

TITLE: QBSafe: a randomized trial of a novel intervention to improve care for people living with type 2 diabetes.

Protocol Number

2000032654: QBSafe randomized trial

Protocol Version

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Synopsis

1. Purpose

Glycemic control is often the main indicator of successful diabetes care, but a singular focus on glycemic control may lead to patients' overall health and wellbeing being overlooked or undervalued. We have previously developed an intervention comprised of (a) a set of conversation cards designed to enable patients to identify aspects of life with diabetes important to them and to share them with their clinician to obtain their input; and (b) materials that help clinicians respond to patient concerns. We now propose to conduct a randomized clinical trial to test the feasibility of the research procedures and efficacy of the intervention with respect to patient reported outcome measures.

2. Primary objective

The primary objective is to determine whether usual care with the QBSafe intervention (comprised of conversation cards and materials) compared with usual care alone improves patient reported outcomes (principally Illness Intrusiveness Rating Scale) and clinical outcomes (change in hemoglobin A1c) among patients with type 2 diabetes and hemoglobin A1c >8%.

3. Secondary Objective

The secondary objectives are: 1) To determine the *feasibility* of the research procedures necessary to conduct a practice-based randomized trial to determine the clinical effectiveness of QBSafe intervention in the care of patients with type 2 diabetes; 2) To estimate the impact of the intervention on other patient reported outcomes (diabetes distress, treatment burden, hypoglycemia, global quality of life); 3) To estimate the impact of the intervention on patient-centered diabetes (time spent discussing QBSafe domains, patient and clinician satisfaction); 4) To explore how patients and clinicians discuss weight and weight loss during clinical encounters; and 5) To explore how patients and clinicians discuss patients' roles in communities of care.

4. Study Design

This is a randomized clinical trial of usual care with a behavioral intervention (use of conversation cards during routine clinical encounters) compared with usual care. The study will randomize 5-8 clinicians and 78 of their patients with type 2 diabetes to each arm. Data collected includes medical record data, patient and clinician surveys, and audio-visual recordings of clinical encounters.

5. Study Date Range and Duration

The intervention will occur at a single clinical encounter with follow-up data collection at 6 months from the time of intervention.

6. Number of Study Sites

Single study site (Fair Haven Community Health Center)

7. Primary Outcome Variables

Primary outcome is the illness intrusiveness measured by the validated Illness Intrusiveness Ratings Scale (IIRS). IIRS is comprised of 13 items that ask patients to rate the degree to which their “illness and/or its treatment” interfere with life domains central to quality of life.

8. Secondary and Exploratory Outcome Variables (if applicable)

Patient-reported outcomes:

- Diabetes distress will be measured by the validated Diabetes Distress Scale (DDS-17).
- Treatment burden will be assessed with the use of the Treatment Burden Questionnaire (TBQ).
- Self-management will be measured using the Summary of Diabetes Self-Care Activities (SDSCA).
- To assess global quality of life, we will use the 0 (worst possible)-to-100 (best possible) single-item visual Analogue Scale, which is a valid, reliable, and responsive measure recommended for use in clinical trials.
- The quality of communication will be assessed with a modified version of 3 questions from the CAHPS Clinician and Group survey.
- Patient satisfaction with the intervention will be assessed with a single-item question on a 5-point Likert scale that addresses whether they would recommend the approach used during their encounter (which could have been usual care alone or with the QBSafe ASK) to other patients.
- To measure hypoglycemia, patients will be asked about the frequency of any hypoglycemia (defined by a glucose level below 70 mg/dl [Level 1 hypoglycemia] or symptoms consistent with hypoglycemia), any blood glucose level below 54 mg/dl (Level 2 severe hypoglycemia), or any hypoglycemia requiring assistance from another person to treat.
- Clinicians will rate on a 5-point Likert scale their satisfaction with the approach used during the encounter (which could have been usual care alone or usual care with the QBSafe ASK).

Clinical outcomes:

- The primary clinical outcome will be the change in HbA1c. We will examine HbA1c levels obtained prior to encounter and closest to the 6 months post encounter.
- We will review medical and pharmacy records to assess the doses and types of diabetes medications prior to encounter, immediately post encounter, and 6 months post encounter.
- We will calculate adherence to diabetes medications based on the proportion of days covered (PDC) 6 months prior to and 6 months post encounter.
- We will assess any referrals made (diabetes education, nutrition services, physical therapy, other specialists) immediately post encounter and up until 6 months post encounter.
- We will assess healthcare utilization: any hospitalizations or emergency department (ED) visits for hypoglycemia or hyperglycemia (based on principal diagnoses), any diabetes-related ED visits or hospitalizations, ED or unplanned hospital visits for any cause, and urgent care visits within 6 months post encounter.

Encounter outcomes:

- As we have done in our prior studies (which now constitute a library of >5000 video recorded visits), we will use a GoPro camera to record all clinical encounters in both trial arms for which both clinicians and patients consent to such recording (~90% of encounters in prior trials). We will determine visit duration, time spent on discussion of each QBSafe domain, who initiated the discussion, and whether and how clinicians addressed each of the concerns raised. We will also explore how clinicians and patients discuss weight and weight loss strategies, and patients' roles in (bidirectional) communities in care .

9. Study Population

The study population includes clinician and their patients recruited from the Fair Haven Community Health Center in New Haven, CT. Eligible clinicians are any physicians, residents, nurse practitioners, and physician assistants who participate in the care of patients with type 2 diabetes and prescribe medications for them. Eligible patients are adults, diagnosed with type 2 diabetes, fluent in either English or Spanish, and with HbA1c >8%.

10. Number of Participants

We will randomize 10-15 clinicians and their 156 patients to the two arms (usual care with QBSafe intervention vs usual care). Our intent is to have enough power to detect important differences in patient reported outcome measures and in changes in glycemic control between the two arms. With this sample size, we will be able to detect a mean between-arm difference of 7.5 points on IIRS (primary outcome) with 13 patients per clinician (N=65, per trial arm). To account for potential attrition, the sample size is increased by 20% to 156 patients (78 per arm). With this sample size, we have 77 and 99% power to detect a between-arm difference in HbA1c at 6 months of 0.3 and 0.6%, respectively.

11. Study Schedule

This trial does not require extra visits, beyond those routinely conducted during clinical care. Consent will be obtained prior to the routine office visit and prior to enrollment. Just prior to the office visit with the clinician, patients and clinicians will complete several questionnaires. Clinical data will be abstracted from the electronic health record. During the visit, audio-visual recording will be done. Patients and clinicians will complete brief questionnaires right after the visit. At 6 months post visit, clinical data from the electronic medical record will be again abstracted and patients will complete additional questionnaires.

Protocol Revision History

Version Date	Summary of Substantial Changes
3/31/2022	First version
5/16/2022	Changes made in response to IRB review
9/27/2022	Clinicians will be able to try out the conversation cards with their patients' verbal assent in order to gain practice with the use of the cards. No data on patients will be collected and these encounters will not be audio-video recorded.
11/17/2022	Allow for recruitment of up to 15 clinicians.
1/17/2023	Storage of videos on external hard drive. Additional details on recruitment of patients and how to handle point-of-care hemoglobin A1c results.
4/25/2023	Modification to the protocol to allow for further revisions of clinician training materials based on the needs of clinicians enrolled in the study. Addition of an information card for patient participants letting them know that they will be contacted for follow up in 4-6 months.
8/17/2023	Modification of the protocol to explore how clinicians and patients discuss weight and weight loss.
10/25/2023	Added communication with clinician participants via email.
4/25/2024	Expanded target enrollment to 156 to account for larger loss to follow up.
9/11/2024	Edits to NOMAD survey and change in timing of NOMAD survey.
2/14/2025	Modification to the protocol to explore how clinicians and patients discuss patients' roles in communities of care.

Statement of Compliance

This document is a protocol for a human research study. The purpose of this protocol is to ensure that this study is to be conducted according to the Common Rule at 45CFR46 (human subjects) and other applicable government regulations and Institutional research policies and procedures.

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Abbreviations

Abbreviation	Explanation
HbA1c	Hemoglobin A1c (glycemic control)

Glossary of Terms

Glossary	Explanation
QBSAFE	Quality of life, Burden of treatment, Safety, and Avoidance of Future Events – key aspects of life with diabetes.

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1 Background/Literature Review

1.1 Background

Diabetes care has traditionally focused on targeting certain levels of glycemic control to reduce the risk of acute and chronic complications.¹ Clinical guidelines consider glycemic control fundamental to type 2 diabetes (DM2) management.¹ In practice, performance measures reward clinicians whose patients achieve target levels of glycemic control.² In research, clinical trials in DM2 compare interventions primarily with respect to their ability to achieve glycemic targets.³ Our prior study found that only 18% of registered diabetes trials included patient reported outcomes as primary endpoints.⁴

The current paradigm is problematic for several reasons. When glycemic control is the main focus of diabetes care, important aspects of patients' health and wellbeing may be overlooked or undervalued.⁵ Implementing evidence-based diabetes guidelines into practice without attention to the specific patient situation may fail to address the burden of diabetes and may increase the burden of its treatment ("illness intrusiveness") worsening how a person with diabetes feels or functions. Further, for patients with poor glycemic control, clinicians all too often focus on intensification of the medication regimen to reduce the HbA1c without understanding and addressing the contextual factors involved, such as competing life demands, capacity to implement the treatment plan, or other social determinants of health that may affect a person's ability to self-manage diabetes.⁶

Cumulative Complexity Model: People living with diabetes are expected to devote significant time and effort to manage their chronic disease but their ability to do this work may be limited due to their capacity. This balance between workload and capacity has been described in the Cumulative Complexity Model (CuCoM).⁷ The capacity to do "patient work" is drawn from the same capacity to do the work of everyday life: working in a job, parenting and other caregiving, volunteering, or hobby activities (*Figure 1*). When the workload of care exceeds the capacity to enact it, an overwhelmed patient may reduce their adherence to treatment and worsen their hyperglycemia. Clinicians may respond to the elevation in HbA1c with intensification of the treatment (e.g., new medications, more complex regimens, increased monitoring) which worsens the imbalance of workload and capacity. At the same time, other symptoms (from diabetes or associated comorbidities) remain unaddressed further reducing the patient capacity to respond. The end result is a patient experiencing high levels of disruption in their life from their illness (diabetes and other) and from its treatment ("illness intrusiveness"), whose glycemic control remains poor.

