparisons of discounting delayed and probabilistic rewards. Psychological Record, 52(4), 479–492. https://doi.org/https://doi.org/10.1007/BF03395199

- Those assigned to the EFT (IC) group may be asked to visualize future events (health information) while completing the DD task.

Memory tasks: Different types of memory processes may be involved in the intervention effects; these include working memory, prospective memory, retrospective memory and episodic memory, which will be measured using computerized tasks or paper/pencil measures. The tasks we will use are the following:

- The "Virtual Week" (Rendell et al., 2007; Rose et al., 2010) is a measure of Prospective Memory (PM) and Retrospective Memory (RM). The task is styled as a board game, with each round (movement across the board) representing one day. Throughout a single day, participants are instructed to complete different tasks either as different events occur (e.g., when someone comes to the door), at different times of day (e.g., when it is 4:00pm), or after different durations of gameplay. The game begins with a training round, so that the participant learns what is expected through the task. While completing the training round, the participant will be provided with any necessary instructions from the study personnel to help them complete the task correctly. After the training round, all participants will complete test rounds of the "Virtual Week."
    - Those assigned to the EFT group may be asked to visualize completing the daily tasks prior to starting each round (e.g., close their eyes and imagine everything that would be involved with calling a fictional person in the game at a certain time).

Rendell, P. G., Jensen, F., and Henry, J. D. (2007). Prospective memory in multiple sclerosis. J. Int. Neuropsychol. Soc. 13, 410–416. doi: 10.1007/s00213-008-1408-0

Rose, N. S., Rendell, P. G., McDaniel, M. A., Aberle, I., and Kliegel, M. (2010). Age and individual differences in prospective memory during a "Virtual Week": the roles of working memory, vigilance, task regularity, and cue focality. Psychol. Aging 25, 595–605. doi: 10.1037/A0019771

- Working memory, measured as the ability to remember sequences of items (e.g., letters, numbers, symbols, or locations), with and/or without distractors present, and potentially in different orders (e.g., forwards/backwards).
- Prospective Memory Task, measured as the ability to remember to do to an extra task (e.g., clicking the mouse, certain keys on the keyboard, typing in a text box), while finding target word's in a word list

Cheng, H. , Yang, Z. , Dong, B. , Chen, C. , Zhang, M. , Huang, Z. , Chen, Z. and Wang, K. (2013), Chemotherapy-induced prospective memory impairment in patients with breast cancer. Psycho-Oncology, 22: 2391-2395. doi:10.1002/pon.3291

- Royal Prince Alfred Prospective Memory Test is a measure of time and event based prospective memory designed to assess retention over both long and short intervals (e.g. 15 minutes to a few days)

Radford, K.A., Lah, S., Say, M.J., & Miller, L.A. 2011). Validation of a New Measure of Prospective Memory: The Royal Prince Alfred Prospective Memory Test, The Clinical Neuropsychologist, 25, 127-140; DOI:10.1080/13854046.2010.529463.

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12.4 Describe any source records that will be used to collect data about subjects (e.g. school records, electronic medical records).

Response:

Electronic medical records and pharmaceutical records will be used. These will include records from patients at UBMD and additional records provided through the use of i2b2/TriNetX and Urban Family Practice.

*12.5 Indicate whether or not **individual** subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings will be shared with subjects or others (e.g., the subject's primary care physician) and if so, describe how these will be shared.*

Response:

We will not be administering any diagnostic tests, and as such will not be sharing results with participant's physicians.

*12.6 Indicate whether or not **study** results will be shared with subjects or others, and if so, describe how these will be shared.*

Response:

Full study results will not be shared with subjects. Findings based on group data may be presented at conferences and published in scientific journals.

13.0 Study Timelines*

13.1 Describe the anticipated duration needed to enroll all study subjects.

Response:

We anticipate it will take up to 6 months to recruit all participants.

13.2 Describe the duration of an individual subject's participation in the study. Include length of study visits, and overall study follow-up time.

