PROTOCOL TITLE:
A Universal Medication Schedule to Promote Adherence to Complex Drug Regimens

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1.0 Objectives

1.1 Specific Aims:

1. Compare the effectiveness of the UMS EHR tools, with or without SMS and/or Portal interventions.
2. Evaluate the 'fidelity' (reliability) of each strategy and explore patient, staff, physician, and health system factors influencing the delivery of the interventions, alone and in combination
3. Assess the costs required to deliver each of the interventions from a health system perspective

1.2 Hypotheses:

H1-2. Compared to enhanced usual care, patients in the SMS only arm [H1] and in the Portal only arm [H2] will have greater adherence to their Rx regimen.

H3. Compared to SMS only arm, patients receiving both the SMS and Portal, will have greater adherence to their Rx regimen [H3].

H4. Compared to the Portal only, patients receiving both the SMS and Portal will demonstrate greater adherence to their Rx regimen [H4].

2.0 Background

2.1 Disease Background

Effective, practical, and scalable approaches are needed to help patients safely use complex Rx regimens.[1-3] We will leverage available technologies and test strategies to impart the Universal Medication Schedule (UMS) in **primary care** to help patients understand, consolidate, safely use, and adhere to their medications.

The Challenge of Managing Complex Drug Regimens.

In ambulatory care, patients assume primary responsibility for safely and appropriately administering Rx regimens.[1] Yet the expectations placed on patients by the healthcare system for medication-related tasks are considerable. In order for patients to gain the benefits of drug therapy while minimizing risks of adverse drug events (ADEs), they must: 1) have a functional understanding of medications and their proper dosing, 2) consolidate their regimen to the most efficient daily schedule, 3) problem-solve around regimen use as changes occur, and 4) continue the behaviors over time. Studies have repeatedly documented that patients have problems performing these routine tasks.[4-7] This is alarming, as adults are being prescribed increasingly complex medication regimens.[8] Over the past decade, the percentage of Americans taking ≥ 5 Rx drugs daily has doubled to nearly 40% of older adults.[8] While long-term adherence is essential to reap health benefits, all forms of non-adherence - failure to fill new prescriptions, incomplete use, and premature discontinuation - are common.[9-14] Non-adherence has been linked to greater morbidity and mortality from chronic conditions. Complex drug regimens also raise the risk for errors and ADEs, many of which are preventable or ameliorable.[15-20] Nearly 10 million outpatient physician visits and 4 million emergency department admissions are attributed to ADEs or side effects annually.[21] These are more likely to occur in primary vs. specialty care, among older patients and those with multi-morbidity.[21-23]

★ **Vulnerable Populations.** Older age poses a significant risk for medication safety and adherence concerns for obvious reasons. The prevalence of multi-morbidity increases with age; approximately 17% of younger adults ages 20-39 live with 2 or more chronic conditions compared to a third of middle-aged adults (40-59), and nearly two thirds of individuals over 60 years old. This, in turn, often translates to a greater number of prescribed medications. As part of the aging process, the challenge of managing complex drug regimens is made ever more difficult by higher rates of cognitive decline and limited health literacy.[24-26]

Literacy. Numerous studies have found limited literacy skills to be significantly associated with patients' poorer recall of medication names and indications, inadequate understanding and demonstrated use of Rx instructions and precautions.[5,6,27-32] Our team found that patients also may overcomplicate multi-drug regimens by taking medicine more times a day than necessary.[4] Lower literate patients were at greater risk for not consolidating regimens [M=6.1 times/daily (SD=1.8); adequate literacy M=5.8 (SD=1.6) vs. low literacy M=6.5 (SD=2.4), p=0.03]. While studies have been inconclusive as to whether lower literacy is associated with non-adherence,[33-36] the evidence clearly suggests that patients with lower literacy are more likely to misunderstand Rx instructions, putting them at greater risk for poor adherence.[7,37]

Language. In addition, limited English proficiency (LEP) presents a formidable barrier in healthcare.[38-43] Interpreters are rarely available to aid physicians and pharmacists in counseling LEP patients on safe Rx use, instructions are frequently unavailable in non-English languages, and multilingual materials are often inaccurate and poorly translated.[44-47] These barriers have been shown to have a deleterious effect on LEP patients' Rx use.[48-50] Wilson, et al. studied 1,200 LEP adults in California.[50] Nearly half encountered difficulties interpreting Rx instructions and 16% experienced an adverse reaction as a result. Similarly, Sleath et al. found that 58% of LEP adults reported difficulty understanding English Rx instructions as a barrier to safe use.[51]

★ **Health System Barriers.** Individual barriers such as older age, limited literacy, and LEP are exacerbated by health system barriers.[52] Multiple studies have shown physicians often fail to discuss with patients basic information around the safe use of prescribed medicines, let alone other relevant concerns (i.e. cost of medications).[53-57] Furthermore, print Rx information is rarely distributed at the point of prescribing. Evidence also suggests that pharmacists equally fail to counsel patients on safe and appropriate Rx use.[53,55,56] While print materials (Rx labels, warning stickers, Medication Guides, patient leaflets) are provided by pharmacies, most are poorly written and confusing.[58-61] In addition, considerable variability has been identified across this process.[62-64] Bailey et al. found Rx instructions written by physicians to be highly variable;[63] Wolf et al. reviewed Rx instructions printed by multiple pharmacies and also found that pharmacy translations often deviated from physicians' instructions.[64] Variable, poor quality physician prescriptions and pharmacy translations and lack of appropriate counseling complicate the task of organizing and properly dosing multi-drug regimens.

2.2 Rationale

An Evidence-Based Solution: A Universal Medication Schedule (UMS).

The IOM 2008 report *Standardizing Medication Labels* recognized the need for setting standards within prescribing and dispensing practices to promote safe and accurate

medication use for patients.[65] Members of our research team (Wolf, Wood) presented the concept of the UMS in this report. As approximately 90% of prescriptions are taken four times a day or less, the UMS specifically proposed to establish four standard time intervals (morning, noon, evening, bedtime) for the prescribing and dispensing of medicine. This would remove current variability in the manner in which prescriptions are written by physicians and transcribed by pharmacists.[62-64] All prescriptions would instruct patients to take their medicine at one or more of these specified times; this would be described in a single, standardized fashion. UMS instructions also use health literacy best practices, like simplified text, numeric characters instead of words to detail dose (1 instead of 'one'), and 'carriage returns' (placing each dose on a separate line) to clearly identify every time a medicine is to be taken.[4]

There is strong evidence supporting the UMS.[4,65-70] Among a multi-site sample of 500 primary care patients, Wolf et al. found those receiving UMS instructions versus a current standard were 33% more likely to accurately interpret R_x instructions.[66] Lower literate adults were more likely to correctly comprehend the UMS instructions. These findings were replicated among 94 patients in Cork, Ireland, and also among 203 LEP patients in Chicago and San Francisco.[68,69,71] Earlier studies also found the use of more explicit time intervals, such as those used in the UMS approach, improved patient understanding and reduced medication errors.[67,72]

In January 2014, our team completed two parallel, 5-year clinical trials testing the UMS as an embedded standard in pharmacy practice [R01HS017687; R01HS016435]. 845 English and Spanish-speaking, low-income patients with type 2 diabetes and hypertension being cared for by one of 8 community health centers in the Washington D.C. area received reduced-cost medications from a collaborating non-profit, central-fill pharmacy. Patients were randomized to receive their bundled medications with UMS label instructions or a current standard modeled after a leading national pharmacy chain (no orientation to UMS provided). Over 9 months, both English and Spanish-speaking patients improved their proper use of multi-drug regimens (OR 1.98, 95% CI 1.02-3.85) with benefits extending to a near two-fold increased adherence rate as measured by pill count (OR 0.58, 95% CI 0.35-0.98). Exploratory analyses also found a non-significant trend with glycemic control between arms (tight control (HbA1c <7.0%: 55.6% (UMS) vs. 46.3% (Standard), p=0.15). As with prior studies, these benefits were greatest for lower literate adults and those taking >5 Rx drugs. *The IOM has repeatedly highlighted this concept, the US Pharmacopeia, American College of Physicians, and National Council for Prescription Drug Programs recommend it as a standard, and California passed legislation in 2011 stating the UMS as a best practice for Rx labeling, also supported by the National Board of Pharmacy*.[65,73,74]

