STU#: STU00209066

PROTOCOL TITLE: Development & Pilot of the Technology-Enabled Alliance for Medication Therapy Management (TEAM)

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STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	
IND / IDE / HDE #	
Indicate Special Population(s)	☐ Children ☐ Children who are wards of the state ☐ Adults Unable to Consent ☐ Cognitively Impaired Adults ☐ Neonates of Uncertain Viability ☐ Pregnant Women ☐ Prisoners (or other detained/paroled individuals) ☐ Students/Employees
Sample Size	120 adults
Funding Source	Gordon and Betty Moore Foundation
Indicate the type of consent to be obtained	☐ Written ☒ Online ☒ Verbal/Waiver of Documentation of Informed Consent ☐ Waiver of HIPAA Authorization ☐ Waiver/Alteration of Consent Process
Site	☒ Lead Site (For A Multiple Site Research Study) ☐ Data Coordinating Center (DCC)
Research Related Radiation Exposure	☐ Yes ☒ No
DSMB / DMC / IDMC	☐ Yes ☒ No

Contents

1.0 Objectives

We will link community pharmacy and primary care practices via a shared electronic health record to improve medication therapy management for older patients taking complex prescription (R_x) regimens. Our specific aims are to:

Aim 1 Evaluate the fidelity and efficacy of the TEAM intervention to promote healthcare provider counseling, medication reconciliation, and safe regimen use among adults taking complex R_x regimens.

Aim 2 Explore patient, healthcare provider (pharmacist, prescriber), community pharmacy and/or primary care practice barriers to implementation.

Aim 3 Determine the costs of the TEAM intervention from both a community pharmacy and primary care practice perspective.

2.0 Background

Primary care practices in the U.S. are increasingly challenged to manage the growing number of patients living with multiple chronic conditions (MCC). More than a quarter of adults have MCC, and this dramatically increases with age. Compared to adults with only one or no chronic health condition, those with MCC have worse clinical outcomes, poorer physical function and mental health, higher healthcare utilization, including a greater risk of hospitalizations and readmissions, worse quality of life, and increased mortality risk. This is clearly detrimental to our healthcare system; according to a 2014 AHRQ report, 71% of U.S. healthcare spending is allocated to patients with MCC. Not surprising, multiple studies have found a gradient trend in healthcare expenditures, with annual outpatient costs increasing with each additional chronic condition. A 2017 study by Soni et al. found older adults with MCC had nearly twice the out-of-pocket costs than older persons with one or no chronic health condition

2.1 Major Consequence of MCC: Polypharmacy

With such a high prevalence of MCC, it is not surprising to see similar trends in the proportion of patients challenged with *polypharmacy*; most commonly defined as taking ≥5 Rx medications. Polypharmacy has dramatically increased 3-fold over the past several years. Among adults age 45-64, one in five contend with polypharmacy, while >40% of individuals over 65 are self-managing complex Rx regimens. These patients are at increased risk for adverse drug events (ADEs), drug interactions, inadequate adherence, poorer functional health status (including fall risk), and worse chronic disease outcomes.

Table 1.

Top 10 Barriers to Medication Adherence
1. Complexity
2. Cost
3. Forgetfulness
4. Misunderstanding
5. Health/Illness
6. Side Effects
7. Stigma
8. Depression
9. Health Literacy
10. Beliefs

Medication Adherence Project, New York Department of Health & Hygiene: www.nyc.gov/html/doh

Adverse Events. Adverse drug events (ADEs) are defined as “any injuries resulting from medication use, including physical harm, mental harm, or loss of function.” Medication errors refer to “any mistake made by a provider or patient that occurs during the process of medication use.” Medication errors do not always result in an ADE, but often impact treatment effectiveness. Medication errors in ambulatory care are more likely to occur in primary vs. specialty care settings, among older patients, and among those with MCC.

Inadequate Adherence. Adherence-related problems are estimated to cost the US healthcare system up to $300 billion a year, compromising the

effectiveness and safety of a patient's treatment and leading to >125,000 deaths annually. Yet half of older patients living with chronic conditions take <80% of prescribed doses. While adherence barriers are varied and often depend upon the treatment in question, a number of key root causes have been identified across multiple contexts **(Table 1);** polypharmacy and regimen complexity is one of the most frequently cited barriers.

2.2 Patient Perspective: Challenges of Self-Managing Complex R_x Regimens.

Patients prescribed multiple drugs face many challenges, such as variable Rx fill dates, forgetfulness, and cost concerns. All of these may keep patients from filling prescriptions on time. Patients also struggle to organize and take daily regimens; studies by our team and others have repeatedly shown older patients often misunderstand Rx instructions and overcomplicate medication schedules (**Figure 3**). Yet patients rarely receive explicit guidance from physicians or pharmacists on appropriate Rx use. When patient education is given, it is often for a single drug as opposed to a full regimen. As a result, patients are unclear on how to organize and simplify daily dosing for multiple drugs to support adherence and safe medication use. This is increasingly difficult with older age, due to memory lapses, health complications, poor self-efficacy, and fatigue.

Figure 3. Example of how older patients overcomplicate a 7-drug regimen

Wolf MS, Curtis LM, Waite K, Bailey, SC, Hedlund LA, Davis TC, Shrank WH, Parker RM, Wood AJ. Helping patients simplify and safely use complex prescription drug regimens. Arch Intern Med 2011; 171; 300-5.

2.3 Primary Care Perspective: Challenges of Managing Older Adults with MCC

Primary care practices, especially FQHCs, contend with diverse patient populations, particularly in terms of age and health status. Yet these practices have limited resources to support more complex patients. Clinic visit times are typically brief, and patient education and care coordination services are minimal compared to subspecialty practices that focus on single conditions. While patient-centered medical homes offer more comprehensive services, this reflects a small minority (~18%) of primary care settings.

A number of challenges have become increasingly apparent as primary care providers face a rising number of older adults taking complex R_x regimens. First, as the number of medications prescribed to a patient increases, so does the potential for medication errors, drug-drug interactions and ADEs. Problems with inadequate medication reconciliation in ambulatory care further complicates this; estimates indicate that 3 out of every 4 patients in ambulatory care may have inaccurate medication lists in the EHR. Such inaccuracies increase the risk of inappropriate prescribing, as providers have an incomplete picture of which medications the patient is actually taking. Finally, medication adherence is rarely assessed systematically in routine primary care, which leaves providers questioning whether the root cause of patients not achieving therapeutic goals is biologic failure of the R_x regimen or poor self-care. Prior studies have found clinicians have difficulty identifying and addressing medication-related concerns, and few clinical resources exist to support and monitor patients' Rx use at home. Poor adherence and other medication challenges often go unrecognized and untreated.

Beyond medication, there is the general criticism that the U.S. healthcare system and our evidence-based guidelines do not properly address MCC, but are focused on single conditions alone. While primary care providers bear the burden of managing the many health problems of these patients, current delivery models lack continuity of care, may not have efficient provider-provider communication channels (especially if subspecialists are not within the same health system, as is true for many FQHCs serving vulnerable populations), and struggle to address psychosocial barriers to self-management and find available community resources for referral.

