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Enhanced Quality in Primary Care for Elders with Diabetes and Dementia (EQUIPED-ADRD) – R33 Trial

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Statement of Compliance

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), any other applicable US government research regulations, and institutional research policies and procedures. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

List of Abbreviations

AE	Adverse Event/Adverse Experience
DSMB	Data and Safety Monitoring Board
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IRB	Institutional Review Board
MOP	Manual of Procedures
N	Number (typically refers to participants)
NIH	National Institutes of Health
PI	Principal Investigator
SAE	Serious Adverse Event/Serious Adverse Experience
SOP	Standard Operating Procedure
US	United States

1. Purpose of Study and Background

1.1 Purpose

The purpose of EQUIPED is to test and evaluate a care quality improvement intervention featuring use of consensus decisional guidance for the medical management of diabetes (DM) patients with Alzheimer's and other forms of dementia (ADRD) in primary care at NYU Langone Health. This quality improvement program will include provider (PCP) workflow enhancements supported by a panel manager (PM) for workflow support, electronic health record (EHR) decision support and feedback, and PCP collaborative learning.

It will test hypotheses about whether care based on explicit standards for DM medical management for people with ADRD will: **H1)** Improve patient symptoms and quality of life while maintaining expected clinical outcomes; **H2)** decrease patient and caregiver management burden and improve care quality based on patient/caregiver preferences;**H3)** (secondary) decrease specialty, ED and hospital utilization.

In order to test and evaluate this program, we will conduct a pragmatic randomized controlled trial (RCT) and evaluate it using mixed methods (surveys and interviews) in 20 NYU Langone Health clinics with the enrollment goal of 500 patients with diagnosed DM and ADRD in the intervention (INT) and control (CON) group (1,000 total).

If EQUIPED demonstrates that patients and family caregivers who receive this quality improvement program achieve established goals for diabetic care in addition to fewer dementia-related symptoms, less caregiver burden and stress, and fewer DM-related adverse events, potentially avoidable and costly utilization may also decrease. This best practice approach could then be widely disseminated to other clinical practices.

1.2 Specific Aims

Specific Aims of the R33 Enhanced Quality In Primary Care for Elders with Diabetes-ADRD (EQUIPED-ADRD) are:

1) Implement and evaluate a pragmatic trial in a large healthcare system using cluster randomization, and the practice change framework, that will: manage people with co-occurring DM and ADRD according to the guidelines developed to test our hypotheses and identify additional patients with cognitive impairment and inappropriate DM management.
2) Test whether EQUIPED-ADRD will increase the proportion of intervention patients who are in desirable glycemic and blood pressure ranges compared to control patients.
3) Test whether the EQUIPED-ADRD intervention will improve dyad perception of care quality and reduce treatment burden.
4) Test whether dementia symptoms will deteriorate less in intervention subjects compared to controls.

Exploratory Aim. Test whether intervention subjects will use fewer health care services than controls and will have less cognitive decline associated with desired changes in glycemic and blood pressure control.

1.3 Background

Over 11 million Americans ≥65 years have Diabetes (DM)[1], a prototypic chronic disease requiring self- management.[2] While the linear increase in prevalence of Alzheimer's disease and related dementia (ADRD) associated with increasing age is well known, diabetic patients of similar ages may have as much as a two-fold risk of developing cognitive impairment and ADRD.[3–6] Emerging evidence suggests pathophysiological links between DM and both AD and microvascular dementia.[7,8] DM management is complex and includes management of co-existing risks, complications and related diseases (hypertension, cardiovascular and microvascular disease). Cognitive impairment likely challenges diabetic self-management placing responsibility and additional stress on family caregivers. Management complexity requires logistical skills, complex decision- making and understanding of risks and disease trajectories so caregivers must be deeply involved in managing DM in dementia patients. Some patients with DM and ADRD are not diagnosed and/or recognized as cognitively impaired[9] and their caregivers may be insufficiently involved, unrecognized or unsupported, further challenging DM management.

Over and under treatment of DM and its medical complications in some ADRD patients,[10] increased hypoglycemia risk,[6,11] and caregiver burden are well documented.[4,12] Adding to the complexity of the co-occurrence of DM and ADRD is the heterogeneity of patients in age, ADRD and DM severity, race/ethnicity, health status, and life expectancy.[13] This heterogeneity argues strongly for a pragmatic trial[14] within a healthcare system representing patient and clinical system diversity. ACCORD,[15] ADVANCE,[16] and related studies provide substantial trial and observational evidence about DM management in elders and DM's relationship to dementia, but clinical uncertainty exists. This suggests that health priorities and preferences of DM-ADRD patients and caregivers should help direct DM management. But the push towards value-based payment and the focus by healthcare systems and payers on diabetes quality metrics that may not apply can lead to particular confusion about management of DM in ADRD patients.

The relationship between diabetes and dementia: Underlying the co-occurrence of DM and ADRD is a 1.5-2.5 times increased risk DM patients have for ADRD.[9,35,36] Pathophysiological links underlie this increased risk and substantial research is directed to find new treatment targets for both conditions.[7] A 2012 meta- analysis found that DM increased risk for AD, vascular and other dementia, and mild cognitive impairment.[37] Vascular dementia may mediate the relationship between DM and AD, making AD clinically apparent.[8] To capture clinically detectable risks, a recent international collaboration developed an empirically validated risk score to predict 10-year dementia risk in DM with reasonable predictive validity.[38] Regardless of causal links, the co-occurrence of DM and ADRD presents a significant challenge for clinicians, patients and CGs because these co-occurring diseases increase clinical uncertainty, complicate management of both conditions, and too often lead to care burden and poor outcomes for patients and CGs, and confusion and frustration for providers.

Cognitive impairment may be undetected in DM: Cognitive impairment and dementia are frequently undetected in DM, leading to poor quality of care for both conditions.[21,35] DM patients with unrecognized cognitive impairment may have trouble with self-management, which could

lead to under- or over- treatment of hyperglycemia, hypertension[9] and poor adherence to diet and exercise.[3] The American Diabetes Association (ADA) and the American Geriatrics Association (AGS) Guidelines advocate screening for ADRD in DM.[39–41] A European intervention to screen DM patients for cognitive impairment is underway[42] and the VA has developed an administrative screen for veterans at risk for hypoglycemia.[10] Multiple screening tools exist for detecting ADRD.[43] One of the most studied and practical is the Mini-Cog™,[44] a brief dementia-screening test created and validated by Dr. Soo Borson (a member of our study team). This has been cited in numerous studies comparing the feasibility and accuracy of several tests.[45]

Patients with DM-ADRD experience DM over-treatment and under-treatment: Diabetes care includes management of hyperglycemia, blood pressure, hyperlipidemia, and monitoring for microvascular and macro- vascular complications, using pharmacologic and non-pharmacologic (diet and exercise) management.[39,46] DM-ADRD patients experience worse DM monitoring,[21] poor non-pharmacologic treatment,[3] and have worse metabolic outcomes than patients with DM alone.[28,35] Under-treatment can potentially lead to symptomatic hyperglycemia such as polyuria, increased infections, weight loss and fatigue. Over-treatment can potentially lead to hypoglycemia, acute confusion, and health care utilization. VA research has shown potential over-treatment of hyperglycemia in veterans with ADRD and DM, ranging from over 50-63% of high risk veterans having HbA1c<7%.[10] Hypertension in DM can be over- or under-treated; ACCORD and ADVANCE provide evidence for moderate management of hypertension in DM.[15,16,47] Under-treatment of hypertension in DM has been well studied but there is VA evidence for hypertension over-treatment in routine clinical practice.[48] Cholesterol management by statins in older DM patients was not specifically readdressed in ACCORD or ADVANCE. In Enhanced Quality In Primary Care for Elders with Diabetes-ADRD (EQUIPED-ADRD) we aim to target glycemic and blood pressure (BP) management based on ACCORD and ADVANCE evidence to decrease both over and under treatment. During the R21 phase of this study we developed consensus decisional guidance related to glycemia (measured as “HbA1c”) and BP targets that also address monitoring for risks of complications, any new cholesterol recommendations, and non-pharmacological DM management with a goal of identifying safe, high quality management guidelines for DM-ADRD patients to be implemented in the R33 phase. These guidelines address 1) screening for cognitive impairment in older DM patients with out-of-desired range of HbA1c or BP but no ADRD diagnosis, 2) CG support, and 3) treatment based on CG preferences.