Shifting Upstream: Implementing the UMS at Prescribing vs. Dispensing Medication.
The above AHRQ/NIH-funded trials revealed several obstacles: 1) over half of patients routinely use multiple pharmacies resulting in their continued receipt of variable R_x label instructions; 2) imparting the UMS only on drug labels was not a sufficient signal to patients to consolidate multi-drug regimens; 3) patients need comprehensive views of the UMS applied to their entire R_x regimen vs. individual R_x labels only; 4) additional reminders may be beneficial to reinforce UMS prescribing after medical encounters, helping patients remember and simplify daily R_x use, and support adherence; 5) the UMS

alone may be insufficient at addressing multifaceted concerns that may warrant more intensive counseling and monitoring (issues with costs, side effects, regimen fatigue, motivation, etc.). Both the pharmacy and patients also expressed a need for improved, plain language R_x information that provides general knowledge to support safe R_x use. Our proposal is based on evidence from the field, extensive experience with EHRs, mobile technology, patient portals, and funded development work [R18HS17220, R21CA132771, R01NR011300, R01NR012745, U19HS021093]. We will shift the implementation of the UMS to primary care, leveraging technologies that are becoming increasingly prevalent per federal mandates (Health Information Technology for Economic and Clinical Health (HITECH) Act), particularly among community health centers.[75] We respond to the Office of the National Coordinator (ONC) 'Meaningful Use' criteria by leveraging an EHR to deliver standard, patient-centered information supporting safe R_x use, as well as by extending the utility of a patient web-based portal.[76]

Leveraging Increasingly Available Technologies to Support Medication Use. There are increasingly available technological solutions that can be leveraged to help patients learn how to safely and appropriately take prescribed medications at a cost that is not prohibitive, including electronic health records (EHRs) with corresponding 'patient portals' and cell phone applications (SMS text messaging).[75,77-80]

★ **'Meaningful Use' of EHRs.** Our team has successfully field tested the UMS strategy at two academic centers using different EHR platforms (EpicCare: R18HS17220, R21CA132771; Cerner: U19HS021093).[77] This included: 1) UMS-mapped standard physician instructions (a.k.a. 'sigs') that were e-prescribed to pharmacies (Epic only), 2) plain language medication information sheets ('MedSheets') incorporating the UMS sig given to patients upon checkout, and 3) a redesigned EHR medication list ('MedList') that organized a patient's entire R_x regimen according to UMS intervals (Cerner only). *These tools are in English and Spanish; we will now export all of these tools into a new EHR platform (GE Centricity) and Epic for this study.*

★ **Mobile Technologies to Promote Health Behavior Change.** While EHRs can be leveraged to provide tools to support appropriate medication use in primary care, additional measures may be necessary to promote safe medication use outside of healthcare settings.[77,81,82] Mobile technologies, specifically SMS text messages, have been used to provide health-centered messages to patients in their daily lives.[83-86] Recent estimates indicate mobile technologies are useful tools for reaching low-income populations and racial/ethnic minorities; 92% of African-American and Latino adults own cell phones.[87] Text messaging capabilities are also commonly used; 81% of cell phone users send or receive text messages.[87] *While use of this technology is more common among younger adults, the number of older adult cell phone (even smart phone and tablet) users is increasing exponentially (89% ages 50-64; 77% ≥65), including those who actively receive and send text messages.*[87] Multiple studies have been conducted to evaluate text messaging as a means of promoting behavior change. [81,83,88] A 2010 systematic literature review by Cole-Lewis and Kershaw evaluated 12 interventions that utilized text messaging as a platform for disease management or prevention.[83] Eight studies in this review reported positive changes in behavioral or clinical outcomes among individuals receiving text messages; outcomes included greater weight loss, smoking cessation, increased blood glucose monitoring and decreased hemoglobin A1c. Recent studies have found text

reminders increased R_x adherence, yet causal mechanisms and implementation 'best practices' remain unclear.[89,90]

★ **Web-Based, EHR Patient Portal.** Increasingly, EHR systems are incorporating 'patient portals'; these are web-based tools that allow patients encrypted access to their medical record.[91-98] A variable list of functions may be offered to allow for self-management support and enhanced communication between patients and healthcare providers (i.e. email physician, schedule appointments, reconcile and refill medicines). *Improving access to and use of portals is important for ONC Meaningful Use stages 2-3 criteria that emphasize greater health information exchange, patient-controlled data and patient involvement in decision making.*

While the potential value of patient portals is undeniable, actual evidence on their acceptability, usability, and effectiveness in benefitting patient care remains limited (Goldzweig et al, 2013).[92] A few studies have found a diverse set of adults (young, old, veterans) to perceive these tools to be valuable. In specific circumstances they have been repeatedly used by patients, and a couple of trials have found portals to significantly improve patients' adoption of recommended health behaviors.[99,100] Nagykaldi et al. found that use of a patient portal among 422 adults at two primary care practices increased patient activation, perceptions of patient-centered care, and compliance with recommended preventive services (uptake of low-dose aspirin, pneumovax, children's immunizations).[101] Little evidence is available specific to use of the patient portal for medication self-management purposes. McInnes et al. examined data from the Veterans Aging Cohort Study and found that HIV+ veterans who used an electronic personal health record were nearly twice as likely to be ≥ 90% adherent to their antiviral regimens (OR 1.80, 95% CI 1.35-2.38).[102] Specific web portal functions used by veterans that aided adherence could not be identified, *yet we still view the ability to review medication lists and lab values, to contact providers via secure messaging, and to seek additional Rx information as viable mechanisms for improvement.* Intensifying the challenge of how to make best use of the portal technology, system designers must account for age, race/ethnic, and literacy barriers.

3.0 Inclusion and Exclusion Criteria

3.1 **Methods of screening for eligibility.** Patients will be screened for eligibility by phone after they have had a regularly scheduled doctor appointment. The screener document details the series of questions that will be asked.

3.2 **Inclusion and Exclusion criteria.**

Patient Inclusion Criteria. Patients must meet the following eligibility criteria:

1) Patient is age 50 and older
2) Patient is English or Spanish speaking
3) Patient has 5 or more R_x medications listed in the EHR list (we exclude 'as needed' (PRN) medicines from all analyses and will not apply the UMS to these medicines) and self-reports being prescribed 3 or more R_x medications during the screener call.
4) Patient owns a cell phone and is able to receive text messages
5) Patient has access to the internet, and has or is willing to obtain a personal email address.

Patient Exclusion criteria. Adults with severe, uncorrectable vision, hearing or cognitive impairments or who are unable to consent, as well as prisoners will be excluded from this research.

COVID-19 Survey Eligibility
Wave 1: We will include any participant who has consented to participate in the main study and who has indicated that they were willing to be contacted for future studies run by Dr. Wolf on the consent form.

Waves 2 – 4: We will include any participant who has consented to participate in the main study, who has indicated that they were willing to be contacted for future studies by Dr. Wolf on the consent form, and who completed at least Wave 1 of the COVID-19 survey.

Waves 5-9:
We will include any participant who has consented to participate in the main UMS Portal study, who has indicated that they were willing to be contacted for future studies by Dr. Wolf on the UMS Portal consent form, and who completed at least Wave 1 of the COVID-19 survey.

Patient Inclusion Criteria: Any provider or staff that works at Erie Family Health Center or Lavin Primary Care, Northwestern University will be eligible to complete the provider/staff survey.

4.0 Study-Wide Number of Subjects

4.1 A total of 1505 patients will be enrolled in the study across all sites.

4.2 We expect around 50 providers and staff will be enrolled for the provider/staff survey but we will not limit responses. All providers and staff that may have been exposed to the study will receive a link to complete the survey.

5.0 Study-Wide Recruitment Methods

5.1 Patient Interviews.

Recruitment will be done by phone by trained Northwestern RAs.

For patients recruited from Erie Family Health Center: first, Alliance will send Erie providers an encrypted file of a list of eligible patients from Erie Family Health Center who have an upcoming doctor appointment scheduled. Providers will indicate if any eligible patients should not be contacted. Providers will be reminded via email to reply with their list of approved patients. Providers will be informed that if they do not respond within two weeks they are giving Northwestern permission to contact all patients on the list. Northwestern will then mail a letter to patients on the list, notifying them that a research coordinator (RC) will be telephoning to invite them to participate in a study. Patients will be given the opportunity to opt out of being contacted by calling a hotline number and leaving a message. RCs will monitor the messages and send Alliance a list of patients who have chosen to opt out. Seven days after the letters have been sent, an RC will call patients

who did not opt out to ask screener questions to determine eligibility and, if eligible and interested, schedule their baseline. Due to COVID-19 restrictions, the study team may not be able to mail letters to all patients. If a letter mailing is not possible, the study team will still obtain permission from the provider to contact their patients but not send recruitment letters.

For patients recruited from Northwestern Medicine Primary Care: potential participants will be identified through reports generated by the Enterprise Data Warehouse (EDW) for patients who have an upcoming appointment scheduled. Per clinic protocol, all eligible patients can be contacted and providers will not receive a list of their patients to indicate who should not be contacted. Research staff will then mail a letter to patients on the list, notifying them that a research coordinator (RC) will be telephoning to invite them to participate in a study. Patients will be given the opportunity to opt out of being contacted by calling a hotline number and leaving a message. RCs will monitor the messages of patients who have chosen to opt out. Seven days after the letters have been sent, an RC will call patients who did not opt out to ask screener questions to determine eligibility and, if eligible and interested, schedule their baseline. Due to COVID-19 restrictions, the study team may not be able to mail letters to all patients. If a letter mailing is not possible, the study team will contact patients by phone after their doctor's visit but not send recruitment letters.

