HMC RESEARCH PROTOCOL

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Medical Research Center

Nurse-led medication self-management intervention in the improvement of medication adherence in adult patients with multi-morbidity: A Feasibility Randomized controlled trial

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NCT- Not available

1. Summary

Back ground & Aims

Adult patients suffering from multimorbidity are at high risk of medication non-adherence. It has been well established that self-management support is an effective strategy to enhance medication adherence for patients with chronic conditions. However, little is known about the effect of the medication self-management intervention in Adult patients with multimorbidity. The aim of this study to evaluate the effectiveness of a nurse-led medication self-management intervention in improving medication adherence and health outcomes in adult patients with multimorbidity.

Methods

This study is a single centre, single-blind, two-arm randomised controlled trial. Adult patients with multi-morbidity will be recruited from NCCCR Qatar. A total of 100 participants will be randomly allocated to receive standard care or standard care plus the medication self-management intervention. The intervention will be delivered by clinical nurse specialists. The 6-week intervention includes three face-to-face education sessions (2st week, 4rd week and 6th week) and two weekly (8th week and 10 week) follow-up phone calls. Participants in the control group continue to receive all respects of standard care offered by healthcare providers, including chronic disease management, drug prescription, referral to hospital specialists, health education and consultations regarding patients' diseases and treatments during centre visits.

Outcome

The primary outcome is medication adherence as measured by the 5-item Medication Adherence Report Scale. Secondary outcomes include medication self-management capacity (medication knowledge, medication beliefs, and medication self-efficacy), treatment experiences (medication treatment satisfaction and treatment burden). All outcomes will be measured at baseline, immediately post-intervention (7th week), and at 3-month post-intervention.

2. Abbreviations and Acronyms

NCCCR- National Cancer Care Center and Research
CNS- Clinical Nurse Specialist
IMB- Information-Motivation-Behavioral Skills

3. Introduction / Background

Adherence is a key factor in the potential effectiveness of the treatment of chronic conditions in patients. According to the World Health Organization, however, 50 per cent of these patients do not comply with the drug regime in developed countries(1). In developing countries, access to health services is limited and there is a shortage of health care providers and financial resources, so it is assumed that this number is higher. Medication non-adherence is often linked to adverse clinical results (2) and decreased quality of life (3)and higher use of health resources(4). Drug non-adherence is widespread among the elderly, and over 55% live with multiple diseases (i.e., multiple chronic diseases) together(5). In addition to the high complexity of multi-morbidity, patients are more likely to receive complex medications(6) , adverse drug reactions(7), and substantial drug burdens (8). Patients need to spend a lot of energy and time taking and administering medicines(9, 10). Multi-morbidity is an obstacle to the self-management of drugs that lead to disease, leading to poor compliance and treatment results(11, 12) . Support for the self-management of medications is an effective strategy for addressing the challenges of taking medications and giving patients the opportunity to take care of themselves. In general, medication self-management programs integrate multiple components to help patients take drugs efficiently and safely, such as changes in health behavior change, patient education, shared decision making, and goal setting. Drug self-management interventions have been established in several conditions(13-15). However, Current clinical trials focus on specific diseases or drugs, limiting their generalization to older patients with multiple diseases(16, 17). Some studies have found the effectiveness of self-management interventions in this complex patient group(18-21) . Unfortunately, most have not significantly improved compliance and health outcomes. A six-month self-management support program for the treatment of multiple diseases based on cognitive behavioral therapy and motivational interviews did not result in any improvements in the outcome of patients, except for self-assessment of health(18). Another personalized self-management intervention by nurses in patients with coronary disease and depression also did not show significant differences in compliance and health outcomes between the intervention and the control group(19) . One explanation is that most self-care programs for elderly patients with multiple diseases are designed to address all aspects of self-care, but not specifically to improve medication self-management capacity or focus on patients with adherence problems. A study by Cochrane concluded that interventions were more effective in targeting specific problems experienced by multi-morbidity patients., such as depression, functional limitation, and non-adherence to medication non-adherence(22) . Interventions with a broader focus, such as case management and changes in treatment for multi-morbid patients, seem to be less effective. Drug management interventions are more effective in addressing specific problems related to the use of drugs. Information about the need to move health education intervention way from the tradition information based and advice-giving model to health coaching using evoking, focusing, planning and motivational interview process. Furthermore, the social behavior model was rarely used to guide study design and explain the mechanisms of previous studies underlying important or non-significant intervention effects. Therefore, although interest in the study of adult patients with multiple diseases is growing, promoting medication adherence of this group of patients is still a challenge for healthcare providers and researchers(23). Information about the need to move health education intervention way from the tradition information based and advice-giving model to health coaching using

evoking, focusing, planning and motivational interview process. The current study aims to implement evidence-based, theoretical and nurse-led drug self-management interventions in adult patients with multi-morbidity.

4. Objectives

The primary objective

To evaluate the effectiveness of a six-week intervention led by a nurse in medication self-management to improve medication compliance in adult patients with multimorbidity and going to discharge, as compared with standard care.

