CARILION CLINIC INSTITUTIONAL REVIEW BOARD

IRB RESEARCH APPLICATION INSTRUCTIONS

NOTE: This is a protected document! Please do not remove protections.

The Carilion Institutional Review Board (IRB) is a committee charged with protecting the rights and welfare of human subjects in research. You must submit this application and receive IRB approval if you wish to conduct human subjects research at Carilion Clinic, including the Jefferson College of Health Sciences, or if you will use Carilion patients or services as part of the research process. The entire application must be completed. If you are unsure if your research meets the definition of human subjects research, please first visit the IRB website for more information.

Research protocols may be reviewed at convened meetings of the IRB or through a single reviewer process involving the IRB Chair and staff. The type of review is determined by the nature of the project, the level of potential risk to research subjects, and the characteristics of the subject population. The final determination of the type of review applicable to a study is made by the IRB.

- **Full Board Reviews:** Greater than minimal risk research requires review at a convened meeting of the IRB. Research that involving vulnerable populations, experimental drugs or devices, invasive procedures, or deception (e.g., in behavioral research) may also require full board review. A schedule of IRB meetings and submission deadlines can be found on the Carilion IRB website.

  Full Board submissions should be sent to Meredith Talmadge at mttalmadge@carilionclinic.org. For further information, call 540-853-0728.

- **Exempt and Expedited Reviews:** Exempt and Expedited studies involve no more than minimal risk to subjects. Federal regulations define minimal risk as the probability that the magnitude of harm or discomfort anticipated in the research are not greater in of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. The Carilion IRB must determine whether proposed studies meet the criteria for Expedited or Exempt review.

  Exempt and Expedited submissions should be sent to Janet McDowell at jdmcdowell@carilionclinic.org. For further information, call 540-981-8015.

Signature pages may be sent electronically or faxed to (540) 985-5323. For further information call 853-0728.

Note: Consent Form and Information Sheets should be submitted in Word rather than in pdf, as IRB staff may need to make revisions and edits to these documents. The CV of the PI should be sent in a separate electronic document so that IRB staff can file them individually in our electronic filing system.

Please do not copy this page when submitting paper copies to the IRB office.

Carilion Clinic Institutional Review Board Application

REGISTRATION WITH DEPARTMENT OF RESEARCH & DEVELOPMENT

Per Institutional Policy, <u>all</u> IRB submissions must include the Research & Development (R&D) Authorization letter stating R&D has given you permission to submit to the IRB. Do you have your R&D Letter?

☒ Yes (If yes, you MUST attach your R&D letter to this submission.)

☐ No *(If no, <u>do not</u> submit this IRB application until you have your R&D letter.* You may contact R&D at 540-985-8510 or go to *http://insidecarilion.org/hubs/office-sponsored-projects/rd-forms-0.)*

FINANCIAL CONFLICT OF INTEREST DISCLOSURE

Per Institutional Policy, <u>all</u> research team members on a <u>funded</u> study must submit a study-specific Financial Disclosure form through the Carilion Organizational Integrity and Compliance Office. Please contact kecooper1@carilionclinic.org immediately to do so.

*Please note it is the PI's responsibility to ensure all members of the research team have disclosed any financial or other relationships to the funding source. Failure to do so may be considered serious noncompliance and result in study suspension or termination.

SECTION I: APPLICATION DATA

Date Completing Form: 3/20/19
(This date MUST be updated by you each time you make changes to this document to submit to the IRB)

Complete Title of Study: Healthy Habits for Type 2 Diabetes

Research Team (All individuals participating in the conduct of research under the direction of the Carilion Principal Investigator, including investigators, coordinators, those obtaining consent, those accessing identifiable data, etc.*. If you need additional entries, visit the IRB website Forms page.):

Carilion Principal Investigator: John Epling Credentials: **MD, MSEd**
Department: Family and Community Medicine
Inter-office address: 1 Riverside Circle, Suite 102, Roanoke, VA, 24016
Mailing Address (if external): Same
Phone: 540-581-0166 E-mail: jwepling@carilionclinic.org Fax:

Other Investigator: Warren Bickel Credentials: PhD
Role & Responsibilities: Co-Investigator
Phone: 540-526-2088 E-mail: wkbickel@vtc.vt.edu

Other Investigator: Jeff Stein Credentials: PhD
Role & Responsibilities: Co-Principal Investigator
Phone: 540-526-2124 E-mail: 540-526-2124

Study Coordinator: Kirstin Gatchalian Credentials: BS
Role & Responsibilities: Program Manager
Phone: 540-526-2071 E-mail: kmgatch@vtc.vt.edu

Other Research Team Member: Megan Stuart Credentials: MS
Role & Responsibilities: Coach/Interventionist
Phone: 540-526-2260 E-mail: stuartma@vtc.vt.edu

Other Research Team Member: Chesley Ammermann Credentials: BS
Role & Responsibilities: Research Assistant
Phone: 540-526-2113 E-mail: chebbie1@vtc.vt.edu

Other Research Team Member: Gemma Porras Credentials: BS
Role & Responsibilities: Research Assistant
Phone: 540-526-2237 E-mail: abrown34@vtc.vt.edu

Other Research Team Member: Jeremiah Brown Credentials: MS.
Role & Responsibilities: Coach/Interventionist

Phone: 540-526-2260 E-mail: jeremiahmbrown@vtc.vt.edu

Other Research Team Member: Julia Basso Credentials: PhD
Role & Responsibilities: Coach/Interventionist
Phone: 540-526-2168 E-mail: jbasso@vtc.vt.edu

Other Research Team Member: Hailey Snyder Credentials: N/A
Role & Responsibilities: Undergraduate intern/research assistant
Phone: N/A E-mail: haileys19@vt.edu

Other Research Team Member: Drew McCauley Credentials: N/A
Role & Responsibilities: Undergraduate intern/research assistant
Phone: N/A E-mail: jd11mcc@vt.edu

Other Research Team Member: Laila Krysta Credentials: N/A
Role & Responsibilities: Undergraduate intern/research assistant
Phone: N/A E-mail: lailak98@vt.edu

*If this research involves external collaborators: If non-Carilion affiliates will be obtaining IRB approval through their home institution, they should not be listed on this application. If you would like to request that one IRB to defer to another, please contact the IRB immediately to discuss the feasibility of this agreement.

Note: All research team members must complete Carilion IRB education requirements before submitting this application. Further information regarding education requirements can be found on the Carilion IRB website.

1. Has the Principal Investigator ever had any research suspended or terminated by an IRB?
   ☐ Yes ☒ No
   - If yes, please explain:
2. Has any version of this research protocol ever been submitted to any other IRB?
   ☐ Yes ☒ No
   - If yes, please attach a copy of all IRB correspondence
3. Has the Principal Investigator ever been convicted of a crime, disciplined by a public or private medical organization, disciplined by a licensing authority or is the Principal Investigator currently the subject of such a proceeding?
   ☐ Yes ☒ No
   - If yes, please explain:
4. Have any of the other investigators or study team members ever been convicted of a crime, disciplined by a public or private medical organization, disciplined by a licensing authority, or are any currently the subject of such a proceeding?
   ☐ Yes ☒ No
   - If yes, please explain:
5. **Location of Research**:
   - Check the facility where research activities will take place (please check all that apply):
     ☐ CRMH ☐ CNRVMC ☐ JCHS ☐ CC Physician's Office
     ☐ CRCH ☐ CFMH ☐ CRMH Rehab ☒ Other: **Fralin Biomedical Research Institute, Corporate Research Center)**
   - List all departments within the facility where research activities will take place: **Center for Transformative Research on Health Behavior (CTRHB) at the Fralin Biomedical Research Institute (FBRI); 1 Riverside Circle**
   - **Virginia Tech Corporate Research Center; 1715 Pratt Drive, Suite 1000, Blacksburg, VA**
6. **Collaboration:**

- Will this research involve collaboration with another institution? ☒ Yes ☐ No
- If yes, name the institution(s):
- **University at Buffalo School of Medicine and Biomedical Sciences, Division of Behavioral Medicine, G56 Farber Hall, 3435 Main Street, Buffalo, NY 14214**
- **Dr. Leonard Epstein is a Co-Investigator on the NIH grant. Dr. Epstein will not be reviewing identifiable Carilion subject data. No human subject activities will occur at the University at Buffalo.**
- If yes, will the collaborating institution's IRB also review the study? ☐ Yes ☒ No
  Note: If the collaborating institution's IRB has already approved the study, please submit their approval letter with this application.