For providers and staff: To investigate healthcare provider and/or healthcare system-level barriers to implementation, we will conduct brief online interviews (n ~25-50) with clinic providers and staff to explore barriers and facilitators to implementing the various intervention strategies. The practice manager, academic manager, or clinician partner at Erie Family Health Center and Northwester Medicine will email providers and staff that may have been involved in some aspects of the study a Redcap link to an online consent. If the provider or staff member consent and click next, they will be taken to a brief online survey. Survey responses will be anonymous.

5.2 **Data Abstraction from the Erie EHR.**

Mr. Hamilton (Quality Informatics), working under the supervision of Dr. Rachman, will write Structured Query Language (SQL) programs to extract data periodically from the EHR database. Also, lists of potentially eligible patients will be generated for recruitment and periodic medication lists will be updated in order to measure medication reconciliation. Data sets containing study identification numbers only will be prepared for sharing with the team.

6.0 Multi-Site Research

6.1 This study is a single-centered study.

7.0 Study Timelines

Timeline: We are anticipating the project to be completed in 4.5 years. The image below describes the timeline of events for this proposed study.

Table 2. Study Timeline	Year 1				Year 2				Year 3				Year 4				Year 5	
TASKS	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2
PREPARATION PHASE:																		
Hire and train staff; convene DSMB	■	■																
Pilot test and refine assessment tools		■	■															
Orient sites, lead training, plan logistics			■															
Implement, de-bug EHR/mobile tech tools		■	■															
INTERVENTION PHASE:																		
Recruit, consent, and randomize participants				■	■	■	■	■	■	■	■	■	■	■	■			
Conduct baseline interviews				■	■	■	■	■	■	■	■	■	■	■	■			
Implement interventions				■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Conduct follow-up interviews				■	■	■	■	■	■	■	■	■	■	■	■	■	■	
Seek process feedback from clinic staff									■				■				■	
Extract EHR data					■				■				■				■	
EVALUATION PHASE:																		
Clean and analyze data						■	■	■	■	■	■	■	■	■	■	■	■	■
Summarize and interpret findings													■	■	■	■	■	■
Submit manuscripts for publication							■				■				■	■	■	■
Present findings at national venues							■				■				■			■

7.1 **Study Duration**.

1. The anticipated duration of participation will be 6 months. Patients will complete an in-person or phone baseline interview after having a regularly scheduled doctor appointment. They will then complete a 6-8 week phone interview, and a 6-month post baseline, in-person interview or phone interview (if unable to complete in person due to NU COVID-19 in-person interview restrictions).
2. We have allotted 36 months to recruit and enroll all participants.
3. We anticipate 9 additional months to finish preliminary analysis. The estimated date to complete analysis is May 2021.

8.0 Study Endpoints

8.1 **Covariates.**

Patient characteristics: Socio-demographic characteristics, language, country of origin, time in US, comorbidities, social support, cognition (the cognitive assessment will not be completed if the baseline interview is completed over the phone), and health status will be collected. A literacy assessment using the Newest Vital Sign (NVS) and brief health literacy screener, and the Consumer Health Activation Index (CHAI) will be administered.

Regimen characteristics: R_x drugs will be collected and grouped into drug class. Regimen complexity will be calculated via the Medication Regimen Complexity Index (MRCI).

Provider-Patient Prescription Communication: We will ask questions adapted from the Consumer Assessment of Health Providers Survey (CAHPS-modified only as

necessary) to evaluate the extent and quality of provider verbal counseling on prescription medications.

Fidelity (Process) Measures:

- *Receipt of UMS materials.* We will collect EHR data on prescriptions and end-of-visit summaries to assess whether the UMS sigs were actually prescribed and whether the MedSheets and Medlists were printed. Similarly, we will review patients' actual medication bottles to determine if the labels reflect the UMS instructions and ask whether they received the MedSheets and Medlists (yes/no).
- *Receipt of SMS text reminders.* At each follow-up, the RC will ask whether patients received text reminders. We also will have texting opt out data from the text message provider.
- *Use of Patient Portal.* At each follow-up, the RC will inquire whether patients used the Patient Portal and if clinic staff followed-up with the patient. We also will obtain data through the EHR on who has accessed the portal and the number of portal logins each participant did during the study.

8.2 **Primary Endpoints.**

Effectiveness Outcomes. For the outcomes described below, we only include R_x chronic medications. Though we document them, we exclude PRN, as adherence concerns are different.

Treatment knowledge. Patients will be asked to identify drug indication; binary classifications will be applied per drug.

Medication adherence. The ASK-12 Adherence Barrier Survey assesses patients' general adherence behaviors and barriers to treatment adherence. Adherence will also be measured for each R_x medication using: 1) Self-report of how many pills and how often each medicine was taken over the last 24 hours. The RC will record how many pills were taken at each time for each medicine. Correct dosing will be measured as yes/no per drug, based on having properly demonstrated dose (# pills), spacing (hours between doses), frequency (times per day), and total pills/day, 2) in-person/phone pill counts of all chronic, pill form medicines, using established guidelines employed by our team [R01HS00167; PI Wolf], 3) the proportion of days covered (PDC), a measurement of days covered with medication, based on pharmacy claims. This is 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 both continuously (PDC) and dichotomously (yes/no - PDC $\geq$80%). Patients will be asked to sign a release at their first and/or last interview allowing us to obtain fill information from pharmacies used during the study. We will request information from pharmacies 6 months prior to baseline to a year post baseline. If the interview is completed over the phone, patients may receive a pharmacy release form by mail to sign and return to the research team. For the pill count during phone interviews, RCs will read a standardized script to ask patients to count study pills using a standardized procedure. If able, participants will be asked to join a video call so the

RC can take a screen shot of the patient's remaining pills-per bottle. The RC will save the screen shot/photograph to the study project folder within the secure GIM server only using the patient's studyid to identify the photograph. No PHI will be captured in the photograph. If the participant does not have video capabilities, the RC will proceed to explain how the patient can count their pills and relay the number to the RC. This script is outlined in the interview script. For patients consented before May 19, 2020 that complete a phone 6 month, a brief script will be read informing patients of the change in the consent in regards to the pill count. The RC will ask the participant to provide verbal consent to allow the study team to take a screen shot/photograph of the patient's pills during a video call in order for the RC to count the pills after the interview. The patient will be notified that no PHI will be captured in the photograph.

Medication reconciliation. Chart reviews will determine whether any discrepancies are present between patient self-report and the chart medication list. Nature of the discrepancy (omission vs. commission) will be recorded.

Clinical Outcomes. Systolic/diastolic blood pressure will be collected on all patients during the baseline and 6 month interview. Low-density lipoprotein cholesterol (LDL) will be obtained from patients' electronic health records. Chart review of hemoglobin A1c (hbA1c) will be reviewed for all diabetic patients. Differences will be measured between the last clinical measurement prior to baseline assessment and the last measured value during the study period (closest to 6 month assessment).

9.0 Procedures Involved

9.1 We will conduct a randomized trial using a 2x2 factorial design to test the effectiveness of UMS interventions to improve safe use and adherence to complex prescription (Rx) regimens. The research will be performed at Erie Family Health Center clinics and Northwestern Memorial HealthCare (NMHC) in Chicago.

9.2 **Research Coordinator Training.** The RCs and the project manager will contact and consent participants, conduct interviews, perform retention and follow-up activities and quality assurance. All have completed human subjects training (CITI) and intensive training from Dr. Wolf in interview protocols and safe data transfer. They also have multiple years of patient interviewing and data management experience. Simulations will be used to monitor interviewer proficiencies. Our staff has ample experience conducting surveys measuring medication-related outcomes.

9.3 **Computer Programming.** We will be using RedCap to collect all data. This allows for straightforward electronic entry of participant responses by the RC and generation of data files compatible with statistical programs. The database is both encrypted and password protected, and is only accessible by approved study personnel at Northwestern. Dr. Kwasny (analyst) will oversee the database structure and quality assurance activities.

9.4 **Data Safety and Monitoring Board (DSMB).** The DSMB will be formed early in the project and be given responsibility to review and approve the methods and analysis plan. It will be organized by Drs. Wolf and Bailey and include 4 health services researchers with related expertise. Meetings will be via video/tele-

conference to review protocols, procedures, and concerns related to research integrity.

9.5 **Trial Registration.** This study is registered at ClinicalTrials.gov (NCT02820753).

9.6 **Implementation and e-bugging of EHR, Portal Tools.** Dr. Wolf will plan the implementation of the EHR tools within the GE Centricity EHR with Dr. Rachman (Alliance CEO), Mr. Hamilton and Ms. Kaleba. All have considerable experience implementing changes to this system. Dr. Wolf has implemented the same processes to be tested in this study within Epic and Cerner platforms. Alliance's informatics analysts will implement the EHR and portal tools, assist with piloting in the electronic test environment, troubleshoot and communicate with GE Centricity if necessary, and roll out tools to Alliance sites. Drs. Wolf, Bailey and Rachman and Ms. Herman will work together to impart the specific functionality (portal survey and electronic views of Medlist, Medsheet) on the Alliance portal, as well as ensuring functionality of the lab reports to the clinic containing the portal survey results. Dr. Wolf will also work with Epic programmers at NMHC to refine the build in Epic for Northwestern clinics. While all functions have already been programmed at Northwestern, some functions may need to be tweaked and turned on accordingly.

