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COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS): a protocol of pragmatic trials within a cohort

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ABSTRACT

Introduction: Due to the rapidly ageing population, there is an increased demand for services for hospitalised older patients with acute medical conditions. The COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS) study will evaluate the effectiveness of comprehensive geriatric assessment (CGA) and multidisciplinary intervention by comparing with conventional care among acute hospitalised older adults in Korea.

Methods and analysis: Multicentre trials within a cohort comprising 3 sub-studies (randomised controlled trials) will be conducted. The intervention includes CGA and CGA-based multidisciplinary interventions by physicians (geriatrician, oncologist), nurses, nutritionists, and pharmacists. The multidisciplinary intervention includes nutritional support, medication review and adjustment, rehabilitation, early discharge planning, and prevention of geriatric syndromes (falls, delirium, pressure sore, and urinary retention). The primary outcome is living at home 3 months after discharge. The analysis will be carried out based on an intention-to-treat principle. In addition to assessing the economic effects of the intervention, a cost-utility analysis will be conducted.

Ethics and dissemination: The study protocol was reviewed and approved by the ethics committees of Seoul National University Bundang Hospital and each study site. The study findings will be published in peer-reviewed journals. Subgroup and further in-depth analyses will subsequently be published.

Trial Registration Details: This study has been registered at https://cris.nih.go.kr/ (trial registration number: KCT0006270)

Strengths and limitations of this study

- The multicentre trials within the cohort study will evaluate the clinical effectiveness and health outcomes of comprehensive geriatric assessment (CGA) and CGA-based multidisciplinary team intervention for acute hospitalised older patients in various clinical settings.
- The study will compare the CGA and CGA-based multidisciplinary interventions, including nutritional support, medication adjustment, rehabilitation, discharge care plan, geriatric syndrome prevention (falls, delirium, pressure sore, and urinary incontinence), with the conventional care.
- This pragmatic study will compare multicomponent intervention by interdisciplinary team with usual care in various clinical setting; thus the result of this study will confirm the clinical effectiveness of CGA-based multidisciplinary intervention in real-world clinical practice conditions.
- This study will be conducted in Korea, and the findings may not be generalisable to other countries due to the difference of healthcare system.

INTRODUCTION

Comprehensive geriatric assessment (CGA) is a multidimensional, interdisciplinary assessment for evaluating the medical, psychological, and physical functions as well as the social status of older patients. It aims to detect unidentified and potentially reversible problems and develop a coordinated and integrated management plan for treatment and long-term follow-up care.[1] Previous studies have suggested that CGA-based multidisciplinary care is superior to the conventional care in reducing the risk of mortality or institutionalisation and improving functional capacity.[2, 3] However, there was a difference in effect between wards and teams, and no randomised controlled trial has been completed in an acute care setting in Korea.

Geriatric medical professionals and multidisciplinary teams for older inpatient management are rare in Korea (with less than 10 academic hospitals), and detailed protocols varies between institutions. Furthermore, a hospitalist system was introduced in 2016 to improve the quality of in-patient care in Korea.[4] Although CGA-based multidimensional intervention is the accepted gold standard in care for older hospitalised patients with frailty, CGA-based intervention needed to be verified in Korea due to differences in insurance and healthcare systems. Because the shortage of geriatric consultants or practitioners caring for hospitalised older patients is also one of the biggest problems in other countries, it is necessary to validate in the setting where the geriatrician exists and it does not.[5]

Randomised controlled trials (RCTs) are considered the gold standard for generating high-quality evidence for the efficacy of an intervention. However, RCT design is sometimes criticised due to its limited external validity, resulting from difficulties and restricted environments in patient recruitment. Consequently, pragmatic trials, aiming to guide decision-making in clinical practice, were proposed.[6] As an implementation of the concepts of both pragmatic trials and RCT, trials within cohorts (TwiCs) enable researchers to conduct several

randomised trials using conventional care comparators within a cohort.[6]

The COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS) was set up according to the TwiCs design. The COMPASS aims to compare the clinical efficacies of the CGA-based multidisciplinary team intervention and the conventional care for pre-frail or frail older patients hospitalized in acute care setting. The COMPASS study comprises 3 nested sub-studies, COMPASS-ER, COMPASS-IN, and COMPASS-ONCO. COMPASS-ER compares the effect of a proactive multidisciplinary team intervention model based on the CGA with that of conventional treatment for patients admitted through the emergency department. COMPASS-IN compares the geriatrician-led care (multidisciplinary team intervention model based on the CGA) and hospitalist-led care (conventional treatment) for hospitalised older patients. COMPASS-ONCO compares the effect of an oncologist-led multidisciplinary team intervention based on the CGA with that of conventional treatment for older cancer patients without the involvement of geriatricians.

We hypothesised that the CGA-based multidisciplinary team intervention increases the likelihood that patients will be living at home at 3 months after discharge (primary outcome). Reduction in the total number of medications or inappropriate medications, length of hospital stay, re-admission, all-cause mortality, quality of life, length of days living at home, incidence of geriatric syndrome during hospitalisation, emergency department visits, functional status, cost-utility analysis, and other indicators will be assessed as secondary outcomes.

METHODS AND ANALYSIS

Trial Design

The COMPASS study will adopt the TwiCs design with 3 RCT sub-studies. Each sub-study will recruit patients from a cluster of institutions (COMPASS-ER: 2 hospitals, COMPASS-IN: 2 hospitals, COMPASS-ONCO: 5 hospitals). The patients recruited from the clusters will be randomised into the intervention or control groups in a 1:1 ratio. Randomisation will be performed through a web-based system according to the pre-embedded, computer-generated, permuted blocks with stratification. Allocation concealment will be secured by preventing researchers from assigning groups using the central system. The recruitment of participants started on 2 November 2021. This study will follow the Consolidation Standards of Reporting Trials (CONSORT) **(Figure 1)**.[7]

Participants and Setting

The study participants are hospitalised older patients with acute medical problems. The inclusion criteria are as follows: (1) 65 years of age or older, (2) pre-frail or frail status assessed by Korean version of the Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight scale (K-FRAIL) questionnaire, [8] (3) having 2 or more of the following diseases (hypertension, diabetes, ischemic heart disease, chronic lung disease, arthritis, stroke, depression, chronic kidney disease, and dementia), (4) living at home for more than 3 months before hospitalisation, (5) (for COMPASS-ONCO only) subject to conventional, primary chemotherapy because local treatment for curative purposes (such as surgery, concurrent chemo-radiotherapy, and radiation therapy) is ineligible (stage 3 or higher), and (6) (for COMPASS-ONCO only) histologically confirmed cancer (gastric adenocarcinoma, colorectal adenocarcinoma, non-small cell and small cell lung cancer, pancreatic adenocarcinoma, or biliary adenocarcinoma).

The exclusion criteria are as follows: (1) planned hospitalisation in the specialised care unit, such as an intensive care unit and/or acute stroke ward, at the time of admission, (2) terminal

status requiring hospice or palliative care, (3) life expectancy of 6 months or less, (4) other serious health conditions that limit the participation in the research, (5) (for COMPASS-ONCO only) oral targeted therapy as a palliative first-line chemotherapy, and (6) (for COMPASS-ONCO only) recurrence within 6 months after adjuvant chemotherapy.

Informed consent will be obtained from the patients. At the request of the sponsor, consent for third party provision of research data and use of secondary ancillary research will be additionally obtained.