2.4 Pharmacy Perspective: Challenges of Serving Adults with MCC

Community pharmacies also face challenges when providing medication services to older patients with complex Rx regimens. An estimated 300 prescriptions are filled daily in U.S. retail pharmacies; community pharmacists rarely have time or resources to counsel patients, despite state and federal mandates. Even if counseling is provided, it is often incomplete, as most pharmacists do not have access to patients' medical records and therefore lack essential information needed to inform counseling (i.e. indication for use, clinical notes). It is also rare for pharmacists to be aware of patients' entire regimen as patients may fill prescriptions at multiple pharmacies to reduce costs. This makes it increasingly difficult for pharmacists to identify potentially dangerous drug-drug interactions or to provide counseling on a patient's entire regimen instead of a single medication alone. Finally, poor communication channels between community pharmacies and primary care practices complicates care coordination; pharmacists often must communicate with physicians via fax or phone if a medication safety concern is identified or further information is needed to fill a prescription. This can be onerous, and often leads to problematic delays.

2.5 Solution: Linking Primary Care to Community Pharmacies

We will address many of these challenges by connecting community pharmacies to primary care so they may provide comprehensive medication therapy management for older adults with complex Rx regimens. Our Technology-Enabled Alliance for Medication Therapy Management (**TEAM**) intervention will link a major, national community pharmacy chain (Walgreens) to primary care practices (Access Community Health Network ('ACCESS')) via a shared electronic health record (EHR) platform (Epic, Verona WI). Through shared access to patients' medical records, pharmacists can perform comprehensive medication therapy management services, document and communicate patients' Rx challenges for review and action by primary care providers. The TEAM strategy enables a pharmacist to help patients on complex Rx regimens via:

Medication Review by Telephone. A Comprehensive Medication Review (CMR) is when a pharmacist reviews with a patient their entire list of medications that they are taking and prescribed. Pharmacists will call patients to conduct a CMR. Pharmacists will be able to document and communicate patients' medication challenges for review and action by primary care providers. A CMR will:

- ensure the primary care physician knows all medications the patient is taking (*reconciliation*)
- investigate if patients are taking medication as prescribed, in a safe manner (*proper use*)
- monitor and detect any drug-related adverse effects (ADEs) (*surveillance*)

- address any questions or concerns patients may have about their medicine (e.g. side effects, treatment alternatives, dietary restrictions, cost, 90 vs. 30 day scripts; *education*)
- inquire about patients' adherence to regimens, what barriers they may experience (e.g. cost, forgetfulness) and if they need assistance (e.g. synchronization requests, pill box or reminder tools, etc.; *adherence*).

Clinical Decision Support. The pharmacist will provide timely notifications via secure, EHR-based messaging direct to prescribers of any medication concerns, based on either 1) pharmacy information (e.g. medications ordered by other prescribers, fill data), 2) patient report of problems during phone-based encounters, or 3) pharmacist review of the patient record. This may pertain to potential issues regarding discrepancies in the medication list, drug-drug or drug-disease interactions, therapeutic duplication, patient report of ADEs or inappropriate dosing, Rx discontinuation, or inadequate adherence and reasons why (e.g. cost, forgetfulness). Specific recommendations will be included to expedite action.

2.6 TEAM Conceptual Framework

The TEAM strategy represents a coordinated healthcare system response to a very challenging set of patient behaviors, specific to the self-management of complex Rx regimens. Thus, our conceptual framework first deconstructs what is required of patients to properly adhere to and sustain Rx treatment; to reduce harm and achieve optimal benefits. However, many of these common patient challenges have root causes that are healthcare system-based. Our TEAM intervention reflects potentially scalable changes to primary care and community pharmacy practices that can reduce cognitive demands of daily Rx use, monitor patients, mobilize care teams, promote safe Rx use and adherence, and improve chronic disease outcomes.

2.7 A Patient Perspective on R_x Use

In their *Model of Medication Self-Management*, Drs. Bailey and Wolf break down the process of successfully managing a multi-drug regimen using a health literacy perspective into 6 steps. For patients to gain the benefits of drug therapy, they must: 1) fill prescriptions in a timely manner, 2) understand R_x instructions, 3) organize and consolidate their regimen to the most efficient, safe daily schedule, 4) take each medication as prescribed, 5) monitor Rx use and report any side effects or concerns to their provider, and 6) sustain use over time. Studies have repeatedly shown patients have problems performing these cognitively-demanding tasks, especially as regimen complexity increases and patients get older; both patient and health system barriers likely impact proper use. *With more informed pharmacists, TEAM can improve patient engagement and regimen use.*

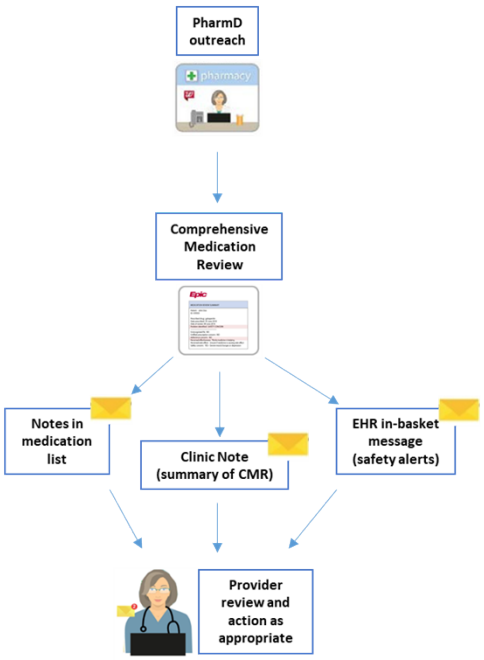
2.8 Behavioral Theories Guiding TEAM

While non-adherence can be unintentional, failure to take drugs appropriately can also result from patients' deliberate choices. Beyond cost, extensive research has identified important determinants that can influence Rx use, such as attitudes or beliefs towards the efficacy of drugs, social influences (e.g. family and friends) and low self-efficacy.

2.9 A Healthcare System Perspective

The many struggles many patients face when contending with polypharmacy and complex daily Rx schedules, can in large part be attributed to the manner in which services are provided in primary care and pharmacy settings; these are the targets of the TEAM strategy. From a health system perspective, TEAM is guided by the Chronic Care Model, which has served as a practice standard for thinking about how healthcare systems could improve their approach to addressing the increasing numbers of individuals with MCC. It is an organizational approach for preparing primary care to manage the care needs of individuals by implementing practical, supportive, evidence-based patient-healthcare provider interactions. The underlying premise of this model is that the current health system structure is not adequately equipped to manage chronic disease, as primary care providers and services are typically time-limited, lacking in care coordination and any capacity to proactively follow-up with patients to optimize outcomes and prevent harm. Higher quality healthcare is achieved through specific transformations within existing health systems and more productive interactions with other healthcare organizations and the community served (*such as with a community pharmacy*). The TEAM intervention integrates and coordinates available resources at community pharmacies serving patients from primary care practices, bringing the pharmacist into the care team for older adults with complex Rx regimens and maintaining productive interactions with the primary care provider to support clinical decision making and provide feedback on patients' regimen use.

Figure 6. TEAM Communication & Information Flow



3.0 Study Endpoints

The primary study endpoint will be the completion of all analysis of the Aims. A secondary study endpoint will be when all patient interviews are completed (n=120).