9.7 **Randomization.** Randomization will occur at the patient level. Patients will be randomized to 1 of 4 arms (1:2:2:2). Because all arms receive the EHR tools, we are able to 'turn on' those features at all participating clinics. The other interventions occur outside of the clinic setting, so we are able to assign patients to those arms at an individual level.

9.8 **Clinic Space, Orientation and Workflow.** Prior to implementation, Dr. Wolf will meet with physicians and staff at each of the sites to familiarize them with the planned study activities, answer questions, provide a printed synopsis of the protocol per site, and give contact information. They will work closely with Dr. Buchanan to coordinate activities at the sites and plan space needs for interviews and study visits.

9.9 **Spanish Translation.** All of the measures identified already have Spanish versions. We will employ Dr. Schoua-Glusberg, from Research Support Services, to translate remaining components (introduction prompts, item probes, surveys, etc.), as well as the consent and recruitment materials into Spanish. Dr. Schoua-Glusberg has specialized in research studies with Hispanic populations, including topics such as methodology for instrument translations and qualitative pretesting of survey instruments in Spanish, since 1984 and we have worked with her extensively. Dr. Bailey (Spanish) will review all materials and facilitate any discussion to reach an agreement on the best words and phrases for the final product.

9.10 **Pilot-testing and Refinement of Study Materials and Protocol.** We will pilot-test the study battery, protocol and patient materials among English and Spanish-speaking patients at Alliance sites. Cognitive interviews will be conducted among a convenience sample of 30 patients (n=15 per language) that meet eligibility criteria to refine and standardize the study materials. We will 1) obtain average completion times for the interview and 2) elicit patient comprehension and acceptability of the interview and patient materials through a set of targeted questions. If problems are

identified, the root cause(s) will be analyzed and modifications made to the interview and materials as appropriate prior to full-scale implementation.

9.11 **Interviews.** The initial interview will be conducted in person or over the phone at the time of patient consent and enrollment. Following the baseline interview, RCs will conduct one telephone interview 6-8 weeks later. Assessments at this interview are aimed to closely track any change in the most proximal outcomes of R_x understanding and behavioral outcomes (self-report adherence). A final in-person interview or phone interview (if unable to complete in person due to NU COVID-19 in-person interview restrictions) will then be conducted 6 months post baseline. Patients will receive financial incentives to attend study visits ($40 for baseline interview, $60 at 6 months). In addition, patients will receive reimbursement for text messaging costs if they do not have unlimited texting = (estimated costs based on greatest possible incurred charge). Patients will be provided $10 for transportation costs or a parking pass.

★ **COVID-19 Waves 5-9 Patient Interviews.** Participants will complete up to five telephone interviews in total, with one interview taking place every 4 months. New, supplement-specific data collection related to COVID-19 will be collected via telephone interviews. See section 9.20 for more information

9.12 **Obtaining Clinical Markers Data.** At in-person baseline and 6 months, trained RCs will use a blood pressure monitor to measure systolic/diastolic blood pressure on all participants. RCs will use an automated, validated device (Omron HEM-907XL) and procedures used in the National Health Examination and Nutrition Survey (NHANES). RCs will ask patients to sit quietly with feet and back supported for 5 minutes before blood pressure is obtained. Three recordings will be taken per visit, spaced at least 5 minutes apart, and the mean of the 2nd and 3rd readings will be used to indicate blood pressure for that visit. Patient positioning, arm selection, cuff size selection and other techniques will follow NHANES procedures. Baseline and 6-month interviews that are completed over the phone will not obtain in-person blood pressure values.

In the event that a patient has a high blood pressure screening (systolic >180 or diastolic >110): For patients with a high blood pressure screening, the RC will proceed to the following Hypertensive Emergency Screening Questions:

<u>Hypertensive Emergency Screening Questions:</u>

Are you currently experiencing…

- Severe pain in the chest and/or upper back?
- Nausea or vomiting?
- New vision changes?
- Severe trouble breathing?
- A headache? (Must say yes to both sub-questions to count as a yes)

- Is it different from prior headaches?
- Is it severe?

The RC will then instruct the patients based on the following for Erie patients:

- For interviews done at an Erie site, and patient has a systolic >180 or diastolic >110: Patient should be transferred in real time to the on-site nurse for a full assessment and provider consultation regardless of responses to screening questions. The RC will provide the patient with their blood pressure values on a piece of paper.
- For interviews done at Northwestern, and patient has a systolic >180 or diastolic >110:
  - Patient should be advised to go to the Northwestern Emergency Department regardless of responses to screening questions before leaving the interview. The RC will provide the patient with their blood pressure values on a piece of paper.
  - The RC should notify Erie Family Health Centers of the patient's blood pressure screening and that the patient was advised to go to the Emergency Department
    - The RC should call Erie directly and follow the phone tree to speak with a Patient Access Representative, 312-666-3494
  - Erie Staff will notify the patient's Primary Care Provider

The RC will then instruct the patients based on the following for Northwestern patients:

- If yes to any screening questions above, patient should either call their PCP's office from the interview room to speak to a healthcare provider for advice, or proceed to the ER.
- If no to all screening questions above, patient should be instructed to call their primary care doctor.

For diabetic patients, a chart review or EDW pull will be done to examine Hemoglobin A1c (hbA1c) levels at their regularly scheduled primary care appointments closest to baseline and 6 month interviews. This is to decrease the burden on the participant – alternatives include taking a blood sample at our interview or asking participants to go to Quest Diagnostics. We felt that was excessive and unnecessary, so will use the EHR data provided by Erie or the EDW report for Northwestern patients.

9.13 **Study Arms.**

Enhanced Usual Care**.** Current usual care includes variable physician prescribing and/or nurse counseling, and no active SMS or surveillance of medication use post-visits.

We are enhancing this usual care by adding UMS materials as a clinic standard, per Erie's request following their current experience with these materials. All patients at Erie or NMHC, thus all patients in this study, will begin to receive UMS-related tools at their primary care visit to support Rx use. These materials have previously been successfully piloted in multiple NIH-funded studies. These include:

1. *UMS Rx Instructions ('Sigs').* The UMS is defined in Section 2.2. We have already successfully replaced existing EHR default sigs for 305 Rx drugs in primary care with UMS instructions [R21CA132771], and tested use of UMS sigs in pharmacy practice [R01HS017687, R01HS019435], in English and Spanish.

2. *MedSheets.* As an additional measure funded by AHRQ [R18HS17220], we created single-page, plain language Rx information sheets following health literacy best practices with content appropriately sequenced from a patient's perspective (drug name, indication, purpose/benefit, how to take, for how long, when to call your doctor, when to stop taking and call your doctor, important information). These sheets pull in the UMS sig to tailor content and serve as a tangible, 'patient-friendly' addition to the after-visit summary. Medsheets for a total of 305 Rx drugs have been embedded within the Epic EHR at NMFF and are automatically generated and distributed at check out to patients with new Rx prescriptions. Lexile analyses were performed on these sheets, confirming each to meet a < 8th grade readability standard. The content was developed by two pharmacists, performing an environmental scan of existing tools. Patients, physicians, and health literacy experts reviewed the material and guided revisions.

3. *MedList.* We re-designed the EHR medication list to impart the UMS to an entire Rx regimen (R18HS17220; U19HS021093). All medicines are listed and instructions consolidated in UMS form (requiring e-confirmation by doctor to ensure patient safety and flagged by clinical decision support tools if harmful interactions exist in regimen – supervised by Dr. Wood) to visually depict patients' morning, noon, evening, and bedtime medicine.

The UMS EHR tools have been piloted in Epic and Cerner, and are now being implemented in GE Centricity for this proposal now. Among 144 patients at the NMFF General Medicine clinic, nearly all (91%) patients received their MedList, UMS sigs, and MedSheets for new medications; 85% reviewed it with their doctor. Feedback from 20 physicians offered unanimous positive feedback on the tools.77 [R18HS17220].

9.14 **SMS Text Reminders.** For those patients receiving text reminders (SMS; SMS+Portal), daily text reminders will be sent post baseline following the UMS intervals. The texts will continue daily, with the option to opt out at any time. Stopping the texts will not impact their continuance in the study. Texts will automatically stop after 6 weeks, with an option at that time for patients to opt back in to the service. Those who opt back in will get the texts all 6 months of the study, or until they decide to stop. In past studies we have sent texts for one week, but recent studies have shown patients may benefit from longer text interventions. A covariate will be to look at the effect of length of text intervention to patient adherence, as well

as whether or not people opted out. Participants without unlimited texting plans will be reimbursed the total cost of receiving the texts. Patients will receive uniform, generic messages around UMS time intervals such as, "Good Morning! Please remember to take your medicines today." and, "Hope you had a great day and remembered to take all your medicine!"