Interventions

The intervention comprises the CGA and CGA-based multidisciplinary interventions. A description of the adapted CGA and multicomponent intervention is shown in **Table 1.**

Table 1. Overview of Comprehensive Geriatric Assessment and Multidisciplinary Team Intervention

Domain	Assessment Tool and Risk Criteria	Assessor/ Provider	Intervention
Nutrition	MNA ≤23 MNA-SF ≤11	Nutritionist APN RN	Dietary change and education (Patient / Caregiver) Oral nutritional supplements Protein/amino acid replacement Dysphagia assessment and rehabilitation if needed Tube feeding Dental care
Medication	Potentially inappropriate medication list, Polypharmacy (≥10)	Pharmacist APN RN Physician	Education (Institution / Patient / Caregiver) Medication reconciliation De-prescription
Rehabilitation	TUGT ≥10 seconds Grip strength (<28 kg in male <18 kg in female) ADL/IADL dependency	APN RN Physician	Early ambulation/rehabilitation Transfer to rehabilitation medicine
Discharge care plan		APN RN	Identify decision-makers among family members and preferred discharge location

		Physician	Check financial and social situation Discharge care planning and consultation Consult with hospital transfer centre or home health nursing centre
Geriatric syndrome (Falls, Delirium, Sore, Urinary incontinency)	(Falls) Hendrich II fall risk model ≥5 or John's Hopkins fall risk assessment tool ≥14, history of falls, TUGT ≥10 (Delirium) history of delirium, K-MMSE 2 ≤26, age ≥80 (Sore) Braden scale ≤18 (Urinary Incontinence) indwelling urinary catheter	Nutritionist Pharmacist APN RN Physician	(Falls) Fall prevention education handouts for patient and caregiver Early ambulation/exercise Consultation to rehabilitation medicine (Delirium) Non-pharmacological delirium prevention (medical optimisation, pain control, sleep hygiene) De-prescribing for medications that potentially cause delirium (Sore) Nutritional support Frequent positioning and application of pressure relief aids Consultation to Pressure sore management team or plastic surgery (Urinary retention) Identification of urinary retention (infection) Residual urine volume check after catheter removal Education for clean intermittent catheterisation Medication treatment if needed.

Notes: ADL = Activities of Daily Living; APN = advanced practice nurse; IADL = Instrumental Activities of Daily Living; MMSE = Mini-Mental State Examination; MNA = Mini Nutritional Assessment; MNA-SF = Mini Nutritional Assessment Short Form; RN = registered nurse; TUGT = timed up-and-go test.

Comprehensive Geriatric Assessment (CGA)

The CGA includes the collection of information on sociodemographic characteristics, functional status (Activities of Daily Living [ADL] [9] and Instrumental Activities of Daily Living [IADL] [10]), comorbidities (the Charlson Comorbidity Index [11]), history of falls, delirium and pressure sores, a medication review, grip strength, Timed Up and Go test (TUGT), nutritional status (Mini Nutritional Assessment [MNA] or MNA short form [MNA-SF]),[12] cognitive function (Korean-Mini Mental State Examination 2 [K-MMSE 2]),[13] and mood (Korean Version of Short Form Geriatric Depression Scale [SGDS-K]).[14] The CGA will be

administered by geriatric advanced practice nurses (APN) or registered nurses (RN) at baseline. The CGA, in our experience, takes approximately 45–60 minutes based on the cooperation of the older patients.

CGA-Based Multidisciplinary Intervention

The standardised geriatric management protocol will be delivered based on the CGA results; the predefined evidence-based intervention is described in **Table 1**. The multidisciplinary intervention team will comprise a geriatrician, nurse, case manager, pharmacist, and nutritionist. If it is difficult to assemble a multidisciplinary team with all the members, physicians will request consultations to a healthcare professional. For the COMPASS-ONCO sub-study, the oncologist will be the principal investigator instead of a geriatrician.

For the participant randomized to the intervention group, RN or APN will monitor whether the individualised intervention plan based on the CGA results is properly applied. The recommended intervention strategy will be communicated to the multidisciplinary team. The intervention team will implement all recommendations as much as possible to facilitate adherence.

Comparison

Patients in the control group will receive the conventional care provided by the study hospital. Since a structured CGA will not be implemented, consultations will be allowed without any restriction if physicians in charge determine that there is a specific problem.