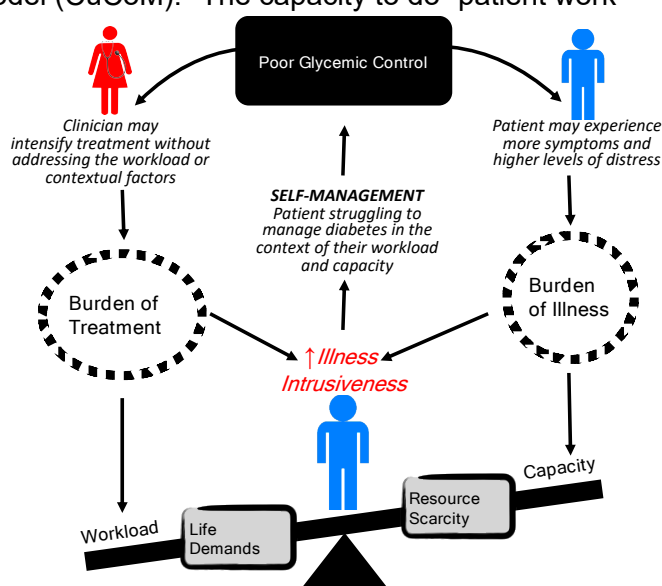


Figure 1: Conceptual Framework for the Trial

Patient capacity: There are multiple factors that impact the capacity of people with DM2 to manage their disease. People living with DM2 are frequently affected by multiple other

chronic conditions and functional impairments.^{8,9} As many as 40% have at least 3 comorbid conditions.^{10,11} Thus, aside from diabetes care, patients are asked to take other medications, visit other clinicians, undergo diagnostic studies, and comply with recommendations about diet or lifestyle changes pertinent to their other conditions.¹² Some comorbidities, such as arthritis, dementia, or depression, directly impair patients' ability to perform self-management tasks, such as glucose monitoring or insulin injections. Some comorbidities, such as advanced heart or kidney failure may make it more difficult to meet self-management goals. Many other comorbidities may compete for patients' attention, increase out-of-pocket costs, and deplete financial resources.¹³ Symptoms, such as chronic pain, fatigue, neuropathy, and insomnia are highly prevalent, affecting 25% to 40% of patients with diabetes;¹⁴ when unaddressed, they interfere with valued activities (increase "illness intrusiveness") and substantially impair self-management.

Workload of diabetes care: In addition, diabetes care can be intensely time-consuming.¹⁵⁻¹⁸ One study estimated that the total time patients need to fully comply with guideline recommendations for diabetes self-care was around 4 hours per day, far more than is reasonably feasible for most people living with the disease.¹⁵ In reality, patients spend less time on diabetes care, but this varies considerably across the population, with adults in poor health reporting more time spent on self-care.¹⁷ This high workload/burden may interfere with patient's valued activities and further increase "illness intrusiveness."

Illness intrusiveness: Illness intrusiveness results from the sum of disease- and treatment-induced disruptions to lifestyles, valued activities and interests.¹⁹ Illness intrusiveness compromises psychological wellbeing and contributes to emotional distress. When clinicians focus on glycemic control without paying attention to how diabetes or its treatment affect patient's lives, emotionally challenging aspects of life with diabetes may remain unaddressed (feelings of deprivation and distress related to dietary changes; challenges in using diabetes technologies [e.g., using, interrogating, downloading and sharing results from glucose meters and monitors]; and financial stressors related to diabetes [e.g. insurance problems, affording medications and healthy foods]). The Cumulative Complexity Model predicts that **when diabetes care accounts for and addresses these outcomes, the balance between workload and capacity is restored, illness intrudes less, patients are able to fit self-management into everyday lives, and glycemic control improves.**

Social determinants of health: The capacity available to manage DM2 and the life demands that contribute to the workload that patients experience, are influenced by the social, economic, and physical contexts of people's lives. Income, employment, education, housing, health literacy, social support, racism and other forms of discrimination, and community safety contribute to poor (vs successful) DM2 self-management.²⁰ An individual clinician may have little ability to influence these important social determinants of health directly. However, a clinician can use information on social determinants of health to tailor medical care based on an individual patient's social context (i.e., "social risk-informed care"), for example by considering food insecurity when designing an insulin regimen.²¹ In addition, a clinician can target social risk factors through a referral to social services or to other community programs (i.e., "social risk-targeted care"), for example to address food insecurity or housing instability.²¹ Although many community health centers are now systematically collecting data on social risk factors, this information is still rarely used to influence care plans.²⁰

In sum, patients with DM2 are expected to devote significant amount of time to diabetes care and many are burdened by the demands of their treatment and by the symptoms of diabetes

and the limitations it poses on their lives. Clinicians typically do not address these aspects of life with diabetes even though they are critical to health and to the wellbeing of our patients. Addressing these concerns is likely to improve the ability of patients to manage their illness and thus avoid poor glycemic control.

These data suggest that a paradigm shift is needed – from the narrow focus on reaching hemoglobin A1c targets – even modified ones – to a more holistic approach that responds to patient needs, fits within the patient’s context and capacity, and prevents iatrogenic harms. To address this, we propose to test a novel approach to DM2 care focused on Quality of life, Burden of treatment (medication administration, costs, and monitoring), Safety (reducing adverse effects), and Avoidance of Future Events (acute and chronic diabetes complications) – the QBSafe approach. Funded by an R21 grant (R21 AG061427), we developed a QBSafe agenda setting kit (ASK), which includes a set of **conversation cards** that enable patients to identify and bring up aspects of QBSafe that would benefit from clinician’s input. The QBSafe ASK also includes materials that help clinicians respond well to these patient concerns.

Conversation cards are a low-tech, high-impact clinical tool. There is no doubt that the best way to address many of the contextual factors affecting illness intrusiveness and glycemic control is through policy changes that directly improve social factors that promote health. No clinical intervention alone could or should replace this policy response. And yet, in caring for patients, clinicians must notice their patient’s needs and respond with competence and compassion. That is precisely where our intervention makes a contribution. Clinicians face competing demands for their attention, which makes it difficult to connect with patients, identify their concerns, and address them effectively. Conversation cards with written plain-language statements have been used to help patients communicate and help clinicians notice and respond effectively to patient concerns.²²⁻²⁸ In palliative care, conversation cards help patients verbalize their wishes and priorities at the end of life that may otherwise be difficult to formulate.^{22,23} In pediatrics, cards help patients with obesity set goals with their clinicians.^{24,26} Like shared decision-making tools, conversation cards allow patients and clinicians to communicate better and to determine jointly how to respond to concerns that arise. In sum, conversation cards can serve as portable, low-tech, low-cost tools that efficiently enable individualized care.

1.2 Prior Experience (if applicable)

Discussion of QBSafe domains during routine clinical care: A video-graphic analysis:

In order to determine how much time during clinical encounters of patients with DM2 is focused on QBSafe domains, we analyzed video-recorded encounters from a clinical trial of shared decision-making tools using the control group that did not receive any intervention.²⁹ Using these data, we sought to determine how often patients and clinicians initiated, discussed, considered, and responded to problems in the domains of quality of life, burden of treatment, social supports, sexual dysfunction, and the risk for hypoglycemia during routine clinical encounters for diabetes. Two coders, working independently, reviewed each video recording after ensuring they could agree on their codes $\geq 90\%$ of the time. During this calibration process, a codebook was created that defined aspects of quality of life, burden of treatment, hypoglycemia, sexual dysfunction, and social supports that were coded during analysis. We included 41 clinical encounters in our analysis; patients’ average age was 62, average HbA1c 8.3%, median encounter length of 15 minutes.³⁰ At least one aspect of QBSafe was raised during 35/41 (85%) of the clinical encounters. QBSafe concerns were predominantly raised by the patient (65% of the time). When QBSafe issues were raised, they involved quality of life discussions (59%), treatment burden (51%), hypoglycemia (10%), and social supports (2%). No discussions took place about sexual dysfunction, how diabetes care interferes with other aspects of life, or of how life interferes with diabetes care.

Although clinicians often acknowledged patient concerns, or proposed to monitor further, they rarely proposed specific actions to address these concerns. Few changes in the treatment program occurred.

These findings suggest that many, but not all, aspects of the QBSafe domains are discussed during routine clinical encounters, but the manner in which they are raised and discussed, when so, do not lead to changes to the care plan.

QBSafe ASK development and acceptability: QBSafe ASK (i.e., the set of conversation cards) was developed with funding from NIA (R21 AG061427) in order to improve patient-centered care for complex patients with diabetes. Specifically, our goals were to promote conversations between patients and clinicians in which they could problem solve together, while targeting issues related to workload and capacity. The design process was iterative and involved a collaboration between Dr. Lipska and Dr. Montori at Yale School of Medicine and Mayo Clinic, respectively, along with a healthcare designer from the Patient Revolution (Maggie Breslin). The first iteration of the intervention involved use of brief surveys about overall quality of life, diabetes-related quality of life, difficulties with management of diabetes, hypoglycemia, and social supports – aspects of life with diabetes deemed to be important and identified both from the literature and from clinical experience.³¹⁻³⁶ In early stages of our work, we found that patients were able to complete the surveys fairly easily, but this did not lead to meaningful conversations during the clinical encounters. We hypothesized that the volume of questions and the format were not conducive to conversation or problem-solving.