Hyperglycemia, hypoglycemia and cognition – a complex story: The relationship between cognition and hyperglycemia or hypoglycemia is complex. People with hyperglycemia perform more poorly on tests of cognition,[49,50] but ACCORD provided no evidence that intensive glycemic control improves cognition or prevents cognitive decline.[51,52] Although intensive glucose control in ACCORD was associated with more hypoglycemia,[53] lower baseline cognition was also associated with increased risk of severe hypoglycemic episodes in ACCORD-MIND[25]. Evidence that hypoglycemic episodes increase the risk of future cognitive worsening is less clear. In ACCORD-MIND/MRI, more hypoglycemic episodes occurred with intensive treatment but there was no difference in rates of cognitive decline between the groups[25] or MRI differences related to hypoglycemic episodes.[52] Observational studies suggest hypoglycemia may increase risk of dementia[23,24,54,55] but risks may be biased because hypoglycemia may occur in people with unrecognized ADRD which is subsequently recognized.[26] Although dementia severity is related to hypoglycemia, the role of glycemic control in causing or preventing hypoglycemia is less clear; thus, hypoglycemia is not an outcome in our study. However, utilization is a study outcome, so

we will observe and analyze hypoglycemia leading to clinic, ED or hospital use, adding to evidence about hypoglycemia's relationship to DM management in ADRD.

Family and friends provide 75% of daily care needs for patients with ADRD living in the community:[56] We refer to these individuals as CGs. When included with the person with dementia, we refer to these as dyads. CGs of patients with DM and CGs of patients with dementia report substantial CG burden.[27,57] A recent European study of CGs of DM-ADRD patients demonstrated increased supervision time.[12] CG burden is known to be linked to patients' behavioral problems, poor cognition, and increased dependency; a recent study demonstrates increased burden related to medications and medical care supervision.[58] CG stress is associated with poor outcomes for dementia CGs themselves, such as depressive symptoms often meeting diagnostic criteria for major depressive disorder[59] and ED visits or hospitalizations.[60] Decreasing CG stress improves outcomes for patients with AD[61,62];CG burden and stress are important outcomes for our study.

ADRD's increase healthcare utilization and costs for DM patients: A comprehensive analysis of 1999 Medicare claims data showed that all types of utilization and costs (hospitals, hospital outpatient, physicians, nursing homes and home health), were increased for dementia patients.[30] For Medicare beneficiaries with a dementia diagnosis, DM was present in 21% versus 16% of non-dementia patients. The same analysis showed significantly different crude rates of hospitalization/1000 beneficiaries (OR 3.36 [2.44-4.44]) for DM- ADRD vs. DM without ADRD. Data from 2007-08, focusing on potentially avoidable hospitalizations for ADRD patients, showed that Medicare costs and utilization are higher and the main driver of increased costs is increased hospitalizations.[31] ADRD patient admissions for short-term and long-term DM complications were higher compared to non-ADRD DM patients (OR: 1.43 [1.31-1.57] and 1.08 [1.02-1.14], respectively).

DM management in ADRD patients – summary of current evidence and gaps: Consensus on best management of DM in ADRD patients is lacking. High quality DM care in people ≥75 in general is undefined,[13] although there is consensus that DM management must be individualized in such patients.[39,40] Life expectancy for DM-ADRD is highly heterogeneous and substantially complicates DM management decisions. These issues add to clinical uncertainty and suggest that dyad care preferences and outcomes that matter to them, like decreased symptoms, decreased care burden, and decreased healthcare use, are important to consider in DM-ADRD guidelines.[63] Despite these challenges, research discussed above (mostly observational, some from trials) concerning DM-ADRD informs management approaches: moderate control of hyperglycemia and BP is appropriate, DM quality improvement is safe, feasible and may improve survival in older DM patients,[64] hypoglycemia is a major risk, "self"-management must be handled by CGs, and CGs need support. However, available evidence has not led to consensus decisional management guidance for patients/CGs and providers (international efforts are beginning),[35,42] or to practical, clinical quality improvement programs to address this. New value-based management makes evidence-based treatment guidance and meaningful outcomes important to define for DM-ADRD patients: The evidence reviewed above points to meaningful outcomes for the patient/CG dyad that high quality DM-ADRD care must achieve – CG support, decreased burden and attention to preferences; improved quality of life based on decreased symptoms and stable function for patients; and decreased healthcare utilization. Too often DM-ADRD patients are not represented in studies used for DM quality metrics and payers may not be aware of ADA and AGS positions. Our project will define high quality management and meaningful outcomes for this vulnerable, rapidly growing patient group.

2. Study Design

The design is a mixed methods evaluation of a pragmatic randomized controlled trial (RCT) of a clinical quality improvement program for patients with diabetes (DM) and Alzheimer 's disease and Related Dementias (DM-ADRD). The RCT will occur at NYU Langone Health and affiliated hospitals and clinics. We are using mixed methods (surveys and qualitative interviews) to better understand patient, caregiver (CG) and provider experiences and outcomes.

3. Subject Population

3.1 Total Number of Subjects and Sites

We will randomize the **20 largest NYU Langone Health primary care practices**, 9 Intervention **(INT)** clinics and 9 control **(CON)** clinics. We will enroll **1,000** patients (and their caregivers) ≥65 with diabetes (DM) and Alzheimers disease and other forms of dementia (ADRD) from these practices based on the Inclusion and Exclusion criteria below. As stated in inclusion and exclusion criteria, patients must have a caregiver who will also be enrolled. The patient and caregiver are referred to as a "dyad."

3.2 Inclusion Criteria

Patient:

1) Patient must receive care at one of the INT or CON clinics.
2) Patient must be 65 years and older.
3) Patient must have DM diagnosis.
4) Patient must have documented cognitive impairment **or** an ADRD diagnosis (ICD-10 diagnosis in Epic).
5) Patient must have someone who is identified as a family or friend who provides caregiving assistance.

Caregiver:

1) Caregiver must have adequate knowledge of identified patient and/or participate in that member's healthcare decisions.
2) Caregiver must be English or Spanish speaking.
3) Caregiver must demonstrate capacity to consent to research participation.
4) Caregiver must be at least 21 years old.

3.2 Exclusion Criteria

Patient:

1) Patient does not receive care at one of the clinics.
2) Patient is not 65 years and older.
3) Patient does not have DM diagnosis.
4) Patient does not have documented Cognitive impairment or an ADRD diagnosis.
5) Patient has end stage dementia, other terminal illness with <6 months to live, and/or is hospice eligible.

6) Patient does not have a caregiver**.**
7) Hearing too poor to use telephone.

Caregiver:
1) Caregiver does not have adequate knowledge of identified patient and/or does not participate in that member's healthcare decisions.
2) Caregiver is not English or Spanish speaking.
3) Caregiver lacks capacity to consent to research.
4) Caregiver is under 21 years old.
5) Hearing too poor to use telephone.

3.3 Vulnerable Subjects

Patients with cognitive impairment and their caregivers are a vulnerable group; however, the procedures employed in this clinical trial are low risk and have been successfully employed without incident in a number of other studies by this research team as well as by other investigative teams. The patient has the right to decline participation for any potential caregiver who assists them or direct the caregiver to withdraw participation at any time. See Section 5.2 for consent procedures that include a Capacity to Consent screen, to ensure subject comprehension.

3.4 Duration of Subject Participation

Participant dyads (patient and caregiver) will be in the study for a maximum of 24 months (surveyed at baseline, 6, 12 and 24 months). Only caregivers will complete surveys and interviews.

4. Quality Improvement Program – Description of the QI intervention

In this quality improvement program, INT and CON clinics will be provided with quality improvement activities for patients with diabetes and ADRD.

For both the INT and CON clinics:

We will provide decisional guidance (the guideline); materials about community and NYU Langone Health resources for managing patients with DM-ADRD, particularly caregiver support services; advice on referrals for both DM and cognitive specialty care; provider education, and basic feedback. We will try to identify a clinical champion in all INT and CON clinics.