We will use EZ Texting, a safe, economical, premium Internet SMS text service plan, to program and schedule discrete UMS-centered text messages. These will be sent at standard intervals for all patients based on their regimen, with a maximum of two times a day (i.e. 1 or 2 times daily depending on regimen). Because these reminders are sent daily, we have limited the number of times sent per day so as not to burden and overwhelm the patient. Generic reminders are used due to the complexity of patient regimens and the SMS text message itself sent around the general time of behavior is a memory support. The premium plan ensures patients do not receive promotional messages with the text. A trained RC will orient and confirm patients can retrieve text messages. The RC will also instruct patients to abstain from reading text messages while driving and instead read messages and take medicines once they can safely concentrate on the task.

9.15 **EHR Web-Based Patient Portal.** The addition of the patient portal will provide opportunities to have ongoing communications with their clinic, real-time reconciliation and updating of medication lists, access to regimen-specific medication information, and to provide a feedback loop informing healthcare providers of adherence-related behaviors and concerns. The encrypted patient portal website will be managed by the Alliance HIT team and the MyChart team, under Dr. Wolf's supervision. Secured instant messaging and email features to communicate with clinic staff are already available within the portal. The additional build out above these informational and communication features will be a periodic requests for patients to (1) identify if they missed taking any of the medicine in their regimen in the past 3 days, and (2) list any concerns or problems related to refill, cost, side effects, or management of their medicines. This process has previously been piloted with patients and can be performed in three minutes or less. Patients in this arm will be asked to fill this survey out 2 weeks, 1, 2, 3, 4, and 5 months post baseline. An email will be sent to patients at these time points, requesting that they access the portal and complete the regimen adherence assessment (embedded in the portal). The information submitted back by the patient will be sent back to the EHR and directed to the responsible doctor or nurse. Identified 'champions' at Erie and NMHC will be trained to review the files and identify patients with regimen-related concerns. Patients who do not complete the assessment within 48 hours will be sent a second email reminder. If they still do not fill out the survey, a third and final reminder will be sent. Patients who self-report any concerns or who demonstrate incorrect or missed doses will also trigger nurse follow-up. The RC will create a MyChart or MyErieHealth account for patients that do not already have a patient portal account, depending on the clinic they attend. For Erie patients, a MyErieHealth account will be created through the MyErieHealth admin page. For Northwestern patients, the RC will obtain a MyChart activation code by accessing a patient's chart through Epic. Erie staff will send encrypted emails weekly or as needed to NU RC's with a list of patients that have completed the portal survey. For Northwestern patients, RC's will

determine if a survey was completed by accessing a patient's chart through Epic to see a record of a completed UMS Portal MyChart survey.

9.16 **Nurse Training.** Nurses will be educated on health literacy and health communication best practices, barriers to medication self-management, and how to briefly counsel patients via face-to-face and telephone using teach-to-goal and implementation intention approaches. Our team has used these techniques in prior studies that tested a low literacy diabetes education strategy in FQHCs. Patients at the time of enrollment will also be extensively oriented to the patient portal and use of the EHR and portal tools. The clinic nurse phone number and email will be provided for technical support.

9.17 **Pharmacy Release.**
To calculate PDC, we will need to collect pharmacy claims data for each patient that grants permission. 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. Once the patients have signed the informed consent, patients will be asked which pharmacies they use to fill their prescriptions. They will be asked to sign the appropriate release(s) allowing us to obtain fill information from pharmacies used during the study. We will request to obtain information for any medicine that was filled 6 months prior to baseline to 1 year post baseline. If the interview is completed over the phone, a pharmacy release form may be mailed to the participant to be filled out and returned to the study team.

★ **COVID-19 Waves 5-9 Pharmacy fill data.** For participants that complete COVID Wave 5-9, participants will be asked if they use Walgreens or CVS to fill their prescriptions. During the COVID consent process, participants will be informed that Walgreens and CVS Pharmacy may access, receive, or use their personal information, based on the pharmacies they utilize.

9.18 **Data Sources.** Data sources for this study will include in-person interviews or phone interview with participants (see attached surveys), blood pressure machine readings during in-person visits, Electronic Health Record chart review, and pharmacy data.

9.19 **Data Collection.** In order for the researchers to evaluate the intervention and how well it is being utilized, we will ask the Alliance to provide some data to Northwestern for Erie patients. For consented patients, the Alliance/Erie Family Health Center will provide data, including basic demographics, current medication lists and clinical outcomes from the patients' medical record. The Alliance/Erie Family Health Center will also provide the above detailed information in the form of de-identified, aggregate data (i.e. frequencies and means (SD) per arm) for all patients, regardless of whether or not the patient consented to participate in the study. All data will be transferred via secure Sharepoint site.

Specifically:

- Alliance will send contact information for identified eligible patients
    - Study ID
    - Patient's medical number

  - Patient name
  - Clinic and provider name
  - Home and cell phone number
  - Address
  - Sex
  - Date of Birth
  - Primary language
  - Date of last primary doctor appointment at Erie
  - All drugs prescribed (name, dose, form, GPI, instruction, date prescribed, number of refills, pharmacy, quantity)

- NU will send Alliance/Erie Family Health Center Study IDs and baseline interview dates, linked by patient ID
- Alliance will send the following information to Northwestern for consented patients:
  - Study ID
  - All values 6 months prior to baseline & 12 months post
    - Blood pressure
    - HbA1c
    - Cholesterol levels
  - Information on all prescribed medicines baseline to 12 months post (name, dose, form, GPI, instruction, date prescribed, number of refills, pharmacy, quantity)
  - Current at baseline and 12 months post
    - Chronic conditions
    - COVID-19 diagnosis and/or results of antibody test
  - All clinic visits/appointments 6 months prior to baseline and 12 months post (date, provider, meds prescribed, visit type)
  - Patient portal survey results, date completed, and possible clinic contact for patients in either of the portal arms
  - Patient portal use 6 months prior to baseline and 36 months post baseline
    - how many times patient logged on to portal
    - what portal was used for
    - when and how often portal was used

For Northwestern patients, the same data that was requested above will be obtained through an additional EDW report, including patient medications, chronic conditions, COVID-19 diagnosis and/or results of antibody test, and healthcare utilization (ED, hospitalization, primary care appointments) as well as hypertension, diabetes and cholesterol clinical values.

For Participants that complete COVID Wave 5-9.

★ EHR Data. Medical record data will be again collected via the Electronic Health Record (EHR) from January 1, 2019 - present. EHR data will confirm comorbidities and medications. We will also extract clinical outcomes (HbA1c, diastolic and systolic blood pressure, cholesterol (LDL, HDL, total, triglycerides), GFR, COVID-

19 lab tests and results, COVID-19 diagnosis, COVID-19 vaccine type and dates, and antibody results), preventive services utilization (cancer screening, immunizations), and health services use (clinic visits (including telehealth), medical subspecialty visits, emergency department visits, hospitalizations). Lastly, we will collect patient portal usage.

9.20 **COVID-19 Survey.** We are proposing an optional sub-study to be contacted from a pool of existing studies conducted by Dr. Michael Wolf (LitCog (STU00026255), REMinD (STU00203777), COPD Multimorbidity (STU00201640), UMS Portal (STU00201639), and TAKE IT (STU00204465). Participants will be invited to participate in an optional one-time brief (5-10 minute) telephone survey to capture one additional outcome pertaining to their knowledge, attitudes, and beliefs about the COVID-19 outbreak in March 2020. This new data will be linked with participant characteristics from the parent study. They will also be asked a series of patient-reported health literacy items. Participants who complete to COVD-19 survey will receive a $10 gift card in the mail.

Recruitment will be done by phone by trained Northwestern RAs. We will contact any who has indicated that they were willing to be contacted for future studies run by Dr. Wolf on the consent form. Verbal consent will be obtained prior to completing the one time brief (5-10 minute) telephone survey.

Waves 2-4:

From the same pool of existing studies included in Wave 1, any participants who completed the Wave 1 COVID-19 survey will be contacted and invited to participate in up to 3 additional telephone surveys (10-30 minutes each) over the course of 4 months to continue to evaluate knowledge, attitudes, and beliefs over time about the ongoing COVID-19 pandemic. Participants who complete the follow-up interviews will receive a $10 gift card in the mail for wave 2 and a $15 gift card for waves 3 and 4 (per survey), for a total of up to $40 for the follow-up activities. For wave 3 and 4, we increased the participant compensation from $10 to $15 due to the longer survey administered at this time point.

Recruitment will be done by phone by trained Northwestern RAs. We will invite anyone who has indicated that they were willing to be contacted for future studies run by Dr. Wolf on the consent form and who completed the Wave 1 survey. Verbal consent for the follow up waves will be obtained prior to completing the Wave 2 telephone survey (initiated 2 weeks after Wave 1). Participants who consent to these follow-up activities will be re-contacted for completion of Waves 3 and 4 at 1 month and 3 months post-wave 2.

Waves 5-9

In March 2020, we recruited a subset of the UMS Portal cohort (n=215), and patients enrolled in four other studies (n=458; Total N=673) to form the Chicago COVID-19 Comorbidities (C3) cohort study. We initially completed four phone interviews

(described above) with them to better understand how older adults with underlying health conditions, at greater risk for COVID-19 complications, were responding and taking action (or not) to prevent infection and disease spread.