4.0 Study Intervention

4.1 TEAM Intervention Arm

Read/write EHR access with established Epic security points will be granted by ACCESS to Walgreens, with permission to more fully access the EHR only for those patients who have consented to the study and are specifically randomized to the TEAM study arm. These individuals will be referred to a designated Walgreens pharmacist using a report issued by the Walgreens Research Analytics Team, which will include Proportion of Days Covered (PDCs) for prescribed medications in the following therapeutic medication classes: hyperlipidemia, hypertension, diabetes, multiple sclerosis, hepatitis C, and HIV. Pharmacists will also be able to view a patient's record (e.g. problem list, medication list, visit diagnoses, clinic notes, orders, etc.) and, with write access, Walgreens pharmacists will be able to initiate medication

reconciliation activities, including adding notes in their medication list for the prescriber, requesting the removal or discontinuation of prescribed drugs that patients report they are no longer taking and adding medications omitted from the ACCESS primary care provider's list. Any medications added by the pharmacist will appear in the chart as "Patient-reported". Any addition of medications or notes to the medication list, will require the acknowledgment of the prescribing physician (Epic security point #282). The pharmacist will also be granted the capability of adding clinic notes and secured messaging to prescribers (Epic security point #77). For direct communications, as with notifying a prescriber of an unfilled order, a secured EHR inbox message will be sent by the pharmacist. This was viewed by ACCESS and Walgreens as the best means for getting the immediate attention of a prescriber. Figure 6 depicts the TEAM Intervention work flow. Specific TEAM activities and their timing are described below:

4.2 Medication Review by Telephone

The Walgreens Research Analytics Team will be notified of all patients randomized to the TEAM intervention on a weekly basis. They will then generate an Adherence Report for all medications in the predetermined six therapeutic medication classes, which will include rolling 12 month PDC per medication. This Adherence Report will be sent directly to the Walgreens pharmacist prior to initiating the CMR by phone. S/he will retrieve contact information for the patient via the EHR and attempt to initiate an introduction via telephone, wherein the pharmacist will explain his/her role, and establish a time (on the introductory call or scheduled for a later date) to perform a medication review. This is estimated to take between 10-45 minutes, depending on the size and complexity of the patient's regimen. The pharmacist will begin by reconciling the Epic EHR medication list with the patient, matching up what the patient is currently taking, what has been discontinued by a prescriber, what is still prescribed but the patient is not taking (and why), and identifying any omissions. Each medication will be reviewed, either in the list or identified by the patient, including a brief review of how patients take the medicine to ensure safe use. Patients will also be probed on whether they are experiencing any symptoms that could be signs of an adverse drug event (ADE). Pharmacists will address any questions or concerns patients may have about their medicine (e.g. side effects, treatment alternatives, dietary restrictions, cost, 90 vs. 30 day scripts), and assess patients' adherence. If missed doses or premature discontinuation is reported, problems (e.g. cost, forgetfulness) will be discussed and assistance offered (e.g. synchronization requests, pill box, reminders).

Pharmacists will document the CMR in real-time based on current practices and chart in the EHR afterwards (add any new medications to the medication lists, send secure messages to providers, create clinic notes). Any medications proposed to be added or discontinued from the medication list will be flagged and accompanied by a clinic note, requiring the prescriber to acknowledge the note and update the list. The pharmacist also will have the option in Epic to mark in the medication list if the patient reports not taking it at this time even though it is prescribed (e.g. intentional non-adherence). Any proposed reconciliation of the medication list will be accompanied by a highlighted note/justification in the EHR. In a similar manner, secured Epic EHR in-basket messages will be sent to prescribers if an ADE or serious side effect is detected, or premature discontinuation of a medication is reported. The pharmacist will generate an overall summary of the CMR, including any clinical recommendations or commentary on patient adherence, in a clinic note, which will populate as a patient encounter in the chart. Ideally, the

CMR will be completed one month post baseline interview and will take place before the follow-up interview conducted at two months.

Additional contact may be made if the Walgreens pharmacist were to discover a patient was recently hospitalized or if serious adherence concerns were detected from pharmacy fill data (see below).

At 6 months, the Walgreens Research Analytics Team will send an additional Adherence Report for patients in the TEAM intervention to the community pharmacist. The pharmacist will review the report and if a patient has poor adherence for at least one medication, they will initiate Therapy Management Review (TMR). This is a call from the pharmacist to the patient checking in specifically about the medication(s) for which they have poor adherence. After the TMR call, the pharmacist will create notes and send an in-basket message to the prescriber as necessary.

4.3 Clinical Decision Support

The Walgreens pharmacist will provide timely notifications via secured Epic messaging direct to prescribers via the EHR of any patient concerns, based on either 1) pharmacy information (e.g. medications ordered by other prescribers, fill data), 2) patient report during phone-based encounter, or 3) pharmacist review of patient record. This may pertain to potential issues regarding discrepancies in the medication list, potential drug-drug or drug-disease interactions, therapeutic duplication, report of ADEs or inappropriate dosing, premature Rx discontinuation, inadequate adherence, and reasons why (e.g. cost, forgetfulness). Recommendations will be included to expedite a prescriber response.

TEAM components were designed with primary care workflow constraints in mind. Clinic staff roles are not modified given limited bandwidth. Instead, community pharmacists will be able to initiate medication reconciliation services and more directly communicate with and mobilize the medical team.

5.0 **Procedures Involved**

Our team will build, implement, and field test the TEAM strategy through a partnership between a large, multi-site FQHC (Access Community Health Network; 'ACCESS') in Chicago and Walgreens.

5.1 Performance Sites:

ACCESS. Access Community Health Network has been on the frontlines of community-based health care in Cook and DuPage counties for 25 years, serving the health needs of underserved communities by providing preventive care, chronic disease management, and other support services. In 2017, ACCESS served more than 183,000 individuals, including 26,117 patients with hypertension and 16,923 patients with diabetes. The patient population is low income and racially/ethnically diverse. ACCESS uses the **Epic EHR** platform (Verona, WI).

Walgreens Co. For 7+ years, our team has partnered with Walgreens on projects centered on innovations, medication therapy management (MTM), and partnerships with primary care. In 2018, Dr. Wolf (MPI) coordinated a master research agreement between Northwestern and Walgreens. We are one of few academic partners formal collaborating with Walgreens through their Center for

Health and Wellbeing Research. With >8,000 stores in the US (heavily populated in medically underserved areas), Walgreens ranks as the largest retail community pharmacy chain.

The following five ACCESS Health Centers have collocated Walgreens community pharmacies and current read-only access for Walgreens pharmacists in place:

1. ACCESS Grand Boulevard
2. ACCESS Genesis
3. ACCESS Hawthorne
4. ACCESS La Villita
5. ACCESS Madison

The TEAM intervention will be rolled out initially at the Hawthorne and Genesis sites. If needed, the pilot will be rolled out at the Grand Boulevard, La Villita, and/or Madison site. The intervention will be rolled out as follows: Walgreens pharmacists will be notified of the enrollment of a patient in the intervention by the Walgreens Research Analytics Team. Each pharmacist will conduct 2-3 CMRs a week at these locations. For this pilot, we will be using trained community pharmacists and possibly community pharmacist residents.

5.2 Phases of the Project

The following activities will be performed during the proposed project, by phase:

Design Phase (months 1-9)

1. Organize Northwestern-Walgreens-ACCESS team; establish project milestones, roles.
2. Convene all stakeholders (primary care providers, Walgreens pharmacists and leadership) to gather feedback on the initial draft standard operating protocol (SOP) for the implementation of TEAM in ACCESS clinics, leveraging Walgreens pharmacists will be developed. This is an iterative process with all TEAM users.
3. Amend existing Walgreens-ACCESS agreements to include new Epic read/write access, given the parameters established by the mutually-agreed upon SOP. This includes the specification of set security points within the ACCESS EHR (Epic) that both allows and controls pharmacist permissions. Our Northwestern team has already worked with ACCESS and Walgreens to detail the TEAM protocol (see section 4.0 study intervention).
4. Devise an implementation evaluation battery capturing process outcomes and also a range of patient-reported medication safety-related outcomes.