We will receive some workflow support for the quality improvement program. This will include Epic-based EHR enhancements such as guidance for MiniCog^{TM} cognitive screening; provider scripts for decisional guidance discussions, especially for care de-escalation and cognitive screening results. Basic feedback and education will occur in both INT and CON clinics including yearly meetings with PCPs for education and feedback on DM and ADRD management.

Preparation for the PCPs will occur either before or very soon after the quality improvement program begins. The research team will meet with clinic providers and staff at a monthly meeting. PCPs will receive a 30-60 minutes in person training including introduction to the

decisional guidance, introduction to clinical resources and possibly other educational materials, such as templates and scripts.

Based on the guideline, providers will be encouraged to develop individualized management targets, particularly for HbA1c and BP, for each patient, and re-evaluate these targets over time. Providers will also be trained in cognitive screening with the MiniCog^{TM}. Clinic staff will be trained in minor workflow changes related to the intervention.

INT Clinics:

In the INT clinics we will introduce the panel manager (PM) to all clinic staff and develop processes for interaction. The PM will work with INT clinic providers to individualize communication methods between the PCP and PM. Each month INT clinic providers will get a list of eligible patients who have appointments with them in the coming month - those with diagnoses of DM-ADRD and those 75 and older with DM who are out of range for HbA1c or BP. This process gives providers monthly reminders about the ongoing quality improvement study and is a more intensive form of QI intervention than provided to CON clinics.

Because this is a pragmatic trial, the clinical team and a project-funded PM will deliver the intervention, fitting it as closely as possible into usual clinical workflow. The clinical team includes PCPs, occasional APNs and PAs (who function as PCPs), RN's, MA's, office staff, and clinic onsite administration. The PM will be part of the team; PMs providing chronic disease self-management support (usually telephonic) are clinic team members in many healthcare systems.

We will assign two PMs to 9 randomly selected INT clinics. Each PM will have 4.5 INT clinics and will engage and focus on their first clinics in a randomly ordered step-wise fashion working within 1-2 clinics over a focused 3-month period before moving on to the next 1-2 clinics for 3 months, then the last 1-2 clinics for 3 months. Our preliminary data suggests 20-50 patients per INT clinic with DM-ADRD ≥65 years; and about an equal number with DM without ADRD who will screen positive for cognitive impairment, most of whom are ≥75 years and identified by HbA1c/BP over or under treatment, or identified by provider referral, which we will allow. With 9 INT clinics, given our preliminary data about patient numbers, each PM will have an anticipated 300 dyads. PMs can engage about 33 patients/month, making initial 300 patient/CG contact in 9 months.

The PM will clinically decide how/which patients to engage in what order. We think that engaging DM-ADRD patients/caregivers around their PCP visit makes the most sense for the dyad, the PCP and the PM and we have established that process. However, as a clinician, the PM may identify other patients with significant needs and may engage them as soon as patient is identified (i.e. patient over 75 with poor BP control, social needs, and PCP suspects cognitive problem). For the INT clinics we think this approach will ensure 1) adequate time to engage all dyads with thorough evaluation for those who meet criteria for care quality improvement; 2) focused presence to engage and be known to the PCPs in that clinic; and 3) time needed to ensure initial follow-up of recommended actions to ensure that recommended care processes are completed. Supporting activities will continue for each previously engaged clinic when moving onto the next clinic. We anticipate patient/caregiver loss over the 3 years of the study and the sample will be refreshed with patients with new diagnoses and who are new to the clinic. Although these patient/caregiver dyads will be followed for shorter durations, they will be enrolled as discussed in 4.2 and they will contribute information until the end of the study.

PM Qualifications and Training: The PM will be a licensed healthcare professional, either an RN or pharmacist. She/he will meet all criteria needed for hiring and credentialing within the NYU Langone Health clinical enterprise. Required qualifications: RN or clinical pharmacist; 2 years' experience in licensed role. Preferred characteristics: Certified diabetes educator (CDE); geriatrics experience, Spanish fluency.

Because we plan to hire two PMs, a combination CDE who is also an RN, and a clinical pharmacist would provide complementary expertise, although a second RN would also be acceptable. As noted below, we plan that the PM will work mainly with particular clinics to develop relationships with providers and clinic staff, but we also anticipate that they will work on relevant cases in any clinic where complementary expertise may be useful. For example, if only one PM speaks Spanish, regardless of INT clinic, that PM would handle Spanish speaking dyads.

We will train intervention PMs in DM and ADRD management for INT clinics. Training will include one-on-one sessions with the mPI's and co-I's, suggested reading, shadowing relevant clinicians, such as social workers in the Alzheimer's Disease Center and geriatrics clinic, and other relevant activities. We expect training will require one month's duration with subsequent continuous learning activities that include continuing meetings with mPIs and co-I's and travel to national conferences.

PM Activities. The PM will reach out to eligible patients with diagnosed DM-ADRD (see section 4.3) and ≥75 year-old patients with over- and under-treatment of HbA1c/BP for cognitive screening using IQ-CODE as defined in the Guideline. For those with a positive screen, in coordination with the PCP, the PM will facilitate further cognitive evaluation. These patients will become part of the quality improvement intervention. The PM will begin telephonic assessment and DM management education of DM-ADRD patients around the time of the scheduled visit (either just before or just after). The PM will conduct a detailed psychosocial and needs assessment with each willing CG and assess the patient based on both a standardized assessment and clinical judgement. The PM will also engage those CGs who live far from the patient and who manage the patient remotely through paid home heath aids (HHA). The CG psychosocial assessment will focus on diabetic management support and family dementia CG support providing referrals as needed to well established New York City programs. The PM will provide PCPs with evaluation data, DM-relevant care suggestions and facilitate PCP visits for care reassessment as clinically appropriate. The PM will assist the PCP and the dyad with developing individualized DM management targets and re-evaluating these targets over time. The PM will maintain dyad follow-ups and monitor patient-level data using EHR follow-up data as per usual clinical care, and an Epic-generated report for relevant issues. The PM will also address dyad goals and treatment preferences and assist with communicating these with the PCP. A key part of PM activity will be determining with each PCP their preferred method of communication (e.g., Epic messaging, order pending, periodic phone calls, etc).

At primary care visits of DM patients with known ADRD or a positive cognitive screen, PCPs, coordinating with PMs, will proceed with DM management according to EQUIPED-ADRD Guidelines. PCPs will have PM information about CG stress, treatment preferences, and need for CG support referrals through the PM notes or Epic "in-basket" communications. PCPs will reassess as needed and encourage referrals. In patients with a positive cognitive screen, PCPs will follow guidelines for further cognitive evaluation per dyad preference. PCPs will have scripts to facilitate discussions, knowing that the PM will follow-up with the dyad after the visit. Clinic

workflow redesign is expected to be minimal. Providers will be alerted to the visit of relevant patients as described in the enrollment section and dyads will have an explanation of the EQUIPED-ADRD program through IRB approved brochures.

Over the 3 years of the study**,** the PM will continue to assist the dyad telephonically with DM-ADRD management support as clinically appropriate to meet management targets, communicating as needed with the PCP. EHR-generated reports on DM management will support intervention PCPs and PMs.

Provider Feedback. In the INT clinics, bi-annual reports will be given to providers and these will be discussed at bi-annual meetings which will be either by webinar or in person; in-person meetings will be held at least once a year. The provider–specific reports will detail DM-ADRD patients' medical management metrics such as numbers of caregiver referrals to community support, any changes in proportions of patients in range for HbA1c and BP, and the number of older adults with DM screened for cognitive impairment. Monthly patients lists will serve as periodic reminders of the quality improvement program. Other feedback and collaborative learning opportunities for INT clinic providers include quarterly "office hour" webinars with the mPI's and co-I's to review the reports and brainstorm opportunities for improvement.

