

COVER PAGE

Combined Study Protocol and Statistical Analysis Plan

Principal Investigator	Heather J. Baer, ScD
Official Study Title	Integrating Online Weight Management with Primary Care Support: Patient-Centered Strategies for Addressing Overweight and Obesity in Primary Care
ClinicalTrials.gov ID	NCT02656693
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PROTOCOL SUMMARY**

Answer all questions accurately and completely in order to provide the PHRC with the relevant information to assess the risk-benefit ratio for the study. Do not leave sections blank.

PRINCIPAL/OVERALL INVESTIGATOR

Heather J. Baer, ScD

PROTOCOL TITLE

Integrating Online Weight Management with Primary Care Support: Patient-Centered Strategies for Addressing Overweight and Obesity in Primary Care

FUNDING

PCORI

VERSION DATE

Version 23: January 11, 2019

SPECIFIC AIMS

Concisely state the objectives of the study and the hypothesis being tested.

The goal of this project is to adapt an evidence-based online weight management program and integrate it with population management support from primary care practices. We then will conduct a three-arm, cluster-randomized trial to compare the effectiveness of 1) the combined intervention (online weight management program plus population management support) with 2) the stand-alone online weight management program and with 3) usual care, among overweight and obese primary care patients with type 2 diabetes or hypertension. The specific aims are:

- 1) a. To adapt an online weight management program and integrate it with population management support, incorporating input from patients, primary care clinicians, and other stakeholders; afterward, we will acquire feedback on the positive and negative aspects of the intervention.
b. To compare the effectiveness of the combined intervention (online weight management program plus population management support) with the stand-alone online program and with usual care.

Hypothesis 1: The combined intervention will lead to greater weight loss at 12 months compared with the stand-alone online program and with usual care.

- 2) To identify mediators of the combined intervention and the stand-alone online program.
Hypothesis 2: The effects of the combined intervention and the stand-alone online program on weight loss will be mediated by patients' level of engagement, changes in self-efficacy, and changes in diet and physical activity.

- 3) To explore whether the effectiveness of the combined intervention and the stand-alone weight management program varies by patient characteristics.

Hypothesis 3: The interventions will be more effective among patients who are younger, white, and higher socioeconomic status, although the population management strategy may help to reduce these differences.

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BACKGROUND AND SIGNIFICANCE

Provide a brief paragraph summarizing prior experience important for understanding the proposed study and procedures.

Overweight and obesity are problems of tremendous clinical and public health importance. Over 35% of U.S. adults are obese (body mass index, or BMI, ≥ 30 kg/m²) and another 33% are overweight (BMI 25-29.9 kg/m²). Overweight and obesity are associated with many serious health conditions, including type 2 diabetes, cardiovascular disease (CVD), and some cancers. Even small amounts of weight loss (3-5%) can lead to significant health benefits, such as reductions in triglycerides, blood glucose, and risk of type 2 diabetes. Based on these findings, lifestyle intervention and counseling (comprehensive lifestyle intervention) are recommended for all patients with BMI ≥ 30 kg/m² and for patients with BMI 25-29.9 who have one or more CVD risk factors or other obesity-related comorbidities. Despite these recommendations, primary care clinicians often do not identify overweight or obese patients or counsel them about weight management. Evidence from a number of studies has indicated that online weight management programs can help people achieve and maintain clinically meaningful weight loss. While the amount of weight loss in online programs may be less than in traditional face-to-face approaches, online programs may increase convenience and decrease cost of lifestyle interventions. Although there are relatively few studies, evidence also suggests that online weight management programs can help patients achieve weight loss in the primary care setting. However, online weight management programs are not being widely implemented in primary care, and it is unclear whether they are effective and scalable in real clinical practice. We will adapt an evidence-based online weight management program called BMIQ which was developed to help healthcare professionals educate and engage patients in the process of lifestyle change and long-term weight management.

RESEARCH DESIGN AND METHODS

Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled by researchers study-wide and by Partners researchers. Provide a brief summary of the eligibility criteria (for example, age range, gender, medical condition). Include any local site restrictions, for example, "Enrollment at Partners will be limited to adults although the sponsor's protocol is open to both children and adults."

Focus Groups and Key Informant Interviews

Several focus groups, each of which will include up to twelve patients, will be conducted at the beginning of the study to obtain their feedback about the BMIQ online program and the population health management support strategy. To be eligible for the focus groups, patients must have a BWH clinician, be between ages 20-70 years old, and have a recent BMI (in the past year) between approximately 27 and 40 kg/m². They should be interested in weight management and/or motivated to lose weight. In addition, they must speak English, and have regular access to the Internet (at least once per week) via a computer, smartphone, or tablet.

Phone interviews will be conducted at the end of the study to solicit feedback on the BMIQ program and the population health management intervention. Patients in the PROPS Study who are assigned to the online program or combined intervention arm, reach the 18-month timepoint, and complete the final study survey are eligible and will be invited to participate. Research staff will recruit and schedule up to 30 participants for the phone interviews.

Key Informant Interviews will be conducted at the beginning and the end of the study. To be eligible, the key informants must be clinicians or other staff who provide services to patients at

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one of the participating BWH primary care practices. There are a total of 165 clinicians in these practices, including staff physicians, residents or fellows, and nurse practitioners or physician assistants. Additional staff who provide services to patients include dietitians and population health managers. Approximately 7 clinicians or other staff who provide services to patients at each time point will be recruited as key informants and will also be asked to complete electronic surveys during the trial. These surveys are a part of the study and completion of these surveys are voluntary.

Trial

After adapting the online weight management program and integrating it with the population management support strategy based on our focus groups and key informant interviews, we will conduct a three-arm cluster-randomized trial to compare the effectiveness of the combined intervention (online weight management program plus population management support) with the stand-alone online weight management program and with usual care. This will be a pragmatic clinical trial conducted in approximately 14 BWH primary care practices.

To be eligible for the trial, patients must have an upcoming scheduled visit with a BWH primary care provider (for some patients this may be a Resident, Nurse Practitioner or Physician Assistant) within the next 2 months, BMI between 27 and 39.9 kg/m² at enrollment, and a diagnosis of Type 2 diabetes or hypertension. They also must be between ages 20 and 70 (inclusive) at enrollment, speak English or Spanish, and have a valid email address and regular access to the Internet (at least once per week) using a computer, tablet, or smartphone. Patients must also be motivated to lose weight. Finally, patients must attend their upcoming scheduled visit with a BWH primary care provider and have their weight measured at the visit. However, in some special situations when a weight from a primary care visit is not available, a weight from another visit may be used instead for enrollment. For example, if a patient's weight was not recorded at their PCP visit, which we are calling the index or baseline PCP visit, or if the patient missed or rescheduled their index PCP visit, a weight taken within 6 weeks before or after the index PCP visit is acceptable for enrollment as long as the weight was taken at a Partners-affiliated institution and it has been recorded in the patient's chart in Epic. If there is no other recorded weight from a Partners-affiliated institution within 6 weeks before or after the index PCP visit, the patient may be scheduled for a separate visit at the Brigham and Women's Hospital Center for Clinical Investigation (BWH CCI) to have their measurements (e.g., height and weight) taken, and these can be used for enrollment. A patient also may be scheduled for a visit at the CCI to have their height/weight measurements taken and used for enrollment if it has been more than 4 weeks since the patient's index PCP visit or other visit at a Partners-affiliated institution or if the patient was referred directly by the PCP but does not have a recent or upcoming scheduled PCP visit or other visit at another Partners-affiliated institution in the next month. In all of these cases, the study will pay for this BWH CCI visit. Participants will also be compensated \$50 and parking vouchers for a BWH CCI visit.

We plan to enroll a total of 840 patients for the study (280 per arm). Patients who enroll in the trial will attend regular primary care visits at their practices and also will complete surveys by e-mail, regular mail, or phone. The enrollment of Spanish-speaking patients will start between July 1 and August 1, 2016 (1-2 months later than the enrollment start of English-speaking patients on June 1, 2016). (HB: Please change to say, "Recruitment/enrollment of Spanish-speaking patients will start around August 1.") This staggered enrollment is due to translating the online program BMIQ from English to Spanish, and making the Spanish version of the online program functional. This staggered enrollment has been approved by PCORI (the Sponsor), as well as reviewed and approved of by the study statistician.

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Briefly describe study procedures. Include any local site restrictions, for example, “Subjects enrolled at Partners will not participate in the pharmacokinetic portion of the study.” Describe study endpoints.

Patient and Stakeholder Partners

Our patient and stakeholder partners, a group of patients and clinicians, will be given access to an initial test version of BMIQ so they can experiment with the various features, review the content, and make initial recommendations about the potential changes and customizations before giving access to the program to our focus group and key informant interview participants.