In response to these early results and with the intent of bringing the contents of the surveys into a conversation during the clinical encounter (where they could be turned into action), we turned our attention toward conversation cards, which can be used to engage patients in agenda setting and care planning.²²⁻²⁶ We developed 12 cards that corresponded to the topics important to patients living with diabetes and reflected by the surveys we had already used. These card prototypes were then refined and field-tested in usual care with patients with diabetes. As a result, we added 2 additional cards, about successes in diabetes care, based on feedback from and observations of their use by diabetes nurse educators.

Finally, we recruited 7 clinicians (endocrinologists, primary care, nurse practitioners, diabetes educators) and their 83 patients with diabetes to understand the acceptability of the cards in clinical practice. Adult patients with diagnosed type 1 or type 2 diabetes were recruited into the study if they spoke English (we have now developed an ASK in Spanish) and had the capacity to make decisions about participation in research. All patients received the QBSafe cards prior to their appointment: some patients received the cards electronically (via email or text link) because they were scheduled for a virtual visit and some patients received their cards after they were roomed and were waiting for their clinician during a routine in-person diabetes visit (the COVID-19 pandemic hit our practices during this evaluation, forcing us to develop an ASK that could be safely shared with patients). Patients were instructed to select 0-3 cards that were most pertinent to their situation. Clinicians were instructed to review the cards at the start of the visit. After the visit, both patients and clinicians filled out brief surveys on the cards' acceptability.

Acceptability of the QBSafe ASK was high: 7 clinicians rated the cards based on their helpfulness during each clinical encounter during which they were used. The majority of patients (64%) reported that the cards helped them talk about topics important to them during their visit and 78% would recommend them to patients like themselves. In qualitative interviews, patients who responded with 'neutral' or 'disagree' categories reported feeling

they could bring up QBSafe topics without the cards because they had an established and positive relationship with their clinician, which also explained why they were more likely to recommend them to other patients than to prefer to use them in their own future encounters.

Team Experience:

Harms of overtreatment: The research program of PI (Lipska) has focused on the recognition of potential overtreatment among older patients with DM2, as well as on the prediction and prevention of hypoglycemia in diabetes care, particularly for older patients with DM2.³⁷⁻⁴⁰ This work showed that a substantial proportion of older Americans achieve hemoglobin A1c levels below 7%, despite having serious co-existing health problems and functional impairments. In addition, this work demonstrated that hospital admissions for hypoglycemia exceed hospital admissions for hyperglycemia and pose a significant health threat to older Medicare beneficiaries. These findings suggest that potential overtreatment is common and warrant greater focus on the safety of diabetes management, particularly among the elderly.

Advancing patient-centered diabetes care: Efforts to improve diabetes care quality are most effective when they center around the patient and the totality of the patient's needs, whether medical, financial, or psychosocial, and are integrated with the totality of the patient's care. Over the past 20 years, Dr. Montori (Co-I) has conducted work to redesign diabetes management, implement the Chronic Care Model, test new models of care to integrate primary and specialty care, and bring evidence-based patient-centered care to diabetes care in primary care settings. Montori is one of the developers of the concept of **minimally disruptive medicine**, which seeks to advance patient goals for health, health care, and life, using effective care programs designed and implemented in a manner that respects the capacity of patients and caregivers and minimizes the burden of treatment the care program imposes on their lives. This led to pioneering work to develop the Cumulative Complexity Model, theories of treatment burden and patient capacity, and measures of **treatment burden**, particularly in patients with diabetes and other chronic conditions, polypharmacy, and personal and social complexity.^{7,34,41-58} Montori also led the development and evaluation of tools to improve **communication and shared decision making** in clinical encounters for patients with diabetes. He founded the only Shared Decision-Making National Resource Center in the country, and conducted, with Ms. Branda as the lead statistician, most of the practice-based randomized trials of shared decision-making interventions for use during clinical encounters in the literature. This experience includes the design and conduct of **cluster randomized trials**, the use of video recordings to determine the fidelity of use of these interventions and their effect on the conversations per se, and the refinement of procedures to conduct these studies within busy primary care practices.^{29,59-65}

In order to improve DM2 care, effective interventions need to be embedded in primary care. Over the past two years, Dr. McCoy (Co-I) has led a successful multi-disciplinary effort within Mayo Clinic Health System's urban and rural primary care practices to redesign diabetes management and improve the reportable diabetes quality metrics (HbA1c, blood pressure, and lipid control, non-smoking, and aspirin use), patient satisfaction, and staff well-being.⁶⁶ Through this and other quality improvement efforts (e.g. a pre-diabetes patient education program, a digital education program for patients with newly diagnosed diabetes, a program to address transportation barriers for accessing primary care), Dr. McCoy has demonstrated leadership in improving DM2 care in primary care settings.

Addressing health disparities in DM2: DM2 disproportionately affects economically disadvantaged and racial/ethnic minority populations. Racial/ethnic minorities with DM2 experience greater barriers to self-management and are more likely to have poor glycemic

control. For over 2 decades, Dr. Camp (Co-I) has led efforts to improve diabetes care in medically underserved communities and has held multiple leadership positions within the HRSA National Health Disparities Collaborative. Her efforts have included organizational system changes to improve DM2 care for underserved groups, program development, and implementation of successful interventions in federally qualified health centers.⁶⁷⁻⁷¹

Methodology: Mrs. Branda, Assistant Professor of Biostatistics and the study statistician, has over 10 years of experience in the design and analysis of multi-centered trials, including practice-based clustered randomized trials, including not only high impact randomized trials but also prospective pilot studies such as this one. She is an Associate Editor for Trials and is an instructor for a graduate level course on the design of clinical trials. She has collaborated with Co-I Dr. Montori on over 12 randomized controlled trials in shared decision making, making her a preeminent expert in the design, conduct, and analysis of trials like the one proposed here.

2 Rationale/Significance

2.1 Rationale and Study Significance

Glycemic control is often the main goal of diabetes care, but a singular focus on glycemic control may lead to patients' overall health and wellbeing being overlooked or undervalued. We have previously developed an intervention comprised of (a) a set of conversation cards designed to enable patients to identify aspects of life with diabetes important to them and to share them with their clinician to obtain their input; and (b) materials that help clinicians respond to patient concerns. We now propose to conduct a randomized clinical trial to test the feasibility of the research procedures and efficacy of the intervention with respect to patient reported outcome measures and for improving glycemic control.

Significance of the research:

1. The new approach to glycemic management will shift the focus of care toward improving how a patient feels and functions. In this way, this research addresses patient-centered goals and needs, instead of prioritizing disease-centered surrogate targets. Most clinical diabetes research is not focused on improving, or even measuring, **patient-reported outcomes**.
2. By focusing attention on the contextual factors in a person's life, the new approach will help clinicians incorporate social determinants of health into clinical care decisions.
3. The intervention is a set of **conversation cards**. Seemingly simple and low-tech, conversation cards can be an effective way to engage patients in care and to "give voice" to difficult issues. They have been used to that effect in the management of obesity among adolescents and in end-of-life decision-making.²⁴⁻²⁶ However, to our knowledge, they have not been previously applied in diabetes care.
4. Since the project is focused on patient-reported outcome measures, it requires the use of surveys and direct observation of clinical encounters. We will use **audio-visual recordings** of the encounters for analysis, as we have successfully done in our prior work, to determine the fidelity with which the intervention is used and the extent to which it improves patient-centered diabetes care.

The trial will take place at the Fair Haven Community Health Care (FHCHC), a federally qualified medical center that cares for a diverse, bilingual (Spanish and English) and vulnerable population including >21,000 patients and >1,500 patients with diabetes. This site has experience in the conduct of federally funded diabetes trials, including being the only federally qualified health center to participate and one of top recruitment sites of the GRADE trial. We chose to test QBSafe in a *primary care setting* because:

- the shift from a disease-centered (HbA1c) to a person-centered (QBSafe) care is consistent with the philosophy of primary care;
- most patients with DM2 in the U.S. receive diabetes care in primary care settings; and
- primary care can often respond well (including the involvement of specialists, nurse educators, social workers, and community resources) to the broad range of issues QBSafe raises.

We chose to test QBSafe at FHCHC because the center cares for a predominantly minority population (with a higher burden of diabetes), younger in age than the general diabetes population (more likely to experience challenges with DM2 management and more likely to benefit from improvements in DM2 control), and with a greater prevalence of actionable social risk factors, such as food insecurity, housing instability, difficulties with transportation

or paying bills,²⁰ that may reduce patient's capacity to self-manage their disease (and thus in need of interventions to achieve care that fits within patient's context).⁷² There are 28 adult or family primary care clinicians at FHCHC and 575 patients with HbA1c >8%.

2.2 Purpose of Study/Potential Impact

The primary purpose of the study is to improve the quality of life and health outcomes of people living with type 2 diabetes.

2.3 Potential Risks and Benefits

2.3.1 Potential Risks

The risks of the intervention in this study – use of QBSafe ASK (14 conversation cards) – include clinician discomfort with issues raised by the cards or patient discomfort with raising some of the issues with their clinician. Time spent answering the survey questions may pose an inconvenience. In addition, patients and clinicians may feel discomfort with the use of video recordings during the office visit. Finally, both patients and clinicians face risk associated with breach of confidentiality. Protections to minimize these risks are described below.

2.3.2 Potential Benefits

When healthcare professionals focus on glycemic control without paying attention to patient reported outcomes, emotionally challenging aspects of living with diabetes may remain unaddressed; these may include interpersonal relationships (e.g., overbearing support or lack of understanding/support from others); dissatisfaction with clinicians; feelings of deprivation and distress related to dietary changes; challenges in using diabetes technologies (e.g., using, interrogating, downloading and sharing results from glucose meters and monitors); and financial stressors related to diabetes (e.g. insurance problems, affording medications and healthy foods). Illness intrusiveness, diabetes distress and unsustainable levels of treatment burden are ubiquitous among patients with type 2 diabetes and need to be better addressed. In order to shift the paradigm of care and to encourage productive conversations in clinical practice, we have developed and propose to test the impact of QBSafe conversation cards embedded in usual care versus usual care alone on feasibility outcomes, illness intrusiveness, and HbA1c change. The results of this trial, if positive, will justify a larger study to determine the impact of the intervention on clinical effectiveness and implementation outcomes; if negative, it will require additional studies to develop the tools and responses needed to address illness intrusiveness in diabetes care.