We will now continue our investigation to better understand the longer-term impact of COVID-19. From the same pool of existing studies, any participants who completed the Wave 1 COVID-19 survey will be contacted and invited to participate in up to 5 additional telephone surveys occurring every 4 months. Interviews will collect information on participants' responses to COVID-19 and changes in lifestyle behaviors, healthcare utilization, physical and mental health, access and adherence to treatment, socioeconomic circumstances and clinical outcomes. We will also collect data from the medical record and pharmacy record abstractions.

Participants who complete additional telephone surveys will receive compensation in the mail. See section 22.2 for further details.

Data from all waves of the COVID-19 telephone surveys will be captured in REDCap.

9.21 **Post-trial investigations**

To investigate patient, healthcare provider, and/or healthcare system-level barriers to implementation, we will conduct brief online survey (n ~25-50) with clinic providers and staff to explore barriers and facilitators to implementing the various intervention strategies. The practice manager, academic manager, or clinician partner at Erie Family Health Center and Northwester Medicine will email providers and staff that may have been involved in some aspects of the study a Redcap link to an online consent. If the provider or staff member consent and click next, they will be taken to a brief, anonymous online survey.

We will also compare the cost-effectiveness of each strategy. Specifically, we will estimate the incremental cost of interventions over the cost of usual care from the perspective of AllianceChicago, Erie Family Health Center, and Northwestern Medicine. The primary operational costs of the intervention strategies include texting related costs and the programming and maintenance costs of the Epic/GE Centricity EHR and the patient portal. We will separately track development costs of the interventions, conditional on having an EHR and portal, which are primarily comprised of software generation and other programming requirements based on programmer hours. Staff/programmer costs will be measured using tracked time spent on developing and running the intervention and converted to dollars using current wages.

10.0 Data and Specimen Banking

10.1 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. Data will be stored on Northwestern encrypted servers and access will be granted through the PI.

11.0 Data and Specimen Management

11.1 Analysis Plan.

Aim 1.

The proposed trial uses patient 1:2:2:2 randomization with random block size to achieve group comparability and balance. Stratified by clinic, each participant will be randomized to one of the four arms. The four arms are the result of a 2x2 factorial design, where SMS text reminder and portal are the two-level factors with all four arms receiving the EHR tools. We conservatively anticipate at least 80% retention for follow-up at six months. This will result in 1505 participants recruited to the study with an anticipated minimum of 1204 (172 participants in EHR arm and 344 per the other arms) available after six months, contributing to primary data analysis. Due to an NIA administrative hold, the interventions were not implemented as planned. Hence it was determined that the primary analysis would be "per-protocol" rather than intent-to-treat to assess the effect of the interventions under optimal conditions. Participants who received the initial 6 weeks of SMS messaging continuously will be considered as receiving the SMS intervention, and participants who logged on to the patient portal and completed at least one survey will be considered as receiving the patient portal.

To ensure adequate balance across treatment arms, baseline outcomes and potential confounders including socio-demographic characteristics, comorbidities, regimen complexity (i.e. # of medications, total pills taken daily), health literacy level, and language will be examined. Variables found to have clinically meaningful differences across treatment groups will be entered as covariates in the generalized linear mixed models (GLMMs) used for formal analyses as described below.

Prescription medication adherence at 6 months is the primary outcome of interest for Aim 1, with treatment knowledge regimen consolidation, and clinical outcomes being relevant to hypotheses of secondary interest. We will use generalized linear mixed-effects models (GLMMs) to test for the effects of SMS text reminder and Portal, specifying the proper link functions based on the distribution of the outcome variable. Analyses will be performed using PROC GENMOD in SAS (v.9.4). SMS text reminder and Portal (both binary) and an interaction term for SMS and Porta are the three variables included in the model to denote the intervention groups and the enhanced usual care group (H1-6). Since adherence will be assessed for each medication, 2-level GLMM will be used with medications nested in participants. We will test for differences in the outcomes between each of the groups and the enhanced usual care arm to determine benefits of SMS texting or portal use, or both by constructing contrasts.

Aim 2.

We will determine the extent to which the interventions were implemented as planned (a process evaluation) across each of the sites and for all four study arms. We will collect EHR data on prescriptions and end of visit summaries to assess whether patients actually received new prescription orders (in after visit summaries) with the

UMS sigs, and review pharmacy records to determine if they were translated accordingly onto patients' drug container labels. We will also observe during patient interviews (that occur after medical encounters) which patients received the MedSheets and MedList. For those receiving SMS text reminders (SMS and SMS+Portal arms), we will ask patients at all follow-up intervals whether they received the text messages. For those electing to turn off the service, we will qualitatively explore and code reasons why. For patients who receive the Portal (Portal and SMS+Portal), we will track usage data, rate of entry errors, review technical support logs for the frequency and nature of calls, and also investigate at each follow-up patient satisfaction, acceptability and usability of the portal.

Aim 3.

We will directly measure and assess the perspective costs of developing and running UMS interventions, alone and in combination. Specifically, we will estimate the incremental cost of interventions relative to usual care from the perspective of the Alliance, Erie, and Northwestern. The primary costs of running UMS technologies involves the limited expenses around printing (printer ink, paper, staff time) as a result of generating new R_x information with after-visit summaries. SMS monthly costs will be easily documented as well as usage. However, we will include estimates for programming maintenance, for both GE Centricity EHR/Epic and the patient portal, and will test the sensitivity of results to changes in the maintenance requirements in terms of programmer hours. We also will separately track development costs for software and other programming requirements based on programmer hours. 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 the potential use of variable staff using different salaries but assuming the same proficiency in terms of time required. Further, we will assess the sensitivity of estimates to different proficiency levels that could arise from learning by doing.

Exploratory Analyses. In addition to the primary per-protocol analysis, we will investigate if there is a "dose response" of either intervention. Specifically, we will look at the total weeks participating in SMS text messages and the total number of portal surveys completed. Additionally, we will repeat all GLMM analyses described for Aim 1 to explore whether differences in interventions vary by relevant covariates representing patient and regimen characteristics known to impact outcomes, specifically adherence. Interaction terms will be included in models accordingly. Statistical significance for a tested interaction ($p<0.05$) will indicate that intervention groups differ in outcomes by the studied variable (i.e. age, literacy level, regimen complexity, drug class, language, activation, comfort with texting or portal, etc.). As adherence has its many measurement challenges, experts recommend triangulating with multiple measures. We will fully investigate and compare results across each adherence measure (24-hour recall, pill count, PDC) and create a general estimate of adherence via single factor score using maximum likelihood estimation. Exploratory analyses will examine HbA1c and blood pressure from baseline to 6 months, although power may be limited.

COVID-19 Survey: By extending each of these studies (LitCog (STU00026255), REMinD (STU00203777), COPD Multimorbidity (STU00201640), UMS Portal (STU00201639), and TAKE IT (STU00204465)) to capture an additional patient-reported outcome related to one's knowledge, attitudes and behaviors related to COVID-19, we can link participants' responses to this longitudinal survey to a minimum data set of participant characteristics that include demographic, socioeconomic, cognitive (including health literacy) and health behavioral characteristics. We will then be able to investigate determinants of COVID-19 knowledge, attitudes and behaviors without duplicating data collection efforts for these variables.

Dr. Peipert will be analyzing data from the Wave 1 health literacy items.

RCs will conduct interviews by telephone using REDCap survey software. Ms. Opsasnick (analyst) will oversee database structure & quality assurance. Participants will complete 5 phone interviews with RCs.

Statistical analyses will be led by Dr. Kwasny, and all analyses will be conducted with SAS 9.4 (Cary, NC). Using data from the C3 cohort, participants' perceived levels of stress has been assessed from the initial onset of the outbreak (March 13-20; C3 W1), through its rapid acceleration (March 27-April 3; C3 W2) and apex phases (May 1-22; C3 W3), and the flattening phase (July 15- August 15; C3 W4) of the COVID-19 pandemic. The additional surveys provides the opportunity to continually assess persistent stress over a span of time that likely will include the pandemic's expected, slow recovery, an anticipated second wave in the fall/winter of 2020/2021, and its eventual recovery as well. Also during this time, there may be new treatments available, as well as a vaccine for COVID-19. Initial models will examine associations between perceived stress as a result of COVID-19 and health and healthcare outcomes over time among C3 participants. As perceived stress, health and lifestyle behaviors are expected to change over time, we will use GLMMs to examine the relationship between stress, and outcomes (diet, alcohol use, smoking, physical activity, diet, weight gain, sleep, social isolation, treatment adherence, self-reported health status) using stress as a time-varying covariate. For data from the EHR, we will assess routine health care use.