Focus groups and key informant interviews

Based on the recommendations of the patient and stakeholder partners, a new customized version of BMIQ will be developed and tested in several focus groups, each of which will include up to twelve patients. The focus groups will be led by an experienced moderator. During the first two focus groups, participants will be introduced to BMIQ and will be asked for feedback about its design, features, content, and usability. They also will be given examples of the type of outreach that will be done by the Central Population Management (CPM) team and will be asked for feedback about this.

For the third focus group (which also may be conducted as individual phone interviews, depending on patients’ availability), patients who have already participated in one of the first two groups will be asked to test out the BMIQ website on their own before attending the third focus group. They will do this using a test account that will be set up for them by a member of the research staff, and they will be sent instructions for how to log in and a list of tasks to try to complete ahead of time. During the third focus group (or phone interviews), these participants will be asked for feedback about the design, content, features, and usability of the BMIQ website.

Key informant interviews will be conducted with approximately seven BWH primary care clinicians or other staff who provide services to patients (including physicians, nurses, medical assistants, dieticians and population health managers. They will be asked to test the customized version of BMIQ before the interview, and during the interview they will be asked for feedback about its design, content, features, and usability; they also will be able to review the detailed population management protocol and give feedback. Patient phone interviews and key informant interviews will be conducted again at the end of the study, to acquire feedback on the positive and negative aspects of the interventions.

Trial List Review Of Potential Patients By Primary Care Providers

Lists of potentially eligible patients will be generated by the research team through an Epic workbench report and/or the Enterprise Data Warehouse (EDW). In all participating practices, primary care clinicians or their delegate (e.g., LPN or RN) will review the patient lists to validate them and to make sure that the patients are appropriate and do not have any medical contraindications for weight loss or physical activity. The population health managers will also assist with this process. If the PCP or the PCP’s delegate (e.g., RN, LPN, PA) does not review his/her list of potentially eligible patients and determine which patients, if any, should NOT be contacted for the study within 1 week of receiving the list, we will move forward with putting the patients from that list on our list of patients who are appropriate to contact. We would then mail these patients a letter describing the study and plan to call patients approximately 1 week after mailing the letter to describe the study to patients and conduct a phone screen if patients are interested in participating in the study. Please note, prior to calling any patients, Research

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Assistants review the patient's chart in Epic to confirm minimal inclusion criteria are met and major exclusion criteria are not present.

We will ask the Medical Director and/or the Practice Manager at each of the participating practices to acknowledge implementation of the 1 week window described above by sending us an email response; we will document their responses accordingly. We will also ask them to send us the names of any providers in their practice who are not in favor in this change; for these providers, we will not contact patients unless we receive the reviewed lists back from the provider. We will report any complaints regarding the 1 week list review period in real-time to the Partners Human Research Committee (IRB) in real-time via an "Other Event" submission.

In addition to mailing recruitment letters to patients approved for contact, we will be sending potentially eligible patients an Epic MyChart message. After the same 2-week list review process as described above, the PROPS Study Team will send the Partners eCare team a monthly list of patients who are potentially eligible and approved for contact. The Partners eCare team will then merge this list with a custom reporting workbench, and identify patients whose MyChart status is active. These patients will then be sent a MyChart message describing the study. Patients will not be able to respond to the message, however, the letter will give patients the contact information for the research study team (e.g., email, phone, website) if they are interested in participating in the study.

For each month of enrollment, we will hold a contest among the participating practices for the highest percent of patients enrolled in the study (i.e., the number of patients enrolled in the study from any one practice out of the number of patients initially identified through EDW and/or Epic workbench report for that practice). The monthly prize will be \$100 which will be routed to the practices fund for luncheons, etc. We hope the contest will encourage teamwork in the practice around the study, reward practices for their hard work on the study and perhaps discourage selective screening of patients depending on what study arm the practice has been assigned to.

Trial Randomization

Participating BWH primary care practices (or teams/clinics within the larger practices) will be randomized to one of three study arms (approximately eight teams/clinics per arm): 0) usual care, 1) online weight management only program, 2) combined intervention. The randomization will be stratified on clinic type (community-based clinic, hospital-based clinic, or community health center), to help ensure balance of the different types of clinics across the three arms, as they have different characteristics and patient populations; in addition, the estimated number of eligible patients at each clinic will be accounted for in the randomization. Of the 24 anticipated participating primary care clinics, 12 are community-based, nine are hospital-based, and three are community health centers. Therefore, when we stratify by clinic type and randomize from within these strata, using a computer algorithm, four community-based clinics, three hospital-based clinics, and one community health center will be randomized to each arm.

Study arms

In Arm 0 (usual care), patients will not be invited to join BMIQ, although they will receive general written information about weight management and they will continue to receive population management support for diabetes and hypertension.

In Arm 1 (online weight management only program), patients will be invited to join BMIQ for 12 months, but they will not receive weight-related population management support from their primary care practice. It should be noted that, separate from the study, as standard clinical

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practice patients may receive support from population health management for other conditions they may have (e.g., hypertension or type 2 diabetes). This research study will not affect this separate care, and this will be made clear to participants in the phone screen and consent form.

In Arm 2 (combined intervention), patients will be invited to enroll in the BMIQ program for 12 months. Patients who enroll in BMIQ will create a personalized weight management plan (which includes setting goals for weight loss, calorie intake, and physical activity), complete structured educational sessions, participate in self-monitoring activities, receive automated messages, and interact with other features of the program. In addition, patients in Arm 2 will receive weight-related population management support from their primary care practice; their BMIQ data will be monitored by the population manager, who will conduct outreach with patients according to the protocol. If patients use Patient Gateway (also known as Epic MyChart), the Population Health Manager and Research Dietitian may communicate with patients using MyChart.

Outcome measures

The primary outcome will be change in body weight at 12 months (pounds), calculated as the difference between each patient's weight at the initial primary care visit and at the follow-up visit 12 months later. Changes in body weight also will be assessed at 6 months and 18 months after the initial visit. In addition, we will examine weight change over the first 3 months for patients who have visits during this time period. Other similar outcome measures will include percentage of weight change, percentage of participants without weight gain, and percentage of participants who lose at least 5% of their initial weight. If a patient has a weight that is not exactly 6 months after the initial primary care visit, the weight closest to this projected follow-up date and +/- 8 weeks of this projected follow-up date will be used. If a patient has a weight that is not exactly 12 or 18 months after the initial primary care visit, the weight closest to this projected follow-up date and +/- 90 days of this projected follow-up date will be used.

Weight-related quality of life will be assessed using the Impact of Weight on Quality of Life (IWQOL)-Lite questionnaire. The IWQOL-Lite is a brief, 31-item self-report measure that was adapted from a longer 74-item questionnaire, the IWQOL, to minimize response burden to subjects participating in clinical trials for obesity treatment.

Other secondary outcomes will be changes in cardiovascular risk factors, including systolic and diastolic blood pressure, total cholesterol, HDL and LDL cholesterol, triglycerides, fasting glucose, and HbA1c levels; changes in diet and physical activity; changes in overall health status; and changes in self-efficacy around weight loss. Diet will be assessed using the PrimeScreen, a 31-item validated questionnaire that was developed as a brief dietary screening tool. Health status will be assessed using a 5-point scale response to a single question from the SF-36, "In general, would you say that your health is (Excellent, Very Good, Good, Fair, Poor)". Self-efficacy will be assessed by asking patients to rate their confidence in their ability to lose weight on a scale from 1 ("not at all confident") to 10 ("very confident"). We have chosen these simple, brief outcome measures to minimize patient burden.

To assess patients' level of engagement with the interventions, we will track a variety of process measures, including the number of logins to BMIQ, number of learning modules completed, number of days with self-monitoring data entered, and number of contacts with the Population Health Manager or other members of the research staff. Patients' satisfaction with the online weight management program and the population management support strategy will be assessed using 5-point Likert scales. Primary care clinicians' satisfaction with different components of the interventions also will be assessed, and the usability of BMIQ will be assessed among both patients and clinicians with the System Usability Scale (SUS). Finally, we

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will track the numbers of patients and clinicians who use certain features within BMIQ and how often they use them.

Statistical analysis

Aim 1a: To adapt an online weight management program and integrate it with population management support, incorporating input from patients, primary care clinicians, and other stakeholders; afterward, we will acquire feedback on the positive and negative aspects of the intervention.