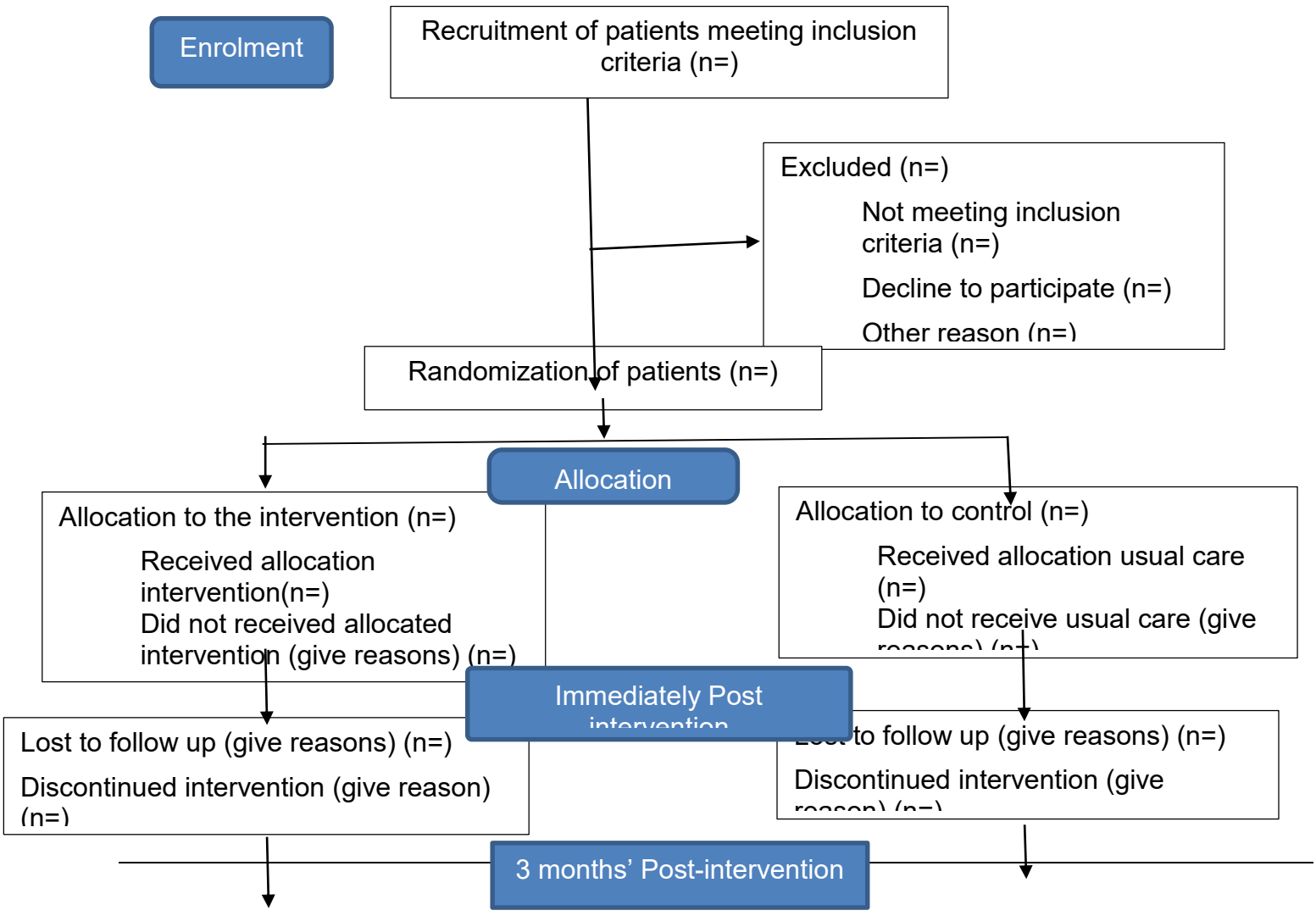
Secondary objectives

To evaluate the effectiveness of the intervention on the improvement of patients' medication self-management capacity (medication knowledge, medication beliefs, and medication self-efficacy), treatment experiences (medication treatment satisfaction and treatment burden), as compared with standard care. *(Retrospective means the data is already in existence when the project is submitted to the IRB for initial (if this is a retrospective chart review, the end date must come before the submission date): mm/dd/yyyy to mm/dd/yyyy*

5. Study Methodology

This is a single Centre open label, two-arm randomized controlled trial with 1:1 randomization at the participant level. The patient population will be patients with at least two comorbidities. The patient recruitment will be done in the National Centre for Cancer Care and Research (NCCCR) in the outpatient department in the clinical nurse specialist counselling room. Participants will randomly be allocated to receive standard care(control) and standard care plus the medication self-management intervention (Motivational Interview). Primary and secondary outcomes of study will measure better medication adherence, medication self-management capacity and treatment experiences, which will be collected from both group including the intervention group and control group (Participants in the control group will continue to receive all respects of standard care offered by healthcare providers) at baseline (T0), in the 7th week immediately post-intervention (T1), and at 3-month post-intervention (T2). This protocol is presented based on the recommendations of the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 statement(24). The results of this trial will be reported as per the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement(25).

An overview of the study design is shown in Fig. 1.



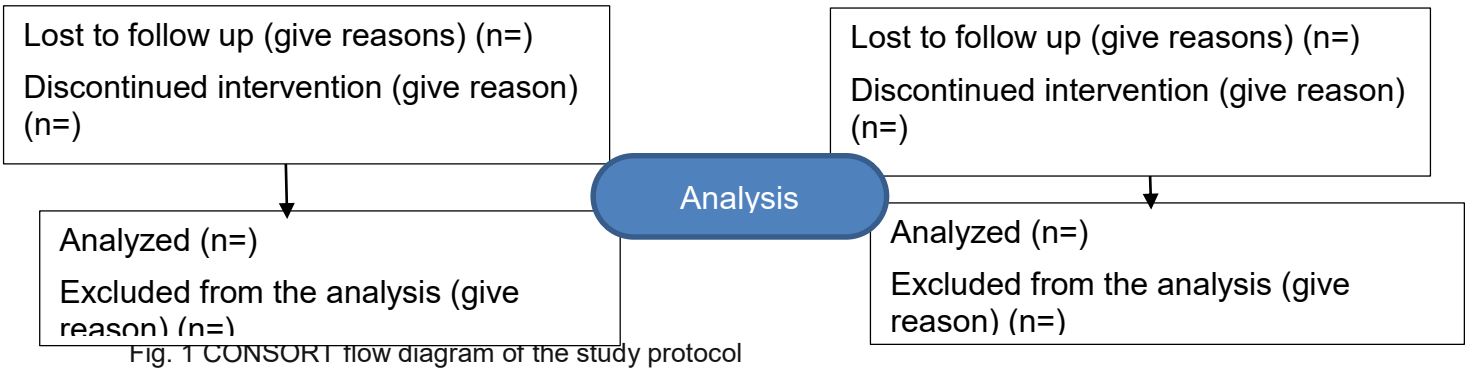


Fig. 1 CONSORT flow diagram of the study protocol

Theoretical framework

Motivational strategies, to reiterate, are built on sophisticated understandings of human behavior in the social environment (HBSE), most of which have been confirmed through real-life experimentation. The theoretical foundation of Motivational intervention(MI) is first and foremost the knowledge that people often modify their behavior as a result of their interaction with others. A related assumption is that therapists who possess critical counselling skills can help facilitate personal change in their clients(26).