CON Clinics:

Providers will get a list of eligible patients DM-ADRD initially, giving them the opportunity to follow the decisional guidance. In addition, the guideline will specify cognitive screening in DM patients, ≥75 years with high or low HbA1cs or BP's because we suspect that these values may represent self-management red flags due to cognitive (especially memory and executive) impairment. During training the CON providers will be encouraged to do cognitive screening as well as follow the guidelines in general. Clinics can decide who does the cognitive screen, such as a RN or MA, using the MiniCog^{TM} we will address this issue in the guideline and during provider training. Per guidelines, any patient with a MiniCogTM score < 3 of 5 should have further cognitive assessment per the guideline and preferences of the patient/caregiver dyad. These patients will also become eligible for the evaluation and can be identified by periodic research staff EHR identification of patients with DM-ADRD diagnoses in the CON clinics. When identified we will enroll them for the evaluation (4.2). As with INT clinic patients, we anticipate patient/caregiver loss over the 3 years of the study and the sample will be refreshed with patients with new diagnoses and who are new to the clinic. The investigators will visit CON clinics yearly to discuss care of patients with DM-ADRD. These meetings will serve to answer questions, get feedback from PCPs and provide general feedback on the progress of the quality improvement program.

5. Methods and Procedures (Evaluation)

5.1 Screening and Identification

We will use NYU Langone Health Epic to identify patients in the INT and CON clinics who meet inclusion and exclusion criteria listed in Section 3.2.

There will be three levels of screening:

- **Level 1:** Initial screening will be automated by settings in the EHR that generate a report based on inclusion criteria (above).

- **Level 2:** The initial list of patients generated by the EHR will be screened by the RA first through chart review for eligibility based on exclusion criteria (see Section 3.2). Should the patient not meet inclusion criteria, for example they don't actually have a diagnosis of diabetes, or speak English or Spanish; the patient will be removed from the list of potentially eligible patients.

- **Level 3:** Those patients who remain eligible following chart review to their PCP's in the INT clinics to notify them about their patients with DM-ADRD. The PCP's will be encouraged to review their list and decide if a patient is misclassified or inappropriate; some will review the lists and some will not. Any patient a PCP indicates as inappropriate or misclassified will be ineligible and will be screen failures. The amended list of eligible patients with both DM and ADRD for both the INT and CON clinics will go back to the RM who will send a letter to the patients informing the patients/caregiver of the quality improvement program and of a potential telephonic survey.

While eligible patients are easily identified by Epic, their caregivers (the respondents to the surveys and interviews to evaluate the quality improvement program) are not always listed in the patient chart. To identify an appropriate caregiver, a letter from the primary care physician will ask the patient to read the letter and then give it to their caregiver. The letter will explain the quality program briefly and state that a research assistant will call the patient's home unless they do not want to be called.

If the dyad, for whatever reason, does not want to participate in a call, they will be asked to opt out using the Standard Operating Procedure (SOP) of NYU Langone Health as outlined in SOP #HSR-312, Version Number 2.0. This SOP states that patients are able to opt-out of the Direct Recruitment process either by phone (1-855-777-7858) or email (research-contact-optout@nyumc.org). Patients who wish to opt out must provide at least three of the following identifiers:

1. Full name
2. Date of birth
3. Address
4. Medical record number

The opt-out phone line and email account are managed by Office of Science and Research (OSR) personnel. Authorized OSR personnel and the Senior Director of Compliance and Privacy are the only individuals authorized to add patients to the opt out list. Should we receive a patient opt out request we will instruct the patient to follow this process. OSR will process this request upon receipt of all required information, and update the patient status in a tracking sheet and in Epic to "Do Not Contact."

5.2 Consent Procedures and Documentation

5.2.1 Process of Consent

The patient and caregiver (dyad) is enrolled in the study (the evaluation of the RCT of a quality

improvement program) when verbal consent (or assent, see E3) is obtained from the patient and caregiver.

Verbal Consent

We are requesting a HIPPA waiver of authorization and documentation of consent in order for caregivers and patients to give verbal consent for the survey, qualitative interview and use of patient data (EHR and claims).

We request the use of verbal consent and a waiver for documentation of consent because:

1) This study presents no more than minimal risks to privacy for subjects. All survey data obtained will be stored in HIPPA compliant REDCap library accessible only to the IRB approved study team. All data exported from REDCap will be fully de-identified, and contain no subject identifiers.

2) It would not be possible to conduct this study without the use and analysis of subject PHI to evaluate the improvement in care for patients, and burden for caregivers. Investigators will take all precautions, outlined in Section 6.2 Protection Against Risks, to protect the privacy and maintain confidentiality of subjects.

3) Surveys and qualitative interviews will occur by telephone making written consent infeasible given enrollment of 1,000 patients and caregiver dyads.

4) Verbal consent provides opportunity to fully explain study procedures, risks and benefits and assess for capacity to consent, an important and necessary procedure in this population both for patients and caregivers.

5) It Requiring an elderly person to recall, interpret, and understand requested instructions for consent purposes through mail will result in many unreturned documents and an unfair prevention of participation for those persons who want to participate but are otherwise “unable” to.

6) Finally, in the clinical space, where HIPPA rules are equally enforced, we conduct verbal consents for release of information when written consents are not feasible and complete that authorization by documentation from a legally authorized representative (in this case, a physician).

Step by step process of consent:

1. **INT**: RA mails letter (see Patient Letter) to patients in INT clinic signed by the clinic director, lead physician, or primary provider (depending on clinic preference) informing them about EQUIPED quality improvement program and evaluation.

2. **INT and CON**: RA calls eligible patient and/or caregiver using contact information from patient chart in EHR. If caregiver information is not available in the chart, the RA will ask the patient for caregiver contact information.

3. **INT and CON**: RA screen Patient and/or Caregiver for Capacity to Consent (See section E3)
    a. If the patient demonstrates capacity, the patient is deemed able to provide verbal consent to have the study team talk to the caregiver to obtain their verbal consent

and to have the study personal obtain and analyze health data (medical records and claims).

b. If the patient does not have capacity and assents to the study, the RA is able to speak to the caregiver who provides verbal consent for the caregiver survey , and the Health Care Proxy (HCP) (who may or may not be the caregiver) provides verbal consent for study personnel to obtain and analyze the patients' health data (medical records and claims).
c. If the patient does not have capacity, and refuses (no assent), the dyad will not be enrolled although the clinical team (Panel Manager) can re-contact that dyad over time to offer improved care quality.

4. **INT and CON**: If the caregiver demonstrates capacity (screened using Capacity to Consent, at the discretion of the RA) verbal consent will be documented by the RA in REDCap and the caregiver will be consented to participate in the study. Caregiver consent covers participation in 4 telephone surveys.

A healthcare proxy is an individual who is designated as a representative/agent through a health care proxy signed by both the subject and the appointed representative/agent. For a health care proxy to be effective, it must have been signed at a time when the subject had decision-making capacity. In addition, the health care proxy must not specifically prohibit research. Determination of the legal authority of a surrogate will be obtained through Epic, or verbally by the patient and/or caregiver.

Potential subjects will be told that their involvement in the study is completely voluntary and that they can withdraw from the study at any point. Caregivers may themselves be elderly and might have cognitive impairment such that it impacts their capacity to consent to research. For all potential participants, we will assess the individual's ability to provide informed consent using IRB approved interview procedures to assess capacity to consent for research. Some subjects may be too hearing impaired to communicate by telephone and the telephone interview is designed to assess for this potential problem and mitigate this issue when possible but this might impair one's capacity to consent. Although we have conducted numerous studies with elderly subjects, this has been a rare occurrence. Nonetheless we will not enroll any caregiver participant who cannot communicate by telephone.

If the patient demonstrates capacity (See E3. Subject Capacity), the patient is deemed able to provide verbal consent to have the RA talk to the caregiver and to have the study personal obtain and analyze health data. If the patient does not have capacity and assents the caregiver will provide verbal consent for the caregiver survey, and the HCP (who may or may not be the caregiver) provides verbal consent for the health data (medical records and claims). If the patient refuses (with or without capacity), the dyad will not be enrolled although the clinical team can re-contact that dyad over time to offer improved quality care.

If the caregiver, after following our standard consent procedures, demonstrates capacity using the below questions, verbal consent will be documented and the caregiver will be consented to the study. Caregiver consent covers participation in 4 telephone surveys. Patient (with capacity) or HCP (if patient assents but does not have capacity) will provide verbal consent for health data (EHR and claims information). The research assistant will document this agreement to participate using a standardized form kept for documentation purposes.