11.2 **Power Considerations.** Study sample size was based on pairwise comparisons of the primary outcome of medication adherence, measured by 24-hour recall, at six months between both the SMS texting arm and the Portal arm compared to enhanced usual care (Aim1, H1-3) and the interactive effect of both SMS and Portal compared to either intervention alone (Aim1, H4-6). We expect 69% of enhanced usual care participants to be adherent at six months. Enrolling 1505 participants from 1 health center and conservatively estimating 80% retention at six months (n=1204; 172 EHR and 344 per other arms), we will have 80% power to detect a minimum absolute difference between study arms of 12% using a Type 1 error rate of 2.5%.

With the sample size set by the primary outcome of 24-hour recall at 6 months, we also show detectable effects for pill count and regimen consolidation, and for all

outcomes comparing additional intervention effects of SMS texting and patient portal to EHR alone (i.e. SMS text reminders vs. enhanced usual care, Portal vs. enhanced usual care, SMS text reminders + Portal vs. SMS text reminders only, SMS text reminders + Portal vs. Portal only). Estimates for the enhanced usual care arm were calculated based on the minimum detectable differences calculated for H1-H3 and a Type 1 error rate of 2.5% was used for these comparisons between each of the three additional arms and enhanced usual care. Note: the minimum detectable differences for consolidation reflect a conservative 25% reduction in sample size; we will remove patients from analyses who misunderstand the dose frequency for any of their medicines (i.e. 2 times daily vs. 3 times daily).

11.3 **Protocol to ensure confidentiality.**

Each subject will be tracked using the RedCap, which is encrypted, password protected and only accessible by approved Northwestern personnel. Identifiers and other related information for coordinating research activities (recruitment outcome, research interview call log and interview visit schedule, etc.) will be in RedCap until it is de-identified.

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 consent forms and 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.

11.4 **Quality Assurance.**

Training will begin after surveys and interview protocols have been refined and standardized. The project manager will lead sessions to orient the research staff to the surveys and study protocols (e.g., interview process, use of laptops, data security). 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 prior to any active recruitment efforts. All interviewers will be required to demonstrate competence in survey administration. Training the entire research staff at once will ensure uniform administration of the study protocols and interviews.

11.5 **Study-wide data management.**

Data Access. The Data Custodian is the Principal Investigator, Dr. Michael Wolf. Only authorized personnel listed on this 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 servers for the length of the study. The Project

Manager or Data Analyst will download the data from REDCap monthly and save to the "Analytic" folder within the UMS Portal 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 Northwestern patients will remain in the secure REDCap system. 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. All identifiable information will be deleted upon completion of the study

Data Coordination Center (Northwestern). The project manager and data analyst at NU will combine the data and maintain the master data file containing all data, create a data dictionary, and be responsible for data cleaning and providing updated data to study investigators when requested.

Data Storage. Data will be stored on the Northwestern server for the length of the study. All identifiable information will be deleted upon completion of the study.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

12.1 **Data Safety and Monitoring Board (DSMB).** The DSMB will be formed early in the project and be given responsibility to review and approve the methods and analysis plan. It will be organized by Drs. Wolf and Bailey and include 4 health services researchers with related expertise. Meetings will be via video/tele-conference to review protocols, procedures, and concerns related to research integrity.

13.0 Withdrawal of Subjects

13.1 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.'

13.2 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. They will then not be contacted for further interviews or visits.

14.0 Risks to Subjects

14.1 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.

15.0 Potential Benefits to Subjects

15.1 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 mobile and computer technologies to support safe and appropriate medication use.

16.0 Vulnerable Populations

N/A

17.0 Community-Based Participatory Research

N/A

18.0 Sharing of Results with Subjects

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

19.0 Setting

19.1 The Alliance of Chicago will identify potential participants who are patients at Erie Family Health Center. Northwestern RCs will identify and recruit potential participants who are patients at NMHC. RCs will recruit and screen participants. In-person interviews will take place in a private space at Northwestern, at Erie clinics, or in community sites in the participant's neighborhood (i.e. private study rooms in libraries). Baseline or follow-up interview that take place over the phone will be completed in a private space/private offices. For interviews that are not able to be

20.0 Resources Available

20.1 **Team.** The research team is comprised of 5 PhD level researchers, 3 Physician-researchers, 2 master's degree level researcher, 1 project manager, and 2 bilingual research coordinators, all of whom have extensive research experience. The co-PIs represent institutions with proven track records in health literacy, medication safety and adherence, and the use of health technologies. All team members have extensive knowledge on health literacy in the context of medication management and health technologies. Co-Investigators on this project include the Chief Operating Officer and Director of Clinical Informatics and Chief Executive Officer of Alliance, as well as the Director of the Health Literacy and Learning Program (HeLP), which seeks to advance the study of limited health literacy and interventions that could improve one's ability to obtain, process, and understand basic information needed to make appropriate health decisions. The investigators have successfully collaborated on numerous previous projects. The project manager has 4 years of experience managing complex research studies and supervising research staff. The research coordinators receive extensive training on research methods, interviewing techniques and the consent process. We have significant experience in recruiting patients from FQHCs (Alliance clinics specifically), conducting studies related to medications, consenting patients to follow-up, and conducting multi-part follow-up with both in-person and telephone interviews. Additionally, the team has experience in managing data in accordance with the best-practices of the IRB to protect patients' confidentiality.

20.2 **Erie Family Health Center.** Performance sites will be clinics from the Alliance of Chicago, an electronic health record (EHR) system user community composed of safety net providers in eight states. The network is an innovator and leader in using health information technology (HIT) among community health centers. Founding members are in Chicago and have a long history of collaboration with Northwestern researchers, and Drs. Wolf and Bailey specifically. The Alliance links 67 community

health center practices in the metropolitan Chicago area alone serving more than 153,000 unique patients. All of these clinics are Public Health Service 330-funded FQHCs with federal mandates to provide care to medically underserved U.S. areas. Patients receiving care at Alliance sites are mostly African American, Latino and low income. We will work specifically at Erie Family Health Center (33,350 patients, 85% Latino). Alliance FQHCs share a common EHR (GE Centricity®) to promote quality improvement. Erie Family Health Center will rely on Northwestern's IRB (IRB Authorization Agreement letter included). The Alliance has an IRB of Record with Chicago Department of Public Health, so will not rely on NU's IRB.

NMHC. NMHC serves a diverse patient population and represents the entire spectrum of socioeconomic status. The practice employs more than 30 attending physicians.

20.3 **Facilities.** The RCs will have access to a private space to consent and interview patients. All follow up calls and data recording will be done from a closed office/private space.

20.4 **Training protocols.** Northwestern staff training. The Northwestern project manager and bilingual RCs have completed Human Subjects Training (CITI) and have received intensive training, led by Drs. Wolf, in interview protocols and safe data transfer. Any new research staff will go through the same rigorous training requirements.

21.0 Prior Approvals

21.1 We have received funding from the National Institute on Aging.

22.0 Recruitment Methods

22.1 For patients from Erie:

Recruitment will be done by phone by trained Northwestern RAs. First, Alliance will send Erie providers an encrypted file of a list of eligible patients from Erie Family Health Center who have an upcoming doctor appointment scheduled. Providers will indicate if any eligible patients should not be contacted. Providers will be reminded via email to reply with their list of approved patients. Providers will be informed that if they do not respond within two weeks they are giving Northwestern permission to contact all patients on the list. Northwestern will then mail a letter to patients on the list, notifying them that a RC will be telephoning to invite them to participate in a study. Patients will be given the opportunity to opt out of being contacted by calling a hotline number and leaving a message. RCs will monitor the messages and send Alliance a list of patients who have chosen to opt out. Seven days after the letters have been sent, a RC will call patients who did not opt out to ask screener questions to determine eligibility and, if eligible and interested, schedule their baseline. Due to COVID-19 restrictions, the study team may not be able to mail letters to all patients. If a letter mailing is not possible, the study team will still obtain permission from the provider to contact their patients, but not send a recruitment letter.

For patients recruited from Northwestern Medicine Primary Care: potential participants will be identified through reports generated by the Enterprise Data

Warehouse (EDW) for patients who have an upcoming appointment scheduled. Per clinic protocol, all eligible patients can be contacted and providers will not receive a list of their patients to indicate who should not be contacted. Research staff will then mail a letter to patients on the list, notifying them that a research coordinator (RC) will be telephoning to invite them to participate in a study. Patients will be given the opportunity to opt out of being contacted by calling a hotline number and leaving a message. RCs will monitor the messages of patients who have chosen to opt out. Seven days after the letters have been sent, an RC will call patients who did not opt out to ask screener questions to determine eligibility and, if eligible and interested, schedule their baseline. Due to COVID-19 restrictions, the study team may not be able to mail letters to all patients. If a letter mailing is not possible, the study team will contact patients by phone after their doctor's visit without sending letters.

If requested by the patient, the RC may text or email the patient confirming their interview date, time, and address. At their baseline interview, the RC will proceed with obtaining their written or verbal consent and administer the baseline interview. The patient will then be eligible to receive the remaining components of the intervention depending on study arm (SMS, portal, SMS+Portal) and to participate in evaluation activities, Participants will give written informed consent or verbal consent using procedures approved by Institutional Review Boards at Northwestern University prior to completing the baseline interview.