The risks to the participants are reasonable since the intervention is noninvasive, the research team has adequate experience with conduct of intervention studies, there is no risk of any significant morbidity or mortality, and precautions are taken to minimize discomfort or breach of confidentiality. There is a high likelihood (e.g., investigators record and expertise, validated methods, statistical power) of obtaining meaningful, useful information.

3 Study Purpose and Objectives

3.1 Hypothesis

QBSafe ASK (intervention) with usual care compared with usual care alone will improve patient centered outcomes (principally illness intrusiveness) and clinical outcome (glycemic control) among people with type 2 diabetes with inadequate glycemic control (HbA1c >8%).

3.2 Primary Objective

The primary objective is to determine whether the QBSafe intervention (comprised of conversation cards and materials) compared with usual care improves patient reported outcomes (principally Illness Intrusiveness Rating Scale) and clinical outcomes (change in hemoglobin A1c) among patients with type 2 diabetes and hemoglobin A1c >8%.

3.3 Secondary Objective (if applicable)

The secondary objectives are: 1) To determine the feasibility of the research procedures necessary to conduct a practice-based randomized trial to determine the clinical effectiveness of QBSafe intervention in the care of patients with type 2 diabetes; 2) To estimate the impact of the intervention on other patient reported outcomes (diabetes distress, treatment burden, hypoglycemia, global quality of life); 3) To estimate the impact of the intervention on patient-centered diabetes (time spent discussing QBSafe domains, patient and clinician satisfaction); 4) To explore how patients and clinicians discuss weight and weight loss during clinical encounters; and 5) To explore how patients and clinicians discuss patients' roles in communities of care.

4 Study Design

4.1.1 General Design Description

This is a randomized clinical trial of a behavioral intervention (use of conversation cards during routine clinical encounters) along with usual care compared with usual care alone. The study will randomize 5-8 clinicians and 78 of their patients with type 2 diabetes to each arm. Data collected includes medical record data, patient and clinician surveys, and audio-visual recordings of clinical encounters.

4.1.2 Study Date Range and Duration

The intervention will occur at a single clinical encounter with follow-up data collection at 6 months from the time of intervention.

4.1.3 Number of Study Sites

Single study site (Fair Haven Community Health Center)

4.2 Outcome Variables

4.2.1 Primary Outcome Variables

Primary outcome is the illness intrusiveness measured by the validated Illness Intrusiveness Ratings Scale (IIRS). IIRS is comprised of 13 items that ask patients to rate the degree to which their “illness and/or its treatment” interfere with life domains central to quality of life.

4.2.2 Secondary and Exploratory Outcome Variables (if applicable)

Patient-reported outcomes:

- Diabetes distress will be measured by the validated Diabetes Distress Scale (DDS-17).
- Treatment burden will be assessed with the use of the Treatment Burden Questionnaire (TBQ).
- Self-management will be measured using the Summary of Diabetes Self-Care Activities (SDSCA).
- To assess global quality of life, we will use the 0 (worst possible)-to-100 (best possible) single-item visual Analogue Scale, which is a valid, reliable, and responsive measure recommended for use in clinical trials.
- The quality of communication will be assessed with a modified version of 3 questions from the CAHPS Clinician and Group survey.
- Patient satisfaction with the intervention will be assessed with a single-item question on a 5-point Likert scale that addresses whether they would recommend the approach used during their encounter (which could have been usual care alone or with the QBSafe ASK) to other patients.
- To measure hypoglycemia, patients will be asked about the frequency of any hypoglycemia (defined by a glucose level below 70 mg/dl [Level 1 hypoglycemia] or symptoms consistent with hypoglycemia), any blood glucose level below 54 mg/dl (Level 2 severe hypoglycemia), or any hypoglycemia requiring assistance from another person to treat.
- Clinicians will rate on a 5-point Likert scale their satisfaction with the approach used during the encounter (which could have been usual care alone or usual care with the QBSafe ASK).

Clinical outcomes:

- The primary clinical outcome will be the change in HbA1c. We will examine HbA1c levels obtained prior to encounter and closest to the 6 months post encounter.
- We will review medical and pharmacy records to assess the doses and types of diabetes medications prior to encounter, immediately post encounter, and 6 months post encounter.
- We will calculate adherence to diabetes medications based on the proportion of days covered (PDC) 6 months prior to and 6 months post encounter.
- We will assess any referrals made (diabetes education, nutrition services, physical therapy, other specialists) immediately post encounter and up until 6 months post encounter.
- We will assess healthcare utilization: any hospitalizations or emergency department (ED) visits for hypoglycemia or hyperglycemia (based on principal diagnoses), any diabetes-related ED visits or hospitalizations, ED or unplanned hospital visits for any cause, and urgent care visits within 6 months post encounter.

Encounter outcomes:

- As we have done in our prior studies (which now constitute a library of >5000 video recorded visits), we will use a GoPro camera to record all clinical encounters in both trial arms for which both clinicians and patients consent to such recording (~90% of encounters in prior trials). We will determine visit duration, time spent on discussion of each QBSafe domain, who initiated the discussion, and whether and how clinicians addressed each of the concerns raised. We will also analyze clinical encounters to understand how clinicians and patients approach conversations about weight and weight loss. We will analyze whether and how patients and clinicians discuss patients' communities of care, including mentions of what community members do to help patients in their care, and how patients balance their care with caregiving responsibilities.

4.3 Study Population

The study population includes clinician and their patients recruited from the Fair Haven Community Health Center in New Haven, CT. Eligible clinicians are any physicians, residents, nurse practitioners, and physician assistants who participate in the care of patients with type 2 diabetes and prescribe medications for them. Eligible patients are adults, diagnosed with type 2 diabetes, fluent in either English or Spanish, and with HbA1c >8%.

4.3.1 Number of Participants

We will randomize 10-15 clinicians and their 156 patients to the two arms (usual care with QBSafe intervention vs usual care). Our intent is to have enough power to detect important differences in patient reported outcome measures and in changes in glycemic control between the two arms. With this sample size, we will be able to detect a mean between-arm difference of 7.5 points on IIRS (primary outcome) with 13 patients per clinician (N=65, per trial arm). To account for potential attrition, the sample size is increased by 20% to 156 patients (78 per arm). With this sample size, we have 77 and 99% power to detect a between-arm difference in HbA1c at 6 months of 0.3 and 0.6%, respectively.

4.3.2 Eligibility Criteria/Vulnerable Populations

Clinician eligibility: Eligible clinicians are any physicians, residents, nurse practitioners, and physician assistants who participate in the care of patients with DM2 and prescribe medications for them.

Clinician Enrollment Process: Eligible clinicians will be recruited (in person or virtually, depending on the evolution of site-specific COVID-19 policies and IRB-approved procedures) after scheduled presentations at the health center and just prior to a scheduled appointment with an eligible patient. As in our prior practice-based trials, clinicians are study participants themselves and must provide written informed consent to participate in the trial prior to enrolling their first patient. An email communication will be sent to clinicians to ensure they have no concerns about the use of data collected during clinical encounters for additional analyses which may not be directly related to the objectives of the QBSAFE trial.

Patient eligibility: Eligible patients are adults, diagnosed with DM2, able to sign informed consent, fluent in either English or Spanish, and with HbA1c >8%. Patients for whom an HbA1c target >8% is clinically reasonable (e.g., those with limited life expectancy) and/or aligned with goals/preferences will not be included.

Patient Enrollment Process: As in our prior practice-based trials, eligible patients will be identified through appointment lists by a trained study coordinator who will recruit eligible patients via phone (asking patients to arrive early to their scheduled appointment to complete the consent process), or in person at the time of their scheduled visit. Clinicians will review the list and identify patients for exclusion if HbA1c >8% target is reasonable. The written informed consent procedure will take place in a private exam room prior to their scheduled appointment. In the spirit of minimally disruptive research, all study activities will occur within scheduled appointments, avoiding the need for additional research-only visits.

No vulnerable populations will be involved in this study.

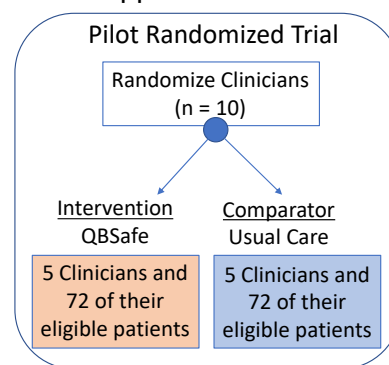


Figure 2: Overview of Trial Design

Study Methods/Procedures

4.4 Study Procedures

The study coordinator will identify potentially eligible patients by review of appointment lists. Clinicians will review the lists to ensure that patient participation is clinically reasonable (i.e., that an A1c target $\leq 8\%$ is clinically sensible and consistent with patient preferences and goals). Patients will be recruited by the trained study coordinator by phone, text, mail, email, or portal message and will be asked to arrive early to their scheduled appointment to complete the consent process. The written informed consent procedure will then take place in a private exam room prior to their scheduled appointment. Given the changing circumstances around the pandemic of COVID-19, patients will also have the option to go over the consent document over the phone, have the opportunity to ask questions, and will be able to complete the written consent electronically (via the e-consent feature within REDCap or EPIC) or by mail ahead of their scheduled appointment. In the spirit of minimally disruptive research, all study activities will occur within scheduled appointments (or ahead of the appointment), avoiding the need for additional research-only visits, unless patients prefer to complete them remotely by phone, electronically, or by mail.