Implementation phase (months 10-30)

5. 'Beta test' the TEAM strategy in the clinical environment to confirm the functionality of all bi-directional information sharing components.
6. Trouble shoot any technical/procedural concerns, modifying the SOP accordingly.
7. Orient participating ACCESS clinical sites and Walgreens staff on the final SOP in preparation for the live implementation to be conducted in the second project phase.
8. Implement the finalized TEAM intervention protocol defined in the Design Phase at ACCESS clinic sites. The strategy includes Walgreens pharmacist outreach with identified

ACCESS patients to: a) perform medication reviews, b) generate automatic and tailored EHR-based alerts; c) provide clinical decision support.

9. Enroll 120 patients into the pilot study.
10. Randomize patients (1:1) to either: 1) the TEAM intervention or 2) enhanced usual care.
11. Conduct baseline (by phone) and 2 month follow-up interview (by phone) with enrolled patients. Interviews will include validated measures and will be completed using RedCAP software for data quality and safety. Data will also be abstracted from patient EHR records at 12 months post-enrollment.

Evaluation Phase (months 31-36)

12. At the completion of the Implementation Phase, conduct structured telephone or in-person interviews (as appropriate) with Walgreens pharmacists and its leadership who were involved in the TEAM project to capture their project-specific experiences, perceptions of benefits, challenges, and other constructive feedback leading to necessary modifications.
13. Collect and merge all pertinent data sources (EHR), Walgreens, pharmacy records, patient report (qualitative and quantitative), perform quality assurance activities in preparation for formal analyses.
14. Conduct details analyses in response to Aims 1-3.
15. Share preliminary analyses with ACCESS, Walgreens and study team.

5.3 Study Arms

Enhanced Usual Care. Patients randomized to enhanced usual care will have the medical record available to a Walgreens pharmacist with 'read only' access. All patients at the five targeted health centers already have read-only access in place. This means the Walgreens pharmacist will have the capability to review an ACCESS patient's record as necessary. 'Read only' permissions are becoming more commonplace with increased adoption and linkage of health information technologies between healthcare organizations. While this health information exchange presents opportunity for a pharmacist to engage patients in a more informed manner for MTM, existing pharmacy practice workflows will remain unchanged. Pharmacists will not have dedicated effort to perform MTM. While they are not prevented from proactively engaging with patients to perform medication reviews or contacting ACCESS prescribers to share information, it is a rare occurrence due to workflow. At present, the pharmacist may refer to the EHR as needed and in a reactive manner; such as if a patient were to request a medication requiring review for billing purposes (i.e. verify insurance, prior authorizations), or if a patient safety concern was raised (e.g. potential drug-drug or drug- disease interaction, therapeutic duplication, etc.). Similarly, read only EHR access means pharmacists must continue to use existing communication channels (e.g. phone, fax) to contact prescribers. These channels can be onerous and inefficient.

Intervention: TEAM strategy. See section 4.0 Study Intervention.

5.4 Randomization & Blinding.

Patient-level randomization will occur within ACCESS health centers. At each site, participants will be randomized via a 1:1 scheme to intervention or 'enhanced usual care' (N=120; n=60 per

arm) in randomized block sizes of 4 or 6 using SAS PROC PLAN. We will blind personnel involved in statistical analyses (Ms. Curtis, Ms. Batio) and also the principal investigators (Bailey, Wolf) and coinvestigators. Site project managers and RCs will have access to study arm assignments to initiate TEAM components to those randomized to receive them.

Limitations to Randomization Scheme. As a 'diffuse' intervention that addresses patients and the health system (ACCESS), we recognize prescribers at ACCESS sites will be caring for patients in both study arms of our trial. While there may be risk of potential contamination, our extensive experience working in time-constrained, resource-limited FQHC practices would suggest this to be of minimal concern. Other randomization options, either by clinic or by prescriber, are more problematic. FQHC practice sites are heterogeneous, and also have prescribing clinicians that work across sites. Our team strongly felt that patient-level randomization, wherein we could also control the receipt or withholding of TEAM services under study, was the most formidable, pragmatic approach.

5.5 Measurement

Outcomes and covariates collected during study visits are described below:

Patient Characteristics. During interviews, RCs will collect patient socio-demographic and health characteristics (including comorbidity and health status) and will administer brief measures of social support, anxiety and depression (PROMIS), and health literacy (3-item screener). These measures have been used in prior studies by our team, are validated, and have been shown in the scientific literature to influence medication use.

Regimen Characteristics. At each interview, RCs will review the medication list in the patients' EHR and those reported by patients. We will use a structured protocol from prior studies to identify medications no longer taken and as well as those prescribed but not on the list. Final medications will be grouped by drug class. Regimen complexity will be calculated using the validated Medication Regimen Complexity Index.

Intermediary Outcomes. We will assess a series of intermediary outcomes designed to determine if the TEAM strategy can reduce patient burden and challenges associated with medication self-management and increase patient engagement in care. Specifically, the Healthcare Task Difficulty (HCTD) scale, an 8-item measure in which patients rate difficulty of particular healthcare tasks (e.g. administering medications) will be administered, along with the Treatment Burden Questionnaire (TBQ). The TBQ assesses the workload of being a patient and its effect on quality of life, and is composed of 15 items measuring burden associated with treatment self-management (e.g. taking medicine and following doctors' advice), issues related to healthcare visits including laboratory tests, arranging appointments, and costs. We will also assess health management related to financial barriers and different tools that may help a patient take their medication. Finally, we will measure self-efficacy using the Self-Efficacy for Managing Chronic Disease tool, a widely-used 6-item scale and patient engagement via our team's validated tool, the Consumer Health Activation Index (CHAI). We will assess patient experience by asking questions on interactions with their provider, pharmacist, and specifically about the TEAM intervention.

Effectiveness Outcomes.

Healthcare provider counseling
We will ask patients (yes/no) whether their prescriber/nurse/pharmacist counseled them about their medications. We will also ask the Health Literacy supplemental items of the Consumer Assessment of Health Providers Survey (CAHPS) to evaluate the extent and quality of provider verbal counseling on Rx medications.

For the outcomes described below, we only include chronic Rx medications. Though we document them, we exclude PRN or limited duration drugs, as adherence concerns are different. All of these measures have been used in multiple studies by our team; results have been published extensively.

Medication Reconciliation

At each interview, commissions (medications listed in the EHR and the patient reported not taking) and omissions (patient reported medications not in the EHR) will be calculated based on medication lists and patient self-report.

Medication knowledge. Medication-specific knowledge will be measured through a series of open-ended questions, capturing patients' knowledge of each of their medication's: 1) indication for use and 2) risks, warnings or potential side effects. Answers will be qualitatively reviewed and independently scored as correct/incorrect by two RCs according to medication information provided from ACCESS and Walgreens For any that the RCs do not have information on or any with discordance between RCs, a pharmacist will qualitatively review and independently score as correct/incorrect.

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Medication dosing errors. We will use a 24-hour recall procedure utilized extensively by this team in prior and current studies to assess Rx dosing errors. At each interview, RCs will review medications reported as taken by the patient and those listed in the EHR to create a final list of medications prescribed to the patient. RCs will then ask patients to report, one by one, how they took each medication over the past 24 hours. Patients will be asked to specify the amount taken (i.e. dose) and when taken (to determine frequency and interval between doses). Patients will be asked to report whether this was how the medication was prescribed, and if not, will be queried: 1) to determine the reason for not taking the medication as prescribed (i.e. forgetfulness, ran out of medication) and 2) to describe how the medication *should* be taken. Data from this exercise will be used to assess correct dosing (yes/no) based upon the instructions for each medication. It will also be used to calculate regimen consolidation, or the total number of time points throughout the 24-hour period that a patient reported taking one or more medicines (count variable, range: 1-24).