Development, implementation and evaluation of interventions are guided by a framework adapted from the Information-Motivation-Behavioral Skills (IMB) model of Fisher and Fisher (27). The IMB model is a well-established social behavioral model for understanding and predicting health-related behaviors. In consideration of the complexity of patients living with multimorbidity, the IMB model was extended by including four interrelated variables (that is, disease burden, treatment burden, depressive symptoms, and medication treatment satisfaction) emerging from comprehensive literature reviews. The extended IMB model demonstrated that in addition to adherence information, motivation, and behavioral skills, medication treatment satisfaction and treatment burden could also directly or indirectly impact medication adherence. Based on the model, it is proposed that individuals who are well informed, highly motivated, having skills to perform medication self-management, highly satisfied with medication treatment, and experiencing low treatment burden are more likely to enact and maintain adherence behavior. The medication self-management intervention might be effective if intervention components focus on addressing each of the above behavioral determinants that affect medication adherence.

6. Study Population and Study Setting/ Location

In this section describe the study population that is to be enrolled in the study, planned recruitment number and Inclusion and Exclusion Criteria to be listed here. Also list the Hospitals in which this study will be conducted (e.g. HGH, Rumailah etc)

The trial will be conducted at NCCCR in QATAR. NCCCR Physician, clinical pharmacist and nurses work collaboratively to provide essential health services to discharged multi-morbidity patients including health education, medical treatment services, and chronic disease management in NCCCR.

Participants

The participants of the trial are discharged adult patients with multi-morbidity. Multi-morbidity is defined using a cut-off of three or more chronic conditions as patients with at least three conditions are more likely to have complex needs and great utilization of healthcare services (28). To avoid the ceiling effect and improve study power to detect changes in adherence, only participants with low medication adherence (Morisky scale<2) are considered eligible for the trial.

Participants' **inclusion criteria** are

- +18 years old or over,
- patients with at least two of the identified comorbidities (Hypertension, Chronic painful condition, Cancer, Inflammatory connective tissue disorders, Diabetes, Lipid disorder, Dyspepsia and gastroenteritis, Heart disease, Chronic obstructive pulmonary disease, Stroke and cerebrovascular disease , chronic kidney disorder , Asthma Thyroid disorders, Anemia, Chronic liver disease, Depression, Epilepsy, Anxiety & other stress related disorders), (3) having at least one medication prescribed for a chronic condition over at least the 3 months prior to inclusion in the study,
- non-adherence to medications, as defined by scoring zero on the 8-item Medication Adherence Report Scale (Morisky -8)(29),
- independently managing their medications (i.e., not rely on a care taker),
- able to speak or understand English/Arabic,
- able and willing to receive phone calls, and
- capable of providing a written informed consent to participate in the study.

Exclusion criteria are

- being institutionalized in a long-term care facility,
- planning to move away from the community in the next 6 months,
- cognitive impairment (Mini-cog scores < 4), and
- currently participating in research involving chronic disease management. Patients with cognitive impairment are excluded because they may not be able to provide valid answers to the questionnaires.

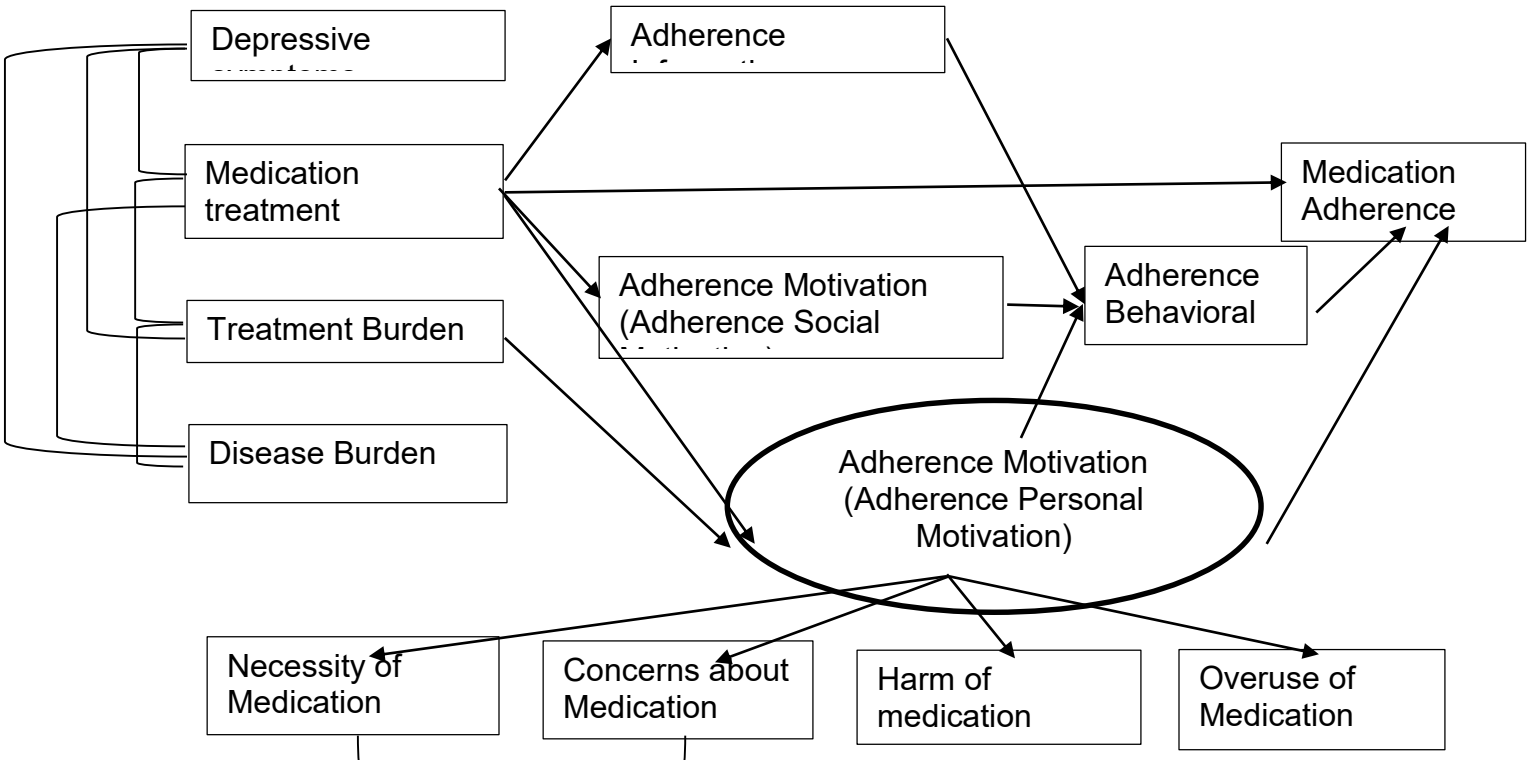


Fig2. Theoretical framework of the study: the extended information motivation behavioral skills model of medication adherence