Since clinicians routinely use point-of-care hemoglobin A1c (HbA1c) testing at Fair Haven, it is possible that some patients may become either eligible or ineligible for the study at the time of their clinic visit. Point-of-care HbA1c is routinely done for patients who have not had an HbA1c done within 3 months of their clinic visit; it is also sometimes repeated in patients with a recent HbA1c if the clinician judges this to be important. When identifying potentially eligible patients, the study coordinator will note whether an HbA1c was done within the 3

months of the planned clinic visit. If the HbA1c was done within the 3 months of the planned clinic visit and is $>8\%$, the patient will be asked to come in early to provide written informed consent and complete study questionnaires. If the HbA1c was done more than 3 months ago, the patient will be asked to come in early to obtain point-of-care HbA1c (as would be routinely done) and to provide written informed consent. If the HbA1c returns as $>8\%$, the patient will then be enrolled in the study and asked to complete the study questionnaires. If the HbA1c returns $\leq 8\%$, the patient will not be included in the study.

Medical assistants regularly measure patients' weight at the start of every visit as part of the routine collection of vital signs (weight, pulse, blood pressure, temperature). The trial protocol will not impact this usual clinic practice.

Once written consent is obtained, all patients will be asked a set of questions about illness intrusiveness (IIRS), diabetes distress (DDS-17), treatment burden, quality of life, and hypoglycemia. Patients who complete written consent ahead of their scheduled clinic, will have the option of completing the questions ahead of their scheduled visit either electronically (via Qualtrics), by phone, or by paper and mail.

Clinicians will be randomized to use QBSafe ASK (a set of 14 conversation cards) during their usual care visits vs usual care alone. Clinicians will not be aware of the study hypotheses and will proceed to provide care to their patients in the usual fashion. Clinicians randomized to the intervention group (QBSafe ASK) will have the opportunity to try out the conversation cards with some of their patients with diabetes (regardless of eligibility for the trial) prior to using them with their randomized study patients. This will allow clinicians to gain experience with the use of the cards. Clinicians will ask their patients for verbal assent for this purpose. No data on patient participants will be collected and these practice sessions will not be audio- or video-recorded. Once clinicians in the intervention arm of the trial feel ready to proceed, patients will be consented and enrolled. In the intervention group, patients will be given the set of 14 conversation cards (QBSafe ASK) as they wait for their clinician either in the waiting room or in the exam room. They will be asked to select 0 to 3 cards that best fit their situation and to bring them up in the consultation. Clinicians will conduct the encounter as usual but will be asked to review and respond to the cards first.

To help clinicians prepare for the trial, practice sessions will be allowed (as above). In addition, to help clinicians respond to some of these cards, the study team will hold training sessions for clinicians ahead of the first study or practice visit. During the training session, clinicians will have the opportunity to view the cards, discuss the issues on the conversation cards, and discuss ways of responding. Clinicians will have access to suggested ways to address the concerns included in the conversation cards (e.g., information about how to address sexual dysfunction). The resources for responses will be available online, via diagrams and brief videos response examples during encounters, which our team has developed and is continuing to refine.

Office visit encounters will be video-recorded and additional information will be obtained immediately following the encounter, including questions about the quality of communication and satisfaction with the encounter, as well as patient assessment of health literacy. Clinicians will be asked to answer 2 items after each clinic visit with a study participant. Additional information will be obtained from the electronic medical record, including age, sex, race/ethnicity, comorbidities, medications (prescriptions and fills), baseline weight and body mass index, and HbA1c level.

The primary outcome will be the Illness Intrusiveness Ratings Scale (IIRS) and will be assessed 6 months after the initial encounter. Patients with type 2 diabetes are typically seen in the primary care office every 3 months. At that time, we will collect data on illness intrusiveness, diabetes distress, treatment burden, quality of life, and hypoglycemia. This will be assessed either during a scheduled visit closest to the 6 month time-point, or by phone, mail, or electronic survey – according to patient preference and feasibility. EMR records will be used to obtain subsequent HbA1c levels at 6 months, as well as data on diabetes medications (prescriptions and fills), healthcare utilization, and referrals.

Once all patients are enrolled and complete the clinic visit, a NOMAD survey will be completed by clinicians randomized to the QBSAFE arm and to any participating clinic staff to examine barriers/facilitators of the implementation of the QBSAFE Toolkit within the primary care practice's routines.

4.4.1 Description of the Intervention

QBSAFE ASK Description

In the intervention group, patients will be given a set of 14 conversation cards (QBSafe Agenda Setting Kit, *Figure 3*) as they wait for their clinician either in the waiting room or in the exam room. They will be asked to select 0 to 3 cards that best fit their situation and to bring them up in the consultation. Clinicians will conduct the encounter as usual but will be asked to review and respond to the cards first. To help clinicians respond to some of these cards, clinicians will have access to suggested ways to address these concerns which we have developed. The resources for responses will be available online, via diagrams and brief video response examples during encounters, which we have developed.

I struggle with remembering, taking, or managing my medications.	I struggle with monitoring my blood sugar.	There are things I would like to do but can't or won't because of my diabetes.	My diabetes limits my ability to work, do hobbies, or spend time with family and friends.	I am frustrated by the amount of time I spend managing my diabetes.
1	2	3	4	5
I am having problems with low blood sugar.	I would benefit from more help managing my diabetes.	I find it hard to follow your suggestions about diet and exercise.	Diabetes is impacting my sex life.	I worry about my ability to pay for my healthcare.
6	7	8	9	10
I have another issue related to my diabetes that I'd like to talk about.	I have something I'd like to share with you but I know you probably won't be able to do much about it.	Diabetes has had some positive impacts on my life.	I have felt moments of pride while managing my diabetes.	 Find and share this tool and others on our website. PATIENTREVOLUTION.ORG
11	12	13	14	

Figure 3: QBSafe Agenda Setting Kit: Conversation Cards

Mode of Use

The conversation cards will serve as guides for conversation, rather than scripted discussions, so clinicians will have flexibility in the manner in which they use the cards, including how and when they use them during the visit. They may even elect not to use the cards with certain enrolled patients, per their own judgment.

Training of Personnel

Designated site staff will be trained to review informed consent documents and obtain necessary signatures from patients and will be observed doing so, by study personnel or research staff, prior to actually consenting patients. Participating clinicians randomized to the intervention as well as other clinical staff (e.g., social worker, pharmacist, dietician, on-site interpreters) will receive brief training on the purpose and use of QBSafe ASK in a group setting. Our preliminary findings suggest that clinicians generally felt confident in responding to patient concerns, making longer training sessions unnecessary. Other clinical staff will be invited in order to improve handoffs and promote team-based care. Study staff will share the 14 conversation cards, and, when opportune, brief videos demonstrating the use of the QBSafe ASK in the clinical encounter. During training, clinicians will have the opportunity to try the cards and to access materials with suggested responses with a colleague and to ask questions about ways to respond directly to concerns raised by the cards, or ways to collaborate with non-clinician team members when concerns fall outside of clinician expertise (e.g., by warm handoff to social worker, dietician, diabetes educator). The resources for responses will be available online, via diagrams and brief video response examples during encounters, which we have developed and will continue to refine and revise based on clinician needs during the study. Clinicians will be reminded that QBSafe should be used to support their conversation with the patient in a manner that makes sense

in their practice. Study staff will be available to answer questions about the use of the intervention throughout trial conduct.

Table 1: Data Collection for the QBSafe Pilot Trial.

	Before Enrollment	Prior to Visit	RANDOMIZATION	During Visit	Post Visit	6 Months Post
Patient Completed Forms						
Informed Consent	x					
Illness Intrusiveness Ratings Scale (13-item scale) ¹⁹		x				x
Diabetes Distress Scale, DDS-17 (17-item scale) ⁷³		x				x
Treatment Burden Questionnaire, TBQ (15-item scale) ³⁴		x				x
Quality of life (1 item) ⁷⁴		x				x
Summary of Diabetes Self-Care Activities (SDSCA) ⁷⁵		x				x
Quality of communication (3 items adapted from CAHPS) ⁷⁶					x	
Patient satisfaction (1 item)					x	
Hypoglycemia questions (4 items)		x				x
Health literacy screener (1 question) ⁷⁷					x	
Clinician Completed Forms						
Informed Consent	x					
Clinician characteristics questionnaire		x				
Clinician satisfaction (2 items)					x	
NOMAD survey (23 items) ⁷⁸					x	
Encounter Data						
Audio-visual recording of visit				x		
Clinical Data Abstracted from EMR						
Hemoglobin A1c	x	x			x	x
Weight/BMI				x		
Diabetes Medications	x	x			x	x
Referrals					x	x
Healthcare utilization		x			x	x

Control Group

Control clinicians will conduct their encounter as usual. To limit contamination, we will limit access to the QBSafe ASK to clinicians allocated to the intervention arm, a feature, along with clinician training, that justifies our choice of using a clustered randomized design.

4.4.2 Data Collection

Clinicians and their patients who agree to participate will have their data captured in the REDCap system, a HIPPA compliant data capture system that has a log of changes as well as password protected. We will document in a recruitment tracking log all potentially eligible patients found to be ineligible or who decline participation. The reason for ineligibility or reason for decline will be captured along with age, sex, race, and ethnicity. At the time of their enrollment, clinicians will complete a demographic survey (*Table below*). After each encounter, study staff will administer appropriate instruments/surveys to clinicians and to patients and encourage them to complete the surveys at that time. If participants request a return envelope, one will be provided to return the survey by mail. If the survey is not received in the 10 days post encounter, a reminder will be mailed to them with a copy of the survey along with a return envelope. A courtesy call will be made within 5 days post mailing. Every effort will be made to complete the survey at the clinic immediately after completion of the clinical encounter as this offers the best chance for complete data collection.

Data from the medical record will be abstracted for all enrolled patients to capture demographic, clinical, and medication prescription and fill data. The time frame for collection will be from prior to enrollment to 6 months post enrollment. For patients who do not have any encounters at the clinic in the 6 months post enrollment, we will call the patient (number of attempts as authorized by the IRB), followed by a postal survey if nonresponse persists. In addition, a scan will be conducted up to 6 months after the 6-month timeline to verify continuity of care at the institution, change in contact information and/or survival status. Of note, this 6-month data collection timepoint is for assessment of outcomes; no recollection of the actual encounter is required nor expected.