7. **Sponsor:**
   - Will this research be sponsored by an institution/entity outside of Carilion? ☒ Yes ☐ No
   - If yes, name the institution/entity: **National Institute of Nursing Research**

8. **Funding Source**: If this study is or will be funded, every research team member MUST submit a study-specific Financial Disclosure form through the Carilion Organizational Integrity and Compliance Office immediately. Please contact kecooper1@carilionclinic.org to do so. The IRB application cannot be approved until it is determined that there is not conflict, or that the conflict has been disclosed and managed.
   - ☐ Carilion RAP grant
   - ☒ Federal/state agency (specify): **National Institute of Nursing Research**
   - ☐ Other grant (specify):
   - ☐ Industry/commercial (specify):
   - ☐ Private, non-profit (specify):
   - ☐ No funding; equipment, supplies, and/or services will be provided (specify company):
   - ☐ No funding; no equipment, supplies, and/or services will be provided
   - ☐ Other (specify):

9. Is this the official project of a VTCSOM medical student as required for graduation and has already undergone scientific review by VTCSOM?
   ☐ Yes ☒ No

10. Anticipated Start Date: **2/2019**

11. Estimated Time Needed to Complete Study: **1.5 years**

SECTION II: DRUG, DEVICE AND BIOLOGIC STUDIES ONLY ☒ N/A

12. What is the name(s) of the drug, device or biologic that will be used in this study:

13. Please attach documentation to confirm FDA approval of this drug, device or biologic. Check one below:
   - ☐ Package Insert
   - ☐ Printed Information from the FDA website confirming FDA approval
   - ☐ Letter from FDA granting approval
   - ☐ Not available; FDA has not approved

14. Does the research study involve an Investigational New Drug (IND) or Biologic? An IND number is required if a drug or biologic is used in a manner outside the labeling approved by the FDA.
   ☐ Yes ☐ No
   - If yes, please provide the IND number assigned by the FDA. If an IND number is not available please explain why an IND was not obtained. If you believe the drug is exempt from IND approval, please submit an IND Determination form that can be found on the IRB web site. Note: Investigators may be asked to have an IND determination application submitted to the FDA.

15. Does the research involve a device that is being used outside the labeling approved by the FDA?
   ☐ Yes ☐ No

If yes:

- Please provide the Investigation Device Exemption (IDE) number provided by the FDA:
- Attach one of the following:
  - ☐ FDA letter granting an IDE
  - ☐ A letter from the sponsor or investigator/sponsor stating the study device is non-significant risk
  - ☐ A letter explaining why the investigation is exempt from IDE requirements

16. Does this study meet the definition of an Applicable Clinical Trial (ACT) that requires registration on ClinicalTrials.gov? Whether yes or no, please complete the ACT Checklist and submit page 1 with your IRB application.

    ☐ Yes ☐ No

SECTION III: STUDY PROTOCOL

17. **Study Abstract:** Provide a brief, non-technical summary of the study, including study purpose and methods.

    In this study, we will test whether a remotely delivered episodic future thinking (EFT) intervention, combined with dietary and activity coaching, as well as self-monitoring, reduces delay discounting and improves weight loss, glycemic control, and other health outcomes in patients with poorly controlled type 2 diabetes. Specifically, the study is a randomized trial comparing the effects of EFT versus a control condition on delay discounting, medication adherence, diet, physical activity, body weight, and glycemic control. Outcome measures will be assessed both remotely (e.g., online) and in the laboratory.

18. **Background:** Summarize background information about the research question(s.) Tell why the research is needed and include the relevance of this research to the contribution of this field of study. Also, provide references to relevant articles in the literature. (If you have more than 10 references, please submit the list of references as a separate attachment. Otherwise, please insert them here.)

    Successful management of type 2 diabetes (T2D) requires a complex repertoire of behaviors, including adherence to physician-recommended medication, dietary, and exercise regimens (1, 2). Most of these behaviors provide little to no short-term benefit and may rather be aversive (e.g., physical exertion and caloric restriction). However, treatment adherence provides critical health benefits in the future, allowing patients with T2D to halt or reverse disease progression and avoid T2D-related complications (e.g., renal disease or diabetic retinopathy). Thus, successful management of T2D requires one's present behavior to be guided by future outcomes. Unfortunately, accumulating evidence indicates that individuals with T2D and those at risk for this disease rapidly devalue the future (3, 4), a phenomenon known as delay discounting). Moreover, within diabetic and prediabetic populations, we and others have shown that high rates of delay discounting are associated with poor treatment adherence and clinical outcomes (3, 4, 5). These data indicate that rapidly devaluing the future likely prevents successful management of T2D through a mechanism in which the health benefits of treatment adherence are too delayed to motivate present behavior. Thus, we believe delay discounting serves as a therapeutic target in T2D, in which improving valuation of the future will improve treatment adherence and, in turn, improve health outcomes such as glycemic control and body weight.

    Episodic future thinking (EFT) is a form of prospection that involves mental simulation of events that might occur in one's future (6). EFT to some extent is an innate human ability that guides decision-making (e.g., simulating the experience of an upcoming job interview or social event); however, populations who discount the future rapidly show deficits in this ability, considering the future infrequently and

demonstrating low-quality EFT content (e.g., fewer contextual and sensory details). Thus, EFT interventions are designed to remediate this deficit and reduce bias toward immediate gratification by guiding individuals to both generate high-quality EFT content and prompting them to engage in EFT frequently. Prior laboratory-based research by the investigative team and others has shown that EFT reduces both delay discounting and a wide range of maladaptive health behaviors and outcomes, including overeating (7), food purchasing (8), and weight control in overweight and obese populations (9).

These therapeutic effects suggest that EFT may be used to reduce the bias for immediate gratification observed in T2D, and thus improve valuation of the long-term outcomes associated with treatment adherence. However, little research has examined the efficacy of EFT in the real world. This gap in knowledge presents a challenge to our understanding of the etiology and treatment of this disease. Therefore, our goal is to leverage prior extensive research to engage our behavioral target, delay discounting, to develop a clinical intervention for T2D. In pursuit of our goal, our objective in this study is to develop a practical, remotely delivered EFT intervention to improve delay discounting and treatment adherence in T2D and, in so doing, improve management of T2D.

Specific Aim 1 will examine the effects of a 4-month, remotely delivered EFT intervention on delay discounting, medication adherence, diet, physical activity, body weight, and glycemic control in patients with poorly controlled T2D. All participants will receive access to a standard behavioral treatment (BT), including lifestyle coaching, dietary and activity education, and daily self-monitoring. Participants assigned to an EFT+BT group will also be asked to generate vivid, episodic events and be sent text-based prompts daily to engage in EFT in the natural environment with the assistance of a study website. Participants assigned to a BT alone group will not receive EFT, but will be asked to access the study website and answer questions about their experience with the same frequency as the EFT group in order to control for use of the technology, effort, attention, and experimenter contact. We will assess outcome measures both during and immediately after the intervention, as well as at a 6-month follow-up session (approximately 2 months following the end of the intervention). This will allow us to estimate both short- and long-term effects changes in behavior, weight, and glycemic control

Specific Aim 2 will examine the acceptability of the remote EFT intervention. In order for an intervention to be effective in clinical settings, it should be easy to use and its helpfulness should be apparent. Thus, during the trial and follow-up, participants will rate all aspects of the interventions along several dimensions, including helpfulness and ease of use. High intervention ratings would suggest that EFT may be implemented with high treatment fidelity in clinical settings and is more likely to be disseminated among treatment providers and adopted by patients.

References

1. Knowler, W. C. et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N. Engl. J. Med. 346, 393–403 (2002).

2. Tuomilehto, J., Schwarz, P. & Lindström, J. Long-Term Benefits From Lifestyle Interventions for Type 2 Diabetes Prevention. Diabetes Care 34, S210–S214 (2011).

3. Amlung, M., Petker, T., Jackson, J. & Balodis, I. Steep discounting of delayed monetary and food rewards in obesity: a meta-analysis. Psychological (2016).

4. Reach, G. et al. Patients' impatience is an independent determinant of poor diabetes control. Diabetes Metab. 37, 497–504 (2011).

5. Epstein, L. N. et al. Delay Discounting and Adherence in Adults with Prediabetes. Health Psychol. (under review).

6. Atance, C. M. & O'Neill, D. K. Episodic future thinking. Trends Cogn. Sci. 5, 533–539 (2001).

7. Daniel, T. O., Stanton, C. M. & Epstein, L. H. The future is now: reducing impulsivity and energy intake using episodic future thinking. Psychol. Sci. 24, 2339–2342 (2013).

8. Sze, Y. Y., Stein, J. S., Bickel, W. K., Paluch, R. A. & Epstein, L. H. Bleak Present, Bright Future: Online Episodic Future Thinking, Scarcity, Delay Discounting, and Food Demand. Clin. Psychol. Sci. 5, 683–697 (2017).

9. Sze, Y. Y., Daniel, T. O., Kilanowski, C. K., Collins, R. L. & Epstein, L. H. Web-Based and Mobile Delivery of an Episodic Future Thinking Intervention for Overweight and Obese Families: A Feasibility Study. JMIR Mhealth Uhealth 3, e97 (2015).

19. **Objectives:** State the research hypothesis or the question that the research will answer. List the research objectives and expected outcomes. **A primary outcome or objective must be identified**. After the statement of the primary objective, secondary objectives may be listed. Objectives should be simple and specific.

We hypothesize that participants assigned to the EFT group will show reductions in delay discounting and glycemic control (primary outcomes), as well as improvements in dietary, weight, and glycemic control and medication adherence (secondary outcomes). If similar behavioral and health changes are also observed for the BT control group, we hypothesize that these changes will be relatively greater for the EFT group. We also hypothesize that participants in both groups will rate the intervention as effective and easy to use, although participants in the EFT group will rate the intervention as more effective.