Medication adherence. Adherence will be measured using: 1) the Ask-12 survey and 2) the proportion of days covered (PDC) according to pharmacy records. The Ask-12 is a brief measure of adherence that covers three domains: inconvenience/forgetfulness, treatment beliefs and behavior. In prior studies, the tool demonstrated good internal consistency reliability (Cronbach's α 0.75) and test-retest reliability (intraclass correlation 0.79); convergent validity was also

demonstrated through correlations with multiple other measures (Morisky, SF-12) and pharmacy claims data. Ask-12 scores range from 12-60, with higher scores indicating poorer adherence. PDC will be calculated by summing the number of days' supply obtained by a patient during a given time period and dividing by the number of days for which the medication was prescribed. For each patient, we will assess adherence within drug class. If a patient fills a prescription for a drug and switches to another drug within the same class, all prescriptions will be summed in the numerator. Adherence will be treated continuously and dichotomously (yes/no; PDC at disease-specific threshold based on Pharmacy Quality Alliance (PQA) standards). PDC data will be automatically obtained from Walgreens as part of the TEAM study.

Clinical Markers. We will abstract relevant clinical markers (e.g. HBA1c for patients with diabetes, LDL cholesterol for patients with hypercholesterolemia, blood pressure for patients with hypertension). Multiple blood pressure measures will be averaged for analyses in accordance with current protocols.

5.6 Process Evaluation

We will determine whether the TEAM intervention was implemented as planned (**Aim 2**) and barriers/facilitators to implementation (**Aim 3**) to optimize the intervention for future dissemination. Mixed methods will be employed to obtain data on intervention implementation. We will capture data from 5 sources: 1) patients, 2) ACCESS EHR, and 3) pharmacies and staff.

Patients receiving the TEAM intervention will be asked to report whether they were contacted by Walgreens for a medication review and if it was useful (1-10 scale). Patients will be asked about their satisfaction with each aspect of the intervention (1-10 scale), whether they refused (yes/no) and why. If applicable, they will be asked if clinic staff contacted them to resolve regimen issues (yes/no) and to rate the quality of these interactions (1-10 scale; CAHPS).

Data from the EHR will be compared to determine whether adherence concerns were properly captured in the EHR (yes/no) and if a clinic response was documented (yes/no). Walgreens fill data will be utilized to document timeliness/completion of prescriptions.

We will conduct focus groups and/or individual interviews with up to 5 participating Walgreens pharmacists and pharmacy staff to explore barriers and facilitators to implementing the TEAM intervention. All focus groups/interviews will be audio-recorded and transcribed. All participants will give informed online consent prior to participation. We will pay pharmacists who complete these interviews $150 in a Visa gift card sent a physical copy via mail or and electronic copy via email.

Cost Evaluation.

Throughout the trial, we will track explicit costs of implementing the TEAM intervention, from multiple sources (clinics, provider, community pharmacies, patient).

6.0 Data and Specimen Banking

Upon completion of all study activities, a final de-identified dataset will be created. This dataset will be stored indefinitely on the GIM server for secondary analyses. Only authorized personnel will have access to the dataset.

7.0 Sharing Results with Participants

Study results will not be shared with participants or anyone else.

8.0 Study Timelines

We anticipate the entire study will take 3 years to complete. The design phase will consist of a nine month window to finalize legal arrangements, an operational protocol and design and development of the evaluation tools. The implementation phase will occur between months 10-30. During this time, a brief pilot study (2-3 months) will finalize materials before the full implementation of the TEAM approach at ACCESS sites, recruiting 120 adults. Participants will be enrolled during a 20 month window and followed for a 12-month period. The evaluation phase will occur for the final 6 months of the study (months 31-36). During this time, quantitative and qualitative data will be collected from a variety of patient and provider sources to determine the extent to which the TEAM approach was delivered, as well as the impact on clinical workflow and patient outcomes.

Individual participants will be screened for eligibility (data pulls from ACCESS to identify new patients done on a quarterly basis) and if recruited and enrolled, will be active study participants for up to 6 months (baseline phone interview, TEAM intervention (if randomized to intervention arm) within 1 month of baseline, follow up phone interview at 2 months, potential TMR at 6 months), with a final EHR data pull completed 12 months post-baseline.

9.0 Inclusion and Exclusion Criteria

In order to participate in this study, patients must meet the following eligibility criteria:

9.1 Inclusion Criteria

Patients meeting inclusion criteria 1-5 below will be identified through ACCESS EHR data pulls on a quarterly basis. For those who qualify for the study based on these pulls, Northwestern RCs will contact these patients by phone to complete an initial phone screener during which time they will confirm criteria 1, 2, 5, and 6 as well as ensure that they do not meet any exclusion criteria.

1) Patient is age 50 and older
2) Patient is English or Spanish speaking
3) Patient has established care at one of the involved ACCESS health centers (defined as 1 visit within 18 months)
4) Patient is an existing Walgreens customer (had 1 or more medications filled at collocated Walgreens pharmacy within past 12 months)
5) Patient is currently prescribed 5 or more Rx medications (excluding antibiotics); that includes at least one medication from any of the following six therapeutic classes of medications: hyperlipidemia, hypertension, diabetes, multiple sclerosis, hepatitis C, and HIV
6) Patient is primarily responsible for administering own medication

9.2 Exclusion Criteria

We will further refine the list of eligible patients during the screening and consent process to exclude those with:

1) Severe, uncorrectable vision
2) Hearing impairments
3) Cognitive impairment (as measured by the 6-item screener)

10.0 Vulnerable Populations

Adults unable to consent and prisoners will be excluded from this research.

11.0 Participant Population(s)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Local	120	120	120
Study-wide	120	120	120
Total:	120	120	120

12.0 Recruitment methods

12.1 Identification of potential participants

Prior to putting the intervention into production, providers and staff at all participating health centers will be oriented to the project. The study will be described to physicians at participating clinics. The Epic data pull will generate lists of their potentially eligible patients (by primary language, established ACCESS patient, age, # Rx taken, existing on-site Walgreens customer). Physicians will receive the list via an inbox message within the EHR; they will indicate if any identified patients should not be contacted. Patients deemed ineligible by providers will be removed from the list of patients to contact.

12.2 Recruitment procedure

Due to COVID-19, there need to be multiple recruitment methods in place in order to do what works best for ACCESS and their health centers, especially since research staff may still be working remotely and not logistically able to perform large recruitment mailings. Therefore, the two recruitment methods in place are recruitment calls and/or recruitment letters. For the first two weeks of the pilot, we will perform recruitment calls. We will reassess after two weeks to determine if we should continue with the recruitment calls or switch to mailing recruitment letters. Regardless of whether the initial patient recruitment occurs via phone or mail, all recruitment activities will be conducted by CITI-certified ACCESS and Northwestern Research Coordinators (RCs).

Recruitment Calls

An ACCESS RC will call patients identified through the Epic patient pull to read through the recruitment letter over the phone. The RC can also email a copy of the recruitment letter if the patient would like to review it. During the call, the RC will read a script that clearly explains that if they are interested, a RC from Northwestern will call them the following week to see if they are eligible for the study and to go through the consent form for this study at that time. The ACCESS

RC will obtain verbal permission from the patient to allow a RC from Northwestern to contact them about the research study.