4.4.3 Adverse Events Definition and Reporting

Potential risks to patient subjects should be minimal. Given that the intervention has been pilot tested and no adverse outcomes occurred, we do not expect early termination due to harm. The intervention is a communication tool (a set of conversation cards) for use during the clinic visit to help patients discuss issues related to their life with diabetes. The tool does not make recommendations or result in prescriptions without the participation of the clinician, and the tool is not to be used outside a clinical visit in which a clinician can place the information in context. All patients randomized to the intervention will receive the standard of care.

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB (using the appropriate forms from the website) and to the funding agency (NIDDK). The investigator will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project through regular study meetings, and additionally via email as they are reviewed by the principal investigator.] The protocol's research monitor(s), i.e, NIDDK, and regulatory and decision-making bodies will be informed of serious adverse events within 5 days of the event becoming known to the principal investigator.

4.5 Study Schedule

In the spirit of minimally disruptive research, all study activities will occur within scheduled appointments, avoiding the need for additional research-only visits, unless patients prefer to complete them remotely by phone, electronically, or by mail. See Table 1 in Section 4.4.1 for the exact timing of data collection.

4.6 Informed Consent

Consent forms describing in detail the study intervention, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting intervention/administering study intervention. The process of obtaining informed consent will minimize undue influence or coercion and offer sufficient time for review. The following consent materials are submitted with this protocol:

- Patient consent form
- Clinician consent form.

4.6.1 Screening (if applicable)

As in our prior practice-based trials, eligible patients will be identified through appointment lists by a trained study coordinator who will recruit eligible patients via phone (asking patients to arrive early to their scheduled appointment to complete the consent process), or in person at the time of their scheduled visit. We will use EPIC (Fair Haven uses this EMR) to identify all patients with HbA1c values >8% within 6 months and closest to or at the time of the appointment office visit; then, a study coordinator will review each chart to assess for exclusion criteria, and approach potentially eligible patients. Clinicians will also review the list and identify patients for exclusion if HbA1c >8% target is reasonable.

4.6.2 Recruitment, Enrollment and Retention (if applicable)

This is a single-site study conducted at the Fair Haven Community Health Center including 10-15 clinicians (physicians, residents, nurse practitioners, and physician assistants) who participate in the care of patients with type 2 diabetes and prescribe medications for them and their 156 adult patients with type 2 diabetes. In order to focus our trial on a population in need of intervention, we will identify patients with poor glycemic control, defined as HbA1c >8%. Clinicians and patients will be recruited by the study coordinator and with support from Dr. Anne Camp. Based on data from 2020, there were 1,513 patients with diabetes at Fair Haven Community Health Center and 38% of them had a hemoglobin A1c above 8% (575 patients), with 390 patients with HbA1c above 9%.

Eligible clinicians will be recruited (in person or virtually, depending on the evolution of site-specific COVID-19 policies) after scheduled presentations at the health center and prior to a scheduled appointment with an eligible patient. As in our prior practice-based trials, clinicians are study participants themselves and must provide written informed consent to participate in the trial prior to enrolling their first patient.

As in our prior practice-based trials, eligible patients will be identified through appointment lists by a trained study coordinator who will recruit eligible patients via phone (asking patients to arrive early to their scheduled appointment to complete the consent process), or in person at the time of their scheduled visit. The study coordinator may also reach out to potentially eligible patients via text message. We will use EPIC (Fair Haven uses this EMR) to identify all patients with HbA1c values >8% within 6 months to and closest to or at the time of the appointment office visit; then, a study coordinator will review each chart to assess for exclusion criteria, and approach potentially eligible patients. The written informed consent procedure will take place in a private exam room prior to their scheduled appointment. In cases of changes due to the Covid-19 pandemic, the consent may also occur over the telephone with the patient signing either an electronic or paper /mail version of the

document. The study coordinator will explain the study, answer any questions, and assess whether participants understood the information about the study. The study coordinator will ask participants to explain in their own words what the research is about, the risks and benefits of the research, and evaluate their understanding of the consent process. In the spirit of minimally disruptive research, all study activities will occur within scheduled appointments, avoiding the need for additional research-only visits. At the time of enrollment, patients will also be asked to express their preference for how they prefer to be contacted for the 6-month outcome if a scheduled visit does not occur during that time (phone, text, email, mailed letter). Each potentially eligible patient will be entered in a patient log and all data will be collected via RedCap. A copy of the consent document will be given to the patient alongside details of the study and contact information for future reference. Staff will keep the original of the signed consent and fax/email a copy to the central office. We will not recruit any special vulnerable population including children, prisoners, and institutionalized individuals.

The primary patient reported endpoint of the study is change in illness intrusiveness (measured by the Illness Intrusiveness Rating Scale, IIRS) between the first visit and the following 6 months. The primary clinical outcome is the change in HbA1c between baseline and the following 6 months. Additional outcomes will include diabetes distress, treatment burden, hypoglycemia, quality of life, and clinical events. In order to ensure retention of participants in research, the following strategies will be used:

- We will clearly communicate our long-term commitment to improving diabetes outcomes of the community. The study coordinator has a long-term history of working at Fair Haven and conducting research on site.
- We will clearly explain to participants the requirements of the study, including the need to collect 6-month outcome data.
- We will be flexible and collect data during already scheduled routine appointments closest to the 6-month time point in order to remain minimally disruptive.
- We will obtain several phone numbers (home, work, cell) for participants so that we can follow up with them easily.
- We will include a written reminder to participants to expect a follow up call 4-6 months after the baseline visit.
- We will offer participants small tokens of appreciation for participation which will include \$25 gift cards during the baseline visit and \$25 for the 6-month completion of study data.
- We will offer participants who are asked to come in early for their point-of-care HbA1c but who do not meet eligibility criteria for the study a \$10 gift certificate for their time.

To ensure participation of clinicians, we have partnered with Dr. Anne Camp, who has been working at Fair Haven for decades now. In addition:

- We will hold a session for clinicians to explain the study (but not the hypotheses) and our commitment to the community.
- We will report research results in formats most useful to clinicians. To accommodate their busy schedules, we will provide a handout that summarizes the findings more succinctly than a journal publication.

- We will provide a gift card for participation (\$200 per participating clinician) to recognize their contributions.

4.6.3 Study Visits (is applicable)

As noted above, in the spirit of minimally disruptive research, all study activities will occur within scheduled appointments, avoiding the need for additional research-only visits, unless patients prefer to complete them remotely by phone, electronically, or by mail.

4.7 Statistical Method

4.7.1 Statistical Design

This clinician-level cluster randomized trial compares the impact of QBSafe ASK (agenda setting kit) embedded in usual care versus usual care alone on illness intrusiveness and glycemic control. The intervention is designed to support patients and their clinicians in identifying aspects of life with DM2 and of diabetes care that require problem-solving discussions. The trial will be registered at ClinicalTrials.gov and the protocol adheres to standard SPIRIT recommendations.

Given the risk of contamination associated with patient-level randomization, we will cluster randomize at the level of the clinician. The trial statistician, Mrs. Branda, will produce a computer-generated random sequence for allocating (on a 1:1 ratio) eligible clinicians to offer care as usual alone or care as usual with QBSafe ASK. The study coordinator will assess eligibility and enroll patients into the trial using the REmote Data Capture (REDCap) system. Except for patients and clinicians, who will be informed that the trial will be testing different ways of conducting diabetes care encounters and be blind to the specific hypotheses of the trial, all study personnel will be able to discern participant allocation.

4.7.2 Sample Size Considerations

Sample size estimations: As we have a fixed number of clusters (N=10 clinicians, 5 per arm),⁷⁹ we determined the detectable effect size on the trial's primary endpoint (IIRS) based on the following assumptions: (a) a standard deviation for IIRS of 14.1; (b) a clustering effect based on a conservative intra-cluster correlation (ICC) of 0.025 (at the upper boundary of the interquartile range for ICCs found in a review of primary care studies across multiple outcomes [median ICC of 0.005 (IQR 0 to 0.021)] and of a large DM2 study [0.0185 (IQR 0.006, 0.037)]); (c) as sample sizes may vary per cluster, we used a coefficient of variance of 0.40; (d) 80% power; (e) two-sided test with alpha = 0.05. Based on these assumptions, we will be able to detect a mean between-arm difference of 7.5 points on IIRS with 13 patients per clinician (N=65, per trial arm). A difference of 7.5 on IIRS between arms is over half of the measure's standard deviation which surpasses the minimally important difference criteria.⁸⁰ To account for potential attrition, the sample size is increased by 20% to 156 patients (78 per arm). Our intent is to have enough power to detect important differences in patient reported outcome measures and in changes in glycemic control. Under the same assumptions listed above, and assuming a standard deviation on the difference in HbA1c of 0.6%,⁸¹ we estimate we have 77 and 99% power to detect a between-arm difference in HbA1c at 6 months of 0.3 and 0.6%, respectively.

4.7.3 Planned Analyses

To determine the *feasibility* of the research procedures necessary to conduct a practice-based randomized trial to determine the clinical effectiveness of QBSafe ASK in the care of patients with DM2 and poor glycemic control. Achievement of this aim will require assessing the feasibility of (a) our methods for recruitment (including screening for eligibility), as well as

the success rates for recruitment and retention of trial participants; (b) completion of study procedures, including the percent complete collection of patient reported outcome measures; (c) assessment of the fidelity with which the intervention was used in audiovisual recordings of clinical encounters; and (d) percent complete collection of data on effectiveness endpoints, namely HbA1c levels and emergency healthcare utilization.

Participant recruitment and retention: The study coordinator will note the time spent and the number of records reviewed to estimate the effort necessary to find eligible patients. We will document in a recruitment tracking log all potentially eligible patients found to be ineligible or those who decline participation. The reason for ineligibility or reason for decline will be captured along with age, sex, race, and ethnicity. This will allow us to determine how many patients need to be screened in order to recruit patients to participate in a future trial. In addition, we will determine the attrition rate, i.e., the proportion of participants who cannot be reached to perform the 6-month assessment of DDS and TBQ, our primary and secondary outcomes, respectively.