Recruitment

Three clinical nurse specialist as a part of research team from NCCCR will deliver the intervention. Nurses' inclusion criteria are (1) Senior clinical nurses with a Master degree or above, (2) having at least 3 years of working experience in HMC, (3) taking on chronic disease management in routine work, and (4) not planning to quit the job in the next 6 months and Nurses who are participating in other research studies on chronic disease management at the time of this study will be excluded. Nurses will recruit participants through approaching potentially eligible participants in NCCCR. Centre appointments by Clinical nurse specialists will be arranged for interested participants and the principal investigator/ co-investigator will determine the eligibility of participants, describe the study to them, obtain written consent forms, and collect baseline data. A one-week period will be allowed for participants to decide whether or not they wish to participate in the study. Participants' reasons for nonparticipation will be recorded.

Sample size; data collection methods
Sample size

Sample size calculation was performed using G*Power Version 3.1.9.7. Estimation is based upon the primary outcome, medication adherence, at 3 months of follow-up between the intervention and control group. Medication adherence is calculated as sum of the scores from each item using Morisky 8. Based on our recent systematic review and meta-analysis on medication adherence interventions among patients with multimorbidity Cohen's effect size (d) of 0.52 on medication adherence is estimated for a medication self-management intervention program. The required sample size will be 94 participants (47 in the intervention group and 47 in the control group) to attain an 80% power with a two-sided α of 0.05. Therefore, for a 5% attrition rate, the final sample size required is 100 participants.

For Arabic speaking patients, the questions will be translated to Arabic by the Arabic speaking research team member.

Randomization & blinding

Consenting participants will be randomized in outpatient clinic in NCCCR. Randomization will be block randomization, and generated by a computer program centrally (Nursing/ Midwifery Research department).

Following recruitment, patients will be randomized to either the intervention or the control arm in a near 1:1 ratio, using a computer-generated randomized permuted block design. The design will use random block lengths of 2, 4 or 6, and include an initial unbalanced block, with a maximum of one additional patient in either arm, to further hide allocation sequences, which means that the ultimate sample size and allocation ratio will vary very slightly from what is planned depend on the unbalanced block.

Each participant will be assigned a special code generated by the computer. The randomization will be kept by the PI and CNS. After the eligibility assessment by CNS, data will be obtaining at the baseline (after completion of informed consent), 7th week and 12th week.

Intervention group

The medication self-management intervention consists of three face-to-face education sessions and two weekly telephone follow-up over 6 weeks. Intervention components are derived from an extensive review of the literature, including the related theoretical framework and current practice. Based on the extended IMB model of medication adherence, this intervention is designed to offer information related to medication treatment, motivate patients to adhere, help build medication self-management skills, and develop adherence improvement plans. The face-to-face meeting will take place in the clinical nurse specialist counselling room in NCCCR. The face-to-face sessions will include all of the following: exploration of medication treatment experience and expectation, medication knowledge education, motivation feedback tailored to the individual's personal and social barriers to adherence, medication self-

management skills building, and goal setting. A patient-centered approach will be adopted considering the complex needs of patients with various combinations of chronic conditions.

A comprehensive assessment of adherence problems will be firstly conducted to identify the factors that affect adherence, including how and why these factors contribute to poor adherence. Medication-related knowledge and skills will be provided based on individual treatments and barriers to adherence. Motivational interviewing techniques will be used for a better understanding of patients' cognitive factors of adherence behavior. Nurses will discuss with patients to explore their preferences and priorities in medication treatments, setting goals that are practical and acceptable for addressing their problems in medication use, and develop individualized adherence improvement plan to reach these goals. Taking patients' complexity into account, strategies to reduce treatment burden will also be incorporated into intervention sessions, including prioritizing medication and other self-management activities using shared decision making, providing communication skills with healthcare providers and encouraging patients to discuss with the physicians about burdensome regimens, exploring patients' family and social network to support their self-care, and helping them to incorporate self-care activities into daily life. Each face-to-face session will last approximately 30– 40 min and will be delivered individually in NCCCR by CNSs. The duration of each session can be adjusted by CNSs in accordance with the patients' barriers and problems to medication adherence. The three face-to-face sessions are designed to complete at 7–10-day intervals over 4 weeks. Before the first face-to-face session, nurses will review patients' clinical health records to confirm the screening criteria.

Patients will be asked to bring all medications to HMC. After the conclusion of the last face-to-face session, education materials containing instructions and information on the name, purpose, side effects, and special tips for each usual chronic medication and medication skills will be provided to participants. After the face-to-face sessions, patients are followed up by two weekly by telephone. Each telephone encounter lasted 10–20 min. The aim, content, and delivery strategy of each session are shown in Table 1.

Control group Participants in the control group will continue to receive standard care from Physicians, nurses, and clinical pharmacists in the NCCCR. Physicians are the primary providers and coordinators of care for patients with chronic conditions. Physicians provide patients consultations and education regarding their diseases and treatments (typically clinician-centred) at each patient visit to the chronic disease clinic. Referral to hospital specialists will be made by physicians as needed. For patients diagnosed with hypertension and/or diabetes, Physicians are required to provide scheduled follow-up via telephone contact. CNSs assist physicians with chronic disease management. In respect of medication management, Physicians will prescribe medication regimens, provide medication consultations (including instructions on the medications' dosage, methods, and frequency), and adjust regimens where appropriate through discussion with patients. No structural medication self-management education session will be provided for patients in standard care group.