Response:

Participants will be in the study for approximately 15 weeks, from the time of the initial online screening survey is completed, and until the final study assessment is completed. An outline of the approximate duration of each session type and corresponding study week is provided below.

Group	Session Type	Session Duration (Hours)	Study Weeks
6-Week	Online Screen	0.5	0
	Assessment (T1)	2.5	1
	Intervention Phone Calls	0.2	7 to 14
	Intervention Sessions	0.58	7 to 14
	Assessments (T2, T3)	2	6, 15
	Total Time	13.24	
8-Week	Online Screen	0.5	0
	Assessment (T1)	2.5	1
	Intervention Phone Calls	0.2	9 to 14
	Intervention Sessions	0.58	9 to 14
	Assessments (T2, T3)	2	8, 15
	Total Time	11.68	
10-Week	Online Screen	0.5	0
	Assessment (T1)	2.5	1
	Intervention Phone Calls	0.2	11 to 14
	Intervention Sessions	0.58	11 to 14
	Assessments (T2, T3)	2	6, 15
	Total Time	10.12	

13.3 Describe the estimated duration for the investigators to complete this study (i.e. all data is collected and all analyses have been completed).

Response:

We anticipate the study will take approximately 1 year to complete.

14.0 Setting

14.1 Describe all facilities/sites where you will be conducting research procedures. Include a description of the security and privacy of the facilities (e.g. locked facility, limited access, privacy barriers). Facility, department, and type of room are relevant. Do not abbreviate facility names.

NOTE: Examples of acceptable response may be: "A classroom setting in the Department of Psychology equipped with a computer with relevant survey administration software," "The angiogram suite at Buffalo General Medical Center, a fully accredited tertiary care institution within New York State with badge access," or, "Community Center meeting hall."

Response:

This research will be conducted at the University at Buffalo (UB), in the the Division of Behavioral Medicine Research Labs, located in G56, G58, G90, G96 and 151 Farber Hall, University at Buffalo South Campus.

14.2 For research conducted outside of UB and its affiliates, describe:

- *Site-specific regulations or customs affecting the research*
- *Local scientific and ethical review structure*

NOTE: This question is referring to UB affiliated research taking place outside UB, i.e. research conducted in the community, school-based research, international research, etc. It is not referring to multi-site research. UB affiliated institutions include Kaleida Health, ECMC, and Roswell Park Cancer Institute.

Response:

☒ **N/A:** This study is not conducted outside of UB or its affiliates.

15.0 Community-Based Participatory Research

15.1 Describe involvement of the community in the design and conduct of the research.

NOTE: Community-Based Participatory Research (CBPR) is a collaborative approach to research that equitably involves all partners in the research process and recognizes the unique strengths that each brings. CBPR begins with a research topic of importance to the community, has the aim of combining knowledge with action and achieving social change to improve health outcomes and eliminate health disparities.

Response:

☒ **N/A:** This study does not utilize CBPR.

16.0 Resources and Qualifications

*16.1 Describe the qualifications (e.g., education, training, experience, expertise, or certifications) of the Principal Investigator **and** staff to perform the research. When applicable describe their knowledge of the local study sites, culture, and society. Provide enough information to convince the IRB that you have qualified staff for the proposed research.*

NOTE: If you specify a person by name, a change to that person will require prior approval by the IRB. If you specify a person by role (e.g., coordinator, research assistant, co-investigator, or pharmacist), a change to that person will not usually require prior approval by the IRB, provided that the person meets the qualifications described to fulfill their roles.

Response:

The Principal Investigator, Dr. Leonard H. Epstein is a Distinguished Professor of Pediatrics, and Social and Preventive Medicine at the State University of New York at Buffalo. Dr. Epstein has published over 300 papers in peer reviewed journals. The project coordinator and research staff have experience in behavioral research using similar methodology and have completed the appropriate certifications: CITI and CPR/First Aid/AED.

Describe other resources available to conduct the research.