Consent for Qualitative Interviews

Caregiver:

Consent procedures as previously described will be followed for those completing qualitative interviews. All who participate will provide verbal consent to be audiotaped (see 6.2 Protection Against Risks), which will be documented by the research assistant using a standardized form kept for documentation purposes. The qualitative researchers will not be blinded due to the purposes of the qualitative study and the type of data they are collecting.

Providers and Staff:

PCPs and staff members will be identified by clinic contacts for participation in qualitative interviews (one interview for each individual). The qualitative study RA will not interview more than one participant type from each clinic and sampling will be by convenience for this study component. Potential participants will be informed that a decline in participation will in no way impact employment and their employers will not know of their agreement or refusal to participate. Those who agree to participate will provide written consent, including consent to be audiotaped, which will be documented by the research assistant using a standardized form kept for documentation purposes (6.2 Protection Against Risks).

E3. Subject Capacity

If the caregiver, after following our standard consent procedures, demonstrates capacity using the below questions, verbal consent will be documented and the caregiver will be consented to the study. As far as patient consent is concerned, should the patient not demonstrate capacity to consent, but not refuse to participate, the RA/RC will follow the assent process and consent the caregiver. Consent covers participation in one survey and a qualitative interview. Once the consent process is completed, the RA will either complete the baseline interview or schedule a time for a follow-up phone call.

When obtaining consent we will use the standard procedures for addressing capacity that we have been used in many prior studies, but may modify this process to be in compliance with the IRB involved in this study as per their request. The following questions will be used:

We have just reviewed what it means to participate in this study. I am going to ask you a few questions just to make sure you understand what we will be doing once we begin.

1. *What would you be doing if you agree to take part in this study? (Examples of acceptable answers: "Take part in an interview/survey," or "Answer questions about my friend or relative.")*
   ☐ Person is able to answer this ☐Person is not able to answer this

2. *What can you do or ask me to do if you are uncomfortable with a particular question in the survey? (Examples of acceptable answers: "Ask to skip the question." "Ask you to read another question.")*

   ☐ Person is able to answer this ☐Person is not able to answer this

3. *What can you do if you decide after we start that you do not want to participate in the study? (Examples of acceptable answers: "Tell you that I do not want to answer any more questions.")*

   ☐ *Person is able to answer this* ☐*Person is not able to answer this*

E4. Subject/Representative Comprehension
Potential subjects will be told that their involvement in the study is completely voluntary and that they can withdraw from the study at any point. Caregivers may themselves be elderly and might have cognitive impairment such that it impacts their capacity to consent to research. For all potential participants, we will assess the individual's ability to provide informed consent using IRB approved interview procedures to assess capacity to consent for research. Some subjects may be too hearing impaired to communicate by telephone and the telephone interview is designed to assess for this potential problem and mitigate this issue when possible but this might impair ones capacity to consent. Although we have conducted numerous studies with elderly subjects, this has been a rare occurrence. Nonetheless we will not enroll any caregiver participant who cannot communicate by telephone.

E5. Documentation of Consent
Those who agree to participate will provide verbal consent, including consent to be audiotaped, which will be documented by the research assistant in the REDCap library for clear documentation purposes. The providers that participate in the qualitative interviews will sign written informed consents and audio consent forms. These documents will be logged and kept in the study binder in a locked cabinet that is accessible only to the PI and the study coordinator.

5.3 Study Specific Procedures

Study procedures include caregiver surveys and interviews to evaluate the quality improvement program described in Section 4.

5.4 Data Collection Overview (Evaluation)

We will collect data from five sources:
1) Caregiver surveys
2) Caregiver qualitative interviews
3) Provider/Staff qualitative interviews
4) Patient data from Epic
5) Patient data from ResDAC (Research Data Assistance Center) claims data

1. ***Caregiver surveys.*** The survey will be administered over the telephone and participant responses will be entered in REDCap survey database. A blinded research assistant interviewer will collect complete telephone survey data from CGs at baseline, 6 months, 12 months and 24 months using a 30-minute survey (see Survey instrument). The RA will enter de-identified survey data from each survey wave into a HIPAA-compliant REDCap electronic database hosted at NYULH.
2. ***Qualitative interviews*** will be conducted with 40 dyads (or until thematic saturation is reached for key content areas) each from the INT and CON clinics. Caregiver Cognitive Interviews will also be conducted with an additional 20 caregivers to evaluate the use of

the Treatment Burden Questionnaire (TBQ) for Caregivers and identify any potential problems that may compromise the quality of data collected using the TBQ with caregivers. The purpose of these interviews is to validate this tool for future studies to measure treatment burden of caregivers. These 60 interviews will be audio recorded (included in verbal consent) and transcribed. Audio tapes will be destroyed once transcriptions are complete, which will be stored in a HIPAA-compliant NYU secure server.

3. **Provider/Staff Qualitative Interviews** will be conducted using purposive sampling framework with members from each category: internal medicine physician; specialty physician; care managements and nursing. Written informed consent will be obtained. Interviews will be conducting via phone. These interviews will be audio recorded and transcribed. Audio tapes will be destroyed once transcriptions are complete, which will be stored in a HIPAA-compliant NYU secure server.

4. ***Patient data from Epic.*** An trained member of the research team (Research Coordinator) who will be blinded to participant INT or CON group affiliation will be responsible for collecting and entering EHR data into REDCap for enrolled patients. The dyad will have consented verbally to review of their medical record in Epic. In order to evaluate this quality improvement intervention, the study team will pull and review administrative data from Epic on patients in the intervention and control clinics. These data will be de-identified and used to monitor safety and evaluate effectiveness of the intervention.

5. ***ResDAC*** *(Research Data Assistance Center) claims data* will be applied for in the 2nd or 3rd year of this study. An IRB modification will be submitted to obtain this data.

Measures
Survey

Table 1							
Measure	**Source of Data**	**How measured**	**Subject**	**Baseline**	**6 Months**	**12 months**	**24 months**
Age	EHR/ Survey*	Years	CG, Pt	**X**			
Gender	EHR/ Survey	Categorical: Male/Female	CG, Pt	**X**			
Race/Ethnicity	EHR/ Survey	Categorical: White, Black, Hispanic, other	CG, Pt	**X**			

Education	Survey	Categorical: < H.S., H.S., Some College, College graduate+	CG	**X**			**X**
Clinical co-morbid conditions	EHR	Charlson comorbidity index8	Pt	**X**	**X**	**X**	**X**
Medication Complexity	EHR	Unique medications (n) + unique multiple administrations/day (n)	Pt	**X**	**X**	**X**	**X**
Prior (1-year) non-acute use	ResDAC	Counts: physician ambulatory visits	Pt	**X**	**X**	**X**	**X**
Prior (1-year) acute use	ResDAC	Counts: ED, hospital visits / bed days	Pt	**X**	**X**	**X**	**X**
Social Support	Survey	MOS Abbreviated Social Support (4-item; 5-point Likert scale)[79,80]	CG	**X**	**X**	**X**	**X**
COVID-19	Survey	Exposure and symptoms, testing status, impact, changes in burden, access to resources	CG, Pt	**X**			
Follow-up COVID-19	Survey	Exposure and symptoms, testing status, impact, changes in burden, access to resources	CG, Pt		**X**	**X**	**X**
DM-ADRD-Specific							
Dementia Diagnosis /Type	EMR	Categorical: Yes/No and if yes, AD, Lewy Body disease, Parkinson's Disease, Vascular, Frontotemporal, and mixed	Pt	**X**			**X**
Dementia Severity	Survey	Dementia Severity Rating Scale[87]	Pt	**X**			**X**
Caregiver relationship to CR	Survey	Categorical: Spouse, child, other relative, friend/other	CG, Pt	**X**			