Table 1 The Nurse-led Medication Self-Management Intervention Sessions

Aim	Content	Delivery strategy
1st face-to-face education session • To identify patients' problems and barriers to medication adherence. • To educate patients on the right information about medication taking and adherence.	(1) Inform patients about the purpose and procedure of the whole intervention. (2) A structured patient-centered adherence assessment, covering a checklist with all the questions about patients' medication experiences, including effectiveness and side effects of the drugs, treatment burden, and barriers to adhering to medications. (3) Educate patients on disease- and medication-related information and correct misinformation, including the name, dosage, frequency, timing, purpose of each medication, potential side effects, and special administration considerations. (4) Encourage patients to ask questions and ensure that they understand what is said to them.	❖ Individualization ❖ Teach-back technique
2nd face-to-face education session • To help patients change negative attitudes and beliefs about medication treatments and become motivated to it. •	(1) Give patients the opportunity to understand the importance of medication adherence and the consequences of non-adherence. (2) Encourage patients to express feelings and barriers to family members and seek assistance, where appropriate. (3) Provide a list of local resource information to patients (e.g., medical care institutions, psychological support organizations, and peer support teams).	❖ Motivational interviewing ❖
3rd face-to-face education session • To help patients develop skills and strategies to overcome practical barriers of their medication treatments. • To help patients set goals and develop a workable adherence improvement plan.	(1) Nurses will educate patients about six skills in medication self-management: 1. Identifying and coping with medication side effects; 2. Incorporating medication treatments into daily life; 3. Obtaining and updating medication adherence-related information; 4. Acquiring, self-cueing and self-administering medications; 5. Effectively communicating with healthcare providers; 6. Acquiring social and instrumental support for adherence. (2) Ask patients to select three skills they most want to learn or help most to take their medications; Discuss with patients	❖ Planning coping responses ❖ Goal setting

	about strategies on how to apply the three skills to their self-management. (3) Set goals and help make an individualized adherence improvement plan based on patients' expectations and preferences.	
2-week Telephone follow- • To further explore the challenges and difficulties in medication self-management. • To provide feedback and suggestions according to patients' performance.	(1) Ask whether patients can adhere to the medications in the last week and if not, the reasons for medication non-adherence will be asked and discussed with patients. (2) Ask whether patients can apply skills in medication self-management and encounter any challenges and concerns in medication-taking. (3) Further adherence education where needed. (4) Conclude what is discussed and encourage patients to contact healthcare providers when they have adherence problems	❖ Active listening ❖ Personalized feedback

Nurses' training Intervention

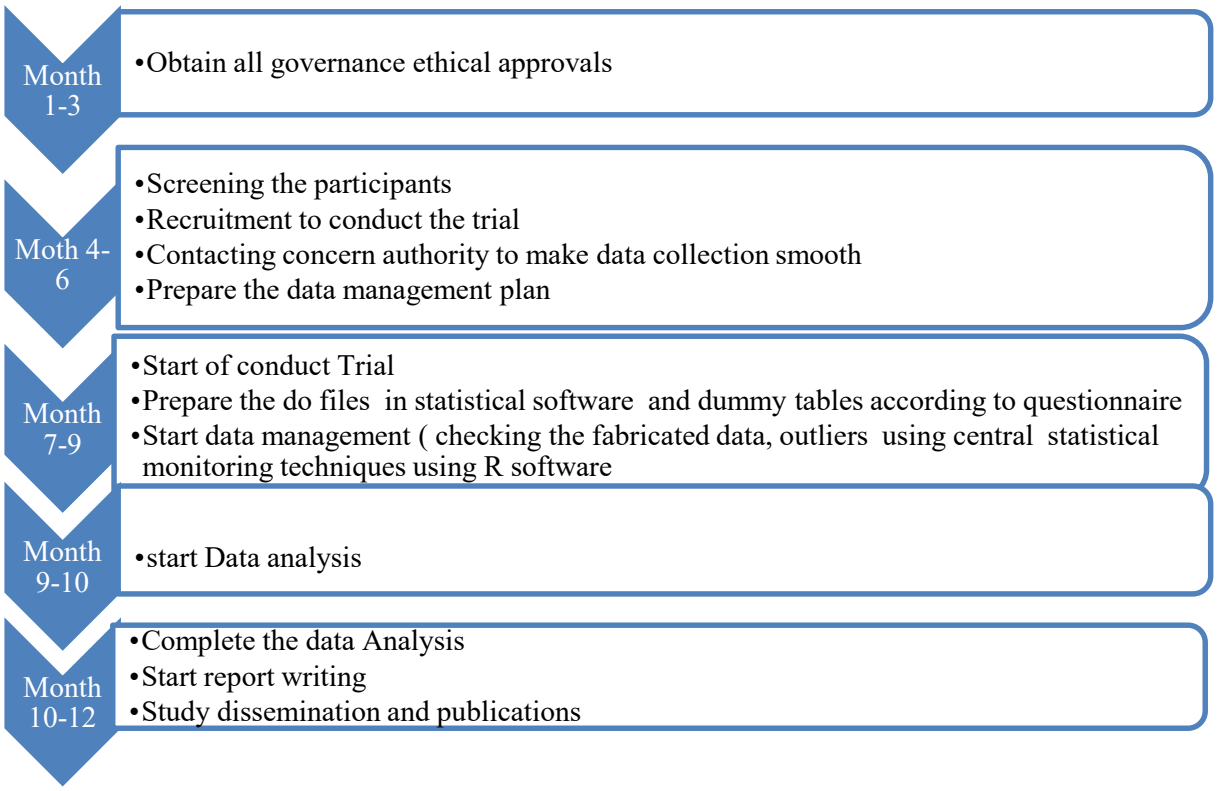
The certified clinical nurse specialists will be informed of the study objectives, procedure, detailed intervention protocol, and ethical considerations. Training sessions will involve medication self-management support, teach-back techniques, shared decision making, and basic motivational interviewing skills, e.g., posing open-ended questions, reflective listening, and expressing empathy(32). Nurses will also receive a detailed study protocol and a manual containing instructions for delivering the intervention.

7. Study procedures

Provide an outline and describe in detail the processes and operations of the study, including logistics

Study Duration and Timelines

The evaluation of the project process will be against the key milestones as described below.



Informed Consent

*a) How people will be **NOTIFIED OR APPROACHED** to consider being a research subject in this study?*

During the OPD visit of the patient the CNS will approach the patients directly based on the inclusion exclusion criteria. All the study details will be explained to the patient in detail at the CNS office. After explaining the study details to the patients, a minimum of one-week time will be given to them before they are decided to take part in the study. After the written informed consent patient will be enrolled to the study and allocated randomly to control and intervention group. For Arabic speaking patients, the informed consent form will be translated in Arabic by the Arabic speaking research team member.

b) Describe the CONSENT PROCESS procedures (When, Where, How, by Whom).