16.2 Describe the time and effort that the Principal Investigator and research staff will devote to conducting and completing the research.

NOTE: Examples include the percentage of Full Time Equivalents (FTE), hours per week. The question will elicit whether there are appropriate resources to conduct the research.

Response:

The Principal Investigator will devote approximately 5-8 hours per week to meet with staff, oversee data safety and discuss recruitment and study specific information.

The Project Coordinator will spend approximately 30% of their time training and supervising staff, including conducting weekly project meetings, 20% coordinating the scheduling of appointments for staff and prospective subjects, 10% coordinating and assisting in the test sessions, and 10% overseeing the development of study materials.

Research Assistants/Interventionists will spend approximately 50% of their time training and running participants, 20% recruiting subjects, 20% developing project materials, including questionnaires, surveys, and forms, and 10% entering data and quality control of the data collected during the study.

16.3 Describe the availability of medical or psychological resources that subjects might need as a result of anticipated consequences of the human research, if applicable.

NOTE: One example includes: on-call availability of a counselor or psychologist for a study that screens subjects for depression.

Response:

We do not anticipate a need for medical or psychological resources stemming from the research procedures. However, if during any of the visits, the participant discloses occurrences of recent life events that appear to cause the participant a high degree of distress (e.g., the participant is crying, appears in shock, etc.) the project coordinator and PI will be notified. These participants will be provided with a list of resources. Additionally, we will follow up with the participant within the next 24 hours of said occurrence.

16.4 Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions.

Response:

All personnel working on the project are required to complete the CITI training as required by IRB. Additionally, there are extensive procedures manuals that are

read and followed by all personnel. The Project Coordinator is responsible for training staff on data collection and recording procedures.

Project coordinator and the principal investigators will be responsible for ensuring proper staff training on study procedures and consistency of data collection between each site. This will be achieved through local training, regular communication between sites and coordinating procedural materials for experimenters.

17.0 Other Approvals

17.1 Describe any approvals that will be obtained prior to commencing the research (e.g., school, external site, funding agency, laboratory, radiation safety, or biosafety).

Response:

☒ **N/A:** This study does not require any other approvals.

18.0 Provisions to Protect the Privacy Interests of Subjects

18.1 Describe how you will protect subjects' privacy interests during the course of this research.

NOTE: Privacy refers to an individual's right to control access to him or herself. Privacy applies to the person. Confidentiality refers to how data collected about individuals for the research will be protected by the researcher from release. Confidentiality applies to the data.

Examples of appropriate responses include: "participant only meets with a study coordinator in a classroom setting where no one can overhear", or "the participant is reminded that they are free to refuse to answer any questions that they do not feel comfortable answering."

Response:

Prospective participants may contact the laboratory of their own free will and are thus controlling access to their privacy. All data will be collected in a secure laboratory environment in password protected databases in which only study staff has access. In sessions, participants will only interact with project research staff and sessions will take place in a private laboratory room that may include a closed circuit television monitoring system that will be monitored by the experimenter to ensure participant protocol adherence and safety. Participants are reminded that they are free to refuse to answer any questions that they do not feel comfortable answering and that all information is kept confidential to the extent provided by law.

The i2b2 data will be protected by only accessing identifiable contact information remotely on IHI's "virtual machine", so the identifiable data never leaves their secure encrypted server. All use of identifiable data is done behind the firewall on IHI's secure system.

In regards to the CDC procedures mentioned in the Procedures section:

In the case of a positive test of an infectious disease, any contact with the Person Under Investigation (PUI) will be disclosed to the Erie county health department as requested/required.

Erie county Department of Health, Epidemiology and Disease control includes forms for identifying reportable infectious diseases and contact information for the appropriate person at the Health department to discuss any personally identifiable information.

http://www2.erie.gov/health/index.php?q=epidemiology-amp-disease-control

18.2 Indicate how the research team is permitted to access any sources of information about the subjects.

*NOTE: Examples of appropriate responses include: school permission for review of records, consent of the subject, HIPAA waiver. This question **does apply** to records reviews.*

Response:

Participants will be recruited using a secure database of interested participants maintained by the Division of Behavioral Medicine and approved for use by previous IRB committees. Potential participants from this database will be contacted if they had indicated that they are willing to be contacted for participation in studies and thus control their own participation.