There will be qualitative analyses of the data collected from patients, primary care clinicians, and population managers during the focus groups and interviews that will be conducted at the beginning and end of the study. The transcribed focus group and interview data will be analyzed according to a standard comprehensive qualitative analysis method, which is comprised of a two-stage coding process: Level 1 structural coding and Level 2 thematic coding. Structural coding follows the structure of the guide; every question receives a structural code that is applied to the appropriate text. Thematic coding is based on themes that arise from the structural coding and are applied in a second pass analysis. These methods are enhanced by the use of a state-of-the-art ethnographic data management software program, NVivo (QSR International) or ATLAS.ti (ATLAS.ti Scientific Software Development GmbH). After the two-stage coding process is completed, comprehensive thematic analysis summary reports will be written.

Aim 1b: To compare the effectiveness of the combined intervention (online weight management program plus population management support) with the stand-alone online program and with usual care.

Hypothesis 1: The combined intervention will lead to greater weight loss at 12 months compared with the stand-alone online program and with usual care.

The goal of the primary analysis will be to compare mean weight change over 12 months among patients in the three study groups. The primary analysis will be intention-to-treat, meaning that all patients will be analyzed in the group to which they were randomized. Before analysis, the data will be examined for errors, inaccuracies, and outliers and cleaned to the extent possible. The outcome variable of 12-month weight change will be examined for normality and, given the large sample size, every effort will be made to retain interpretability through use of linear regression; however, transformations will be considered if absolutely necessary. Patients who become pregnant or have bariatric surgery during the follow-up period will be censored and only weights before those events will be included in the analyses.

We will examine baseline characteristics (e.g., age, sex, race/ethnicity, educational level, medical conditions) of patients in the three study groups; data on these variables will be obtained from the EHR and from surveys, and the adequacy of the data will be assessed. We will use repeated measures mixed effects linear regression, which will be implemented with the MIXED Procedure in SAS, to compose a longitudinal model for the progression of weights in the three study groups. Weights at baseline, 6 months, 12 months, and 18 months will be the outcomes in the mixed effects model, and we will include three indicator variables for the 6, 12, and 18-month time points. We also will include two indicator variables for the three study groups as well as interaction terms between group and time. We will adjust for covariates such as age, sex, race/ethnicity, educational level, medical conditions, and any other factors that may differ between the groups. In addition, we will include clinic type (community-based clinic, hospital-based, or community health center) as a fixed effect in the model to account for the stratified randomization. Clinic, provider, and patient will be included as random effects to account for correlation within-clinic, within-provider, and over time within-patient. To determine whether

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there is a significant difference in the primary outcome of 12-month weight change across the three study groups, we will use a likelihood ratio test with two degree of freedom to examine the statistical significance of the interaction terms between group and the 12-month time point.

For the primary analysis, we will use α (probability of type I error) = 0.05 for the global likelihood ratio test across the three study groups. If we find a significant difference in weight change based on this analysis (i.e., $p < 0.05$), we will do two pairwise comparisons to compare mean weight change in the combined intervention group (online program plus population management) to usual care and the combined intervention group to the stand-alone online program. We will adjust for multiple comparisons using the Holm procedure, which is a sequentially rejective Bonferroni test.

The same general modeling approach will be used to compare other continuous outcomes across the three study groups, including weight-related quality of life, weight across the entire follow-up period, weight change at 6 months, weight change at 18 months, percentage weight change, and changes in cardiovascular risk factors, diet, and physical activity. Secondary outcome measures that are binary (e.g., prevention of weight gain, weight loss of $\geq 5\%$) will be summarized using frequencies, and we will then compare them across the three groups using a mixed effects logistic regression model, which will be implemented with the GLIMMIX Procedure in SAS. Health status and self-efficacy will be collapsed into dichotomous variables (e.g., patients reporting Excellent/Very Good health or reporting self-efficacy ≥ 8) for these analyses, rather than using ordinal scales, in order to make the findings more intuitive. These models also will adjust for clinic, age, sex, and the factors mentioned above, as well as within-clinic, within-provider, and within-patient correlation.

While will use several strategies to try to minimize attrition over the course of follow-up, we still expect there to be approximately 20% attrition, based on previous studies of online weight management interventions in primary care settings; as a result, there will be patients with missing follow-up data on weight and other outcomes. We will monitor and report the amount of missing data and reasons for drop-out, according to the CONSORT (Consolidated Standards of Reporting Trial) Group statement and the extension of this statement for reporting of pragmatic trials. To reduce bias, we will use Markov chain Monte Carlo multiple imputation, which will be implemented with the MI Procedure in SAS, to predict missing weights at 12 months and other time points, based on patients' available weight measurements and data on covariates such as age, sex, race/ethnicity, risk factors, and medical conditions. The same general approach will be used for other outcomes with missing data. In sensitivity analyses, we also will explore using a saturated means mixed effects model with indicators for missing data, and we will compare these results to those from the multiple imputation to determine whether the assumptions affect the interpretation of results.

Aim 2: To identify mediators of the combined intervention and the stand-alone online program.
Hypothesis 2: The effects of the combined intervention and the stand-alone online program on weight loss will be mediated by patients' level of engagement, changes in self-efficacy, and changes in diet and physical activity.

We first will use Spearman correlation coefficients to examine the strength of the associations between each potential mediator (measured as ordinal or continuous variables) and weight change over 12 months. We then will add each of these factors individually to the mixed effects linear regression model from Aim 1, and we will examine changes in the estimated coefficients for study group using the causal-steps approach of Baron and Kenny to detect mediation effects. In sensitivity analyses, we will explore using a more sophisticated, state-of-the-art method called parallel process latent growth curve modeling.

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Aim 3: To explore whether the effectiveness of the combined intervention and the stand-alone online program varies by patient characteristics.

Hypothesis 3: The interventions will be more effective among patients who are younger, white, and higher socioeconomic status, although the population management strategy may help to reduce these differences.

The goal of this analysis will be to examine whether the effects of the combined intervention and the stand-alone online weight management program vary by patient characteristics such as age, race/ethnicity, and socioeconomic status. To do this, we will stratify the study cohort on these patient characteristics and conduct separate analyses within pre-specified subgroups (e.g., age < 50 vs. age ≥ 50, white vs. non-white, college degree or higher vs. less than college degree). For example, we will stratify by age at baseline (< 50 vs. ≥ 50 years) and compare mean weight change across the three study groups within each of these age categories, using a similar modeling approach as for Aim 1. We will examine the coefficients for the time-by-study group interaction terms to see whether the effectiveness of the combined intervention and/or the stand-alone online program appear to vary within different subgroups. Although we did not design this study to detect effect modification, we will use three-way interaction terms between time, study group, and each of these factors in models based on the entire cohort.

Sample size and power

Although the primary analysis will involve a single, two-degree of freedom test comparing weight change at 12 months between the three study groups, we have calculated the sample size so as to have 80% power for the two subsequent pairwise comparisons. As such, the initial likelihood ratio test will be over-powered (see below), in order to have sufficient power to compare the combined intervention group with the usual care group and the combined intervention group with the stand-alone online program, using appropriate adjusted p-values.

We assumed a mean 12-month weight loss of 3 kg in the combined intervention group, 1.5 kg in the stand-alone online program group, and 0.5 kg in the usual care group, with a standard deviation of 5 kg for weight change in each group; this standard deviation incorporates the serial within-patient correlation between baseline and 12-month weight measurements that will be estimated and adjusted for in our mixed effects longitudinal regression. We also accounted for multiple comparisons using the Holm procedure, with $\alpha = 0.025$ for the first comparison and $\alpha = 0.05$ for the second comparison. We initially assumed that weight measurements in each individual patient were independent, not influenced by within-clinic or within-provider clustering. Based on these assumptions, we would need an effective sample size of 176 patients with baseline and 12-month weight measurements in each of the three study groups. With 176 patients per group as the effective sample size, we would have over 99% power for the global test of interaction, comparing 12-month weight change across the three groups. As mentioned above, while this initial global test is overpowered, having 176 patients per group does give us the necessary 80% power for the two subsequent pairwise comparisons. The large sample size also has the additional advantage of allowing us to examine the effects of the interventions within pre-specified subgroups (see below).

To account for the correlation among patients within a given clinic, we use the following formula:

$$N = N_1 \times [1 + (m - 1)\rho]$$

where N_1 is the sample size under the assumption of independence, m is the average number of study patients within each clinic, and ρ is the intra-class correlation coefficient (ICC).

Assuming an average of 28 study patients per clinic and using an ICC of 0.01, based on ICCs that have been observed for weight and similar measures in other cluster-randomized trials in primary care,¹²¹ the actual required sample size is 224 patients per group (224 patients divided

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by 8 clinics per arm \approx 28 patients per clinic). Assuming an attrition rate of approximately 20%, we plan to enroll 280 patients per group, for a total of 840 patients in the trial.