If the patient answers and agrees to being contacted by the Northwestern RC, the ACCESS RC will add that patient to the list that will be sent to NU. If the patient answers and would like to opt out, the ACCESS RC will remove the patient from the list. If the patient does not answer, the RC will leave a voicemail for the patient. The ACCESS RC will make up to four attempts by phone to recruit the patient before categorizing them as a passive refusal and removing them from the patient list.

At the end of the week, the ACCESS RC will send a list of patients that agreed to be contacted to Northwestern. The Northwestern RC will then screen the patient to determine eligibility (English or Spanish-speaking, responsible for administering medication regimen, taking 5+ medications, prescribed at least one medication from any of the selected six therapeutic classes (confirmed via brief chart review), no severe cognitive, hearing, visual impairment). If eligible, the RC will obtain informed online or verbal consent at the end of the call. If the patient is unable to stay on the phone to consent, the RC will schedule a follow up call to consent the patient before the baseline will be done. During the screening and consent call, the Northwestern RC will schedule the call to conduct the baseline assessment and randomize the patient to study arm. Prior to the baseline interview, the Northwestern RC will conduct a more thorough review of the patient medication list through either receiving a file from ACCESS or through read ability in EPIC for patient charts.

Recruitment Letters

An ACCESS RC will mail a letter to patients remaining on the list, notifying them that a RC from Northwestern University will be phoning to invite them to participate in a study. Patients will have the opportunity to opt out of being contacted. Ten days after the mailing, the Northwestern RC will start to contact patients by phone to ask if they would be interested in participating. If interested, the RC will screen the patient to determine eligibility (English or Spanish-speaking, responsible for administering medication regimen, taking 5+ medications, prescribed at least one medication from any of the selected six therapeutic classes (confirmed via brief chart review), no severe cognitive, hearing, visual impairment). If eligible, the RC will obtain informed online or verbal consent at the end of the call. If the patient is unable to stay on the phone to consent, the RC will schedule a follow up call to consent the patient before the baseline will be done. During the screening and consent call, the Northwestern RC will schedule a phone interview to conduct the baseline assessment and randomize the patient to study arm. Prior to the baseline interview, the Northwestern RC will conduct a more thorough review of the patient medication list through either receiving a file from ACCESS or through read ability in EPIC for patient charts.

Training will begin after questionnaire and interview protocols have been refined and standardized. The PIs and project manager will lead sessions to orient the research staff to the surveys and study protocols (e.g., interview process, use of laptop PCs, data security). All interviewers will be required to demonstrate competence in survey administration. All interviews will be conducted via REDCap, a secure, web-based application. Recruitment outcomes along with identifiable data necessary to contact participants will be recorded in NU's REDCap. Interviews will be conducted by research coordinators (RCs) over the phone. RCs will read each question aloud and record patient

responses directly onto a password protected laptop or PC computer using REDCap. Study interview data does not contain any identifiable information, and are identified by project staff by an assigned study ID. All identifiable information will remain in the secure REDCap system. Contacts with enrolled participants will be made via email, USPS and telephone.

13.0 Compensation for Participation in Research Activities

Patients will receive incentives for study visits ($50 gift card or money order for baseline and a $50 gift card or money order for 2 month follow up phone call). Compensation will be mailed to the patient's home address.

14.0 Withdrawal of Participants

In the case that subjects are unresponsive for 6 months past the date their follow up interview was due, they will be labeled as 'lost to follow up' and will be withdrawn from the study.

Participants can choose to withdraw from the study at any time. If a participant chooses to withdraw from the research, any data collected up until the point of withdrawal will still be utilized as it will not include identifying information.

15.0 Risks to Participants

Participation in the study poses minimal risk of psychological, social and economic harm. Informing subjects in advance that they may decline to answer any questions asked during the interview and discussion group will mitigate any risks associated with expressing their opinions (e.g., feeling uncomfortable). They will also be assured they can terminate their participation in the study at any time without penalty. The risk/benefit ratio is low. Minimal to no risk is expected for subjects in this study.

16.0 Potential Benefits to participants

It is possible that subjects enrolled in the intervention study arms may directly benefit in that they may have, as a result of this study, a better functional understanding of their medication. The results of this study may provide important information regarding how strategies can be implemented via the EHR and enhanced provider and pharmacist communication to support safe and appropriate medication use.

17.0 Data Management and Confidentiality

17.1 Analysis Plan

All analyses will be performed in SAS v9.4 (SAS Institute, Cary, NC). Ms. Batio will perform analyses under the direct supervision of Ms. Curtis and Drs. Wolf and Bailey.

Aim 1. Evaluate the fidelity and efficacy of the TEAM intervention to promote healthcare provider counseling, medication reconciliation, and safe regimen use among adults taking complex Rx regimens.

Quantitative analyses will be performed using SAS v9.4 (SAS Institute, Cary, NC). To ensure adequate balance across treatment arms, baseline outcomes and potential confounders including socio-demographic characteristics, comorbidities, regimen complexity, health literacy

level will be compared using ANOVA models and $\chi 2$ tests, as appropriate. Variables found to have significant differences ($p < .05$) across treatment groups will be entered as covariates in the generalized linear mixed models (GLMMs) used for formal analyses as described below. Treatment arm will serve as the primary independent variable. Analyses will be performed using PROC GLMMIX in SAS (v.9.4). A binary variable will be included in the model to denote the intervention group vs. usual care. As we will use stratified randomization by site, we will include in the GLMM an indicator variable for site and any potential confounding covariates noted in the descriptive studies. For outcomes assessed for each medication, 2-level GLMM will be used with medications nested in participants. Additionally, as there may be some effect of provider on adherence, we will explore the effect of any PCP by including provider as a random-effect. Using similar models as described above, we will assess the impact of TEAM on clinical markers (HBA1c, blood pressure, cholesterol) among patients with diabetes and hypertension.

Aim 2. Explore patient, healthcare provider (pharmacist, prescriber), community pharmacy and/or primary care practice barriers to implementation.

We will determine the extent to which the TEAM intervention was implemented as planned at each site in order to optimize the intervention for future dissemination opportunities. Mixed methods will be employed using a convergent parallel design to obtain data on intervention implementation. Quantitative and qualitative findings will be synthesized together to yield a more comprehensive understanding of: 1) whether the interventions were implemented as planned; 2) if (and how) the TEAM intervention might be modified based on user feedback. In this approach, both analyses are conducted separately and synthesized for side-by-side data comparisons. For quantitative data (patient report, EHR, pharmacy data), frequencies will be generated to determine outcomes related to receipt of notifications and feedback and perceived helpfulness of TEAM processes. Similar GLM models as described in Aim 1 analyses will be performed, with TEAM intervention arm as the primary independent variable.

For qualitative data, the study team will review common themes found throughout the pharmacist interviews drawn from the discussion guide and the pharmacists responses. We will use an iterative approach to identify and group emergent themes. Pharmacist quotes will be identified to highlight themes. Attention will be paid to facilitating factors and impeding factors identified during the interviews. An additional layer within impeding factors would be whether or not factors are modifiable, and under facilitating factors, if they are replicable.

Aim 3. Determine the costs of the TEAM intervention from both a community pharmacy and primary care practice perspective.