20. **Study Design:** Give a description of the research design including use of placebo, randomization and an explanation of what is experimental. Include type of study: descriptive, retrospective, cross-sectional, longitudinal, prospective observational, pilot, experimental (controlled or non-controlled) or pilot.

This is a randomized control trial in which we randomly and experimentally assign participants to either an EFT or control group and examine the impact of that assignment on study outcomes. All participants will also receive access to a lifestyle intervention, case management, and self-monitoring.

21. **Study Population:** Describe the subject population, including age, gender, ethnic characteristics and health status. State the inclusion/exclusion criteria along with how this was determined, and by whom. Please state whether pregnant women, children, or other vulnerable groups will be included or excluded. Provide rationale for using or excluding special populations. State the number of subjects or subject records necessary to complete the research.

We will enroll up to 150 patients with type 2 diabetes (N = 54, plus addition to account for screen failure following an initial screening session, possible dropout, etc.). Recruitment will focus on patients who do not adequately control their blood

sugar because this is the subpopulation of diabetes patients in greatest need of intervention. .

Inclusion Criteria:
- **age 18 or over**
- **type 2 diabetes diagnosis**
- **prescribed or recommended oral glucose-lowering medication for type 2 diabetes**
- **HbA1c level of ~8% or greater**
- **body mass index of 25 or greater**

Exclusion criteria
- **current insulin therapy for type 2 diabetes**
- **history of gestational diabetes**
- **pregnant or lactating (if female), or plans to become pregnant in the next 6 months**
- **not ambulatory**
- **intellectual impairment that would impact treatment adherence or the ability to provide informed consent**
- **medical conditions that affect behavioral or medical adherence: Participants should not have a medical condition that would limit participation such as individuals with medical conditions that may affect their ability to use the computer for a prolonged period of time or follow study protocol will also be excluded, current diagnosis with an eating disorder or an unmanaged psychiatric disorder**
- **abnormal glucose related to medications (e.g. atypical antipsychotic medications or glucocorticoids)**
- **prior participation in similar studies: Individuals who have recently participated in a laboratory study using similar methods may also be excluded.**

22. **Methodology:** List all activities or procedures that will be performed (pre-treatment tests and medications, tests and medications used during therapy, diagnostic tests, x-rays, lab tests, questionnaires and other forms, interviews, chart reviews etc.) Describe how, when and where research activities will be administered and analyzed. **Distinguish any standard processes from those that are research.** Please describe activities/procedures in a step-by-step chronological order. State the length of time subjects will be in the study and the expected amount of time required for each study visit or activity.

Individuals who are likely eligible based on the online screening questionnaire (see Appendix A: pre-screening questionnaire) will be invited to attend a lab session. After providing informed consent at the lab session, participants' blood HbA1c, height, and weight will be measured, as well as provide demographic, health, and medication information, and complete delay discounting and food purchase tasks. Participants who are verified to be eligible from lab-based and online screening, will continue with the remainder of the study and will be randomly assigned to either an EFT+BT group or BT control group. Those who are deemed ineligible at this stage (e.g., due to low HbA1C) will be provided with prorated compensation and informed that they do not qualify. If participants are determined to be eligible, they will be given a detailed orientation of what will be expected of them during the study, including tasks they need to complete, recording food consumption and activity levels, and frequency of visits to our lab.

Eligible participants will then initiate further study procedures, consisting of: 1) laboratory assessment sessions, 2) physical activity assessments, 3) case management meetings, 4) daily self-monitoring of diet, weight, and activity, and 5) EFT or control engagement. The intervention will last approximately from Weeks 0-16, with an additional follow-up assessment at Week 24).

-Laboratory Assessment Sessions (Weeks 0, 8, 16, and 24)
At assessment sessions, we will collect measures of blood HbA1c, blood pressure, height, and weight. Participants will also complete delay discounting tasks, food purchase tasks, and complete other study questionnaires (e.g., demographics).

-Physical Activity Assessments (Weeks 0, 8, and 16).
Participants will be provided with an Actigraph accelerometer for use during the study and instructed how to properly wear it. At each assessment (Weeks 0, 6, and 16), participants will be asked to wear the accelerometer for a continuous 7-day period. Although these assessments are scheduled to take place during Weeks 0, 8, and 16, the 7-day period may occur during adjacent weeks, in whole or in part, to facilitate scheduling. After the 7-day period of Actigraph wear, participants will be asked to return the device until the next assessment or at the end of the study.

-24-hour Dietary Recalls (Weeks 0, 8, and 16)
On three days during approximately the same period that participants wear the Actigraph, participants will be asked to complete 24-hour diet recalls using the Automated Self-Administered 24-hour Dietary Assessment Tool (ASA-24). Participants may complete these recalls online.

-Case management meetings (Weeks 0-16).
All participants in both groups will attend weekly (during approximate Weeks 1-8) and bi-monthly (during approximate Weeks 8-16) meetings with a case manager. These meetings will occur over the phone, unless the participant prefers to visit the laboratory. At these meetings, participants will be provided general information on healthy diet, physical activity and medication adherence. Participants will also be provided instruction regarding a number of different healthy habits for patients with type 2 diabetes, including: 1) The Traffic Light Diet, which utilizes RED, YELLOW, and GREEN labels for food to guide participants toward the goal of consuming low energy dense, low glycemic, high nutrient dense foods; 2) the Traffic Light Activity Program, which also utilizes RED, YELLOW and GREEN labels for different levels of caloric expenditure, 3) a variety of behavioral techniques, including meal planning and 4) use of EFT or the control condition. Participants will be provided with educational reading materials for each of these topics, be asked to read these materials in between meetings, and be asked to complete quizzes to assess mastery (see Appendix B: Healthy Habits Manual + Quizzes). These materials will most often be provided in Qualtrics software, but may also be provided in paper form. These meetings will also review information about weight loss and maintenance, engage in problem solving for participants who are struggling with behavior change, behavior change techniques, and diet and activity self-monitoring, and other topics relevant for weight and diet management. The case manager will also provide instruction for using either EFT for behavior change for the EFT+BT group, as well as how to access the study website for the BT control group.

At the end of the intervention period (approximately Week 16), case management meetings will be discontinued. However, participants will retain access to educational materials in Qualtrics through Week 24.

-EFT/Control engagement (Weeks 3-16).

Beginning in Week 2, participants will be randomly assigned to either the EFT+BT or BT control groups. Participants in the EFT+BT group will be asked to generate episodic cues similar to the tasks used in our previous studies on EFT's effect (Daniel et al., 2013). Participants will list and describe events for different time periods. The episodic component of the thinking task will occur while the participants are asked to describe what they are imagining about each event (e.g., vacations, weddings, parties, health goals, etc.). EFT participants will list positive future events they are looking forward to and list events that could happen at different general future time points (e.g., 1 month, 2-6 months, 7-12 months). Participants will also create text-based cues for each event, which will consist of descriptions of the future event (e.g., "In about 6 months, I am attending my sister's wedding in Montana. I am enjoying the crisp air and getting to see my family again."). In contrast, the BT control group will not generate these events.
For the remainder of the intervention, participants in both groups will be sent text-based prompts via cell phone to access the study website (built in Qualtics survey software). Once accessed, the study website will guide EFT+BT participants to engage in EFT by presenting cues. Brief questions may also be presented asking participants to describe their study experience (e.g., "Have you encountered any diet or activity challenges today?"). Participants in the BT control group will only be prompted to access the study website to answer these questions.

Experimenters will train participants in both groups on how to access the study website from their cell phone or alternative internet accessible device (e.g. laptop, tablet, desktop computer), as well as how to pay attention to and think about the cues, and how to adhere to the study's expectations for utilizing the cues (EFT+BT group only). Participants may be prompted several times a day to access the website and, for the EFT+BT group, instructed to use their cues any time that need to, especially around eating episodes.

At the end of the intervention period (approximately Week 16), participants will retain access to educational and other materials in Qualtrics through Week 24. However, participants will not be provided with prompts to access these materials during this period and will not be required to use the website.

-Diet, activity, and weight self-monitoring (Weeks 1-16).
Participants will be taught how to record food, drink, exercise, and at home weight measurements in MyFitnessPal (see Appendix C: Study Websites). MyFitnessPal is a smartphone and web based app that tracks diet and exercise and can record the number of calories, macro and micronutrients consumed. Participants will be asked to use MyFitnessPal for self-monitoring throughout the study, recording the amount and types of food they eat and activity they engage in, as well as their weights. User accounts will be created for participants and will not include any identifying information.

At the end of the intervention period (approximately Week 16), participants may retain access to MyFitnessPal through Week 24 to continue self-monitoring of diet, exercise, and weight. However, participants will not be required to use this software during this period.

References

1. Sze, Yan Yan, Tinuke Oluyomi Daniel, Colleen K. Kilanowski, R. Lorraine Collins, and Leonard H. Epstein. "Web-based and mobile delivery of an episodic future thinking intervention for overweight and obese families: a feasibility study." JMIR mHealth and uHealth 3, no. 4 (2015).

23. **Data Collection:** Describe below the data collection methods and how data be compiled for assessment. Attach a copy of your data collection tool or spreadsheet listing exactly what data is to be gathered during this research study. If all data is retrospective, please state date range from which data will be collected and note that data must be in existence at time of submission of this application.