For Aim 2, we will have 93% power to detect a correlation coefficient of 0.15 between each of the potential mediating factors and weight change at 12 months, and we will have > 99% power to detect a correlation coefficient of 0.2. For Aim 3, we should have sufficient power to examine the effects of the interventions separately within pre-specified subgroups. For example, based on preliminary data, we expect that approximately 35% of patients in the study will be less than age 50 and 65% will be 50 or older at baseline. In the younger age category, we will have almost 95% power to detect a difference in weight change across the three study groups, assuming a mean 12-month weight loss of 4 kg in the combined intervention group, 2.5 kg in the stand-alone online group, and 0.5 kg in the usual care group, with a standard deviation of 5 kg in each group. In the older age category, we will have over 80% power to detect a difference across the study groups, assuming a mean 12-month weight loss of 2.5 kg in the combined intervention group, 1 kg in the stand-alone online group, and 0.5 kg in the usual care group, with a standard deviation of 5 kg in each group.

For studies involving treatment or diagnosis, provide information about standard of care at Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care. Provide information on available alternative treatments, procedures, or methods of diagnosis.

There is currently no formal standard of care for management of overweight and obesity by BWH primary care clinicians. The online weight management program and population health management protocol will be more than the usual standard of care.

Describe how risks to subjects are minimized, for example, by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk or by using procedures already being performed on the subject for diagnostic or treatment purposes.

There are no major risks to clinicians or patients involved in this study. Clinicians and patients can decide whether or not to participate in the interviews and focus groups.

There will be minimal risks to patients due to participation in the online weight management program or the population management strategy. The physical risks are similar to those that are typically undertaken in the receipt of routine medical care, since all of the measurements (e.g., weight, blood pressure, cholesterol, HbA1c) are recommended as part of standard clinical practice guidelines for these patients. It is possible that participation in the study could lead to weight change that would affect the management of medications for type 2 diabetes, hypertension, or other medical conditions; therefore, primary care providers will be notified when patients enroll in the study and if patients lose a substantial amount of weight. Another possible risk for patients is psychological risk associated with being labeled as overweight or obese, with self-monitoring of diet and physical activity, or with completion of surveys; however, these risks are outweighed by the potential health benefits associated with weight loss. There is also a risk of potential loss of privacy or confidentiality, although this is extremely low.

Perhaps the most important risk to address for both patients and clinicians is the risk created by the cluster-randomized trial design of the proposed study. The main concern is that of withholding the interventions from the subjects in the usual care clinics.

Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria for removing a subject from the study, for example, objective criteria for worsening disease/lack of

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improvement and/or unacceptable adverse events. The inclusion of objective drop criteria is especially important in studies designed with placebo control groups.

We will undertake multiple approaches to protect human subjects from risks. We will treat all study data as highly confidential and in accordance with Section 903c of the Public Health Service Act. Patients and clinicians will be assigned a study-specific identification number. All personal identifiers will be kept in a separate location from the data, and only the research assistant and the Principal Investigator will have access to the linked data. All machine-readable files will be stored online with appropriate security measures, and other sensitive written materials will be kept in locked filing cabinets. All of these procedures are in accordance with the regulations of the Partners IRB.

The electronic health record (EPIC) and the BMIQ online program are fully compliant with HITECH (Health Information Technology for Economic and Clinical Health) and HIPAA (Health Insurance Portability and Accountability Act) privacy standards and have multiple built-in security features. Because this will be the first time that BMIQ has been used at BWH, it also will undergo an additional Risk Evaluation that will be conducted by Partners Information Services. This is an IRB requirement of all new technology tools. (Note: the Risk Evaluation for BMIQ has been completed and approved; documentation is included with this submission.) For electronic surveys, we will use a secure, web-based application called REDCap (Research Electronic Data Capture), which also is HIPAA compliant.

In all practices, primary care clinicians or their delegate (e.g. LPN or RN) will review the lists of eligible patients to validate them and to make sure that the patients are appropriate and do not have any medical contraindications for weight loss or physical activity such as those listed below or any others. The Population Health Managers will also assist with this process. If the PCP or the PCP's delegate (e.g., RN, LPN, PA) does not review his/her list of potentially eligible patients and determine which patients, if any, should NOT be contacted for the study within 1 week of receiving the list, we will move forward with putting the patients from that list on our list of patients who are appropriate to contact. We would then mail these patients a letter describing the study and plan to call patients approximately 1 week after mailing the letter to describe the study to patients and conduct a phone screen if patients are interested in participating in the study. Please note, prior to calling any patients, Research Assistants review the patient's chart in Epic to confirm minimal inclusion criteria are met and major exclusion criteria are not present.

We will ask the Medical Director and/or the Practice Manager at each of the participating practices to acknowledge implementation of the 1 week window described above by sending us an email response; we will document their responses accordingly. We will also ask them to send us the names of any providers in their practice who are not in favor in this change; for these providers, we will not contact patients unless we receive the reviewed lists back from the provider. We will report any complaints regarding the 1 week list review period in real-time to the Partners Human Research Committee (IRB) in real-time via an "Other Event" submission.

To minimize potential physical risks to patients that may be associated with weight loss, we will exclude patients who are on insulin for treatment of their diabetes, since insulin is associated with weight gain and there also may be some risk of hypoglycemia. We also will exclude patients who have had a myocardial infarction, stroke, or an atherosclerotic cardiovascular disease (ASCVD) procedure (including percutaneous coronary intervention (PCI), coronary angioplasty, coronary artery bypass grafting (CABG), and carotid endarterectomy) in the last 6 months; patients with unstable angina; patients who are currently pregnant or planning to become pregnant during the study period (since weight loss may be contra-indicated); patients

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who have had bariatric surgery or are planning to have bariatric surgery; patients who are planning to re-locate within the study period; patients who have had significant weight loss (>5%) within the last six months; patients with severe psychiatric illness or impaired mental status (including, but not limited to, active substance abuse, active or history of schizophrenia, active or history of borderline personality disorder, active or history of bipolar disorder, uncontrolled depression, any history of suicidal attempts or suicidal ideation, or any psychiatric hospitalization in the past year); patients with active or diagnosed history of and/or self-reported history of eating disorders; patients with self-reported average consumption of >14 alcoholic drinks/week; patients with any serious medical condition that would affect weight loss or for which weight loss is contraindicated, including end stage renal disease (ESRD) on dialysis or active cancer (except non-melanoma skin cancer) or currently being treated for cancer; Patients should not have received chemotherapy in the past 3 months and have no plans for further chemotherapy (i.e., cancer believed to be in remission); patients on comfort care measures, hospice or in nursing home; patients with an Intern listed as the PCP; patients where the PCP states s/he is not the patient's PCP and/or is unfamiliar with the patient's medical history; patients participating in contra-indicative research studies; females who are currently lactating; patients on prescription or over-the-counter weight loss medications or an all-liquid diet program in the last 6 months or currently (note: if patients used weight loss medication or an all-liquid diet program for < 2 weeks and stopped > 1 month ago, they may still be considered eligible); and patients with any other medical contraindication for weight loss or physical activity, or patients that the PCP or their delegate (e.g. LPN or RN) did not deem appropriate for the study for any other reason. Patients for whom we discover and/or are alerted by patients and/or providers for meeting exclusion criteria after enrollment, will be evaluated by the PI, Co-Investigators, and physicians on the study staff on a case-by-case basis. A decision will be made about whether the patient should be withdrawn from the study based on the exclusion criteria. For example, a female patient who becomes pregnant during the course of the study will be withdrawn from the study since weight loss is contraindicated during pregnancy. The PCP also may be involved in the decision about whether or not a patient should be withdrawn.

During the 18-month study period, if a patient falls into any of the following categories we will proceed with the plan below: 1) patient's Brigham PCP is leaving the Brigham; or 2) a patient is leaving their Brigham primary care practice (e.g., patient is moving/relocating; patient is changing insurance plans; patient is following their Brigham PCP who is leaving the practice; etc.).

The research team will review the patient's chart in Epic to see whether the patient has been assigned to and has established care with a new Brigham PCP. If the patient has been assigned to a new Brigham PCP, we will document this change in our database and the patient may remain in the study without any changes to the arm protocol to which they have been assigned.

If the patient has not been assigned to a new Brigham PCP, the research team will contact the patient and prompt the patient to find a new Brigham PCP or obtain the name of their new non-Brigham PCP.

1. If the patient has a new Brigham PCP, the patient may remain in the study without any changes to the arm protocol to which they have been assigned.
2. If the patient has a new non-Brigham PCP, we will document the new non-Brigham PCP's name in our database. Patients assigned to the Usual Care arm or Online Program may remain in the study with no changes to the existing protocol. Patients assigned to the Combined Intervention arm of the study will receive outreach from the

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research team rather than the Brigham Population Health Manager. We will notify patients of this change.

Whether or not the patient's new PCP is a Brigham PCP, study staff will encourage the patient to mention and discuss their ongoing trial participation in the PROPS Study with their new PCP.