COVID-19 Surveys Recruitment Waves 1 and Waves 2-4: Recruitment will be done by phone by trained Northwestern RAs. We will contact anyone who has indicated that they were willing to be contacted for future studies run by Dr. Wolf on the consent form and who completed the Wave 1 survey. Verbal consent for the follow up waves will be obtained prior to completing the Wave 2 telephone survey (initiated 2 weeks after Wave 1). Participants who consent to these follow-up activities will be recontacted for completion of Waves 3 and 4 at 1 month and 3 months post-wave 2).

COVID-19 Surveys Recruitment Waves 5-9: All methods of recruitment will be done by trained Northwestern RCs.

We will first mail a recruitment letter introducing the study to all eligible patients prior to contacting them by telephone. If the participant is not interested in participating or being contacted by the researcher, he/ she can opt out by calling the toll-free number within 7-10 days and the RC will not contact the participants. Due to COVID-19 restrictions, the study team may not be able to mail letters to all patients. If a letter mailing is not possible, recruitment will be done by phone by trained Northwestern RCs and will let the patient know about the opportunity to continue their participation and see if they are interested in learning more about it.

If they are interested in participating, the RC will engage patients in the informed online or verbal consent process and HIPAA Authorization, as approved by the

Northwestern University Institutional Review Board. After obtaining consent, RCs will conduct the telephone interview or schedule it to be completed at a later date.

For providers and staff: To investigate healthcare provider and/or healthcare system-level barriers to implementation, we will conduct brief online interviews (n ~25) with clinic providers and staff to explore barriers and facilitators to implementing the various intervention strategies. The practice manager, academic manager, or clinician partner at Erie Family Health Center and Northwester Medicine will email providers and staff that may have been involved in some aspects of the study a Redcap link to an online consent. If the provider or staff member consent and click next, they will be taken to a brief online survey.

22.2 **Participant Payment.**

Research Interview	Payment	Form of Payment
baseline	$ 40	cash at close of in-person interview or money order or gift card mailed if phone interview completed
6-8 week	$ 0	(very brief, included in other interviews)
6 month	$ 60	cash at close of in-person interview or money order or gift card mailed if phone interview completed

COVID-19 Survey: Participants who complete the wave 1 COVID-19 survey will receive a $10 gift card in the mail. Any participants who completed wave 2 will receive a $10 gift card; participants who complete wave 3 will receive a $15 gift card for their time; participants who complete wave 4 will receive a $15 gift card for their time (for up to $40 for all follow-up activities). All participants who verbally consent and complete any portion of the telephone interviews will be compensated.

COVID-19 Waves 5-9: Participants will receive the following compensation for each interview they complete:

Timepoint	Compensation
Wave 5	$20 gift card
Wave 6	$20 gift card or money order
Wave 7	$30 gift card or money order
Wave 8	$30 gift card or money order
Wave 9	$40 gift card or money order

Money orders may issued for subject compensation for COVID-19 supplement surveys if Visa gift cards are problematic for the subject.

23.0 Local Number of Subjects

23.1 A total of 1505 participants will be recruited from Erie Family Health Center clinics and NMHC.

24.0 Confidentiality

Only authorized research personnel will have access to study related data. Each participant will be tracked using Access and RedCap. Identifiers and other related information for coordinating research activities (recruitment outcome, research interview call log and interview visit schedule, etc.) will be kept on the secure FSM network drive. Only the PI, project manager, and RCs will have access this database. Identifiers included in the database include: name, MRN, address, phone number, DOB. Upon completion of all study-related data collection the database with identifiable information will be deleted. Study generated data will be collected and stored in RedCap and SharePoint and will be download (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.

25.0 Provisions to Protect the Privacy Interests of Subjects

25.1 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 master study tracking database via Microsoft Access will contain information linking participants to their study id numbers. This database will be encrypted and password protected, kept on a secure server and only accessible by study personnel. Survey data will be stored in a REDCap. The data will not contain any identifiable information. Individual study identification numbers will be assigned to each participant and only this number will appear on the survey.

Subjects will be informed that participation in any part of this research study may result in a loss of privacy, since persons other than the investigators may view their study records if deemed necessary for oversight purposes. However; they will be identified by a unique identification number ("study id"), not by name, and any other identifying information (e.g. personal and/or contact information) will be kept separate from the other data; all information will be kept in secure, password-protected files. Personal information will be encrypted and linked to the study number. Further, subjects will be told that unless required by law, only the study investigators, members of the project staff, and representatives of the Northwestern University and local Institutional Review Boards will have the authority to review any study records. In such case, they too will be required to maintain confidentiality.

25.2 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).

25.3 All enrolled participants will provide written or verbal consent, include HIPAA authorization for the collection of all data, including review of the patient's medical records.

26.0 Compensation for Research-Related Injury

N/A

27.0 Economic Burden to Subjects

N/A

28.0 Consent Process

28.1 Written consent will be obtained for all participants, prior to their participation. The consent process will take place in a private room at NMHC, Erie clinic, in community sites in the participant's neighborhood (i.e. private study rooms in libraries), or over the phone (RC will be in a private space). For patients unable to complete the in-person interview/in-person written consent due to COVID-19, we request a waiver of documentation of informed consent and an alteration to obtain verbal HIPPA Authorization. Due to restrictions to in-person interviews during the COVID-19 pandemic, in-person interviews will not be able to be completed in-person to protect patients' safety and to follow Northwestern guidelines. Research can not practicably be conducted without the waiver or alteration. After verbal consent and HIPPA Authorization is obtained, the consent date and the name of the research coordinator that obtained the consent will be recorded in Redcap prior to starting the baseline interview. Participants will be provided a consent form in their preferred language (English or Spanish). A bilingual (English/Spanish) research coordinators will work with participants who prefer Spanish language, and will communicate in Spanish with potential participants. Informed consent 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.

28.2 **Verbal consent process for COVID-19 survey**:

Subjects will be informed about the nature of the study by a CITI-certified RC and asked to provide verbal consent. They will be informed that they may withdraw from the study at any time and given contact information for the PI and RC. A verbal consent, or a waiver of documentation of consent, is deemed appropriate because the nature of the study involves minimal risk and no PHI will be collected. If a patient agrees to participate after the RC reads the consent, the RC will record the patient's

name on the consent form and the RC will sign their own name on the form. These consent forms will be locked in a file cabinet only accessible to necessary research staff. Patients will be given the option to receive a blank consent form for reference if they request it.

For the follow-up waves of the COVID-19 survey, the same verbal consent process will be followed as above prior to wave 2.

28.3 **Online and verbal consent process for COVID-19 Waves 5-9:**

Subjects will be informed about the nature of the study by a CITI-certified RC and asked to provide online consent with HIPPA authorization and complete the wave 5 interview after consent is obtained. If interested, the RC will send patients a link to Redcap either by email or SMS 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 enter their first and last name, signature, date of birth, and date of consent to complete the online consent.

If a patient is unable to complete the online consent due to inability to use technology for online consent, we request a waiver of documentation of informed consent and an alteration to obtain verbal HIPPA Authorization. After verbal consent and HIPPA 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 first phone 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.

Once online consents are filled out, they will get an automatic email with the signed version of the consent. Patients will also be informed that they may print their screen to keep a copy of the consent. For patients that complete a verbal consent, they will be offered a copy of the consent document to be sent via email or mail for their records according to their preference.

28.4 **Online consent process for Provider/Staff survey**

We will ask providers and staff to consent to complete a brief online survey to obtain feedback about the trial. Providers and staff will be informed of the nature and details of the survey via email. They will be asked to complete an online consent to complete the brief survey. We request a waiver of documentation of consent for the provider/staff consent. A waiver of documentation of consent is deemed appropriate

because the nature of the survey involves minimal risk and no PHI will be collected. In order to complete the online consent, participants will be asked to click if they agree or disagree before moving forward to the online survey.

29.0 Process to Document Consent

29.1 Written or verbal consent will be obtained for all participants, prior to their participation. The consent process will take place in a private room at NMHC, Erie clinic, in community sites in the participant's neighborhood (i.e. private study rooms in libraries), or by phone (RC will be in a private space). Participants will be provided a consent form in their preferred language (English or Spanish). A bilingual (English/Spanish) research coordinators will work with participants who prefer Spanish language, and will communicate in Spanish with potential participants. Informed 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. If the participant agrees to participate in the study, they will be asked to sign and date the consent form before proceeding with the interview. The research coordinator guiding the consent process will then sign and date the consent form. If a written consent is obtained, participants will receive a copy of the signed consent form. After the interview, signed consent forms will be stored in locked cabinets in General Internal Medicine. For phone interviews, the patient will complete a verbal consent and verbal HIPPA Authorization. Patients will be emailed or mailed a blank copy of the consent document for their records.

29.2 Provider/Staff survey. Online consent will be obtained from providers and staff. All participants will be told that their participation is voluntary; they can stop at any time, and whether they participated or not will not be disclosed to their superiors. If the provider/staff does not want to participate or decides to stop before completing the survey, this will not be disclosed to any superiors.

30.0 Drugs or Devices

N/A