All protected health information will be stored on a password-protected spreadsheet on RedCap provided through Carilion Clinic and linked only to subjects through a subject ID number.

Additional de-identified study data will be collected and stored using Qualtrics survey software. These data will be linked to the participants through their subject ID (in RedCap).

These de-identified study data include the following measures, which may also be found in the attached appendix (see Appendix D: Study Measures).

--Demographic variables and health behavior data. Race/ethnicity, household income, and educational level will be assessed at baseline using a survey-based questionnaire. Participants will also be asked about their health and related behaviors (e.g., mental health, medical history, financial behaviors, and food consumption.)

--Eating Disorder Diagnostic Scale. This 22-item self-report scale screens for the presence and severity of symptoms associated with anorexia nervosa, bulima nervosa, and binge-eating disorder assess. Participants who provide scores consistent with an eating disorder will be provided with referrals to the National Eating Disorder's Helpline (800-941-2237), local resources, and/or will be counseld to speak with their personal physician.

--Weight, height, BMI. Participants' weight will be assessed using a digital scale. Height measurements will also be collected. On the basis of height and weight, BMI is calculated according to the following formula: (BMI=kg/m2).

--Blood HbA1c. Hemoglobin A1c (HbA1c) will be measured using the Alere Affinion system.

--Blood Pressure. Blood pressure will be measured in triplicate using an automated blood pressure device by trained personnel. The latter two readings will be averaged.

--Dietary restraint. Participants will complete the three-item "Dietary Restraint" portion of the Three Factor Eating Questionnaire (TFEQ) (Stunkard & Messick, 1985), a validated instrument to detect dietary restraint (Allison, Kalinsky, & Gorman, 1992).

--Treatment effectiveness and ease of use. Participants will rate multiple components of the intervention (e.g., EFT prompts, self-monitoring) on dimensions of perceived effectiveness and ease of use using 5-point Likert scales.

--Delay discounting. Participants will complete hypothetical delay discounting tasks for different commodities (e.g. delayed money, weight loss). These tasks assess preference between a small, immediately available reward (e.g., $50 now) and a larger, delayed reward (e.g., $100 in 6 months) across multiple trials and delays (e.g., 1 day through 25 years). This task reveals how the subjective value of a reward decreases with increases delay. The steepness of the discounting curve, estimated by the parameter k, provides a measure of delay discounting.

--Medication adherence. Adherence to oral glucose-lowering medication (e.g., Metformin) will be assessed by both a self-report questionnaire and by direct observation (pill count). In the self-report questionnaire, participants will complete a questionnaire in which they report how often they have taken their prescribed medication in the recent past. In the direct observation assessment, participants will be asked to bring their prescription bottles to both baseline and follow-up visits. Remaining pills will be counted and medication adherence will be calculated as: (quantity dispensed – remaining)/(quantity prescribed per day * days since last refill))*100, yielding a measure of percent adherence.

--Relative reinforcing efficacy of food. Hypothetical food purchase tasks will assess the relative reinforcing efficacy of a range of foods. In this task, participants report the hypothetical quantity of foods they would purchase to consume across a range of prices (e.g., $0.01 - $30 per serving).

--Dietary intake. Diet will be assessed by self-reporting using the Automated Self-Administered 24-hour Dietary Assessment Tool (ASA-24)

--Corsi block tapping task. In this test of working memory, blocks are presented on a computer screen, which light up one at a time in random order and in sequences of increasing length. After each presentation, participants attempt to reproduce the patterns shown.

--Physical activity. Physical activity will be measured using an Actigraph accelerometer. Participants will complete three Actigraph assessments during the study, with each assessment lasting 7 days. Total activity counts and activity in the moderate to vigorous (MVPA) and vigorous (VPA) ranges, among other measures, will be estimated.

--Patient Health Questionnaire. This questionnaire assesses frequency of depressive symptoms.

24. **Statistical Analysis:** State how qualitative and/or quantitative data will be analyzed. This must include a statement from a statistician that there is sufficient power to determine the primary study outcome or objective. Other outcomes may be listed as secondary and descriptive. If this is a proof of concept or feasibility study that includes limited efficacy testing, there must be a statistician statement that the appropriate design is in place to determine whether an intervention should be recommended for broader efficacy testing. If a study is meant to be solely descriptive, then results apply only to the sample being studied and conclusions cannot be drawn about the larger population; therefore, the primary outcome or objective must be limited in scope.

Sample size justification:

We propose a total sample size N = 54 completed participants. To estimate an effect size for this study, we examined multiple prior data sets. First, our prior laboratory-based data on effects of EFT on delay discounting and ad-libitum food intake and on effects of remotely delivered EFT on dietary intake and BMI revealed generally "large" effect sizes (f > .40). However, due to the uncertainty with which similarly large effect sizes would be observed for each of the broad range of additional measures used in the present study (e.g., medication adherence), we chose to power the proposed study for a more conservative, "medium" effect size of f = .25. Using this effect size, our power analysis indicated 54 total participants would be required based on an ANOVA model with group (EFT/control) as a between-subjects factor, time as a within-subjects factor, as well a group x time interaction. This analysis was performed in G*Power 3.1, a type 1 error rate of α = 0.05, correlation between repeated measures of .50, 95% statistical power. This provides 95% power to detect effects of EFT on lab-based measures assessed at baseline and follow-up assessments (e.g., HbA1c, BMI).

Data analysis:
We will use repeated measures ANOVA to examine changes in delay discounting, glycemic control, dietary intake, physical activity, medication adherence, BMI, and body composition (Specific Aim 1), as well as acceptability of the intervention (Specific Aim 2) in subjects who are randomly assigned to EFT and control conditions. Covariates will be included, as appropriate, including gender and socioeconomic status.
We will test for attrition bias by comparing participants who drop out versus those who complete the study. We will use intention to treat methods, and include all randomized subjects. We have a rigorous retention plan but expect up to 15% attrition. We will use maximum likelihood-based procedures to impute missing data. This approach is associated with more accurate parameter estimates than other approaches (e.g., last-observation carried forward), and is appropriate even when missing data are not missing at random

Statistical review was conducted by: **Jeff Stein, PhD** (name of statistician)
Fralin Biomedical Research Institute (Department/Institution of statistician)
If no statistical review was done, explain why:

SECTION IV: RISKS AND BENEFITS

25. Summarize the possible risks to subjects and how they have been minimized in the study design. Include risk of psychosocial harm (e.g., emotional distress, embarrassment, breach of confidentiality), economic harm (e.g., loss of employment or insurability, loss of professional standing or reputation, loss of standing within the community) and legal jeopardy (e.g., disclosure of illegal activity or negligence), as well as known side effects of study medication, if applicable, and risk of pain and physical injury. Define the level of risk (minimal risk, risk but with potential benefit to patient, risk but no benefit to patient). Describe any procedures that will be used to prevent or minimize risks or discomforts. Note: Most studies create at least a small risk of breach of confidentiality or privacy.

Overall, the risks of study participation are minimal. Participants will be informed of the risks associated with the study.

In subjects who are enrolled with an A1c between ~8% and 9.9%, an A1c over 10% will trigger a notification of their physician or appropriate medical referral. In

subjects who are enrolled with an A1c >= 10%, any 1 percentage point increase over baseline will trigger a notification of their physician or appropriate medical referral.

Participants 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.

Participants might feel uncomfortable disclosing some personal information such as medical history. Participants might experience adverse effects associated with changes in diet, including feeling hungry, fatigue, or headache.

Participants may, if they are on sulfonylurea or glinide medications, experience symptoms associated with hypoglycemia. Given that insulin use is an exclusion for this study, this is likely to be an uncommon and mild clinical issue. Participants will be instructed to discuss the possibility of hypoglycemia with their treating physician and the case managers will educate participants about hypoglycemic reactions and advise those on hypoglycemic medications to carry an additional source of ready sugar.

Participants may experience possible discomfort from blood glucose testing (e.g, momentary pain, skin irritation).

To protect confidentiality, we will use only ID numbers and keep all data in in locked offices and/or password-protected databases. Any data sharing between sites will involve de-identified data only and files will be encrypted or password protected. These screening, monitoring, and confidentiality procedures have been in effect for more than 15 years and for more than 2,000 subjects across the various protocols employed by our group.

26. Describe all costs, if any, subjects may incur as a result of being in this study.

    Costs to the patient include required to travel to the FBRI or CRC sites where participants will complete assessment sessions. However, the compensation provided for participation should adequately cover these costs, including a bonus for completing this 6-month study. The intervention itself has been designed to be remotely delivered and, thus, pose minimal costs.

27. Describe how subjects will be compensated for injury incurred as a result of being in the study.

    Subjects will not be compensated if they are in some way injured because of participation in this study.

28. Is any deception used in the study or any aspect of the study kept secret from the subjects, such as the full purpose of the study?

    ☐ Yes ☒ No

    - If yes, describe the deception involved and the debriefing procedures:

29. Describe any direct benefit to individual subjects, to the group of individuals with the disease process you are researching, and/or to society based on scientific knowledge gained. Explain how the potential benefits offered by this research outweigh the risks. (Please note: payments, gifts, or other free services given as a token for participation are not benefits, but instead are classified as compensation.)