CNS will approach the patients directly based on the inclusion exclusion criteria. All the study details will be explained to the patient in detail at the CNS office. After explaining the study details to the patients, a minimum of one-week time will be given to them before they are decided to take part in the study. We will contact the patient to confirm their participation in the study. If they agreed to participate in the study, will advise to come to the outpatient visit for face to face interview.

c) Describe HOW LONG potential participants will have to decide on participation.

1 week

d) Describe how subjects will be SCREENED FOR ELIGIBILITY for the study.

Based on Inclusion and exclusion criteria

e) Describe how subjects will be ENROLLED into the research study below.

Based on screening & randomization tool

Risk

In this section describe the anticipated risks associated with participation in the research (i.e. illness, injury, death)

No risk is anticipated as part of study

Bio-Specimens & Sample Collection

In this section describe what specimens or samples will be collected specifically for research, if specimens will be stored long-term and/or destroyed. Consider what happens to data/specimens if subject withdraws consent

NA

Outcomes

In this section provide details on the outcome measures and the anticipated primary & secondary outcomes

Outcome assessment

The nurses masked to the participant allocation will collect follow-up data through telephone interview. Participants will be assessed at baseline (T0), in the week immediately post-intervention (7th week) (T1), and at 3-month post-intervention (T2). Table 2 provides an overview of primary and secondary outcomes as well as covariates at each time point. Permission will be obtained from the original authors to use the scales for this study.

Primary outcome

Medication Adherence

The English version of Morisky-8 will be administered to assess medication adherence of the participants(29). The Morisky-8 is a self-reporting measure of unintentional and intentional medication non-adherent behaviors with a yes and no response. The total score of the moresky-8 ranges from 0 to 8, with a higher score representing higher adherence to medication.

Table 2 Schedule of enrolment, interventions, and assessments

TIMEPOINT	STUDY PERIOD				
	Enrolment	Baseline T0	Intervention	Follow-up	
				T1	T2
ENROLMENT					
Eligibility screen	X				
Informed consent	X				
Allocation		X			
INTERVENTION					
Intervention group			X		
Control group			X		
ASSESSMENTS					
Primary outcome					
Medication adherence (Moresky-8)		X		X	X
Secondary outcomes					
Medication knowledge (PKMUQ)		X		X	X
Medication beliefs (BMQ)		X		X	X
Medication self-efficacy (SEAMS)		X		X	X
Treatment burden (TBQ)		X		X	X
Potential covariates					

Socio-demographics (Patients questionnaire)	X
Number of prescribed medications (one-item question)	X
Depressive symptoms (PHQ-9)	X

Secondary outcomes

Medication Knowledge

The Patients' Perceived Knowledge in Medication Use Questionnaire (PKMUQ) is used to determine participants' medication knowledge(33). The PKMUQ comprises five items covering two dimensions: general knowledge in medication use and drug interaction knowledge. The response scale ranges from 1 = strongly disagree to 5 = strongly agree, and the response scores of all 5 items will be summed. Higher scores indicate a higher level of medication knowledge.

Medication beliefs

Medication beliefs will be measured by using the Beliefs about Medication Questionnaire BMQ). The BMQ is an 18-item self-reported questionnaire consisting of two subscales: the BMQ-Specific which evaluates representations of medications prescribed for personal use and the BMQ-General which evaluates beliefs about medications in general(34). The BMQ-Specific subscale consists of two subscales: the 5-item Specific-Necessity subscale assesses beliefs about the necessity of medications and the 5-item Specific-Concerns measures concerns about the medications. The BMQ-General contains 8 items which include two 4-item subscales: The General-Harm subscale which evaluates beliefs about the harm of medication and the General-Overuse subscale which evaluates beliefs about overuse of medication by doctors. Participants will be asked to rate the degree of agreement with each statement. A 5-point Likert scale ranging from 1 = strongly disagree to 5 = strongly agree is used. A higher score indicates stronger beliefs about the corresponding concepts in each subscale.

Medication self-efficacy

The Self-Efficacy for Appropriate Medication Use Scale (SEAMS) will be used to determine participants' medication self-efficacy(35). The SEAMS consists of 13 items that evaluate participants' confidence in taking medications under various challenging circumstances. Each item has a 3-point scale ranging from 1 = not confident to 3 = very confident. The score of scale ranges from 13 to 39, with a higher medication self-efficacy by a higher score.

Treatment burden

The treatment burden will be measured by the 10-item Multi-morbidity Treatment Burden Questionnaire (MTBQ)(36) . It assesses the wide range of behavioral and emotional burdens involved in treatment implementation and treatments associated with taking multiple medicines, self-monitoring their health and making lifestyle changes. Each item is scored on 6-point Likert scale, ranging from 0 = does not apply to 5 = most difficult. Scores are summed to derive a total score ranging from 0 to 50 with a higher score indicating a higher level of treatment burden.

Potential covariates

Socio-demographic characteristics and the number of prescribed medications

Socio-demographic characteristics will be collected at baseline from patients. Patients will be asked about age, gender, educational level, marital status, monthly income, and the number of prescribed medications.

Intervention fidelity and contamination

The principal investigator will be responsible for monitoring the procedure of the whole study. The intervention logbook will be used by participating nurses to record the number, duration, and administration date of face-to-face sessions and follow-up phone call sessions. To ensure that the delivery of motivational interviewing is consistent with its principals, all motivational interviewing sessions will be audiotaped if permitted by the participant. A random 20% sample will be reviewed using Motivational Interviewing Treatment Integrity Coding Manual 4.2.1 (37) by the local motivational interviewing nurse expert throughout the duration of the intervention. The principal investigator will meet with intervention nurses to discuss the experiences and difficulties to deliver the intervention sessions and provide feedback weekly. Intervention logbooks will also be examined weekly by the principal investigator and further training for nurses will be considered if the delivery of the intervention is not per protocol. Contamination may occur whereby control group participants also receive usual nursing care or interact with intervention group participants. However, the current study is expected to be at a low risk of contamination because (1) patients with chronic diseases predominately receive medication management by physicians, the involvement of nurses in medication treatment and consultation is rare, (2) the multifaceted interventions with individualized cognitive behavior component cannot easily be transferred from one participant to another. Also, the following strategies will be introduced to minimize contamination. First, participants and nurses will be provided with clear information on the nature and purpose of the study. Second, Nurse/researchers will ask participants keep the education materials to themselves until the end of the study. Finally, only intervention nurses will receive training to deliver the intervention and they will be requested not to discuss the intervention with their colleagues who might be involved in the control group. At the end of the trial, participants in the control arm will be asked whether they have received any information or education on their medications, causal average effect analysis will be considered if high degree contamination occurs (38).