Primary care clinicians at all of the practices will need to approve patients for participation before they are contacted by the research team and also will be asked to exclude patients who they feel are not appropriate for weight loss or physical activity. All of the patients included in the study will be under the care of a BWH primary care clinician and will continue to be monitored by their clinician throughout the study. PCPs will be notified when a patient enrolls in the study and if the patient has a substantial amount of weight loss. We may also periodically send lists of enrolled patients to PCPs via email to serve as a reminder. Any electronic communications containing participants' personally identifying information or other sensitive text (e.g., the consent form) will be sent in accordance with Partners Information Security guidelines by adding "- SEND SECURE" to the title of the electronic communication. Although there may be some small psychological risk for patients due to self-monitoring activities and completion of surveys, these risks are far outweighed by the potential health benefits associated with weight loss.

Regarding the potential risks to clinicians associated with integrating the BMIQ online weight management program with the electronic health record (i.e., unfavorable workflow, overdependence on technology), this is balanced by the evidence suggesting that the online program and population management support will improve the quality and efficiency of patient care. In addition, it is essential to point out that the proposed interventions are enhancements of the existing electronic health record and population management tools, not the implementation of a whole new system of care. There will be extensive testing prior to implementation of the online weight management program and the population management protocol prior to launching them for the study, to ensure that everything runs as smoothly and efficiently as possible.

Although there is the risk associated with withholding interventions from patients, due to the cluster-randomized design of the study, there remains considerable skepticism about the potential for these kinds of health IT interventions to improve care, both in general and specifically for treatment of overweight and obesity. Therefore, a randomized controlled trial is justifiable and necessary to assess the true benefit of the interventions. If the interventions are found to be effective, we hope that they can be broadly implemented throughout all BWH primary care practices as well as in other primary care settings across the U.S.

FORESEEABLE RISKS AND DISCOMFORTS

Provide a brief description of any foreseeable risks and discomforts to subjects. Include those related to drugs/devices/procedures being studied and/or administered/performed solely for research purposes. In addition, include psychosocial risks, and risks related to privacy and confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

There will be minimal risks to patients due to participation in the online weight management program or the population management strategy. The physical risks are similar to those that are typically undertaken in the receipt of routine medical care, since all of the measurements (e.g., weight, blood pressure, cholesterol, HbA1c) are recommended as part of standard clinical practice guidelines for these patients. It is possible that participation in the study could lead to weight change that would affect the management of medications for type 2 diabetes, hypertension, or other medical conditions. For this reason, PCPs will be notified when a patient enrolls in the study and if a patient has a substantial amount of weight loss. Another possible risk for patients is psychological risk associated with being labeled as overweight or obese, with

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self-monitoring of diet and physical activity, or with completion of surveys; however, these risks are outweighed by the potential health benefits associated with weight loss. There is also a risk of potential loss of privacy or confidentiality, although this is extremely low.

Perhaps the most important risk to address for both patients and clinicians is the risk created by the randomized controlled trial design of the proposed study. The main concern is that of withholding the interventions from the subjects in the usual care clinics.

EXPECTED BENEFITS

Describe both the expected benefits to individual subjects participating in the research and the importance of the knowledge that may reasonably be expected to result from the study. Provide a brief, realistic summary of potential benefits to subjects, for example, “It is hoped that the treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects.” Indicate how the results of the study will benefit future patients with the disease/condition being studied and/or society, e.g., through increased knowledge of human physiology or behavior, improved safety, or technological advances.

This research has the potential to increase weight loss among primary care patients in the intervention clinics, as well as to improve cardiovascular risk factors and patient-centered outcomes such as weight-related quality of life. There are no immediate potential benefits to patients in the control clinics, who will receive usual care during the study; however, if the interventions are found to be effective, the hope is that they will be implemented in all BWH primary care clinics. The potential risks associated with participation in this study are very small compared to the potential benefits of weight loss and control of cardiovascular risk factors, especially for patients with type 2 diabetes or hypertension.

EQUITABLE SELECTION OF SUBJECTS

The risks and benefits of the research must be fairly distributed among the populations that stand to benefit from it. No group of persons, for example, men, women, pregnant women, children, and minorities, should be categorically excluded from the research without a good scientific or ethical reason to do so. Please provide the basis for concluding that the study population is representative of the population that stands to potentially benefit from this research.

All primary care clinicians or other staff who provide services to patients at participating BWH primary care practices are eligible to participate in the key informant interviews. All BWH patients who are ages 20-70 years old and have a recent BMI (in the past year) approximately between 27 and 40 kg/m² are eligible to participate in the focus groups. They should be interested in weight management and/or motivated to lose weight. In addition, they must speak English, and have access to the Internet via a computer, smartphone, or tablet. For the main trial, we will include all BWH patients who are ages 20-70 years old at enrollment, have a BMI between 27 and 39.9 kg/m², have either hypertension or Type II diabetes, speak English or Spanish, have a valid email address and regular access to the Internet (at least once per week), are motivated to lose weight, and don't have any medical contraindications for weight loss and/or physical activity. A subset of current PROPS Study patients who are assigned to the online program or combined intervention arms and complete the final, 18-month study survey are eligible to participate in the focus groups or phone interviews that will be conducted at the end of the study.

When people who do not speak English are excluded from participation in the research, provide the scientific rationale for doing so. Individuals who do not speak English should not be denied participation in research simply because it is inconvenient to translate the consent form in different languages and to have an interpreter present.

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We will enroll people who speak either English or Spanish in the main trial. However, because all primary care clinicians and other staff who provide services to patients at BWH speak English, the key informant interviews will be conducted in English. The focus groups will only include patients who speak English because the current version of the online program is in English. However, it will be adapted for Spanish-speaking patients later in the course of the study.

At the end of the study, phone interviews will be conducted with patients. These materials will be translated into Spanish so that Spanish-speaking patients could be included in the interviews. The online program has also been made available in Spanish now.

For guidance, refer to the following Partners policy:

Obtaining and Documenting Informed Consent of Subjects who do not Speak English

[https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English Speaking Subjects.1.10.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English%20Speaking%20Subjects.1.10.pdf)

RECRUITMENT PROCEDURES

Explain in detail the specific methodology that will be used to recruit subjects. Specifically address how, when, where and by whom subjects will be identified and approached about participation. Include any specific recruitment methods used to enhance recruitment of women and minorities.

Focus Group and Key Informant Interviews:

Focus group recruitment will be conducted using two methods. The primary recruitment method will be to identify potential participants by asking several BWH primary care clinicians and other providers to refer patients who may be eligible and interested. A letter about the focus groups, including the eligibility criteria, will be sent to some primary care clinicians and other providers to ask for their assistance with recruitment.

After providers have given their permission to contact specific patients about the focus groups, the research staff will send two letters (one from the provider and one from the Principal Investigator) and an information sheet about the focus group to patients. Alternatively, the provider also may distribute these materials to patients directly. The information sheet will include contact information for the study (phone number and email address) if patients would like to learn more. Research staff may also contact patients by phone after mailing the letter and information sheet to assess their interest. When they speak with patients by phone, research staff will describe the focus groups in more detail and schedule patients to attend, if they are eligible and interested. A flyer to recruit patients for focus groups also will be distributed at the BWH Program for Weight Management and at primary care practices.

The secondary recruitment method will be to identify eligible patients through an Epic workbench report and/or the Enterprise Data Warehouse (EDW). After identifying potential participants, patients' primary care providers will be contacted to verify eligibility and to obtain their permission to contact these patients. Outreach will then be conducted via mail and phone,

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similar to the primary recruitment method already described, to assess the patients' interest in participating in a focus group. Patients will also have the opportunity to discuss any questions with the research staff.

At least one week before each focus group, a research assistant will mail a reminder to scheduled participants. This reminder will include more information about the sponsorship of the study, its local leadership, and contact information for the Principal Investigator and the IRB administrator, should any questions or concerns arise.

After the first two focus groups, a research assistant will contact patients who participated in one of the first two groups by phone to tell them about the third focus group and see whether they are interested in participating. The third focus group will include testing of the BMIQ online program; therefore, during the phone conversation, a research assistant will obtain verbal consent from the patient for trying out the BMIQ program. If the patient agrees to test the BMIQ program and to participate in the third focus group, the research assistant will set up a test account for them (which is not associated with the patients' name, email address, or any other personal information; it is purely a test account.) The research assistant will send the patient instructions for how to log in to the website with this test account and a list of tasks to try out once they are logged in. This information will be sent to the patient by email or by regular mail, depending on the patient's preference (no patient information will be included). It will also include a reminder about the date, time, and location of the focus group. A research assistant will also call the patient a few days later to make sure that they received the information and that they are able to log in to the website for testing. All of the data that is entered into the BMIQ website and mobile version during this testing process will be deleted after finishing data analysis for the third focus group.