    Participants may benefit from possible weight loss and improved glycemic control.

SECTION V: RECRUITMENT

30. Number of Subjects/Enrollment Goal. The enrollment goal must match the number of subjects needed to meet the primary outcome. If this is a retrospective record review, this figure is the number of records that will be used for analysis. Prior IRB approval must be given to exceed the enrollment goal.

Locally: **Up to 150 enrolled, (N = 54 target completion goal, plus additional if necessary to account for possible dropout, screen failure, etc.)** At all Sites: **up to 150**

*****If this study is a retrospective record review only, you may skip to Section VII*****

31. Will subjects receive any compensation or gifts to participate?

☒ Yes ☐ No ☐ N/A

- If yes, specify payment amount, how it will be prorated and how payment will be made: **Participants may receive up to $300 for completion of all study procedures, as follows.**

- **Assessment Session 1 (Week 0): $20**
- **Assessment Session 2 (Week 8): $30**
- **Assessment Session 3 (Week 16): $35**
- **Assessment Session 4 (Week 24 follow-up, post-intervention): $40**
- **Physical Activity and Diet Assessments 1-3 (Weeks 0, 8, and 16): $20 per assessment week ($60 total possible). These will occur outside the laboratory. At each assessment, participants will be asked to wear the Actigraph accelerometer to measure physical activity for a period of seven days. On three of those days, participants will also be asked to complete the ASA-24 dietary recall questionnaire online.**
- **Brief Online Assessments (Weeks 3, 9, and 15). $5 per assessment ($15 total possible). Participants will be asked to complete brief online assessments (e.g., delay discounting, food purchasing) outside of the laboratory. EFT+BT participants will also be asked to complete an EFT event/cue-generation exercise.**
- **Participants will also receive an additional bonus at Week 24 of $100 for completing 90% or more of all assessment sessions and at-home assessments (Actigraph, brief online assessments, and diet recalls). The magnitude of this bonus was chosen in order to motivate attendance at the follow-up assessments for the majority of participants and thus minimize the occurrence of missing data, including from those participants who may have been less successful in the intervention or follow-up period.**
- **To allow for payments that are both convenient and rapidly available, we may pay participants with reloadable prepaid cards through Greenphire ClinCard (www.greenphire.com), an FDIC-insured payment provider that specializes in clinical trial stipend payments that comply with IRB privacy regulations and considerations. At the beginning of the study, the participant will receive a prepaid MasterCard debit card that can be used anywhere that accepts MasterCard. As payments are earned in the course of the study, additional funds will be added to the account for that participant. Funds are immediately available when added and participants can check their balance as desired. This system will allow frequent, immediately available payments. Payments may also be made via check or cash, however remote debit card payments and checks will be used most often.**
- **Compensation will be prorated.**
- **To minimize barriers to participation, participants may also be provided with travel compensation in addition to the amounts above if they live outside of Roanoke or if travel to FBRI from within Roanoke is prohibitive to participation. Travel compensation, if provided, will be calculated using an hourly rate equal to the US minimum wage.**

32. Will you, the sponsor, or Contract Research Organization offer any fee to physicians for the referral of potential subjects?

☐ Yes ☒ No

33. Will recruitment materials be used?

☒ Yes ☐ No

If yes, check all that apply and include with this submission:

- ☐ Brochure
- ☐ E-mail
- ☒ Recruitment letter
- ☒ Flyer/Poster
- ☐ Clinical trial website posting
- ☐ Radio/Television script
- ☐ Newspaper Ad
- ☒ Website advertisement (including Facebook, Craigslist, etc.)
- ☐ Telephone or in-person script
- ☒ Other (please specify): **Roanoke Valley Metro bus**

STEP 1: IDENTIFICATION OF POTENTIAL SUBJECTS

To "identify" a potential subject refers to steps you plan to take to determine which individuals may qualify to participate in your study so that you can decide which individuals to contact about taking part.

34. How do you plan to identify potential subjects? (check all that apply)

- ☒ Medical Chart Review, Clinic Schedule Review, or QA-QI Database Review (own patient population)
  **Study team requests Waiver of Informed Consent and, if any HIPAA identifiers are collected, a Waiver of HIPAA Authorization for recruitment purposes*
- ☒ Medical Chart Review, Clinic Schedule Review, or QA-QI Database Review (other physicians/practices patient population)
  **Study team requests Waiver of Informed Consent/HIPAA Authorization for recruitment purposes*
- ☒ Potential subjects will not be directly identified by the researchers. The potential subject will obtain IRB-approved written information about the study from his or her health care provider/faculty or from an advertisement, flyer, brochure, website, etc. The potential subject would then contact the researcher if he or she is interested.
- ☐ Researchers who ARE NOT treating clinicians of potential subjects will ask treating clinicians for referrals of eligible patients interested in the study. Treating clinicians identify potentially eligible patients and provide researchers with patient contact information with patient permission documented (e.g. email/letter to researcher from treating clinician states patient permission given. Researcher documents permission in research record.)
  **Study team requests Waiver of Informed Consent/HIPAA Authorization for recruitment purposes*
- ☐ Contact information will be provided by a patient's Carilion health care provider without the patient's knowledge to the researchers AND this is a minimal risk study that does not involve investigative drugs, devices, biologics or medical or surgical procedures.
  **Study team requests Waiver of Informed Consent /HIPAA Authorization for recruitment purposes*
- ☐ Review of Registry/Database in which individuals have previously signed a consent giving their permission to be contacted for future studies
- ☐ Student Records
  **Study team requests Waiver of Informed Consent for recruitment purposes*
- ☐ Other – please explain:

35. Please describe the identification process. List all information you plan to collect during the identification process prior to contacting potential subjects. This includes the inclusion/exclusion criteria and demographics to determine if a person qualifies for a study before contacting that person to be a potential subject.

Carilion Clinic personnel will conduct a data pull of potentially eligible patients from participating Carilion Family and Community Medicine clinics in the greater Roanoke Metropolitan area. An additional data pill may also include the New River Valley area. Data pulls will use the inclusion criteria of age≥ 18, and may include BMI, HbA1c, prescribed glucose-lowering medications, as well as ICD-10 code for type 2 diabetes. The corresponding ICD-9 codes may also be used due to the transition from ICD-9 to ICD-10. Carilion Family and Community Medicine physicians will have an opportunity to review a list of their patients who have been identified as potentially eligible for this study at each data pull. These physicians will be able to request removal of any patient from the recruitment process. The data pull will use the exclusion criteria of no telephone number and patient stipulation of "Do Not Contact" as indicated in the medical record. The data pull will result in a list of potentially eligible patients, which will be provided to the PI. Identifying information in the data pull will consist of potentially eligible patients' names, addresses, and phone numbers. {

36. Who will conduct the identification process?

- ☒ Principal investigator
- ☐ Other investigator (specify):
- ☐ Research coordinator (specify): **.**
- ☒ Other research team member (specify): **Health Analytics**

STEP 2: CONTACTING OF POTENTIAL SUBJECTS

To "contact" a potential subject refers to the initial contact method you plan to use to reach a potential subject to determine if he or she would be interested in taking part in your study.

37. How will potential subjects be contacted? (please check all that apply)

- ☐ Direct in-person contact
- ☐ Telephone call
- ☒ Letter
- ☐ E-mail
- ☒ Potential subject will not be contacted. Potential subject will contact the researchers by responding to a flyer, brochure, e-mail, etc.) **(Please skip to #39.)**

38. Who will contact the potential subject? (please check all that apply and ensure they are listed as a member of the study team)

- ☐ Principal investigator
- ☒ Other investigator (specify names): **Jeff Stein**
- ☐ Research coordinator (specify names):
- ☒ Other research team member (specify names): **Megan Stuart, Chesley Ammermann, Gemma Porras, Jeremiah Brown, Julia Basso**

39. If potential subjects are patients of Carilion Clinic, please check the appropriate scenario:

☒ **Patients will be contacted by the researcher who is also the treating clinician** or by a member of his/her treatment personnel or by his/her Carilion research personnel. Potential subjects will be assured that their decision will not affect their treatment or care or relationship with the treating clinician.
**Submit letter, email, or phone script (if applicable) using appropriate IRB template.*

☒ **Patients will be contacted by their treating clinician who is not the researcher** by letter with information about the research study. ** Submit letter using appropriate IRB template.*
Check all that apply:

- ☐ The letter will be co-signed by the principal investigator and sent by the research team. **Study team requests Waiver of Informed Consent/HIPAA Authorization for recruitment purposes*
- ☒ The letter will indicate that the patient will be called by researchers to discuss study. The letter will include a telephone number to call or post card to return to indicate patient does not want to be contacted. **Submit phone recruitment script.*
- ☐ The research involves the collection of sensitive information (e.g. illegal behavior, drug, or alcohol use; mental illness; sexual behavior.) The letter will include a telephone number to call or post card to return if patient is interested in learning more. Patient will not be contacted until he/she calls or returns post card.