Data Collection, Management & Confidentiality

a) Indicate below HOW study data will be collected for the proposed research.

☒ *Study Forms* ☐ *Study Database* ☐ *Study Web-Based/App* ☐ *Other*

Please detail how study data will be coded:

The research data including participants' personal information will be recorded in two different files. All research-related data will be linked with a study ID number with no identifying information. Original questionnaires and tapes will be locked in a secure cabinet, with limited access by designated research team members only. The link between the code and the identifier will be destroyed once the study finishes and the de-identified data will be stored for at least five years.

b) Describe below WHERE and HOW the study data is physically stored.

Research data will be stored on a password-protected computer and backed up on a password-protected hard drive Research Department 322A 3rd floor 302.

c) Describe below WHO controls access to the study data

Only the PI and Statistician

d) Describe below WHO has access to the study data.

PI and statistician will have the access of full data

e) Describe below HOW the study data is accessed.

The collected data from the questionnaire will be transferred to Microsoft excel.

f) Will subject identifiers be shared outside of HMC? If YES describe below WHOM the study data is shared

No

Subject Withdrawal/ Withdrawal of Consent

In this section describe why a subject may be withdrawn from the study by the PI, what happens to the data or bio-specimens if a subject withdraws consent

If the subject withdrawn from the study before the randomization, then we will report as a screened participant if the subjects withdrawn from the study after the randomization we will include him / her in the analysis.

8. Statistical Consideration and Data Analysis

Our primary analysis will be the 'intention-- to-treat' population, which will include all randomized patients analyzed according to their original treatment allocation, irrespective of their subsequent adherence or how they were actually treated. All data will be analyzed using STATA 17.0 software. Descriptive statistics will be used to describe and compare socio-demographic data on participants between the intervention and control group. Continuous variables that follow a normal distribution will be expressed as means and standard deviations, whereas categorical variables will be presented as frequency counts and percentages. Median values and interquartile ranges will be calculated for continuous data with a skewed distribution. Mann-Whitney U-test or t-test will be performed for continuous data to compare baseline characteristics between groups, and Chi-squared test or Fisher's exact test will be used for categorical variables. The distributions of the outcome variables will be evaluated, and normalizing transformation will be applied as needed. Primary and secondary outcomes will be analyzed following the intention to treat principle at the individual participant level. Changes in repeated outcome measures across different time points between the intervention and control group will be analyzed using generalized estimating equation models with adjustment for potential confounders of the baseline variables. All statistical tests are two-sided, and $p < 0.05$ will be statistically significant.

9. Adverse Event Reporting

In this section, provide a definition of anticipated adverse events that are related to the research, including a description of how SAEs will be assessed, tracked and reported

There will not be any adverse events related to intervention because it is educational intervention. If some adverse event related to out outcome reported during the study, we will notify to the IRB.

10. Ethical Consideration

A statement that the study will be conducted in full conformance with principles of the "Declaration of Helsinki", Good Clinical Practice (GCP) and within the laws and regulations of MoPH in Qatar.

The study will be conducted in full conformance with principles of the "Declaration of Helsinki", Good Clinical Practice (GCP) and within the laws and regulations of MoPH in Qatar.

11. Sponsor, Funding & Collaborator Information

Provide basic details of the lead sponsor and/or funding bodies, including name, and contact information, allocated number for the research, etc. For example QNRF

From Medical Research Center' .

12. Dissemination of Results and Publication policy

List any meetings or conferences where you will be presenting the data and the results of your study. Please provide timeline for finalizing manuscript and when and where you plan to submit for publication. Any presentation, abstract, or manuscript must be made available for review by The Medical Research Center prior to submission.

We plan to conduct stakeholder's workshops, conferences, public forum that will help us to disseminate the study results by reporting and presentation the various interdisciplinary health care professional and policy makers.

We plan to publish our study results in both internationally known journals and electronic open access journals. Finally, our plans for dissemination include assisting other researchers on the phases of the project, trans –disciplinary perspective and other related methodological issues.