Patient-reported outcomes measure collection: We will determine the proportion of patients and clinicians who complete each and all of the patient reported outcomes measures and determine the completeness of surveys returned. We will keep track of how surveys are filled out, the time needed to do so, the need for assistance from study personnel, and evaluate whether survey format (paper immediate, paper delayed (postal) or electronic) affected data collection.

Fidelity of the Intervention: Trained observers will use a checklist to review recordings obtained in both trial arm and describe the extent to which the QBSafe ASK was used as intended during the encounter in the intervention arm (where it describes fidelity) and in the control arm where, if it happens, would describe contamination.

Collection of effectiveness endpoints: We will determine the timing, timeliness, and completion rate of routinely collected HbA1c levels from EMR, as well as frequency of healthcare utilization for hypoglycemia, hyperglycemia, diabetes-related events, and for any cause, at 6 months post-encounter, for both groups.

Clinician and staff assessment: To capture the potential for QBSafe ASK to become embedded in practice in a future large effectiveness trial, participating clinic staff and clinicians will complete the NOMAD survey, a 23-item instrument that captures barriers and facilitators to the adoption of new interventions in clinic routine,⁷⁸ based on Normalization Process Theory.⁸² This will be done after the last patient completes their QBSAFE clinic visit.

Since a definitive trial will require evidence of efficacy, we will power this trial to also estimate the extent to which, compared to usual care alone, usual care with QBSAFE ASK can improve:

Patient-reported outcomes, principally illness intrusiveness (measured with the Illness Intrusiveness Rating Scale), as well as diabetes distress (measured with the Diabetes Distress Scale – DDS-17), treatment burden (measured with the Treatment Burden Questionnaire), hypoglycemia, and global quality of life (measured with a 1-item analogue scale) from baseline to 6 months post intervention.

Clinical outcomes, measured as change in HbA1c between baseline and 6 months.

Patient-centered diabetes care judged by (a) rating the audiovisual recordings of clinical encounters (including the total visit time and the time spent discussing QBSafe domains), and (b) patient satisfaction (using the ambulatory CAHPS survey) and clinician satisfaction (using post-encounter clinician satisfaction survey) with how the encounter went.

Completing analyses and reports: The study will be conducted and analyzed according to the intention-to-treat principle, including all clinicians and patients enrolled in the arm to which they were randomly assigned. Full reports will include cohorts with complete data and intention-to-treat cohorts in which imputation methods will be used to address missing data (where data is missing > 10%). The measure of fidelity will enable a secondary per-protocol analysis including only encounters that were adherent to the protocol.

Baseline characteristics will be reported in the study results with continuous values being reported as means and standard deviations and categorical values reported as counts and frequencies. Baseline characteristics will be assessed for clinical and statistical differences, which – if seen – will be accounted for in regression models that adjust for intervention arm as well. Any baseline imbalances ($p < 0.05$) will be explored as possible factors to adjust main analyses. As the clinician is a clustering effect, a hierarchical generalized linear model (HGLM) will be conducted to assess each outcome of interest. This is an appropriate approach for analyzing clustered data and will allow us to account for potential imbalances between arms. For analysis of the outcomes collected prior to visit and at 6 months post enrollment (IIRS, DDS-17, TBQ, quality of life, HbA1c, hypoglycemia, medication adherence, and healthcare utilization), the 6-month response/value will be modeled adjusting for the baseline value, arm of interest and random effect of clinician. If the baseline value is missing, a dummy variable will be included in the model to indicate missing or not so that the patient's response can still be assessed. Mean difference between arms with a 95% confidence interval will be reported. Results will adhere to the CONSORT guidelines for cluster randomized trials to ensure transparent reporting to allow for assessment of the trials soundness.^{83,84}

Next, we will explore potential interactions between the intervention and pre-specified patient factors (age, sex, health literacy, and language). While we are not powered to test for these interactions given the pilot nature of the trial, we will explore any trends that should be accounted for in further work with a sufficient sample size. To conduct this analysis, the models will be extended using interaction terms to examine several types of heterogeneity of treatment effect (HTE) due to possible changes or improvements in effectiveness of the intervention (interaction of intervention with patient characteristic). These will be reported in study findings as appropriate.

For video-graphic analysis, we will determine visit duration, time spent on discussion of each QBSafe domain, who initiated the discussion, and whether and how clinicians addressed each of the concerns raised. Separate analyses will be conducted to explore conversations about weight and weight loss during these encounters. We will develop a codebook to define aspects of weight and weight loss discussions based on the existing literature and clinical input. The domains coded will be determined a priori and include: time spent discussing weight, who initiated the discussion (patient or provider), categories of words used during discussion, types of recommendations made for weight management, and nature of the discussion. Two coders working independently will review each video recording after ensuring they can agree on their codes ≥90% of the time. Descriptive analyses will be used to summarize findings. We will then compare the findings between encounters with clinicians and patients in the QBSAFE vs control arm of the trial.

4.7.4 Analysis of Subject Characteristics (if applicable)

Baseline characteristics will be reported in the study results with continuous values being reported as means and standard deviations and categorical values reported as counts and frequencies. Baseline characteristics will be assessed for clinical and statistical differences, which – if seen – will be accounted for in regression models that adjust for intervention arm

as well. Any baseline imbalances ($p < 0.05$) will be explored as possible factors to adjust main analyses.

4.7.5 Interim Analysis (if applicable)

Not applicable.

4.7.6 Handling of Missing Data

We will make every effort to minimize missing data. Trial enrollment and the fidelity of follow-up procedures will be reviewed during bi-weekly conference calls. A study biostatistician will conduct frequency reports to assess for missing data, and the study team will troubleshoot any problems encountered. We will report rates of missing data for each outcome by study arm and send missing data reports to sites. Should data be found to be missing at a greater than 10% rate within an outcome, and the missing data is determined to be Missing At Random (MAR) then we will use multiple imputation as a sensitivity analysis where imputed findings will be compared to results of complete data findings where both will be reported for transparency.

5 Trial Administration

5.1 Ethical Considerations: Informed Consent/Assent and HIPAA Authorization

a. Informed Consent and Recruitment

Prior to initiating the study, all subjects (clinicians and patients) will provide written informed consent using standard consent forms. Consent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. One of the medical doctors (PI or site PI, neither involved directly in caring for the potential participant), or a trained study coordinator, will explain the research study to the participant and answer any questions that may arise. This conversation will take place in a private room, or – depending upon Covid-19 precautions – may occur over the phone, prior to the patient arriving for the office visit. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants will have the opportunity to discuss the study with their family or surrogates (if they wish to do so) or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants will be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. For participating patients, permission to review the medical record for research purposes will be obtained using informed consent (compound authorization). There will be modest monetary reimbursement to participants, including patients and clinicians. All recruitment materials and contact will be approved by the Yale IRB and adapted to be consistent with evolving COVID-19 procedures.

b. Protection against risk

Confidentiality: The research team is committed to protecting the confidentiality of information obtained in connection with this research study. We will follow several procedures in order to protect participant's and clinician's confidentiality. Each participant will be given a unique study code that will be used instead of their name or other personal information for the purpose of identifying and tracking all participants in the study. All information will be stored electronically using REDCap which is HIPAA compliant. Any electronic files in this study will be immediately transferred to secure and password-protected servers which only authorized research personnel will have access. Using a

HIPAA compliant procedure governed by a Yale-Mayo data use agreement and following protocols the Mayo team has perfected in prior multicenter federally funded trials, we will use SharePoint to transfer audiovisual recordings with direct identifiers (voice, video, or audio recordings, and/or voice print data) to the Mayo site. At Mayo, these files will be saved in secure password-protected servers behind the institutional firewall with logged access set up for analyses. All information reported in any published medical journals or scientific discussions, will include aggregate and non-identifiable data.

Specific Risks and Precautions Proposed: Information about illness intrusiveness, diabetes distress and treatment burden are important for delivery of high-quality care. Some patients may report high levels of illness intrusiveness, diabetes distress, or treatment burden. We will work with practice leadership to develop protocols that respond to high levels of distress; while this may affect patient reported outcomes in both arms, we feel that leaving an overwhelmed distressed patient without access to intervention would not be ethical. In addition, some patients may feel discomfort or embarrassment when issues of cost or nonadherence are discussed; we believe these emotions will be minimized because patients will identify these issues, rather than clinicians. Time spent answering the survey questions may pose an inconvenience. Clinicians may feel discomfort or lack of expertise addressing concerns raised by the patients with the use of the QBSafe cards. Finally, both patients and clinicians may feel discomfort with the use of video recordings during the office visit. Several precautions will be used. First, participants will be assured that all patients in the study will be asked the same survey questions. Participants can choose not to answer any questions that they do not feel comfortable answering during the study. They may also voluntarily withdraw from the study at any point. If they do not feel comfortable with video recordings, they can choose an option of audio recording only. The data collection for the study as well as the medical record review could result in the risk of confidentiality breach, but the risk will be minimized by the procedures described above in the Confidentiality section.