Functional State	Survey	14 items: ADL/ IADL for CG; within DSS for Pt	CG, Pt	**X**	**X**	**X**	**X**
Marital Status	Survey	Categorical: Single/never married, married, divorced, widowed	CG, Pt	**X**			**X**
Substance use history	Survey	Current: Yes/No; Past history: Yes/No	CG, Pt	**X**	**X**	**X**	**X**
Mental illness history	Survey	Yes/No: Depression, schizophrenia, PTSD, other	CG, Pt	**X**			
Diabetes care questions	Survey	diet, blood sugar testing, exercise	Pt	**x**	**x**	**x**	**x**
Hypoglycemia	Survey	Number, number documented, treatment, number seek medical attention	Pt				
Neuropathic pain	Survey	Yes/no	Pt	**X**	**X**	**X**	**X**
Urinary symptoms	Survey	Counts: frequency, dysuria, incontinence, urgency	Pt	**X**	**X**	**X**	**X**
Falls	Survey	Number, number injurious in last year and then since last survey, number ED or other falls requiring medical attention	Pt	**X**	**X**	**X**	**X**
Syncope	EHR	Number, number ED diagnoses or other events requiring medical attention	Pt	**X**	**X**	**X**	**X**
Structural Measures							
General							
Change in PCP–past 6 mo./last survey	EHR	Yes/No	Pt	**X**	**X**	**X**	**X**
Consistent PCP care	EHR	% Visits by PCP versus other ambulatory providers	Pt	**X**	**X**	**X**	**X**

New home health aide or increased hours	Survey	Yes/no; HHA resource changes	Pt	**X**	**X**	**X**	**X**
New home health care services	Survey	Yes/no	Pt	**x**	**x**	**x**	**x**
Insurance	EHR	Categorical: Yes/No, Medicare, Medicaid, HMO	Pt	**X**	**X**	**X**	**X**
DM-ADRD-Specific							
Has a caregiver (Defined: Sec. B5)	EHR	Yes/No	Pt	**X**	**X**	**X**	**X**
Caregiver living arrangement	Survey	Categorical: Live with subject, close proximity (miles), other	CG	**X**	**X**	**X**	**X**
Clinic-Specific							
Clinic Size	Admin	Number primary care providers / number of patients	Clinic	**X**			**X**
Clinic Support	Admin	Number of clinic support staff / provider	Clinic	**X**			**X**
Proportion Medicare/ Medicaid	Admin	Insurance data specific to Medicare/Medicaid categories	Clinic	**X**			**X**
EQUIPED Process of Care Measures							
Provider use of structured template	EHR	Counts: visit note/templates; proportion of visits with templates	PCP		**X**	**X**	**X**

Provider educational attendance	Admin	Proportion (n, %) of educational sessions attended	PCP		**X**		
PM – PCP Communication	EHR	Counts: emails, forwarded notes between PM and PCP	PM/ PCP		**X**	**X**	**X**
Change in diabetic medication	EHR	Counts: change (add, delete); dosing (increase, decrease)	Pt	**X**	**X**	**X**	**X**
Change in antihypertensive medication	EHR	Counts: change (add, delete); dosing (increase, decrease)	Pt	**X**	**X**	**X**	**X**
Medication complexity	EHR	Sum of unique medications, daily dosing frequency/differences	Pt	**X**	**X**	**X**	**X**
Anticholinergic medication burden	EHR	Anticholinergic medication burden scale	Pt	**X**	**X**	**X**	**X**
PM – CG contact frequency	EHR	Counts: CG visits with PM (by type: email, phone, in-person)	CG		**X**	**X**	**X**
Referrals for CG-support services	EHR	Proportion (n, %) of CGs referred to programs / receipt of service	CG		**X**	**X**	**X**
Cognitive screening of eligible patients	EHR	Proportion (n, %) of DM-eligible patients screened w/ MiniCog^{TM39}	Pt		**X**	**X**	**X**
Outcome Measures							
General							
Hemoglobin A1C Change	EHR	Proportional change: patients with in-range values versus not	Pt	**X**	**X**	**X**	**X**

Blood pressure change	EHR	Proportional change: patients with in-range values versus not	Pt	X	X	X	X
Treatment Burden Questionnaire	Survey	15-item survey modified for CG administration (0-10 likert)[85]	Pt	X	X	X	X
Non-acute care use	ResDAC	Counts: provider ambulatory visits / all health system contacts	Pt	X	X	X	X
Acute care use**	ResDAC	Counts: ED, hospital / #bed days	Pt	X	X	X	X
Sub-acute care use	ResDAC	Counts: # bed days	Pt	X	X	X	X
LTC use	ResDAC	Counts: # bed days	Pt				
LTAC or Hospice use	ResDAC	Counts: # bed days	Pt				
DM-ADRD-Specific							
Dementia symptoms	Survey	DSS	Pt /CG	X	X	X	X
Diabetes caregiver distress	Survey	Diabetes Caregiver Distress Scale	CG	X	X	X	X

LEGEND: CG=Caregiver; Pt=Patient; EHR=Electronic Health Record; ResDAC=Research Data Assistance Center; DM=Diabetes mellitus; ADRD=Alzheimer's disease and related dementias; ADL=Activities of Daily Living; IADL=Instrumental Activities of Daily Living; HABC-M=Health Aging Brain Care-Monitor; PTSD=Post-traumatic Stress Disorder; ED=Emergency Department; PCP=Primary Care Provider; PM=Panel Manager; MYLOH=Managing Your Loved One's Health; MOS=Medical Outcomes Study TBQ= Treatment Burden Questionnaire; Note – the survey is always given to the caregiver (CG)*

*and includes questions about the CG and about the patient; ** Baseline utilization variables will have 20 month look-back through claims and EHR*

As shown in Table 1, many variables for the evaluation will be collected from the EHR or from claims. However, many caregiver-reported variables will also be collected using scales that have been validated for patients, but usually not for caregivers noting that some have been widely used to investigate how a caregiver perceives the patient's conditions. Below we discuss instruments used for caregiver reported variables, as well as the use of EHR and claims to measure patient-related variables. (Table 1 does not reflect the qualitative evaluation. The qualitative study as discussed in Section 3 and elsewhere above, will investigate the experiences of caregivers, patients and providers.)

Variables describing the patients, caregivers and clinics include: a) characteristics of patients and of caregivers, including demographics, marital status, living arrangements, and general health and function; b) patient medical and utilization characteristics, including comorbid conditions, medication complexity, patient symptoms potentially related to diabetes or to medication use and changes, depression and history of substance uses and healthcare utilization in the prior year. Dementia specific characteristics of the patients include type of dementia, its severity, and function. The survey respondent is always the caregiver, although the questions may measure patient or caregiver status.

We will also measure structure of care variables. These include patient use of consistent PCP care, home health services, and patient insurance. Clinic characteristics are size, support staff number, proportion of Medicare and Medicaid patients. Several baseline variables relate to diabetes but because they are also outcome variables they will be described later. As shown in table 1, many of these baseline and control variables are measured in the EHR and Epic administrative reports, or by claims. Some are measured by validated survey instruments, which are discussed briefly below.

We will collect many process of care measures at baseline and at follow-up. These include: a) provider use of Epic templates and tools; b) provider attendance at educational sessions; c) PM-PCP communication; d) PM-caregiver contact frequency; e) referral for caregiver-support services; f) cognitive screening of diabetes patients over 75; g) change in diabetes medications; h) change in hypertensive medications; i) change in anticholinergic burden; j) change in medication complexity. These variables are measured by EHR review and Epic administrative systems.

Outcome variables include HbA1c level and blood pressure. These variables will be measured at 0, 6, 12 and 24 months when available. Our main outcome is the proportion of patients achieving consensus HbA1c targets. BP will be measured by proportion of patients achieving consensus BP targets per our guideline. Theses variables will be measured by the EHR.

Utilization outcome variables are ED, hospital, SNF and ambulatory clinic utilization measured by EHR and by claims (for non-New York Langone Health utilization). SNF days must be measured by claims; Epic reports have discharge destination but do not have SNF days. Utilization variables will be measured at 6, 12, 24 months; the baseline measures include a 20 month look back at utilization.

Multiple caregiver reported outcomes about the caregiver and about the patients will also be

collected at 0, 6, 12, 24 months. General outcomes include: a) caregiver perception of care quality (our main caregiver-reported outcome), dyad care goals, preferences, and satisfaction; b) treatment burden; c) caregiver global health. Dementia and diabetes specific outcomes include: a) patient dementia symptoms; b) caregiver diabetes stress.

Below is a brief description of the instruments we will use, all of which have been studied and validated, although not always with caregivers.

- **Social Support MOS-5.** This survey instrument has been used to investigate social support for caregivers of dementia patients and is well studied.[79, 80] It has 5 questions.