13. References

Cite the sources of all reference materials used to support the hypothesis

1. Organization WH. Adherence to long-term therapies: evidence for action: World Health Organization; 2003.
2. Walsh CA, Cahir C, Tecklenborg S, Byrne C, Culbertson MA, Bennett KE. The association between medication non-adherence and adverse health outcomes in ageing populations: A systematic review and meta-analysis. British journal of clinical pharmacology. 2019;85(11):2464-78.
3. Khayyat SM, Mohamed M, Khayyat SMS, Hyat Alhazmi RS, Korani MF, Allugmani EB, et al. Association between medication adherence and quality of life of patients with diabetes and hypertension attending primary care clinics: a cross-sectional survey. Quality of life research. 2019;28(4):1053-61.
4. Aznar-Lou I, Fernández A, Gil-Girbau M, Sabés-Figuera R, Fajó-Pascual M, Peñarrubia-María MT, et al. Impact of initial medication non-adherence on use of healthcare services and sick leave: a longitudinal study in a large primary care cohort in Spain. British Journal of General Practice. 2017;67(662):e614-e22.
5. Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: a systematic review of the literature. Ageing research reviews. 2011;10(4):430-9.
6. Wimmer BC, Cross AJ, Jokanovic N, Wiese MD, George J, Johnell K, et al. Clinical outcomes associated with medication regimen complexity in older people: a systematic review. Journal of the American Geriatrics Society. 2017;65(4):747-53.
7. Calderón-Larrañaga A, Poblador-Plou B, González-Rubio F, Gimeno-Feliu LA, Abad-Díez JM, Prados-Torres A. Multimorbidity, polypharmacy, referrals, and adverse drug events: are we doing things well? British Journal of General Practice. 2012;62(605):e821-e6.
8. Eton DT, de Oliveira DR, Egginton JS, Ridgeway JL, Odell L, May CR, et al. Building a measurement framework of burden of treatment in complex patients with chronic conditions: a qualitative study. Patient related outcome measures. 2012;3:39.
9. Gonzalez-Gonzalez AI, Brünn R, Nothacker J, Dinh TS, Brueckle M-S, Dieckelmann M, et al. Everyday lives of middle-aged persons living with multimorbidity: protocol of a mixed-methods systematic review. BMJ open. 2021;11(12):e050990.
10. Rosbach M, Andersen JS. Patient-experienced burden of treatment in patients with multimorbidity–a systematic review of qualitative data. PloS one. 2017;12(6):e0179916.
11. Wong MC, Liu J, Zhou S, Li S, Su X, Wang HH, et al. The association between multimorbidity and poor adherence with cardiovascular medications. International journal of cardiology. 2014;177(2):477-82.
12. Smaje A, Weston-Clark M, Raj R, Orlu M, Davis D, Rawle M. Factors associated with medication adherence in older patients: a systematic review. Aging medicine. 2018;1(3):254-66.
13. Conn VS, Ruppar TM. Medication adherence outcomes of 771 intervention trials: systematic review and meta-analysis. Preventive medicine. 2017;99:269-76.
14. Marcum ZA, Hanlon JT, Murray MD. Improving medication adherence and health outcomes in older adults: an evidence-based review of randomized controlled trials. Drugs & aging. 2017;34(3):191-201.
15. Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock SJ, Wines RC, et al. Interventions to improve adherence to self-administered medications for chronic diseases in the United States: a systematic review. Annals of internal medicine. 2012;157(11):785-95.
16. Yarnall AJ, Sayer AA, Clegg A, Rockwood K, Parker S, Hindle JV. New horizons in multimorbidity in older adults. Age and ageing. 2017;46(6):882-8.
17. Williams A, Manias E, Walker R. Interventions to improve medication adherence in people with multiple chronic conditions: a systematic review. Journal of advanced nursing. 2008;63(2):132-43.
18. Reed RL, Roeger L, Howard S, Oliver-Baxter JM, Battersby MW, Bond M, et al. A self-management support program for older Australians with multiple chronic conditions: a randomised controlled trial. Medical Journal of Australia. 2018;208(2):69-74.
19. Barley EA, Walters P, Haddad M, Phillips R, Achilla E, McCrone P, et al. The UPBEAT nurse-delivered personalized care intervention for people with coronary heart disease who report current chest pain and depression: a randomised controlled pilot study. PloS one. 2014;9(6):e98704.

20. Bogner HR, de Vries HF. Integrating type 2 diabetes mellitus and depression treatment among African Americans. The Diabetes Educator. 2010;36(2):284-92.
21. Boult C, Leff B, Boyd CM, Wolff JL, Marsteller JA, Frick KD, et al. A matched-pair cluster-randomized trial of guided care for high-risk older patients. J Gen Intern Med. 2013;28(5):612-21.
22. Smith SM, Wallace E, O'Dowd T, Fortin M. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. Cochrane Database of Systematic Reviews. 2016(3).
23. Wilhelmsen NC, Eriksson T. Medication adherence interventions and outcomes: an overview of systematic reviews. European Journal of Hospital Pharmacy. 2019;26(4):187-92.
24. Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jeric K, et al. Declaración SPIRIT 2013: definición de los elementos estándares del protocolo de un ensayo clínico. Rev Panam Salud Publica. 2015;38(6):507.
25. Turner L, Shamseer L, Altman DG, Schulz KF, Moher D. Does use of the CONSORT Statement impact the completeness of reporting of randomised controlled trials published in medical journals? A Cochrane reviewa. Systematic reviews. 2012;1(1):1-7.
26. Corbett G, Trainer RMC, Valley PLNM. Motivational interviewing. 2012.
27. Fisher JD, Fisher WA. Changing AIDS-risk behavior. Psychological bulletin. 1992;111(3):455.
28. Fortin M, Stewart M, Poitras M-E, Almirall J, Maddocks H. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. The Annals of Family Medicine. 2012;10(2):142-51.
29. Tan X, Patel I, Chang J. Review of the four item Morisky medication adherence scale (MMAS-4) and eight item Morisky medication adherence scale (MMAS-8). INNOVATIONS in pharmacy. 2014;5(3):5.
30. Faul F, Erdfelder E, Lang A-G, Buchner A. G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior research methods. 2007;39(2):175-91.
31. Krska J, Cromarty JA, Arris F, Jamieson D, Hansford D, Duffus PR, et al. Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. Age and ageing. 2001;30(3):205-11.
32. Miller WR, Rollnick S. Motivational interviewing: Helping people change: Guilford press; 2012.
33. Renier CM, Morse J. Development and validation of a survey to assess patient-perceived medication knowledge and confidence in medication use. Journal of Nursing Measurement. 2014;22(1):120.
34. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. Psychology and health. 1999;14(1):1-24.
35. Risser J, Jacobson TA, Kripalani S. Development and psychometric evaluation of the Self-efficacy for Appropriate Medication Use Scale (SEAMS) in low-literacy patients with chronic disease. Journal of nursing measurement. 2007;15(3):203-19.
36. Duncan P, Murphy M, Man M-S, Chaplin K, Gaunt D, Salisbury C. Development and validation of the Multimorbidity Treatment Burden Questionnaire (MTBQ). BMJ Open. 2020;8(4):e019413. doi: 10.1136/bmjopen-2017-019413.
37. Moyers T, Manuel J, Ernst D, Moyers T, Manuel J, Ernst D, et al. Motivational interviewing treatment integrity coding manual 4.1 (MITI 4.1). Unpublished manual. 2014.
38. Keogh-Brown M, Bachmann M, Shepstone L, Hewitt C, Howe A, Ramsay CR, et al. Contamination in trials of educational interventions. 2007.

14. Appendices

List in this section all intended forms or resources that will be used in the conduct of research to collect data, interview people, recruit participants.

1. Screening & randomization questionnaire
2. Medication adherence using Morisky scale
3. BMQ questionnaire
4. The Self-Efficacy for Appropriate Medication Use Scale (SEAMS)