At the end of the study, study staff will also conduct a series of phone interviews with PROPS participants in the online program and combined intervention arms to solicit feedback on their experience in the study. Patients in these arms who reach the 18-month timepoint and complete the final study survey will be eligible and invited to participate. Two versions of the patient interview letter have been created: one for patients who expressed interest in participating as part of the 18-month survey and the other for patients who have not. Research study staff will contact patients by mailed letter and phone to provide more information about participating in the phone interviews, assess interest level, and address any questions.

Primary care clinicians and other staff who provide services to patients will be recruited to participate in the key informant interviews through e-mail announcements to the primary care practices and/or phone calls to clinicians and other staff who provide services to patients. Clinicians will be able to respond by email or phone for more information. A member of the research staff will discuss the interviews with clinicians and schedule them to participate if they are interested. The interviews are a part of the study and their completion is voluntary. Because the key informant interviews may be done via phone rather than in person, the clinicians will provide verbal consent rather than written informed consent. The interviews will be conducted in-person when possible or by phone if in-person is not possible. Verbal consent will be obtained at the beginning of the interview.

Recruitment, Data Collection, and Follow-up for the Main Trial:

The research team will use information from Epic and the Enterprise Data Warehouse (EDW) to identify eligible patients (age 20-70, BMI 27 - 39.9 kg/m², and a diagnosis of either Type II diabetes or hypertension) who have an upcoming visit with a BWH primary care provider (for some patients this may be a Resident, Nurse Practitioner, or Physician Assistant) in the next 2

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months. In all practices, primary care clinicians or their delegate (e.g., LPN or RN) will review the patient lists to validate them and to make sure that the patients are appropriate and do not have any medical contraindications for weight loss or physical activity. The Population Health Managers will also assist with this list review process. If the PCP or the PCP's delegate (e.g., RN, LPN, PA) does not review his/her list of potentially eligible patients and determine which patients, if any, should NOT be contacted for the study within 1 week of receiving the list, we will move forward with putting the patients from that list on our list of patients who are appropriate to contact. We would then mail these patients a letter describing the study and plan to call patients approximately 1 week after mailing the letter to describe the study to patients and conduct a phone screen if patients are interested in participating in the study. Please note, prior to calling any patients, Research Assistants review the patient's chart in Epic to confirm minimal inclusion criteria are met and major exclusion criteria are not present.

In addition to mailing recruitment letters to patients approved for contact, we will be sending potentially eligible patients an Epic MyChart message. The PROPS Study Team will send the Partners eCare team a monthly list of patients who are potentially eligible and approved for contact. The Partners eCare team will then merge this list with a custom reporting workbench, and identify patients whose MyChart status is active. These patients will then be sent a MyChart message describing the study. Patients will not be able to respond to the message, however, the letter will give patients the contact information for the research study team (e.g., email, phone, website) if they are interested in participating in the study.

We will ask the Medical Director and/or the Practice Manager at each of the participating practices to acknowledge implementation of the 1 week window described above by sending us an email response; we will document their responses accordingly. We will also ask them to send us the names of any providers in their practice who are not in favor in this change; for these providers, we will not contact patients unless we receive the reviewed lists back from the provider. We will report any complaints regarding the 1 week list review period in real-time to the Partners Human Research Committee (IRB) in real-time via an "Other Event" submission.

Patients in all three arms who are approved by the PCP will be mailed an introductory letter which will have their PCP's name on it, saying that they may be eligible for the study. Also enclosed will be a letter signed by the PI which describes the study, along with information about how to opt out or, if interested in the study, the number at which they may call us to hear more about the study and see if they are potentially eligible. A Research Assistant will call patients who do not opt out to screen them and assess their motivation to lose weight.

There may be some cases in which the PCP refers specific patients to the study who have just had an appointment or have an upcoming appointment. In these cases, if the PCP has already discussed the study with the patient, we will not mail the introductory recruitment letters to patients and will instead begin with the phone screen. If the PCP has not mentioned the study to the patient, we will send the introductory letter and study information as usual.

Patients will be asked to rate how motivated they are to lose weight in the next 6 months using a 10-point Likert scale (1="not at all motivated" to 10="completely motivated"); this simple measure has been used in previous studies and is associated with behavior change. Only patients who report their level of motivation to be 7 or higher will be eligible. If patients are motivated and interested in participating, and meet all of the other inclusion/exclusion criteria, the Research Assistant will email the patient the consent form through Redcap which will have a fillable signature field. At the patient's election, the research assistant will either review the consent form with the patient on the phone at the time of the eligibility screen call, or will

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schedule a call with the patient within 1 week of emailing the consent form to review the form with the patient and answer any questions the patient may have.

In addition to completing the screening questions by phone with the Research Assistants, patients will also be able to complete the screening questionnaire electronically on their own via RedCap. Patients will be able to access the questionnaire via a link through an auto-reply on the study email inbox, or via a link through the study website. For patients who complete the screening questionnaire electronically on their own via RedCap, a Research Assistant will review it after it is submitted. If the patient is eligible based on the screening questionnaire, the Research Assistant and/or other members of the study staff (e.g., Co-Investigators, MD consultants) will review the patient's record in Epic to confirm eligibility (this is mentioned in the screening questionnaire and the patient will need to give permission for this); if there are any questions, the patient's primary care provider also may be contacted and involved in the decision about the patient's eligibility. If the patient is still eligible after this review, the Research Assistant will then email the consent form to the patient and schedule a time to review it by phone within the next week. If the patient is not eligible after the review, the Research Assistant will contact the patient to let him or her know.

After speaking with the Research Assistant, if the patient remains interested in the study and consents to the study, s/he will electronically sign the consent form in Redcap. The Research Assistant will electronically sign the consent form and email the consent form signed by both the patient and research assistant back to the patient. Any electronic communications containing participants' personally identifying information or other sensitive text (e.g., the consent form) will be sent in accordance with Partners Information Security guidelines by adding "- SEND SECURE" to the title of the electronic communication.

In addition to signing the consent form in Redcap, patients will also be offered the option of completing the consent process by Adobe PDF Echo signature; printing, signing and scanning the consent form; or by regular mail, if they do not want to or are not able to return the form by email. To be eligible for the trial, patients must have an upcoming scheduled visit with a BWH primary care provider (for some patients this may be a Resident, Nurse Practitioner or Physician Assistant) within the next 2 months, BMI between 27 and 39.9 kg/m² at enrollment, and a diagnosis of Type 2 diabetes or hypertension. They also must be between ages 20 and 70 (inclusive) at enrollment, speak English or Spanish, and have a valid email address and regular access to the Internet (at least once per week) using a computer, tablet, or smartphone. Patients must also be motivated to lose weight. Finally, patients must attend their upcoming scheduled visit with a BWH primary care provider and have their weight measured at the visit. However, in some special situations when a weight from a primary care visit is not available, a weight from another visit may be used instead for enrollment. For example, if a patient's weight was not recorded at their PCP visit, which we are calling the index or baseline PCP visit, or if the patient missed or rescheduled their index PCP visit, a weight taken within 6 weeks before or after the index PCP visit is acceptable for enrollment as long as the weight was taken at a Partners-affiliated institution and it has been recorded in the patient's chart in Epic. If there is no other recorded weight from a Partners-affiliated institution within 6 weeks before or after the index PCP visit, the patient may be scheduled for a separate visit at the Brigham and Women's Hospital Center for Clinical Investigation (BWH CCI) to have their measurements (e.g., height and weight) taken, and these can be used for enrollment. A patient also may be scheduled for a visit at the CCI to have their height/weight measurements taken and used for enrollment if it has been more than 4 weeks since the patient's index PCP visit or other visit at a Partners-affiliated institution or if the patient was referred directly by the PCP but does not have a recent or upcoming scheduled PCP visit or other visit at another Partners-affiliated institution in the next

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month. In all of these cases, the study will pay for this BWH CCI visit. Participants will also be compensated \$50 and parking vouchers for a BWH CCI visit.

Patients who provide consent and attend their upcoming scheduled visit with their PCP (or CCI visit or other visit with a measured weight, as described above) will be enrolled in the study. However, prior to officially enrolling the patient, a Research Assistant and/or other members of the study staff (e.g., Co-Investigators, MD consultants) will review the patient's record in Epic (if not already done previously) to confirm that the patient meets all eligibility criteria and that there are no reasons for exclusion; this is explained to the patient during the screening and consent process. In some cases, if there are any questions about the patient's eligibility, the patient's primary care provider also may be contacted and involved in the decision about whether the patient can be enrolled.