A HIPAA waiver has been completed for the recruitment of participants through medical records (i2b2, TriNetX, Urban Family Practice), which is completed through the physician's office with the consent of the primary care physician. The research team may also contact primary care physicians and pharmacists at their preferred pharmacy to confirm eligibility after participants have completed consent/HIPAA/medical/pharmacy release forms.

Any information through recruitment from Trialfacts will be deleted from there servers upon completion of the study and all information will be transferred to a secure database of interested participants maintained by the Division of Behavioral Medicine and approved for use by previous IRB committees. Potential participants from this database will be contacted if they had indicated that they are willing to be contacted for participation in studies and thus control their own participation.

19.0 Data Management and Analysis*

19.1 Describe the data analysis plan, including any statistical procedures. This section applies to both quantitative and qualitative analysis.

Response:

Pill count and MEMS data displayed as a percentage of doses taken will be displayed graphically to enable visual analysis of changes in means and trends of dependent variables across the different phases of the study.

Borckardt, J., & Nash, M. (2014). Simulation modelling analysis for small sets of single-subject data collected over time. Neuropsychological Rehabilitation, 24(3-4), 492–506. https://doi.org/10.1080/09602011.2014.895390

Kratochwill, T., Hitchcock, J., & Chezan, L. (2015). What Works Clearinghouse Standards and Generalization of Single-Case Design Evidence. Journal of Behavioral Education, 24(4), 459–469. https://doi.org/10.1007/s10864-015-9224-1

19.2 If applicable, provide a power analysis.

NOTE: This may not apply to certain types of studies, including chart/records reviews, survey studies, or observational studies. This question is asked to elicit whether the investigator has an adequate sample size to achieve the study objectives and justify a conclusion.

Response:

A power analysis is not applicable to this multiple baseline design. We are collecting weekly data from participants and will have enough data points to ensure we will be able to achieve the study objectives. The results of this study will be analyzed graphically as well as assessing the degree of change from baseline to treatment across the three replications. For an example of a study that utilized a multiple baseline design, see:

Spaulding, S., Devine, K., Duncan, C., Wilson, N., & Hogan, M. (2012). Electronic Monitoring and Feedback to Improve Adherence in Pediatric Asthma. Journal Of Pediatric Psychology, 37(1), 64–74. https://doi.org/10.1093/jpepsy/jsr059

19.3 Describe any procedures that will be used for quality control of collected data.

Response:

The principal investigator will be responsible for ensuring data integrity and safety monitoring for human subjects who are involved in the research and communicating any negative outcomes of the data and safety monitoring plans (DSMP) reviews or any serious event or problem (SEP) that occur to the UB IRB and other required offices/agencies. Materials will be checked to make sure that all study data are coded with a unique participant ID. The ID will be linked only by a name through a master list kept by the project coordinator in a password-protected file.

20.0 Confidentiality*

A. Confidentiality of Study Data

*Describe the local procedures for maintenance of confidentiality of **study data and any records that will be reviewed for data collection**.*

*20.1 A. Where and how will all data and records be stored? Include information about: password protection, encryption, physical controls, authorization of access, and separation of identifiers and data, as applicable. Include physical (e.g. paper) **and** electronic files.*

Response:

The i2b2 data will be protected by only accessing identifiable contact information remotely on IHI's "virtual machine", so the identifiable data never leaves their secure encrypted server. All use of identifiable data is done behind the firewall on IHI's secure system.

Urban Family Practice patient data will be protected by only accessing identifiable contact information remotely. Urban Family Practice will send us an encrypted file, containing this contact information that will be stored on a password protected server that only the research staff will have access too.