☒ **Researchers who ARE NOT treating clinicians of patients will contact patients**:

- ☐ after patients have given permission to a treating clinician to share contact information with the research team and permission is documented
- ☒ without the patients' prior permission AND this is a minimal risk study that does not involve investigative drugs, biologics or surgical procedures. *Check one:*
- ☒ Contact will be via letter, phone, direct-email. **Submit letter, email, phone script using the appropriate IRB template.*
- ☐ Potential subjects will be approached in person while at a Carilion Clinic hospital or clinic. **Submit recruitment script using the appropriate IRB template.*

40. Describe what will be said to potential subjects to introduce them to the research. If an investigator has direct authority over potential subjects who are students, medical residents or employees, then explain how recruitment will avoid undue influence. For example, someone from the research team who does not have direct authority will make the initial contact OR potential subjects will be assured a decision not to participate in the research will not affect grades or job evaluations. Submit any letter, email, phone or other recruitment script that will be used.

Please see attached recruitment letter.

STEP 3: SCREENING OF POTENTIAL SUBJECTS

To "screen" a potential subject refers to additional information that will be collected or activities that will take place after he or she has been identified and contacted and prior to obtaining informed consent for the study. This could include asking questions to a potential subject to determine whether he or she meets eligibility criteria. Note: To comply with HIPAA regulations, only the minimum necessary protected health information may be collected at this time. This means only questions relating to the inclusion and exclusion criteria may be asked.

41. Please describe the screening process for your study. Please include whether you plan to ask potential subjects to do anything or answer questions prior to signing an informed consent document. For example: patients will answer questions about their medical history, be expected to come to the first screening visit after fasting, stop taking medications, change diet, etc.

The screening process will occur via a website or in person. The screening will ask about age, gender, pregnancy status, and other demographic and health information related to inclusion/exclusion criteria. Patients will be scheduled for an informed consent session that will require no change in routine behavior.

Potential participants will be asked to provide a unique study code during screening so that PHI is not collected/stored in the same database as their answers to screening questions. Study personnel will inform participants that the screening information they provide will be kept confidential and not shared with anyone outside of the study team.

Screening data will be collected online using RedCAP (for PHI) and Qualtrics. Stored screening data will not include any HIPAA identifiers. Names and other identifying information of patients identified through query of Carilion Medical Records will be stored in a secure share on a Carilion portal/server.

Carilion patients will be recruited through direct mailings, including a link to the screening questionnaire, to adults 18 years and older. Interested participants will additionally be screened in person to ensure they meet the inclusion criteria as previously described.

In addition, participants will be recruited through flyers posted in Carilion Clinics and other places in the community, such as at health and wellness centers and fairs, schools, libraries, coffee shops, stores, restaurants, etc. People who are interested in the study will contact our research center via phone or email or in person, or access the screening questionnaire directly.

☐ N/A **(If N/A, please skip to Section VI)**

42. Who will conduct the screening?

☐ Principal investigator
☐ Other investigator (specify):
☐ Research coordinator (specify):
☒ Other research team member (specify): **Megan Stuart, Chesley Ammermann, Gemma Porras, Jeremiah Brown, Julia Basso**

43. List all information you plan to record during the screening process. (Attach screening data collection tool or an inclusion/exclusion checklist.) **Study team requests Waiver of Informed Consent and, if any HIPAA identifiers are collected, a Waiver of HIPAA Authorization for recruitment purposes.*

Please see attached screening questionnaire

SECTION VI: STUDY POPULATIONS

44. Does the research involve intervention or interaction with individuals? (Examples include physical procedures, written or verbal communication with individuals, or surveys.)

☒ Yes ☐ No

*****If no, you may skip the remainder of this section and go directly to Section VII*****

45. Which vulnerable populations may be included in this study? Check all that apply:
- ☐ Children/Minors (less than 18 years old)
- ☐ Wards of State
- ☐ Pregnant women
- ☐ Fetuses
- ☐ Neonates of uncertain viability OR non-viable neonates
- ☐ Prisoners (Please contact IRB prior to submission of application.)
- ☐ Mentally disabled persons*
- ☐ Cognitively impaired persons*
- ☐ Limited or non-readers
- ☐ Non-English speakers (You must use either a translated consent form or short form. Contact IRB office.)
- ☒ Economically disadvantaged persons
- ☒ Educationally disadvantaged persons
- ☐ Employees under the investigator's supervision or authority
- ☐ Students under the investigator's supervision or authority
- ☐ Patients in emergency situations
- ☐ Terminally ill patients
- ☐ Others that may be vulnerable to coercion:

**If persons are without decision making capacity, please submit a Legally Authorized Representative Investigator Assurance Form. This form is located on the IRB website.*

46. If persons in any of the vulnerable groups checked above will be enrolled into this study, please explain the additional safeguards that will be used to protect the rights and welfare of those subjects. Check all that apply:
- ☒ For economically disadvantaged subjects, there will be no financial screening of potential subjects and any eligible patient will be allowed to enroll regardless of financial standing or insurance status.
- ☒ For educationally disadvantaged subjects, additional time will be spent with them to ensure their understanding of the research participation by answering questions and clarifying any issues. The consent form will be read to them if necessary.
- ☐ For limited or non-readers, the consent will be read to them and additional time will be spent with them to ensure their understanding of the research participation by answering questions and clarifying any issues. This process and the subject's signature will be witnessed by someone who is not part of the research team.
- ☐ For students, medical residents, or employees under investigator's authority, an investigator, research coordinator, or other member of the research team that does not have direct authority over the students or employees will obtain informed consent.
- ☐ Other (specify):

47. If this research does not exclude children, please assess the level of risk involved (check only one):
- ☒ N/A
- ☐ Minimal risk (no greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations)
- ☐ Greater than minimal risk but has potential benefit
- ☐ Greater than minimal risk but no foreseen benefit

48. For research involving children, will an assent form be used? Assent is not required if the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of research. Please note: if the child is <7 years of age, a discussion is not required.

☐ Yes ☐ No ☒ N/A

49. Do you request a waiver of assent?

☐ Yes ☐ No ☒ N/A

If yes, please justify:

50. Does the research exclude pregnant women? ☒ Yes ☐ No

If you marked No above, then please affirm the following by marking each box:

☐ Preclinical studies and clinical studies have been conducted and provide data for assessing potential risks to pregnant women and fetuses, **or** it is not scientifically appropriate to do this.
☐ The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman and/or fetus; **or,** if there is no such prospect of benefit, the risk to the fetus is minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means.
☐ Any risk is the least possible for achieving the objectives of the research.
☐ The research holds out the prospect of direct benefit to the pregnant woman and/or fetus, **or** no benefit for the woman nor fetus **and** risk to the fetus is minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.
☐ Each individual providing consent will be fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate.
☐ No inducements, monetary or otherwise, will be offered to terminate a pregnancy.
☐ Individuals engaged in the research will have no part in any decisions as to the timing, method or procedures used to terminate a pregnancy.
☐ Individuals engaged in the research will have no part in determining the viability of a neonate.

Please affirm the following by marking each box <u>if they apply to your research</u>:

☐ If the research holds out the prospect of direct benefit solely to the fetus, then the consent of the pregnant woman and the father will be obtained (father's consent need not be obtained if he is unavailable, incompetent, or temporarily incapacitated; or the pregnancy resulted from rape or incest).
☐ For children who are pregnant, assent and permission will be obtained.

51. If you plan to enroll subjects that may be cognitively impaired, describe how you plan to assess decision making capacity prior to consent: **N/A**

- Will consent be obtained from a surrogate decision-maker for incompetent subjects?

  ☐ Yes ☐ No

SECTION VII: INFORMED CONSENT

For guidance on required elements for a Carilion informed consent document, please visit the Carilion IRB website; see New Submissions, Section 2, Informed Consent Guidelines.

52. Are you planning to obtain written (signed) informed consent from subjects for this research?

☒ Yes, I am planning to obtain consent and signature using a consent form **(If yes, please skip to #54)**
☐ No, I am planning to obtain consent without a signature using an information sheet **(Please go to #53)**
☐ No, I am planning to obtain only verbal consent **(Please go to #53)**
☐ No, I am requesting a <u>Waiver of Informed Consent</u> **(Please skip to #61)**

<u>Waiver of the Requirement to Obtain Signed Consent</u>

53. Please answer the following questions to request a <u>Waiver of the Requirement to Obtain Signed Consent</u>:

- Is the informed consent document the only record linking the subject and the research, and is the principal risk the potential harm resulting from a breach of confidentiality?

  ☐ Yes ☐ No

  If yes, you must ask the participant if they want documentation linking them to the research, and the subject's wishes shall govern.

- Does the research involve greater than minimal risk or any procedure for which written consent is normally required outside of the research context?

  ☐ Yes ☐ No

- Will you provide the subject with a written statement regarding the research?
  ☐ Yes ☐ No

- Are the subjects or their legally authorized representatives members of a distinct cultural group or community in which signing forms is not the norm, and is there is an appropriate alternative mechanism for documenting that informed consent was obtained?
  ☐ Yes ☐ No

54. Describe the process of obtaining informed consent, parental permission, and/or assent from the subject in detail (ex: who, when, where, how), and how this process will be documented.