Required Coursework - Responsible Conduct of Human Research by Study

Personnel: Yale University and its component parts, including the Yale School of Medicine, believe that all individual research and research training activities should be conducted in a scientifically responsible and ethical manner. Towards this goal the University has developed principles and practices to ensure the highest possible standards for conducting research: *A Guideline for the Responsible Conduct of Research at the Yale University School of Medicine*, first published in 1991, defines the responsibilities of researchers and institutional officials and describes accepted standards for the conduct of research. This document specifically discusses issues related to management of data, authorship of scientific papers, and the evaluation of research. *Policies and Procedures for Dealing with Allegations of Academic Fraud at Yale University* details procedures for dealing with allegations of academic fraud at the University. *Yale University Policy on Conflict of Interest and Conflict of Commitment* is intended to increase the awareness of faculty, staff and students to the potential for conflicts of interest and commitment, and to establish procedures whereby such conflicts may be avoided or properly managed. *Yale University Patent and Copyright Policies* provides further guidance to trainees in the areas of ownership of data. *Human Subject Research Protection and Institutional Animal Care and Use* policies and procedures aid members of the Yale research community in fulfilling their obligations to ensure that research is designed, conducted, and approved consistently and in compliance with applicable laws, regulations and Yale's commitments to the responsible conduct of research. Yale University also requires training of all faculty and staff who deal with human subjects, human subject data, or utilize animals in their research in the protection of human subjects and animals. These courses are managed by Yale's Human Research Protection Program and the Institutional Animal Care and Use Committee.

All Yale investigators and all investigators from Fair Haven Community Health Center have completed the Yale IRB's mandated certification in the responsible conduct of research.

c. Vulnerable Subjects

No vulnerable populations will be involved in this study.

5.2 Institutional Review Board (IRB) Review

The protocol will be submitted to the IRB for review and approval. Approval of the protocol will be obtained before initiating any research activity. Any change to the protocol or study team will require an approved IRB amendment before implementation. The IRB will determine whether informed consent and HIPAA authorization are required.

A study closure report will be submitted to the IRB after all research activities have been completed.

5.3 Subject Confidentiality

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, representatives of the Institutional Review Board (IRB), or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at the clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or, if applicable, sponsor requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored electronically using REDCap which is HIPAA compliant. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the Yale on a secure server.

Because the study will rely on a statistician who is at the Mayo Clinic, data will be shared with Mayo. Using a HIPAA compliant procedure governed by a Yale-Mayo data use agreement and following protocols the Yale-Mayo team has perfected in prior multicenter federally funded trials, we will use SharePoint to transfer audiovisual recordings with direct identifiers (voice, video, or audio recordings, and/or voice print data) to the Mayo site. At Mayo, these files will be saved in secure password-protected servers behind the institutional

firewall with logged access set up for analyses. All information reported in any published medical journals or scientific discussions, will include aggregate and non-identifiable data.

5.4 Deviations/Unanticipated Problems

Given that the intervention has been pilot tested and no adverse outcomes occurred, we do not expect early termination due to harm. The intervention is a communication tool (a set of conversation cards) for use during the clinic visit to help patients discuss issues related to their life with diabetes. The tool does not make recommendations or result in prescriptions without the participation of the clinician, and the tool is not to be used outside a clinical visit in which a clinician can place the information in context.

That being said, our team will (PI, Dr. Lipska) will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the study sponsor. The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number;
- A detailed description of the event, incident, experience, or outcome;
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- UPs that are serious adverse events (SAEs) will be reported to the IRB and study sponsor, if applicable within 5 days of the investigator becoming aware of the event.
- Any other UP will be reported to the IRB and study sponsor during an annual review.
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) during an annual review of the IRB's receipt of the report of the problem from the investigator.

Protocol deviations will be monitored by the PI and site PI and discussed during weekly team meetings. Site PI will directly supervise the study coordinator(s), observe study procedures and study documents. Dr. Camp, site PI, will review all data collected on an ongoing basis for data completeness and accuracy as well as protocol compliance. A statement reflecting the results of the review will be sent to the NIDDK in the annual report. Any serious protocol deviations will be reported to the IRB within 5 days of PI becoming aware.

5.5 Data Quality Assurance

All data will be collected according to a standardized protocol and directly into REDCap to ensure completeness and reliability. Research study staff have prior experience with participation in NIH-sponsored clinical trials. However, all study staff will be trained to understand study procedures, and will participate in the development of the study procedures manual. All study staff will be supervised by the study PI. Dr. Camp, site PI, will review all data collected on an ongoing basis for data completeness and accuracy as well as protocol compliance.

5.6 Study Records

Study records will include study protocol, consent forms, HIPAA forms, case report forms, surveys, data abstracted from the medical record, and audio-visual recordings.

5.7 Access to Source

Source data will be maintained per Medical Records policy in a password protected, secure, Health Insurance Portability and Accountability Act (HIPAA) compliant, web-based electronic database with a built-in audit trail (REDCap). Video data will also be stored in a password-protected encrypted external hard drive.

Only Institutional Review Board (IRB) approved research team members who have current HIPAA and Collaborative Institutional Training Initiative (CITI) Good Clinical Practice (GCP) and human subjects protection training will be authorized to access records.

5.8 Data or Specimen Storage/Security

All information will be stored electronically using REDCap which is HIPAA compliant. Video data will also be stored in a password-protected encrypted external hard drive. Any other electronic files in this study will be immediately transferred to secure and password-protected servers which only authorized research personnel will have access. Using a HIPAA compliant procedure governed by a Yale-Mayo data use agreement and following protocols the Mayo team has perfected in prior multicenter federally funded trials, we will use SharePoint to transfer audiovisual recordings with direct identifiers (voice, video, or audio recordings, and/or voice print data) to the Mayo site. At Mayo, these files will be saved in secure password-protected servers behind the institutional firewall with logged access set up for analyses. All information reported in any published medical journals or scientific discussions, will include aggregate and non-identifiable data.

5.9 Retention of Records

In order to comply with federal regulations, study records will be retained for at least 3 years with plans to retain de-identified study data for 9 years. The master list linking the unique subject number to the research data will be destroyed as soon as is feasible (data entered and cleaned) and, at the latest, by the end of the study.

5.10 Study Monitoring

Data and safety monitoring are essential for the integrity of the clinical trial. Data and safety monitoring will be conducted by Dr. Lipska as described in detail below. Since this is a Phase II study of a behavioral “low risk” intervention and the study population does not include vulnerable subjects, a formal Data Safety Monitoring Board (DSMB) is not required nor necessary.

The study includes a behavioral intervention (use of QBSafe conversation cards during clinical encounters) and it is expected to result in low risk of adverse events of any kind. Expected risks include discomfort with responding to the QBSafe topics raised with the use of cards, discomfort with audio-visual recordings of the clinical encounters, and risk of confidentiality breach. Adverse events will be monitored by the trained study coordinator on site at Fair Haven Community Health Center and by the site PI, Dr. Camp, and reviewed during weekly team meetings. Any serious adverse events (SAE) will be reported to the IRB and NIH/NIDDK as soon as they are known and no later than 5 business days from their report. Safety and study progress reviews will be reviewed *monthly* during the proposed duration of the trial. Review will be conducted by Dr. Lipska and Dr. Camp, with participation of the study statistician, Mrs. Branda. The safety review plan will address whether adverse events are consistent with pre-study assumptions, reasons for dropouts from the study, whether all participants met entry criteria, whether continuation of the study is justified on the basis that additional data are needed to accomplish the study aims, and conditions whereby the study might be terminated prematurely (e.g., voluntary dropout of >40% of cohort). Study participants would be precluded from participation if they no longer met inclusion/exclusion

criteria for the study or chose to voluntarily withdraw from the study. The measures to protect participants against foreseeable risks are described in the section titled Protection of Human Subjects. Specifically, we will utilize:

- Informed written consents for the study for both the clinicians and patients participating in the trial;
- Protections to safeguard subject privacy (all information will be securely stored with access to study staff only);
- Monitoring and disclosure of any conflicts of interest that may potentially challenge participant safety or bias the data;
- Data security system in place to protect the confidentiality of the data (password protected encrypted electronic records).

Dr. Camp, site PI, will review all data collected on an ongoing basis for data completeness and accuracy as well as protocol compliance. A statement reflecting the results of the review will be sent to the NIDDK in the annual report.

Dr. Lipska (PI) will be ultimately responsible for data monitoring and will obtain a weekly report from the statistician. No outcome data will be reported to the study PI until after the study has been completed. The study statistician will complete all monitoring of the endpoint data. The electronic data (e.g., HbA1c) will be drawn from the electronic medical records of participating practices and entered into REDCap.

We will not use names on any research data (e.g. surveys), but rather a unique study code number. The link between the code number and study participant's identity will be stored in a remote data capture (RDC) system behind the firewall in a secure Yale research server accessible only to study personnel. Medical records will be abstracted electronically using encrypted computers. Names of those who decline participation in the study will be maintained in a do-not-contact list, so they will not be contacted again. We will maintain secure locked file cabinets and electronic records where protected health information is stored. In the clinical environment, consenting of subjects will occur in private areas (e.g. in examination rooms, not in the lobby or busy hallway).

The PI (Dr. Lipska) will take responsibility to ensure that the proposed study is registered on ClinicalTrials.gov prior to enrollment of the first participant. Dr. Lipska and the research team will take responsibility for updating information on the website as the study moves from active enrollment to completion.

5.11 Study Modification

Any changes to the study team, funding, design/methods, or any materials used for participant recruitment, enrollment, follow up, or data collection will be submitted to the IRB for approval before they are implemented.

5.12 Study Completion

This is a 3-year study with funding starting 4/1/2022. The study will be completed by 3/30/2025 and the PI holds responsibility for notifying the IRB when the study is completed. A study closure report will be submitted to the IRB after all research activities have been completed.

5.13 Funding Source

Salary support for this study is provided by NIH.

5.14 Conflict of Interest Policy

The QBSafe intervention under evaluation is not part of any existing effort to commercialize or profit from its use; the researchers involved in this study have not received -- and will not receive with their application in this study -- any royalties or other monetary benefits, directly or indirectly, from the use of the conversation cards. The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical.

Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the trial. All study group members will be asked to disclose all conflicts of interest and the study PI will establish a mechanism for the management of any and all reported dualities of interest.

5.15 Publication Plan

The Study PI (Dr. Lipska) holds primary responsibility for publishing the study results and reporting them to clinicaltrials.gov. All information reported in any published medical journals or scientific discussions, will include aggregate and non-identifiable data.

1. Appendices

Appendix #	Title	Section	Topic
1	Patient survey questions		
2	Clinician survey questions		

References:

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