We will directly measure and assess the costs of developing and running the TEAM intervention. The incremental cost of both strategies will be estimated relative to usual care and each other from both the perspective of the FQHC sites and the Walgreens pharmacies delivering the MTM services. The primary resources for running TEAM include from pharmacy: 1) Walgreens pharmacist time for contacting patients, conducting medication reviews, documentation, messaging prescribers; 2) Walgreens clinical analyst to program adherence reports. Resources to implement TEAM from the primary care practice include: 3) discrete ACCESS programming time for linking Walgreens pharmacies with read/write access; 4) clinic orientation to the newly-available TEAM process and available safety alerts and adherence data, and training on how to respond. The costs of the pharmacist, analyst time (for both ACCESS and Walgreens) are easily

documented. For costs associated with staff training, estimates will be made, with sensitivity analyses performed assuming orientations performed by staff at varying levels of experience based on internal data on wages as well as nationally representative estimates from the Bureau of Labor Statistics.

We will also include estimates for the cost of programming maintenance at each site for the Epic EHR, testing the sensitivity of results to changes in maintenance requirements (in programmer hours) along with internal data on wages. Costs associated with diverted time and changes to workflow to attend to alerts and messages from the pharmacist will also be estimated, as well as changes in the efficiency within a pharmacy due to more rapid communication channels with prescribers. Development costs for software and other programming will be separately tracked. Staff/programmer costs will be measured using tracked time spent on the intervention and wage estimates. We will test the sensitivity of operational costs to different assumptions about potential use of variable staff using different salaries but assuming the same proficiency in time required. We will also assess the sensitivity of estimates to different proficiency levels that could arise from learning by doing.

17.2 Protocol to ensure confidentiality.

Each subject will be tracked using an Access database. The database, containing identifiers and other related information for coordinating research activities (recruitment outcome, interview call log and interview visit schedule, etc.) will be kept on the secure Northwestern network drive. Only the PI, project manager, and RC will have access to this database. ACCESS participants will be additionally tracked in their EPIC EMR system, only accessible by ACCESS study personnel.

Data will be collected via REDCap. REDCap is a secure, encrypted online data collection tool, which can only be access by NU authorized personnel listed on the project's IRB.

Several methods will be employed to reduce the risk of breach of confidentiality. A study identification number will be assigned to each subject in the study. The research data collected and stored will have the study identification number and no other identifying information on it. The de-identified study data will be kept in a separate locked file cabinet. Using this method, if someone were to gain illegal access to the locked filing cabinet with study data, they would have no way to link this data to any identifying information.

17.3 Quality Assurance.

Training will begin after surveys and interview protocols have been refined and standardized. A training session will be conducted by Drs. Wolf and Bailey. The training will include tailored discussion of 1) roles and responsibilities; 2) HIPAA and IRB mandates (completion of Human Subjects Training Program - CITI; 3) effective recruitment communication and interviewing with attention paid to health literacy and culture; and 4) gathering and recording data including administering the structured survey electronically. Role playing will be used to fine tune training for obtaining informed consent and interviewing patients. Institutional Review Board (IRB) approval will be attained at both sites prior to any active recruitment efforts. All interviewers will be required to demonstrate competence in survey administration.

17.4 Study-wide data management.

Data collected includes patient consent forms, data gathered using the ACCESS patient lists, and data collected during the study interviews.

Data Access. The Data Custodian is the Principal Investigator, Dr. Michael Wolf. Only authorized personnel listed on each institutions IRB will have access to the data. Any information that could allow identification of individual participants, including the master list, will be kept strictly confidential.

Local Data Storage. Data will be stored in REDCap, a secure, web-based application, and on the Northwestern secure server for the length of the study. The Project Manager or Data Analyst will download the de-identified data only from REDCap monthly and save to the "Analytic" folder within the TEAM project folder on the FSM department servers which are located in a HIPAA compliant data center. These data files do not contain any identifiable information, and are identified by project staff by an assigned study ID. All identifiable information for ACCESS patients will remain in the secure REDCap system. Upon completion of all study activities, a final de-identified dataset will be created and all identifiable information will be deleted. This dataset will be stored indefinitely on the GIM server for secondary analyses. Only authorized personnel will have access to the dataset. All identifiable information will be deleted upon completion of the study

18.0 Provisions to Monitor the Data to Ensure the Safety of Participants

18.1 Data Safety and Monitoring Board (DSMB)

This study involves no greater than minimal risk. Due to this, we will not be convening a DSMB for this study.

19.0 Provisions to Protect the Privacy Interests of Participants

19.1 Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). In order to preserve participants' confidentiality rights, research subjects will be assigned code numbers that will be used to identify all the information collected. Using these codes, none of the collection forms will contain the names of the participants. All electronic data will be stored in on a password-protected computer. A Microsoft Access master study tracking database will contain information linking participants to their study id numbers. This database will be encrypted and kept on a secure server and only accessible by study personnel.

19.2 Survey data will be stored in a REDCap. Individual study identification numbers will be assigned to each participant and only this number will appear on the survey. Subjects will be told that unless required by law, only the study investigators, members of the project staff, the funding agency and representatives of Institutional Review Boards will have the authority to review any study records. In such cases, these parties too will be required to maintain confidentiality. The final data set will be stripped of identifiers. Data will be shared via presentations at national and international meetings and in peer reviewed publications. Furthermore, all results will be shared with the funding institute.

19.3 Participation in the study poses minimal risk of psychological, social and economic harm. Informing subjects in advance that they may decline to answer any questions asked during the interview will mitigate any risks associated with expressing their opinions (e.g., feeling uncomfortable).

19.4 All enrolled participants will provide e-consent, include HIPAA authorization for the collection of all data, including review of the patient's medical record. For those who are unable to provide e-consent due to inability to access the required technology, they will undergo verbal consent with an alteration of HIPAA Authorization, as described below in sections 22.0 and 24.0.

19.5 Only authorized personnel listed on each institutions IRB and approved by the PI will have access to the data.

20.0 Compensation for Research-Related Injury – N/A

21.0 Economic Burden to Participants – N/A

22.0 Consent Process

22.1 Process to Document Consent in Writing

Due to COVID-19 in-person interview restrictions, we will complete an online consent with HIPAA authorization and complete the baseline by phone after consent is obtained. The RC will send patients a link to REDcap either by email or text to be able to read through the consent with the RC following the protocol below. If the patient agrees to participate, they will be asked to sign and date the online consent.

If a patient is unable to complete an online consent due to inability to use or access technology for online consent, we request a waiver of documentation of informed consent and an alteration to obtain verbal HIPAA Authorization. Due to restrictions during the COVID-19 pandemic, we are no longer planning to conduct any in-person interviews to protect patients' safety and to follow Northwestern guidelines. Research cannot practicably be conducted without the waiver or alteration. For patients that are unable to complete online consent, research cannot practicably be conducted without the waiver or alteration. After verbal consent and HIPAA Authorization is obtained, the consent date and the name of the research coordinator that obtained the consent will be recorded in Redcap by the RC prior to starting the baseline interview.

Informed online and verbal consent will be viewed as a process, i.e. at several times during review of the IRB approved consent document, the subject will be asked to explain in his/her own words what his/her understanding of the consent. This will enable the research personnel to enter into a dialogue with the subject and ensure that the subject understands that he/she is free to withdraw at any time without penalty. Information will be provided to the subjects in terms that they can fully understand. There will be no exertion of any overt or covert coercion. They will be encouraged to ask questions prior to giving consent.

The participant will be informed that they are free to withdraw at any time without penalty and all information will be provided to the subjects in terms that they can fully understand. Once the RC

is satisfied that the participant understands the consent process and the nature of their participation in the research study, the RC will ask the participant if they would like to participate in the study.