- **Global Health (Promis Scale v1.2):** This commonly used instrument from the Promis series of instruments[83] assesses the general health of the caregiver and is reported by the caregivers. It has 10 questions.

- **Diabetes Caregiver Distress Scale:** This scale is adapted from the diabetes distress scale.[84] We were unable to find a diabetes care distress or care burden scale that is directed at caregivers, even when checking literature for type 1 diabetes and children with diabetes. We therefore will use this instrument for caregivers although it is usually given to patients. It has 7 questions.

- **Mental Health and Substance Use:** These 5 questions ask about caregiver history of mental health, including stress and depression, alcohol and illicit drug use.

- **Treatment Burden Questionnaire (TBQ):** This instrument has been used in studies with patients but not with caregivers who are supervising or providing care for care-patients (patients). The form has 15 questions. In order to publish our findings, we are working with experts to conduct psychometric evaluation to validate the TBQ for use with caregivers.

- **Dementia Severity Rating Scale (DSRS):** This is a caregiver questionnaire that asks about the patient's dementia characteristics.[87] It has been used in many studies, including studies by our group, and is well validated. This scale includes questions related to the patient's functional ability.

- **COVID Questionnaire:** This instrument assesses the impact of COVID-19 pandemic and its associated mitigation efforts on study subjects. Specifically, it includes COVID-19 status, related symptoms, and the social, medical and functional impact of the pandemic on caregivers and care recipients. We will attempt to complete this instrument at least once (baseline or follow-up) with every caregiver/care recipient dyad.

- **Follow-up COVID Questionnaire:** This survey will capture any changes that may have occurred since the first COVID survey and will be administered to any participant that has already completed an initial survey.

Most variables measured by EHR and claims are self-explanatory. However, two other instruments will be used with EHR and claims.

- **Patient: Charlson Comorbidity Index:** This well-known modified index will be calculated from the EHR and/or claims.[88]

- **Patient: Anticholinergic Cognitive Burden Scale:** This is also a commonly used scale derived from chart review that has been used in the past by our group.[89]

6. Risk and Benefit Assessment

6.1 Risks

No pharmacological intervention or medical procedures will be used in this study. Rather this study aims to develop and test the use of consensus decisional guidance for the medical management of DM in patients with ADRD.

No survey or qualitative interview data will be gathered without patient and caregiver consent (or in some cases, patient assent). However, some questions may cause anxiety, embarrassment or be emotionally upsetting. The RA/RC will receive training in minimizing emotional impact or discomfort and remind subjects that they may discontinue participation at any time. Dr. Dickson is experienced in qualitative interviews and will also minimize emotional impact or discomfort. In the event of significant emotional upset, the mPIs will be notified and will intervene to address any concerns.

Subject loss of confidentiality is another risk of clinical trials like the one proposed here and with this type of data collection. However, the computerized assisted telephone interview (CATI) and in some cases, in person, data collection method using a REDCap survey tool that we utilize is specifically designed to mitigate such loss as no data is collected with personal identifiers and contact names, addresses and telephone numbers, which are maintained in separate databases.

6.2 Protection Against Risks

All study personnel have completed training in Human Subjects Research and HIPPA standards and we have a strong record of quality assurance and maintained confidentiality from prior projects. NYU MCIT and DataCore, the data management experts who will manage the administrative data and the combined database have multiple data security elements in place (see below) and all personnel are trained in Human Subjects Research HIPPA standards, and data security.

To further protect against risk to loss of subject confidentiality, all records will be coded with anonymous identifiers. Only de-identified data will be shared with the research team without a need to know identifying information. Documentation of consent will be encrypted and will not be known by the PM and clinical team. We will keep one separate and password protected and encrypted computer file that contains identifiable data that is necessary to contact subjects (phone numbers and U.S. mailing addresses). This file will be the only file that can link subject names,

addresses, and/or telephone numbers to the study unique codes, and is only accessible by the study Principal Investigators and Research Coordinator.

Qualitative interviews with caregivers and providers/staff will be audio recorded should patients verbally consent. Audio recording is necessary for transcription and qualitative analysis of interviews. Audio tapes of subject interviews will be labeled with subject anonymous identifier (described above), only linked in a secure file accessed only by IRB approved study team. Audio tapes will be destroyed once transcriptions are complete, which will be stored in a HIPAA-compliant NYU secure server.
All other computer files containing data from this study (survey and interview files and files containing medical record and claims data) will be stripped of identifiable data, and subjects will only be differentiated by unique study codes. Data will be compiled from all of the subjects in the study and aggregated for analysis and publication. All identifying data will be eliminated from files before the statistician analyzes the data. All electronic data will be kept in password-protected databases and program files.

Procedures for maintaining confidentiality will be reviewed quarterly with the research team to assure compliance. Audiotaped intervention sessions that will be used to ensure the quality of the intervention and judge treatment fidelity will be reviewed by Dr. Dickson and subsequently destroyed. A separate consent for audiotaping will be obtained. All study personnel will be trained in data confidentiality, Human Subjects Research and HIPPA compliance, as will the panel managers. Even though the panel managers are part of the clinical team and not the research team, they will interact with the research team and the patient/caregiver dyad and need to understand the context and relationship of the quality improvement program and the research evaluation.

6.3 Potential Benefit to Subjects

We anticipate that participants may receive benefit either from enhanced panel management or usual care and for all we anticipate some immediate benefit regardless of the arm into which they are randomized. All subjects will be recipients of care in clinics that have received guidelines for enhanced care and will be offered referral information for caregiver support services and other informational materials. Contact from an RA may be a break from what for some will be the loneliness of caregiving. We expect some improved caregiver knowledge, decreased sense of burden and improvement in mood for at least intervention subjects. Care recipients may benefit through improved health outcomes. They may also receive increased medical care quality through attention to previously unattended medical issues. Finally, both caregivers and care recipients may receive increased levels of community support through mobilized informal supports and through community agency assistance. This study poses minimal risk to subjects, since the study does not involve tests or treatments beyond that which they would normally receive as part of their normal care. Therefore, the potential benefits outlined above exceed the risks of participation in the study.

For PCPs and staff, participation in interviews poses minimal risk. The opportunity to contribute to better understanding about health service delivery may provide some personal satisfaction and benefit. Information gathered from these interviews may lead to an improved work environment providing direct benefit to participants and colleagues. The interview may also be a place where

PCPs and staff feel free to voice concerns or objections to clinical approaches and this may present a safe space in which to do this.

7. Data Analysis

We will begin all analyses with descriptive summary statistics and graphical displays of all variables. Continuous variables will be summarized with means, medians, standard deviation and interquartile range; categorical variables will be summarized with frequencies. We will assess the balance by treatment assignment of patients in the INT and CON clinics with respect to demographic and clinical characteristics (e.g., age, gender, Charlson Index, socioeconomic status, baseline TBQ, etc.) using standard tests (t-tests, Wilcoxon rank-sum tests, and $\chi 2$ tests as appropriate). Any factors that appear to be unbalanced by treatment assignment will be considered as adjustment factors in the primary analyses. All hypothesis testing will be two-sided and conducted using a significance level of 0.05.

The primary outcome of 'on target' HbA1C values will be measured for each patient as a binary indicator. The primary analysis will use a generalized linear mixed model approach, with a logit link, for the probability of being 'on target.' The treatment group (CON vs INT) will be the primary fixed effect of interest; we will also include the practice as a random effect to accommodate clustering of patients within clinics. We will also explore non-parametric methods such as quantile regression or other rank-based approaches. As noted above, randomization should obviate the need for any additional covariate adjustment, but we will explore whether adjustment for clinic-level characteristics (e.g., clinic size) and provider-level characteristics (e.g., provider demographics and panel size) is necessary. We will use standard assessments of goodness-of-fit, including residual plots, to evaluate the models. Finally, in addition to reporting the treatment difference in terms of the odds ratio from the logistic regression, we will report absolute risk difference as well.

The secondary outcome of TBQ score, transformed into a binary outcome using an appropriate threshold (e.g., the median) will also be assessed using generalized logistic mixed models as described above; the treatment group (CON vs INT) will be the primary fixed effect of interest, with practice included as a random effect. As with the primary outcome, we will assess the need for adjustment using demographic or clinical characteristics, and will evaluate goodness-of-fit using standard approaches. We will also evaluate the TBQ as a continuous score using a linear mixed model. We will assess the validity of the linearity assumption, and seek a suitable transformation of the TBQ score if it appears to be violated. The statistical power for this analysis will be greater than that for the binary version of the outcome because of the additional information provided when using the scale in its original form.