Trialfacts recruitment data will be protected by only accessing survey information remotely. Trialfacts will send us an encrypted file/ Google spreadsheet, containing this information that will be stored on a password protected server that only the research staff will have access too.

Potential participants who have filled out the online screening survey will have their responses stored on a password protected server that only the research staff will have access too. Additionally, if there are paper copies of the screening survey responses they will be de-identified and stored in a locked filing cabinet in a locked room (G96/G56 Farber hall) which only research staff has access to.

Participants will be assigned a unique identification number to ensure the confidentiality of the data. A master list that links subject ID and participant's name will kept in a secure file that is password protected on a password protected computer. Only research staff will access to the master list. Paper files (that may include forms such as: medical release/ pharmacy release forms and other study materials) will be kept in locked lab offices at the Division of Behavioral Medicine Research Lab and electronic files will be kept on password protected computers in password protected/encrypted databases only accessible to members of the research staff. When the results of the study are presented and/or published, only group data will be provided; no individual participant will be identifiable.

20.2 A. How long will the data be stored?

Response:

All study data will be retained for a period of at least three years. The master list linking the study ID with the participant name will be kept in a locked cabinet in G56 for three years after the completion of the study at which point it will be destroyed. Any identifiable information from participants (i.e. medical release forms/ pharmacy release forms) will be kept in a locked cabinet in G56 for three years after the completion of the study at which point it will be destroyed. De-identified data will be retained indefinitely. Information about potential participants provided to us by Urban Family Practice and Trialfacts will be deleted upon completion of the study.

20.3 A. Who will have access to the data?

Response:

Only the principal investigator and research staff associated with the study will have access to the data.

20.4 A. Who is responsible for receipt or transmission of the data?

Response:

The principal investigator takes primary responsibility for the data.

20.5 A. How will the data be transported?

Response:

Data will be transported in password protected/encrypted files via email. All transferred data will be de-identified.

B. Confidentiality of Study Specimens

*Describe the local procedures for maintenance of confidentiality of **study specimens**.*

☐ **N/A:** No specimens will be collected or analyzed in this research. *(Skip to Section 21.0)*

20.6 B. Where and how will all specimens be stored? Include information about: physical controls, authorization of access, and labeling of specimens, as applicable.

Response:

All and urine samples will be analyzed during session it is collected or immediately after the appointment and will not be saved (i.e., stored). Specimens will not be banked for future use.

20.7 B. How long will the specimens be stored?

Response:

N/A, specimens will not be stored

20.8 B. Who will have access to the specimens?

Response:

Research staff conducting appointments will have access to the specimens during or immediately after the appointment. However, specimens will not be stored.

20.9 B. Who is responsible for receipt or transmission of the specimens?

Response:

N/A, there is no receipt or transmission of the specimens.

20.10 B. How will the specimens be transported?

Response:

N/A, the specimens will not be transported.

21.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

NOTE: Minimal risk studies may be required to monitor subject safety if the research procedures include procedures that present unique risks to subjects that require monitoring. Some examples include: exercising to exertion, or instruments that elicit suicidality or substance abuse behavior. In such cases, N/A is not an acceptable response.

21.1 Describe the plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe.

Response:

Data will be reviewed weekly and secured in Division of Behavioral Medicine Research Lab. The Principal Investigator, Leonard H. Epstein, PhD, will be responsible for ensuring data integrity and safety monitoring for human subjects who are involved in the research and may work with a Data Safety Officer consistent with our NIH DSMP.

21.2 Describe what data are reviewed, including safety data, untoward events, and efficacy data.

Response:

Study questionnaires and measurements that are collected by study personnel will be reviewed and monitored.

21.3 Describe any safety endpoints.

Response:

This study poses no greater than minimal risk; therefore, there are no safety endpoints.