Patients interested in participating will be provided with the written consent form during their scheduled visit to the FBRI or CRC. They will also be given time in a quiet room in the laboratory to read and consider the form. Consenting personnel will review each element of the written consent form with the potential participant. The potential participant will be given the opportunity to ask questions and will have as much time as they need to decide whether they would like to participate in the study. They will be encouraged to speak with whomever they wish before making this decision. Personnel will reiterate that the patient may choose to decline participation in the study at that time or at any time thereafter without consequence. The potential participant and person obtaining consent will sign the consent form after the potential participant verbally states that s/he understands the conditions of the study. Patients will also be offered the opportunity to take home the consent form, consider it more carefully, and provide informed consent (if they choose) at a later date.

55. Who will conduct the consent discussion with the subject? (Check all that apply):

    ☐ Principal investigator
    ☒ Other investigator (specify): **Jeff Stein, PhD**
    ☐ Research coordinator (specify):
    ☒ Other research team member (specify): **Megan Stuart, Chesley Ammermann, Gemma Porras, Jeremiah Brown, Julia Basso**
    ☐ For Survey Studies only: Information sheet will be mailed and no discussion will take place

56. Will a student (VTCSOM, Jefferson College, other college or university) be obtaining consent from subjects? (This does not include questionnaire or survey studies.)

    ☐ Yes ☒ No

    If yes, then the Principal Investigator must sign an attestation of training at the end of this form.

57. Where will informed consent process take place:

    ☒ In a private room
    ☐ In a waiting room
    ☐ In an open ward
    ☐ In a group setting (Group consent is allowed only in special situations. Explain process):
    ☐ At potential subject's residence

☐ In emergency situations (Explain process):
☐ Online (Explain process):
☐ Over the phone (Phone consent is allowed only in special situations. Explain process):
☐ Other (specify):

58. How will you assure there is sufficient opportunity for the subject to consider whether to take part? Check all that apply:

☒ Subjects will be allowed to take home unsigned consent form for consideration prior to signing it
☐ Subjects will be allowed a waiting period of hours to consider their decision
☒ Other (specify): **Participants will be encouraged to ask questions about any concerns that they have.**

59. What questions will be asked to assess the subjects' understanding of informed consent? Check all that apply:

☒ What is the purpose of this research?
☒ What are the risks and benefits of being in this study?
☒ How is being in this study different from ordinary treatment?
☒ How long will you be in this study?
☐ Other (specify):

60. Please use Carilion IRB Informed Consent Templates located on our website. How will you assure the consent form or information sheet is written at a level that can be understood by the research subjects?

☐ Determine grade level and reading ease by using spelling and grammar function in Microsoft Word
Provide Scores Here:
☒ Use another readability formula or index (specify type used and results here): **SMOG Grade Level: 9.1**
Note: Consent Forms with difficult reading scores may be returned for editing and may delay IRB review

*****If you are not requesting a Waiver of Consent for any participants, you may skip the remainder of this section and go directly to Section VIII*****

Waiver of Informed Consent

61. Does the research involve more than minimal risk (no greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations) to subjects or to their privacy?

☐ Yes ☐ No

62. If the research involves using identifiable private information or identifiable biospecimens, could the research be carried out without using such information or biospecimens in an identifiable format?

☐ Yes ☐ No ☐ N/A (no identifiable data or specimens being used)

If no, please describe why identifiers are necessary to answer the research question:

63. Will the waiver adversely affect the rights and welfare of the subjects?

☐ Yes ☐ No

64. Please check the appropriate option below describing why obtaining consent is impracticable. Note, by choosing any option in this category, you confirm that data will not include psychotherapy notes and that the study is not subject to FDA research regulations.

- This study is a retrospective medical record review and/or retrospective review of specimens collected for purposes other than this research. Obtaining informed consent is impracticable because of the large number of records and/or specimens involved. Note: If data/specimens are sought from a small group of patients, obtaining consent may be considered practicable even it is inconvenient.

  ☐ Yes ☐ No

- Obtaining informed consent is impracticable because the sample size is so large (e.g. population-base studies or epidemiology trials) that including only those samples/records/data for which consent can

be obtained would prohibit conclusions to be drawn or bias the sample such that conclusions would be skewed.

☐ Yes ☐ No

- Obtaining informed consent is impracticable because the research is looking at issues such as outcomes/morbidity data where not having access to data from all subjects would affect the statistical outcome of the study.

  ☐ Yes ☐ No

- Other reason obtaining informed consent is impracticable:

65. Will the research yield information of direct clinical relevance for the subjects?

☐ Yes ☐ No

66. Will subjects or their Legally Authorized Representative be provided with additional pertinent information after participation?

☐ Yes ☐ No

SECTION VIII: HIPAA FOR PROTECTED HEALTH INFORMATION (PHI)

67. Will this study require the creation, use, access, or disclosure of a Carilion Clinic patient's Protected Health Information (PHI), including access their medical record for screening or recruitment?

☒ Yes ☐ No **(If no, please skip to #69)**

68. Please check whether these items will be collected, recorded, or created from a Carilion healthcare record:

• name	☒ Yes ☐ No
• a geographic subdivision smaller than state except for the first three digits of the zip code	☒ Yes ☐ No
• an element of a date, except year, for dates related to an individual, including birth date, admission date, discharge date and date of death; and all ages over 89 and all elements of such ages may be aggregated into a category of age 90 or older	☒ Yes ☐ No
• telephone numbers	☒ Yes ☐ No
• fax numbers	☐ Yes ☒ No
• electronic mail address	☒ Yes ☐ No
• social security number	☒ Yes ☐ No
• medical record number/ master patient index (MPI)	☒ Yes ☐ No
• health plan beneficiary numbers	☐ Yes ☒ No
• account numbers	☐ Yes ☒ No
• hospital account receivable (HAR)/contact serial number (CSN)	☐ Yes ☒ No
• certificate/license numbers	☐ Yes ☒ No
• vehicle identifiers, including license plate number	☐ Yes ☒ No
• device identifiers and serial numbers	☐ Yes ☒ No
• Web Universal Resource Locators (URLs)	☐ Yes ☒ No
• Internet Protocol (IP) address numbers	☐ Yes ☒ No
• biometric identifiers, including finger and voice prints	☐ Yes ☒ No
• full face photographic images and any comparable image	☐ Yes ☒ No
• any other unique identifying number, characteristic, code	☐ Yes ☒ No

69. Do you plan to collect or record individually identifiable health information about subjects from a healthcare record at any other non-Carilion healthcare provider, health plan (e.g. insurer), employer, or healthcare clearinghouse (e.g. billing service) at any point in the project? (See list of identifiers above.)

☐ Yes ☒ No

- If yes, please list all identifiers you plan to collect:
-

70. Will the individually identifiable data be related to or linked to the past, present, or future physical or mental health condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual?

☒ Yes ☐ No ☐ N/A, we are not collecting or recording any identifiers listed above

71. Will the individually identifiable data be created or received by any person or entity that is a health care provider or an employee of any part of Carilion?

☒ Yes ☐ No ☐ N/A, we are not collecting or recording any identifiers listed above

If you answered "yes" to #67 OR if you answered "yes" to #69, #70, AND #71 then you must either 1) obtain written HIPAA authorization from each research subject (in the informed consent form) or 2) request a HIPAA waiver.

72. Do you request a HIPAA waiver to conduct your research? ☐ Yes ☒ No

******If no, please skip to Section IX*****

A HIPAA waiver can only be granted if the research cannot practicably be conducted without the waiver and the use of the PHI poses no more than minimal risk to the privacy of the individuals.

Waiver of Authorization (HIPAA Waiver)

73. Describe how the use of PHI in this study poses no greater than minimal risk to participants' privacy.

74. Could the research be carried out practicably without the use of PHI?

☐ Yes ☐ No

75. Is the waiver needed because obtaining HIPAA authorization is impracticable? Please check the appropriate option below.

- This study is a retrospective medical record review and/or retrospective review of specimens collected for purposes other than this research. Obtaining HIPAA authorization is impracticable because of the large number of records and/or specimens involved. Note: If data/specimens are sought from a small group of patients, obtaining consent may be considered practicable even it is inconvenient.

  ☐ Yes ☐ No

- Obtaining HIPAA authorization is impracticable because the sample size is so large (e.g. population-base studies or epidemiology trials) that including only those samples/records/data for which consent can be obtained would prohibit conclusions to be drawn or bias the sample such that conclusions would be skewed.

  ☐ Yes ☐ No

- Obtaining HIPAA authorization is impracticable because the research is looking at issues such as outcomes/morbidity data where not having access to data from all subjects would affect the statistical outcome of the study.

  ☐ Yes ☐ No

- Other reason obtaining authorization is impracticable:

76. Do you assure that any data identifying subjects used in this study will not be disclosed to anyone other than the research team, sponsor, and oversight groups?

☐ Yes ☐ No

77. Do you assure that you will not use this data for any other research unless you receive IRB approval?

☐ Yes ☐ No

SECTION IX: DATA PROTECTION PLAN

78. Is the private information being requested the minimum necessary to meet the research goals?

☒ Yes ☐ No ☐ N/A

79. What records or data will you be using or collecting? Check all that apply:

☒ New data for this study
☐ Data already collected for another research study
☐ Data already collected for administrative purposes
☒ Medical records; approximately how many records: **150**
☐ Electronic information from clinical database
☐ Other:

80. Will any sensitive information be collected, such as information regarding sexual behavior, HIV status, recreational drug use, illegal behaviors, physical abuse, mental health disorders, etc.?