Once the patient is enrolled, he/she will be notified and will be asked to complete (by Redcap, paper or by phone interview) a brief survey about their past experiences with weight loss and their weight-related quality of life, diet and physical activity, health status, and self-efficacy around weight loss. A notation that a patient is participating in this research study will be made in Epic (including uploading of the consent form) and the PCP will be notified when a patient is enrolled in the study. The study team may also periodically send lists of enrolled patients to their PCPs via email, as a reminder of their patients' participation in the study.

Any electronic communications containing participants' personally identifying information or other sensitive text (e.g., the consent form) will be sent in accordance with Partners Information Security guidelines by adding "- SEND SECURE" to the title of the electronic communication.

Eligible patients in Arm 2 (combined intervention) or Arm 1 (online weight management only program) will be contacted by a Research Assistant after the primary care visit; the Research Assistant will help them register for BMIQ and set up their account, and they will also instruct them about how to use BMIQ. Patients in Arm 2 (combined intervention) or Arm 1 (stand-alone online weight management program) will have certain study information from the online program BMIQ shared with their PCPs via Epic. These procedures have been reviewed and approved by the HIM Executive Committee and the PeCare Research Council. Information that may be shared includes: a dietitian progress note if they have a consultation with the Research Dietitian; a summary report of the patient's self-reported weight, goals, and food and activity tracking; and notifications about substantial changes in weight. The information will be shared in an Epic progress note and/or a file printed to PDF from the online program BMIQ and uploaded to the Epic media tab via the existing "Research – Flowsheet." The progress note and the media tab file will be entered or uploaded accordingly by the Population Health Manager or the Research Dietitian. Patients in Arm 0 (usual care) will not receive any information about BMIQ but will receive general written materials about weight management, which will be selected with input from the patient and stakeholder partners.

Height, weight, and blood pressure will be measured during the visit for patients in all three arms of the study. The research team will provide information to the medical assistants and other staff at all of the practices about how to obtain the most reliable weight measurements to standardize them across clinics, and they will ask the practices what their usual procedures are. We will ask the medical director and/or practice manager to complete a very brief Outpatient Inventory questionnaire in Redcap so that we can have basic information about the practice, for example, what type of scale is used to measure weight and who in the practice is responsible for taking weights. In addition, a blood sample will be taken at some visits, if ordered by the PCP, for measurements of fasting glucose, triglycerides, cholesterol, and HbA1c levels; these

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laboratory tests are recommended as part of routine clinical care for patients with hypertension or diabetes.

Patients in Arm 2 will be contacted by the Population Health Manager within one week after they are registered for BMIQ to remind them about how to log in and use BMIQ, and they will continue to be monitored and receive support from the Population Health Manager and other members of the research team (e.g., the Research Dietitian) over the next 12 months, according to the population management protocol. If patients use Patient Gateway (also known as Epic MyChart), the Population Health Manager and Research Dietitian may communicate with patients using MyChart. Patients in Arm 1 also will receive a reminder within one week after the visit about how to log in and use BMIQ, and they will continue to be monitored by the Research Assistant and/or other members of the research team. Patients in Arm 1 and Arm 2 will be offered an initial telephonic consultation with the Research Dietitian when they enroll. Patients in Arm 1 will be offered a second opportunity for a telephonic consultation with the Research Dietitian six months after enrolling in the study. The Research Dietitian may also follow-up with patients in certain situations (e.g., if they are losing weight too quickly or if they are not losing weight). Since all consultations with the Research Dietitian are provided by a Dietitian who is funded by the study, patients will receive this service at no charge to them. Patients in Arm 1 and Arm 2 also will be mailed a letter from the Principal Investigator and the study team if they have not used BMIQ in 3 months or more, in order to try to re-engage them with the program. For patients in Arm 2 who have not used BMIQ in 3 months or more, the primary care provider also will be notified and asked to help re-engage the patient, and the provider will be asked to co-sign the letter from the Principal Investigator.

Patients in all three arms will have follow-up visits at their primary care practice at approximately 6 months, 12 months, and 18 months after enrollment; height, weight, and blood pressure will be measured at all of these visits, and fasting glucose, triglycerides, cholesterol, and HbA1c levels will be measured if requested by the clinician; these values usually are measured every 6 months, and at least every 12 months, for patients with hypertension or diabetes. The research staff and/or the primary care practices will send reminders to patients about these scheduled visits by e-mail, text message, or phone, depending on patients' preferences. If a patient misses the 12-month visit at their primary care practice, he or she will be contacted and asked to attend a 30-minute study visit at the Center for Clinical Investigation (CCI) to measure their weight. If the patient refuses or fails to attend the study visit, they will be asked to self-report their weight by phone or e-mail.

In addition, patients in all three arms will be asked to complete follow-up surveys at 6 months, 12 months, and 18 months; they will be able to choose the modality for completing these surveys (by e-mail, by regular mail, or by phone.) The surveys will assess important patient-reported outcomes, including weight-related quality of life, diet, physical activity, health status, and self-efficacy around weight loss. For patients in Arm 1 or Arm 2, the 6-month and 12-month surveys also will include questions about the usability of BMIQ and their satisfaction with the interventions. Primary care clinicians in all three arms will be asked to complete surveys by e-mail at the beginning and the end of the intervention period to assess their attitudes about management of overweight and obesity. On the post-intervention survey, clinicians in Arms 1 and 2 will be asked about the usability of BMIQ and their satisfaction with the interventions. These surveys are a part of the study and completion of these surveys are voluntary.

We will use several strategies over the course of follow-up to minimize attrition and to ensure that data are collected thoroughly and systematically. As mentioned previously, we will only include patients who are motivated to lose weight. Most of the outcome data will be collected at routine primary care visits; patients will not need to attend additional study visits, which should

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minimize burden and possibly reduce attrition. If patients miss their 12-month primary care visit, we will schedule a study visit to measure their weight; if they miss the study visit, we will try to obtain their self-reported weight by phone or e-mail. Patients will be asked to complete surveys at several time points, but they will be able to choose how they want to do them. Each survey will take no more than 15 minutes to complete, and patients will receive \$25 per survey as compensation. They also will be entered into a monthly drawing to win a \$100 check.

Provide details of remuneration, when applicable. Even when subjects may derive medical benefit from participation, it is often the case that extra hospital visits, meals at the hospital, parking fees or other inconveniences will result in additional out-of-pocket expenses related to study participation. Investigators may wish to consider providing reimbursement for such expenses when funding is available

We will ask patients to complete a set of surveys at four different times over the 18-month study period: baseline (the same day or shortly after patients attend their initial upcoming scheduled visit with their PCP), 6 months after enrollment date, 12 months after enrollment date and 18 months after enrollment date. Subjects will be compensated \$25 by mail within 6 weeks after completing the set of surveys for each time point. They also will be entered into a monthly drawing to win a \$100 check.

If for some reason a subject misses his/her routine primary care visit at one of the time points above and/or a weight was not taken at the patient's index PCP visit, research staff may schedule a separate visit at the Brigham and Women's Hospital Center for Clinical Investigation (BWH CCI) to have the subject's measurements (e.g., height and weight) and routine labs (e.g., glucose levels for patients with type 2 diabetes) taken. The study will pay for these measurements and routine lab results to be taken. Participants will also be compensated \$50 and parking vouchers for a BWH CCI visit.

We will also conduct several focus groups at the beginning of the study. If patients participate in one of the focus groups, they will be compensated \$50 and given BWH parking vouchers for attending. Refreshments also will be provided during the focus groups. At the end of the study, we will conduct phone interviews with patients. Patients who participate will receive a \$25 check as compensation.

According to Partners Hospitals' policy, in order to issue a compensation check, we will need to collect social security number and mailing address. We will keep this information in a password-protected database within our secure Partners network shared file area. Only the research staff who will be submitting subject compensation will have access to this database.

For guidance, refer to the following Partners policies:

Recruitment of Research Subjects

[https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment Of Research Subjects.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment%20Of%20Research%20Subjects.pdf)

Guidelines for Advertisements for Recruiting Subjects

[https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines For Advertisements.1.11.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines%20For%20Advertisements.1.11.pdf)

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Remuneration for Research Subjects

[https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration for Research Subjects.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration%20for%20Research%20Subjects.pdf)

CONSENT PROCEDURES

Explain in detail how, when, where, and by whom consent is obtained, and the timing of consent (i.e., how long subjects will be given to consider participation). For most studies involving more than minimal risk and all studies involving investigational drugs/devices, a licensed physician investigator must obtain informed consent. When subjects are to be enrolled from among the investigators' own patients, describe how the potential for coercion will be avoided.