21.4 Describe how the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with participants).

Response:

Participants will be encouraged to contact study personnel if they experience any problems or difficulties, and if any adverse events (AE) are reported, the study personnel contacted will record the AE. AE will be recorded as soon as they are reported, and the PI and study coordinator will be made aware. The study coordinator will summarize the AE in a memo; the participant will be called and the summary will be read to them to ensure that the information is accurate. The memo will then be submitted to the University at Buffalo IRB and the PI. If the PI, or the IRB decide that further action is warranted, the PI and study coordinator will then formulate and carry out a plan to respond to the AE. The study coordinator will write a memo summarizing such actions; this memo will then be forwarded to the IRB. Safety information will be collected and reported to both the UBIRB and the Safety Officer in the time frames outlined by the UBIRB.

21.5 Describe the frequency of safety data collection.

Response:

Data will be reviewed weekly and secured in G56 and 252A Farber Hall. A weekly review of these data will be conducted by the principal investigator and project coordinator during their staff meetings with study personnel.

21.6 Describe who will review the safety data.

Response:

Serious Events and Problems (SEP) will be monitored by the principal investigator and project coordinator as well as reported to both the IRB and the Safety Officer in the timeframes outlined by the IRB.

21.7 Describe the frequency or periodicity of review of cumulative safety data.

Response:

Cumulative data will be reviewed approximately six months to a year based on the requirements of the Grant and NIH committee.

21.8 Describe the statistical tests for analyzing the safety data to determine whether harm is occurring.

Response:

N/A, there are no discontinuing criteria.

21.9 Describe any conditions that trigger an immediate suspension of the research.

Response:

N/A, there are no discontinuing criteria.

22.0 Withdrawal of Subjects*

☐ **N/A:** This study is not enrolling subjects. This section does not apply.

*22.1 Describe **anticipated** circumstances under which subjects may be withdrawn from the research without their consent.*

Response:

Subjects who do not adhere to the protocol procedures and study instructions may be withdrawn from research analyses, as determined by the Principal Investigator and/or NIH Data Safety Committee. In addition to not adhering to study instructions, possible reasons for removal include nonsystematic responding to questionnaires. If a participant is withdrawn from the study without their consent, they will be debriefed about the nature of the study and be compensated for the amount of time spent in the study. We may also stop an ongoing session, or end participation in the study because we have collected all the information we need.

22.2 Describe any procedures for orderly termination.

NOTE: Examples may include return of study drug, exit interview with clinician. Include whether additional follow up is recommended for safety reasons for physical or emotional health.

Response:

Participants will be debriefed about the nature of the study and the reason for their removal. No additional follow-up is needed.

22.3 Describe procedures that will be followed when subjects withdraw from the research, including retention of already collected data, and partial withdrawal from procedures with continued data collection, as applicable.

Response:

Participants can withdraw from the research at any time. If participants withdraw, no further data will be collected, but any information that had been provided may be retained by the researcher and analyzed.

23.0 Risks to Subjects*

23.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to their participation in the research. Consider physical, psychological, social, legal, and economic risks. Include a description of the probability, magnitude, duration, and reversibility of the risks.

NOTE: Breach of confidentiality is always a risk for identifiable subject data.

Response:

There may be some sensitivity associated from certain questions asked when filling out questionnaires or having body measurements taken and subjects might feel uncomfortable disclosing some personal information such as medical history. Subjects can refuse to answer any questions that they are not comfortable answering. Subjects will be free to withdraw from the study at any time, and their refusal to continue will not affect other medical care provided at any healthcare facility.

Breach of confidentiality is another potential risk. To protect confidentiality, we will use only ID numbers and keep all data in locked cabinets or in locked offices and password protected electronic files in password protected computers.

There are no other risks anticipated. All personnel on the study will be CITI course certified and have completed the good research practices certification. All identifiable data will be password protected and only the research team will have access to that information. Subjects will be informed of the risks associated with the study.

23.2 Describe procedures performed to lessen the probability or magnitude of risks, including procedures being performed to monitor subjects for safety.