For online consents, patients will be informed they can print their screen to keep a copy of the consent. For patients that complete a verbal consent, they will be emailed or mailed a blank copy of the consent document for their records.

23.0 Non-English Speaking Participants

All study materials are available in both English and in Spanish and our RCs are bilingual. We have included Research Support Services as part of the grant to provide Spanish translations for materials that have yet to be created. Patients who do not speak either Spanish or English will be ineligible to participate. Patients will be asked their language of choice as they are consented. Research coordinators will be able to conduct all interviews and schedule phone calls in either language. Pharmacists delivering the intervention will do so in the patient's preferred language.

24.0 Protected Health Information (PHI and HIPAA)

24.1 Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). In order to preserve participants' confidentiality rights, research subjects will be assigned code numbers that will be used to identify all the information collected. Using these codes, none of the collection forms will contain the names of the participants. All electronic data will be stored in on a password-protected computer. A Microsoft Access master study tracking database will contain information linking participants to their study id numbers. This database will be encrypted and kept on a secure server and only accessible by study personnel.

Survey data will be stored in a REDCap. Individual study identification numbers will be assigned to each participant and only this number will appear on the survey. Subjects will be told that unless required by law, only the study investigators, members of the project staff, the funding agency and representatives of Institutional Review Boards will have the authority to review any study records. In such cases, these parties too will be required to maintain confidentiality. The final data set will be stripped of identifiers. Data will be shared via presentations at national and international meetings and in peer reviewed publications. Furthermore, all results will be shared with the funding institute.

24.2 All enrolled participants will provide either e-consent or verbal consent, which will include HIPAA authorization for the collection of all data, including review of the patient's medical record. For patients who are unable to provide e-consent and signed HIPAA Authorization, we are requesting an alteration of HIPAA Authorization in order to obtain HIPAA Authorization verbally. These patients would otherwise be unable to participate in this research study and therefore this research could not practicably be conducted without this alteration in place. Only authorized personnel listed on each institutions IRB and approved by the PI will have access to the data.

Due to restrictions during the COVID-19 pandemic, we are no longer planning to conduct any in-person interviews to protect patients' safety and to follow Northwestern guidelines. If a patient is unable to complete an online consent due to inability to use or access technology for online consent, we request a waiver of documentation of informed consent and an alteration to obtain verbal HIPAA Authorization. For these patients that are unable to complete online consent, research cannot practicably be conducted without this waiver or alteration. After verbal consent and HIPAA Authorization are obtained, the consent date and the name of the research coordinator that obtained the consent will be recorded in Redcap by the RC prior to starting the baseline interview.

As this research could not practicably be conducted without the waiver or alteration of HIPAA, it could also not practicably be conducted without access to and use of PHI. The main intervention component of this study involves a pharmacist reviewing the patient's medications with them and making notes (with EPIC security points in place) in their EHR for the patient's provider to see. It would not be feasible to conduct the study and implementation of the intervention without the access and use of PHI.

Identifiers and other related information for coordinating research activities (recruitment outcome, research interview call log and interview visit schedule, etc.) will be password protected and kept on the secure FSM network drive. Only the PI, project manager, and RAs will have access to this database. Identifiers included in the database include: name, MRN, address, phone number, DOB. Upon completion of all study-related data collection the Access database will be deleted. Study generated data will be stored within REDCap and OneDrive and will be downloaded (void of all identifiers) into the project's Analytic folder on the FSM server. Upon completion of the study, a final dataset, void of all identifiers will be created, and stored indefinitely for secondary analyses.

PHI will not be used or disclosed to a third party except as required by law, for authorized oversight of the research study, or for other research uses and disclosures permitted by the Privacy Rule.

25.0 **Qualifications to Conduct Research and Resources Available**

25.1 Team. Drs. Wolf and Bailey, as well as Dr. Parker (Co-Investigator) are internationally recognized for their expertise and extensive work in the space of health literacy, medication safety and adherence. For more than a decade, Drs. Wolf and Bailey have collaborated and co-led numerous NIH, AHRQ, foundation and industry-sponsored pragmatic trials testing health system interventions aimed at helping patients better understand, safely use, and adhere to complex prescription regimens. Combined, Drs. Wolf, Bailey and Parker have more than 200+ peer-reviewed publications addressing safe medication use. Dr. Tarn (UCLA) is a member of the study team for her medication communication and clinical expertise, as well as her assistance in creating opportunities for dissemination within the UCLA Epic platform. Her involvement will facilitate more rapid dissemination opportunities and learnings.

Over the past 3 years, Dr. Wolf has worked to establish a master research agreement with Walgreens Co., which is now in effect as of Spring 2018. The goal of the agreement is to allow for more expedited project opportunities with Northwestern that support improvements in both medical

and pharmacy practices. Drs. Wolf and Bailey, along with Northwestern Memorial Healthcare's Epic Innovations Team, are also leaders in leveraging electronic health records to promote patient engagement, medication therapy management, and follow-up opportunities (via portal and other modalities) for monitoring medication use, adherence and mobilizing clinical teams if regimen concerns arise. In addition to the unique strengths of the Northwestern team and Emory partner, Walgreens Co. is one of the largest community pharmacy chains in the world, and the only 'global' pharmacy with its Walgreens Boots Alliance. The potential for scale is unprecedented. Further, Walgreens team members have successfully worked with Dr. Wolf over the past 7 years.

ACCESS also has ample experience working with the Northwestern team, with partnerships with Drs. Wolf and Bailey dating back nearly two decades. As one of the largest FQHCs in the country, the diversity in their patient population and focus on medically underserved adults offers an exceptional environment to test the TEAM strategy and its ability to benefit disparities-affected populations.

25.2 Health Centers. Performance sites will be health care centers affiliated with Access Community Health Network. All ACCESS health centers use Epic® EHR (version 2016; Verona, WI) to promote quality improvement; Drs. Bailey and Wolf have collaborated extensively in the past on EHR-based research projects and have worked on many research studies and proposals with ACCESS key personnel.

ACCESS. Access Community Health Network has been on the frontlines of community-based health care in Cook and DuPage counties for 25 years, serving the health needs of underserved communities by providing preventive care, chronic disease management, and other support services. In 2017, ACCESS served more than 183,000 individuals, including 26,117 patients with hypertension and 16,923 patients with diabetes. The patient population is low income and racially/ethnically diverse. ACCESS uses the **Epic EHR** platform (Verona, WI). Data queries indicate ~3,900 potentially eligible patients at our six study sites (by age, ≥5 R_x medications, and using Walgreens as their primary pharmacy).

Clinic Space, Orientation and Workflow. Dr. Lazar will coordinate activities and plan space needs with clinic liaisons for patient recruitment and study visits. A patient flow chart will be developed to detail optimal timing of intervention delivery, recruitment and data collection. All study clinics will receive onsite orientation to the study during regularly scheduled business meetings. Dr. Lazar will work with clinic liaisons to plan protocol responses to patient regimen issues (e.g. discrepancies, ADEs, adherence) communicated to them by the pharmacist.

25.3 Walgreens. For 7+ years, our team has partnered with Walgreens on projects centered on innovations, MTM, and partnerships with primary care. In 2018, Dr. Wolf (MPI) coordinated a master research agreement between Northwestern and Walgreens. We are one of few academic partners formally collaborating with Walgreens through their Center for Health and Wellbeing Research. With >8,000 stores in the US (heavily populated in medically underserved areas), Walgreens ranks as the largest retail community pharmacy chain.