Health care utilization outcomes will be analyzed using similar generalized linear mixed models; indicators of use will employ the logistic link function, and counts of days in various facility types will employ Poisson regression with the log link function. Treatment burden (using the Treatment Burden Scale) and dementia symptoms/cognitive function (using the DSRS) will also be evaluated as important secondary outcomes. We will have repeated assessments of these items at 6, 12, and 24 months, and will apply longitudinal mixed effects models to evaluate the trajectories and assess whether they differ by treatment group. Specifically, we will model time using indicator variables, and include interaction terms between time indicators and treatment group (CON vs INT); the statistical significance of the coefficients of the interaction terms will indicate whether

the trajectories in the outcomes over time differ by treatment group. We will also explore more parsimonious ways of modeling time, for example as a linear or polynomial effect. We will choose link functions that address ordinal outcomes, such as the log link for ordered categorical outcomes, in the context of proportional odds or multinomial logistic regression.

All clinical trials are at risk for missing data. Although we will attempt to retain as high a fraction of participants as possible, we acknowledge that some attrition is likely, leading to missing outcome values. The generalized linear mixed models proposed for the primary and secondary analyses incorporate an assumption of data that are missing at random (MAR), meaning that the likelihood of a value being missing depends on observable characteristics (e.g., sex, age, baseline clinical status, etc). In sensitivity analyses, we will assess the impact of different assumptions about the missing data mechanism, and will determine the robustness of trial results to these different assumptions. These sensitivity analyses will take the several forms. The first extreme value imputation, in which we assume that all members of one intervention group experience either a success or a failure (e.g., HbA1 on or off target) while the opposite occurs in the other intervention group. We will also apply a more formalized assessment using the Index of Sensitivity to Nonignorability, developed by Dr. Troxel and colleagues, which provides an objective assessment of the robustness of trial results to different assumptions about the missing data mechanism.

8. Data and Safety Monitoring

This study will be monitored by **1)** the multiple Principle Investigators (mPIs) and **2)** the Data Safety Monitoring Board (DSMB).

8.1 mPI responsibilities:

- Provide oversight of daily operations and on-site monitoring of data accuracy and quality, adherence to the research design, methods and procedures outlined in the protocol
- Monitor AE and SAE and follow-protocols for those events outlined in Section 10, including reporting these events to the IRB and DSMB.

8.2 DSMB responsibilities:

- Review the research protocol, informed consent documents and plans for data safety and monitoring;
- Advise the NIA on the readiness of the study staff to initiate recruitment;
- Evaluate the progress of the trial, including periodic assessments of data quality and timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of the trial sites, and other factors that can affect study outcome;
- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants, and outcomes or ethics of the trial;
- Review study performance, make recommendations and assist in the resolution of problems reported by the mPrincipal Investigators;
- Protect the safety of the study participants;
- Report to NIA on the safety and progress of the trial;

- Make recommendations to the NIA and to the Multiple Principal Investigators concerning continuation, termination or other modifications of the trial based on the observed beneficial or adverse effects of the treatment under study;
- Review interim analyses to assess study recruitment and outcome milestones which are clearly defined in advance of data analysis and have the approval of the DSMB;
- Ensure the confidentiality of the study data and the results of monitoring; and,
- Assist the NIA by commenting on any problems with study conduct, enrollment, sample size and/or data collection.

There will also be a data monitoring committee consisting of the statistician, Dr. Troxel, a DataCore representative, and Co-I Dr. Horwitz. This committee will meet twice yearly during the first three years of the trial to review the survey data and any data to be presented to the DSMB. In the last year, when utilization information from the EHR and claims are becoming available, this group will meet every two months.

9. Ethics/Protection of Human Subjects

9.1 Ethical Standards

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Subjects of Research codified in 45 CFR Part 46.

9.2 Institutional Review Board

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

10. Data Handling and Record Keeping

10.1 Data Storage and Management Responsibilities

All study personnel will be trained in data confidentiality, Human Subjects Research and HIPPA compliance. Data will be stored using HIPAA-compliant REDCap electronic database hosted at NYU Langone Health. To protect against risk to loss of subject confidentiality, all records exported from REDCap will be coded with anonymous identifiers. Only de-identified data will be shared with the research team without a need to know identifying information. Documentation of consent will be encrypted and will not be known by the PM and clinical team. Data will be compiled from all of the subjects in the study and aggregated for analysis and publication. All identifying data will be eliminated from files before the statistician analyzes the data. All electronic data will be kept in password-protected databases and program files. Procedures for maintaining confidentiality will be reviewed quarterly with the research team to assure compliance. Audiotaped intervention sessions that will be used to ensure the quality of the intervention and judge treatment fidelity will be reviewed by Dr. Dickson and subsequently destroyed.

NYULH has privacy provisions that are strictly adhered to, including mandatory Security Awareness and HIPAA training of all employees from custodial staff to Administration; mandatory training for all clinical trials staff, which includes Protection of Human Subjects training. All staff must sign a confidentiality agreement upon employment, and NYULH meets or exceeds all HIPAA requirements. These requirements pertain both to our study personnel and to any MCIT or data management personnel who come into contact with our databases, which are stored on NYULH IT secure servers.

All resources, including web, database, and file servers, are protected from outside intrusion by a firewall that blocks unauthorized access to the LAN by any unauthorized user originating from the Internet by using a sophisticated combination of secure application proxies and packet filtering. Internal network security is maintained through Active Directory authentication. Intrusion detection software is employed to scan for attempted break-ins. User IDs and passwords are assigned and controlled as per SOP "SD004: Study Security", and users are required by the system to change their passwords regularly. Access to clinical trials or other sensitive data is strictly limited and is granted only by the Director of the Technical Support Unit.

10.2 Study Record Retention

In compliance with NIH policy, study records will be retained for a minimum of 3 years after study completion.

10.3 Publication and Data Sharing Policy

This study will comply with the NIH Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

11. Investigator's Qualifications and Experience

Our multidisciplinary team is expert in health system design science. Dr. Blaum, mPI, an expert in multiple chronic conditions (MCC), DM in older adults, and practice change, has led both VA and Medicare practice change projects. Dr. Chodosh, mPI, an expert in cognitive assessment, CG research, and care delivery model implementation for cognitively impaired patients, is the Outreach and Recruitment Core Leader for the NYU Alzheimer's Center, is co-PI on a large NY State grant to provide supportive services for dementia CGs. His ADRD research experience is invaluable as we navigate systems and human subject issues. Dr. Zabar, Division Director of General Internal Medicine and an expert on physician training and interdisciplinary practice, will assist with practice change and provider interface with panel managers (PMs). Dr. Horowitz is Director of the Healthcare Delivery Science Division in the Department of Population Health. A former Beeson Scholar, she is PI of the NYU CMMI Primary Care Transformation Project and has worked on practice change interventions, and electronic health records (EHR) and claims data related to the NYU healthcare centers. She has expertise in behavioral economics and practice change. Dr. Dickson, an expert on qualitative research methodology, has conducted self-management interventions in ethnically diverse patients, including those with low health literacy.

Ira Goldberg, a prominent lipid researcher, is Division Director of Endocrinology. Although a basic scientist, he has a particular interest in diabetes management in complex populations. Dr. Simon Jones is a prominent statistician with substantial experience in public health, delivery system redesign, and implementation research. Our consultants have critical expertise. Dr. Borson is well known for her research in dementia screening and CG burden, Dr. Boustani is known for his work in dementia care and screening, and Dr. Williamson from Wake Forest was Co-PI of ACCORD-MIND.

12. Study Finances

12.1 Funding Source

This study is financed through a grant from the National Institute on Aging (NIA).

12.2 Costs to Subjects

There are no costs for participation.

12.3 Payment for Participation

Caregivers will be provided a $20 gift card upon completion of each of the 4 surveys (baseline, 6 months, 12 months and 24 months) and an additional $20 gift card should they complete a qualitative interview.

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