Response:

We have several provisions in place to ensure participants' privacy and safety is protected while the data is being collected. The lab facilities of the Division of Behavioral Medicine research laboratory consist of private interview rooms that will be used. Only the relevant research staff and participant will be present in the room during sessions. Data is recorded such that not even the person putting it in the file would ever be able to associate the data with the identity of the person providing it. Data and files that have been de-identified and encrypted will be shared between sites. Therefore, there is no reasonable risk of a breach of confidentiality.

Should an emergency situation occur, access to further medical care is available via a telephone located in the laboratory and the following emergency plan will be followed:

1. Have the subject immediately stop any activity and lay down.

2. Call for help! ON CAMPUS EMERGENCY (716-645-2222) or POLICE (911).

3. If the subject is unconscious – assess breathing and heart rate. Initiate CPR (if trained) and call on campus emergency services or police as necessary.

4. If the subject is conscious – continue to observe subject.

*23.3 If applicable, indicate **which procedures** may have risks to the subjects that are currently unforeseeable.*

Response:

N/A, subjects will be allowed to refuse to answer any questions they are not comfortable with.

23.4 If applicable, indicate which research procedures may have risks to an embryo or fetus should the subject be or become pregnant.

Response:

N/A, we will not be enrolling pregnant participants.

23.5 If applicable, describe risks to others who are not subjects.

Response:

N/A, no foreseeable risks to others who are not subjects.

24.0 Potential Benefits to Subjects*

24.1 Describe the potential benefits that individual subjects may experience by taking part in the research. Include the probability, magnitude, and duration of the potential benefits. Indicate if there is no direct benefit.

*NOTE: Compensation **cannot** be stated as a benefit.*

Response:

Participants may benefit from improved health due to better adherence to their prescribed medication(s). Participants may also learn about the experimental research process and their health.

25.0 Compensation for Research-Related Injury

☒ **N/A:** The research procedures for this study do not present risk of research related injury (e.g. survey studies, records review studies). This section does not apply.

26.0 Economic Burden to Subjects

26.1 Describe any costs that subjects may be responsible for because of participation in the research.

NOTE: Some examples include transportation or parking.

Response:

Participants will be responsible for transportation to/from the laboratory for their scheduled sessions. If participants do not have their own personal mode of transportation, they may be reimbursed in the amount of standard bus/train fare. Participants will not incur parking fees at our laboratory.

☐ **N/A:** This study is not enrolling subjects, or is limited to records review procedures only. This section does not apply.

27.0 Compensation for Participation

27.1 Describe the amount and timing of any compensation to subjects, including monetary, course credit, or gift card compensation.

Response:

Participants will receive $35 for completion of each assessment session ($35 x 3 = $105), and will receive additional compensation bonuses if they (a) complete all three assessment sessions ($25), and (b) return the MEMS cap ($20). The total possible compensation for participation in the study is $150.

28.0 Consent Process

28.1 Indicate whether you will be obtaining consent.

NOTE: This does not refer to consent documentation, but rather whether you will be obtaining permission from subjects to participate in a research study. Consent documentation is addressed in Section 29.0.

☒ ***Yes*** *(If yes, Provide responses to each question in this Section)*
☐ ***No*** *(If no, Skip to Section 29.0)*

28.2 Describe where the consent process will take place. Include steps to maximize subjects' privacy.

Response:

Online/Phone Screening

Interested participants will be screened over the phone or have an opportunity to complete the survey online. Consent to screen for eligibility will be obtained verbally over the phone or through an action (e.g. electronically signing) online (see Phone Script for related details). Screening consent will be obtained prior to asking any contact or eligibility questions.

In-Lab Screening/Assessment 1

Documented informed consent will be obtained in a private room at the Division of Behavioral Medicine Research Lab during the scheduled laboratory appointment.

28.3 Describe how you will ensure that subjects are provided with a sufficient period of time to consider taking part in the research study.

NOTE: It is always a requirement that a prospective subject is given sufficient time to have their questions answered and consider their participation. See "SOP: Informed Consent Process for Research (HRP-090)" Sections 5.5 and 5.6.