☐ Yes ☒ No

- If yes, what sensitive information will you be collecting?
- If yes, will you be obtaining a Certificate of Confidentiality? ☐ Yes ☐ No

81. Where will data be stored? Please note that **no other storage options are permitted,** including the use of Carilion provided or personal laptops, encrypted flash drives or other portable devices. Data must not be placed in a cloud or other hosted environment. Any exceptions must first be approved by the Carilion Privacy and Information Security Officer and documentation provided to the IRB.

Please check all that apply:

☐ Hardcopy data in a locked office in a locked cabinet
☒ Electronic data on a password protected, secure drive on a Carilion server (contact mmtenzer@carilionclinic.org to set up a shared drive)
- Select the software to be used: ☐ Excel ☐ Access ☒ Other: Describe Qualtrics

☒ REDCap (contact mmtenzer@carilionclinic.org to discuss use of REDCap). If all data, including the code link, will be stored in REDCap, skip to #82.

82. The standard at Carilion to protect identifiable data used in research is to use a code and link system. Two files should be kept in two separate secure locations. One file should use a unique code for each subject in connection with any sensitive or health information. The other file (the link) associates the unique code with subject identifiers (e.g. name, medical record number). Please describe how you will store data using the options below.

☐ **Retrospective Record Review Research Only:** The master list will contain direct subject identifiers such as name and MRN along with a unique subject code. It will be stored separately from the coded research data set at all times. The research data set will not include any HIPAA identifiers with the exception of a date.
☒ **Prospective Collection of Data**, including surveys or collection of new data: While initial collection of research data may contain identifying information, it must be stored using a code linked to the subject's identity using a master list, or will include only anonymous or de-identified data. All HIPAA identifiers will be stripped from the initial research data collection data tools and replaced with a unique subject code.
☐ **Prospective Collection of Sensitive Data**, including surveys or collection of new data: Research data will be linked to identifiers by a unique subject code at all times. The code will be linked to a master list that contains identifying information. The master list and coded research data will be stored in separate locations.

83. Please describe how you plan to protect identifying information from improper use and disclosure by answering the questions below.

a) Who will have access to identifiers? **Trained study team personnel**
b) How will you limit access to the identifiers? **Identifiers will be stored separately on a password protected master list in Carilion Red Cap or on a Carilion server.**

84. When will study files, including informed consent documents, study documents, and the code link with identifiers be destroyed?

Please note that you must retain research records for the greater of:

- At least three years after completion of the research.

- If the study involves Protected Health Information, research records must be maintained for a minimum of six years after the completion of the research.
- For drug studies conducted under an IND, two years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until two years after the investigation is discontinued and FDA is notified.
- For device studies conducted under an IDE or abbreviated IDE, two years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol.
- The retention period required by the sponsor
- The retention period required by local, state, or international law.
- The retention period required by a site that is not part of Carilion Clinic.

☒ **10** Years after the study has been closed with the IRB (enter # of years)
☐ Other (please specify):

SECTION X: MEDIA USE

85. Will any media be used to record subjects' voice or image?

☐ Yes ☒ No

- If yes, describe what media will be used, how the media will be used, and justify why it is necessary to use the media to collect data:

86. Will the subjects' voice or image be recorded without their knowledge?

☐ Yes ☒ No

- If yes, describe the deception and the debrief procedures:

SECTION XI: SAFETY & MONITORING

87. Describe the process for dealing with adverse events and unanticipated problems.

We do not anticipate any adverse events/unanticipated problems, but these will be reported to the IRB immediately upon occurrence

88. Is there a Data Safety Monitoring Board or other safety oversight committee?

☐ Yes ☒ No

- **If yes:**

What is the name of the board or committee?
If the DSMB is local, please name the members.
How frequently will the data be reviewed for safety?

☐ Every 3 months ☐ Every 6 months ☐ Annually ☐ Other:

- **If no:**

How will the data be monitored to ensure the safety of subjects? **The proposed study poses minimal risk to patients, and therefore no safety monitoring is required.**

89. Are there plans for visits by sponsor monitors or auditors to review study documents for regulatory requirements?

☐ Yes ☒ No ☐ N/A

- If yes, Identify the group that will be conducting the monitoring/auditing visit(s) and the number of times you anticipate this occurring over the next year:

90. Does this project involve research using any of the following?

☐ Yes	☒ No	Mammalian cell/tissue culture (includes established cell lines or primary isolation of cell lines from tissue, blood, etc.)
☐ Yes	☒ No	Cultivated microorganisms (isolated, grown *in vitro* and used for non-diagnostic research, i.e. isolation of biohazardous organisms from patient samples)
☐ Yes	☒ No	Research animals
☐ Yes	☒ No	Molecular cloning, recombinant DNA or gene therapy techniques

If you checked yes on any of the above boxes, you are required to contact the Carilion Clinic Research Safety Committee at 985-8510 for important guidance.

SECTION XII: STORED DATA AND HUMAN BIOLOGICAL MATERIALS REPOSITORIES

Databases and specimen repositories, also known as registries or banks, are used to store data and/or specimens for future use. When the use is for clinical purposes or quality improvement, IRB approval is not required. However, when the use is for research purposes, the databases/repositories must be approved by the IRB (45 CFR 46 and 45 CFR 160 & 164).

91. Will this research collect and store data/specimens (blood, urine, biopsy tissue, saliva, etc.) for future research beyond the parameters of this study?

☐ Yes ☒ No

*****If no, you may skip the remainder of this section and go directly to Section XIII*****

92. Will the data/specimens collected for this research be stored in an existing repository at Carilion that is used for future research?

☐ Yes ☐ No

- If yes, provide repository name:

93. Will the data/specimens collected for this research be stored in a non-Carilion repository that is used for future research?

☐ Yes ☐ No

- If yes, attach a protocol or other information describing the repository operations.

94. Will the data/specimens collected be stored in a repository for future research that will be developed and operated by the researcher(s)?

☐ Yes ☐ No

- If yes, you must also submit a Specimen/Data Repository Application to the IRB

SECTION XIII: SUBMISSION INCLUSIONS

Please check which of the following required materials you are including with this submission. If information is submitted electronically, signature pages must be faxed or hand delivered (mailed).

- ☐ Protocol (Not required for investigator-initiated research; this application serves as protocol.)
- ☒ Grant application
- ☒ Main consent form(s), or Information Sheet
- ☐ Tissue banking consent form
- ☐ Assent form, if required for research involving children
- ☐ Legally Authorized Representative Investigator Assurance Form
- ☒ Recruitment script or other recruitment materials
- ☒ Any subject questionnaire or survey
- ☒ Any data collection tool that will be used to record subject information
- ☐ Inclusion/Exclusion Checklist
- ☐ Applicable Clinical Trial (ACT) Checklist, if study involves drugs, devices, or biologics
- ☐ Investigator brochure for drug studies
- ☐ Completed Form 1572 for drug studies
- ☐ Manufacturer reference material for device studies

☐ Curriculum Vitae for PI
☐ IRB fee, if applicable:
☐ $1,500 application fee for full-board industry-sponsored research
☐ $750 application fee for expedited industry-sponsored research

SECTION XIV: CERTIFICATIONS

Certification of Principal Investigator:
By signing this document I confirm that I have read and will carry out my responsibilities as Principal Investigator as outlined in INVESTIGATOR GUIDANCE: Investigator Obligations (IRB-800).

_____ _____
Carilion Principal Investigator (signature) Date

_____
Carilion Principal Investigator name (printed)

Certification of Department Chair:
My signature indicates that this project has been reviewed by the appropriate departmental parties who have judged that 1) there is a scholarly and scientific justification for the protocol, that the study is feasible, and that the proposed methods are scientifically valid, 2) the PI is sufficiently qualified by training and experience to conduct the research, 3) that the department has made the space and time commitment necessary to carry out the project, 4) that the financial implications of the research have been considered and deemed acceptable to the department.

_____ _____
Department Chair or designee (signature) Date

_____
Department Chair or designee name and title (printed)

Principal Investigator Attestation of Informed Consent Training for Students: I certify that the following student(s) who will be obtaining informed consent for this study will have observed a mock informed consent discussion or actual informed consent discussion conducted by an experienced research team member and have been observed conducting a mock informed consent discussion or actual informed consent discussion by an experienced research team member before being allowed to interact with study subjects. In addition, I certify these students have 1) Completed the Cornerstone research modules on "The Informed Consent Process for Clinical Research" and "Recruitment of Study Subjects." 2) Viewed the video General Informed Consent Requirements" posted on the Education tab of the Office for Human Protections website https://www.hhs.gov/ohrp/education/training/ded_video.html 3) Viewed the 3 informed consent videos posted on the IRB website.

_____
Student name (printed) Name of School

_____

Student name (printed)	Name of School
Student name (printed)	Name of School
Principal Investigator (signature)	Date
Principal Investigator name (printed)	