Focus groups and Key Informant Interviews

Focus group and phone interview participants will be required to give verbal consent in order to participate. Using a focus group or phone interview guide, the focus group or phone interview moderator will ask participants to consent to participating in the focus group and to having their answers recorded. Members of the research staff will be available to answer any questions. Because the key informant interviews may be done via phone rather than in person, the clinicians and other staff who provide services to patients will provide verbal consent as well. The interview will be conducted in-person when possible and when convenient for the clinician or other staff who provides services to patients.

Trial

If according to phone screen patients are potentially eligible, motivated and interested in participating, a Research Assistant will email the patient the consent form which will have a fillable certified signature field. The Research Assistant will call the patient within 1 week of emailing the consent form to review the consent form with the patient and answer any questions the patient may have. After speaking with the Research Assistant, if the patient remains interested in the study and consents to the study, s/he will electronically sign the consent form and email the signed consent form back to the research assistant. The Research Assistant will electronically sign the consent form and email the consent form signed by both the patient and Research Assistant back to the patient. Patients will also be offered the option of completing the consent process by regular mail, if they do not want to or are not able do it by email. To be eligible for the trial, patients must have an upcoming scheduled visit with a BWH primary care provider (for some patients this may be a Resident, Nurse Practitioner or Physician Assistant) within the next 2 months, BMI between 27 and 39.9 kg/m² at enrollment, and a diagnosis of Type 2 diabetes or hypertension. They also must be between ages 20 and 70 (inclusive) at enrollment, speak English or Spanish, and have a valid email address and regular access to the Internet (at least once per week) using a computer, tablet, or smartphone. Patients must also be motivated to lose weight. Finally, patients must attend their upcoming scheduled visit with a BWH primary care provider and have their weight measured at the visit. However, in some special situations when a weight from a primary care visit is not available, a weight from another visit may be used instead for enrollment. For example, if a patient's weight was not recorded at their PCP visit, which we are calling the index or baseline PCP visit, or if the patient missed or rescheduled their index PCP visit, a weight taken within 6 weeks before or after the index PCP visit is acceptable for enrollment as long as the weight was taken at a Partners-affiliated institution and it has been recorded in the patient's chart in Epic. If there is no other recorded weight from a Partners-affiliated institution within 6 weeks before or after the index PCP visit,

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the patient may be scheduled for a separate visit at the Brigham and Women's Hospital Center for Clinical Investigation (BWH CCI) to have their measurements (e.g., height and weight) taken, and these can be used for enrollment. A patient also may be scheduled for a visit at the CCI to have their height/weight measurements taken and used for enrollment if it has been more than 4 weeks since the patient's index PCP visit or other visit at a Partners-affiliated institution or if the patient was referred directly by the PCP but does not have a recent or upcoming scheduled PCP visit or other visit at another Partners-affiliated institution in the next month. In all of these cases, the study will pay for this BWH CCI visit. Participants will also be compensated \$50 and parking vouchers for a BWH CCI visit.

Patients who provide consent and attend their upcoming scheduled visit with their PCP will be asked to complete (by Redcap, paper or by phone interview) a brief survey about their past experiences with weight loss and their weight-related quality of life, diet and physical activity, health status, and self-efficacy around weight loss.

Any electronic communications containing participants' personally identifying information or other sensitive text (e.g., the consent form) will be sent in accordance with Partners Information Security guidelines by adding "- SEND SECURE" to the title of the electronic communication.

NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-making capacity, complete the forms for Research Involving Children as Subjects of Research and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the New Submissions page on the PHRC website:

<https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb>

For guidance, refer to the following Partners policy:

Informed Consent of Research Subjects:

[https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed Consent of Research Subjects.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed%20Consent%20of%20Research%20Subjects.pdf)

DATA AND SAFETY MONITORING

Describe the plan for monitoring the data to ensure the safety of subjects. The plan should include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the planned frequency of review; and (3) who will be responsible for this review and for determining whether the research should be altered or stopped. Include a brief description of any stopping rules for the study, when appropriate. Depending upon the risk, size and complexity of the study, the investigator, an expert group, an independent Data and Safety Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring activity.

NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects under his/her care.

Because the potential risks to patients and clinicians are minimal, we do not plan to employ a Data Safety Monitoring Board and have chosen not to employ formal interim analyses or guidelines for early termination of the trial. However, we will form an Internal Oversight

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Committee that will include Dr. Baer and several of the Co-investigators (e.g., Drs. Block, Bates, Halperin, and Orav). This committee will closely track any adverse events, report them to the Partners IRB and to PCORI, and notify patients' primary care clinicians. If the primary care clinician feels that it is appropriate, the patient can be withdrawn from the study. In the event that adverse events seem to occur more frequently in either of the two intervention groups, however, we will alert the Partners IRB and PCORI as soon as we are aware and take further action as needed.

Describe the plan to be followed by the Principal Investigator/study staff for review of adverse events experienced by subjects under his/her care, and when applicable, for review of sponsor safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include the plan for reporting of adverse events to the FDA and, when applicable, to investigators at other sites.

NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal investigator must follow the Partners Human Research Committee guidelines for Adverse Event Reporting

Although we do not anticipate any direct adverse events from this study, we will promptly report any such adverse events to the IRB and halt the study until such potential adverse effects are addressed.

MONITORING AND QUALITY ASSURANCE

Describe the plan to be followed by the principal investigator/study staff to monitor and assure the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who will be responsible for monitoring, and the planned frequency of monitoring. For example, specify who will review the accuracy and completeness of case report form entries, source documents, and informed consent.

NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is ultimately responsible for ensuring that the study is conducted at his/her investigative site in accordance with the IRB-approved protocol, and applicable regulations and requirements of the IRB.

Again, because the potential risks to patients and clinicians are minimal, we do not plan to employ a Data Safety Monitoring Board and have chosen not to employ formal interim analyses or guidelines for early termination of the trial. However, we will form an Internal Oversight Committee that will include Dr. Baer and several of the Co-investigators (e.g., Drs. Block, Bates, Halperin, and Orav). This committee will closely track any adverse events, report them to the Partners IRB and to PCORI, and notify patients' primary care clinicians. If the primary care clinician feels that it is appropriate, the patient can be withdrawn from the study. In the event that adverse events seem to occur more frequently in either of the two intervention groups, however, we will alert the Partners IRB and PCORI as soon as we are aware and take further action as needed.

For guidance, refer to the following Partners policies:
Data and Safety Monitoring Plans and Quality Assurance

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[https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP in Human Subjects Research.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP%20in%20Human%20Subjects%20Research.pdf)

Reporting Unanticipated Problems (including Adverse Events)

[https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting Unanticipated Problems including Adverse Events.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting%20Unanticipated%20Problems%20including%20Adverse%20Events.pdf)

PRIVACY AND CONFIDENTIALITY

Describe methods used to protect the privacy of subjects and maintain confidentiality of data collected. This typically includes such practices as substituting codes for names and/or medical record numbers; removing face sheets or other identifiers from completed surveys/questionnaires; proper disposal of printed computer data; limited access to study data; use of password-protected computer databases; training for research staff on the importance of confidentiality of data, and storing research records in a secure location.

NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be considered and are strongly encouraged when the research involves the collection of sensitive data, such as sexual, criminal or illegal behaviors.

To ensure patient privacy and confidentiality, all information collected for the study will be stored within the Partners Healthcare System firewall, password protected, and anti-virus software enabled. Only study staff will have access to the study data on Shared File Areas. Only de-identified data will be used for the purposes of publication or presentation. Data collected and housed in the online weight management program called BMIQ will be securely stored by BMIQ. BMIQ will undergo a full Risk Evaluation by Partners Information Services to ensure they meet Partners policies and procedures regarding privacy and confidentiality. (Note: this Risk Evaluation has been completed and BMIQ has been approved. Documentation is included with this submission.)

SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE PARTNERS

Specimens or data collected by Partners investigators will be sent to research collaborators outside Partners, indicate to whom specimens/data will be sent, what information will be sent, and whether the specimens/data will contain identifiers that could be used by the outside collaborators to link the specimens/data to individual subjects.

We do not anticipate sending specimens/data to research collaborators outside Partners.

Specifically address whether specimens/data will be stored at collaborating sites outside Partners for future use not described in the protocol. Include whether subjects can withdraw their specimens/data, and how they would do so. When appropriate, submit documentation of IRB approval from the recipient institution.

We do not anticipate sending specimens/data to research collaborators outside Partners.

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RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE PARTNERS

When specimens or data collected by research collaborators outside Partners will be sent to Partners investigators, indicate from where the specimens/data will be obtained and whether the specimens/data will contain identifiers that could be used by Partners investigators to link the specimens/data to individual subjects. When appropriate, submit documentation of IRB approval and a copy of the IRB-approved consent form from the institution where the specimens/data were collected.

We do not anticipate receiving any information from outside Partners.