Response:

There will not be a significant interval of time between obtaining and documenting consent and the actual participation in the initial research procedures (i.e. shortly after the person signs the document they will begin research procedures at their scheduled convenience). However, if a subject requests more time to review the consent form, they are able to take the consent home to review and discuss with family members, then schedule a visit at a later date.

28.4 Describe any process to ensure ongoing consent, defined as a subject's willingness to continue participation for the duration of the research study.

Response:

Participants will be seen both weekly and monthly at different points of the intervention; after initial consent, participants will have the ability to discontinue the study at any time.

28.5 Indicate whether you will be following "SOP: Informed Consent Process for Research (HRP-090)." Pay particular attention to Sections 5.4-5.9. If not, or if there are any exceptions or additional details to what is covered in the SOP, describe:

- *The role of the individuals listed in the application who are involved in the consent process*
- *The time that will be devoted to the consent discussion*

- *Steps that will be taken to minimize the possibility of coercion or undue influence*
- *Steps that will be taken to ensure the subjects' understanding*

Response:

☒ We have reviewed and will be following "SOP: Informed Consent Process for Research (HRP-090)."

Non-English Speaking Subjects

☒ **N/A:** This study will not enroll Non-English speaking subjects. *(Skip to Section 28.8)*

Cognitively Impaired Adults

☒ **N/A**: This study will not enroll cognitively impaired adults. *(Skip to Section 28.9)*

Adults Unable to Consent

☒ **N/A**: This study will not enroll adults unable to consent. (*Skip to Section 28.13)*

Subjects who are not yet Adults (Infants, Children, and Teenagers)

☒ **N/A**: This study will not enroll subjects who are not yet adults. *(Skip to Section 29.0)*

29.0 Waiver or Alteration of Consent Process

Consent will not be obtained, required information will not be disclosed, or the research involves deception.

☒ **N/A:** A waiver or alteration of consent is not being requested.

29.1 If the research involves a waiver of the consent process for planned emergency research, please review the "CHECKLIST: Waiver of Consent for Emergency Research (HRP-419)" to ensure you have provided sufficient information for the IRB to make these determinations. Provide any additional information necessary here:

Response:

N/A, this research does not involve a waiver for planned emergency research.

30.0 Process to Document Consent

☐ **N/A:** A Waiver of Consent is being requested.
(Skip to Section 31.0)

30.1 Indicate whether you will be following "SOP: Written Documentation of Consent (HRP-091)." If not or if there are any exceptions, describe whether and how consent of the subject will be obtained including whether or not it will be documented in writing.

NOTE: If your research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, the IRB will generally waive the requirement to obtain written documentation of consent. This is sometimes referred to as 'verbal consent.' Review "CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)" to ensure that you have provided sufficient information.

If you will document consent in writing, attach a consent document with your submission. You may use "TEMPLATE CONSENT DOCUMENT (HRP-502)". If you will obtain consent, but not document consent in writing, attach the script of the information to be provided orally or in writing (i.e. consent script or Information Sheet).

Response:

☒ We will be following "SOP: Written Documentation of Consent" (HRP-091).

31.0 Multi-Site Research (Multisite/Multicenter Only)*

☒ **N/A:** This study is not an investigator-initiated multi-site study. This section does not apply.

32.0 Banking Data or Specimens for Future Use*

☒ **N/A:** This study is not banking data or specimens for future use or research outside the scope of the present protocol. This section does not apply.

*32.1 If data or specimens will be banked (stored) for **future use, that is, use or research outside of the scope of the present protocol**, describe where the data/specimens will be stored, how long they will be stored, how the data/specimens will be accessed, and who will have access to the data/specimens.*

NOTE: Your response here must be consistent with your response at the "What happens if I say yes, I want to be in this research?" Section of the Template Consent Document (HRP-502).

Response:

We do not plan to use the data collected for future research.