Outcome Measures

This study aims to assess the clinical effectiveness and cost-effectiveness of the CGA-based multidisciplinary intervention. The primary outcome is living at home at 3 months after discharge. The secondary outcomes are living at home at 6 months after discharge, reduction in the total number of medications or inappropriate medications at discharge, reduction in the length of hospital stay, unplanned re-admission, all-cause mortality, quality of life, length of days living at home, the incidence of geriatric syndromes during hospitalisation, emergency department visits, functional status at 3 months after discharge, and cost-utility.

In addition to the outcomes measured in the entire COMPASS study, additional outcomes will be measured in the sub-studies: In the COMPASS-IN study, the readiness for hospital discharge [15], family interaction [16], a therapeutic alliance between patient and provider [17], and empowerment [18] will be investigated, and frailty status will be followed-up at 3 and 6 months [8]; In the COMPASS-ONCO study, overall treatment utility, recognition of advance directives, changes in body composition, and validity of anticancer drug toxicity prediction model will also be assessed. [19] Overall treatment utility is a clinical outcome measure incorporating objective and subjective measures of anticancer efficacy, tolerability and acceptability. [20]

A cost-utility analysis will be conducted. For cost analysis, direct medical costs and programme operating costs will be assessed. Direct medical costs will be evaluated based on the difference in the health care expenses between the intervention and control groups. Based on the fee for service reimbursement system, the medical cost can be calculated by adding the costs of all medical treatments, examinations, and other input resources from hospitals. The program's cost will be determined using the medical claim data of the participating hospitals. The duration of participation of the health care professionals in the intervention team will be assessed by medical staff by asking for the additional time used for the intervention. The wages

of the health care professionals and the duration of participation in the intervention team will be used to determine the minute-wise cost of the program. The index of clinical effectiveness will be used as the reference in the cost-utility analysis, such as EQ-5D and the activities of daily living (ADL) The results will be analysed as incremental cost-utility ratios (**Table 2**).

Table 2. Outcome variables

Domain	Variable	Source (target population)	Outcome Type	Timeline			
				t_1	t_2	t_3	t_4
Clinical effectiveness							
Living at home		Survey & EMR	Primary & Secondary			X	X
Inappropriate medications		Survey &EMR	Secondary	X	X		
Total number of medications		Survey &EMR	Secondary	X	X		
Length of hospital stay		Survey &EMR	Secondary		X		
Health care utilisation (re-admission and visit to emergency department)		Survey &EMR	Secondary			X	X
Mortality		Survey &EMR	Secondary				X
Quality of Life		Survey using EQ-5D	Secondary	X		X	
Length of days living at home		EMR	Secondary				X
Geriatric syndrome during hospitalisation		Survey &EMR	Secondary		X		
Activities of daily living		Survey &EMR	Secondary	X		X	
Readiness for hospital discharge (Only in COMPASS-IN)		Survey	Secondary		X		
Family interaction (Only in COMPASS-IN)		Survey	Secondary		X		
Therapeutic alliance (Only in COMPASS-IN)		Survey	Secondary		X		
Empowerment (Only in COMPASS-IN)		Survey	Secondary		X	X	
Frailty (Only in COMPASS-IN)		Survey & EMR	Secondary			X	X
Overall treatment utility (Only in COMPASS-ON)		Survey &EMR	Secondary			X	
Recognition of advance directive (Only in COMPASS-ON)		Survey	Secondary		X		
Changes in body composition (Only in COMPASS-ON)		Survey & EMR	Secondary	X		X	X
Economic effectiveness							
Economic evaluation		Survey using EQ-5D, ADL	Secondary	X		X	

t_1: Before intervention measurement (baseline); t_2: After intervention measurement (at discharge); t_3: Follow-up measurement (3 months after discharge); t_4: Follow-up measurement (6 months after discharge); EMR: Electronic medical record; ADL: Activities of Daily Living

Data Collection and Management

Research assessors who are registered in this study will collect data according to the standardised protocol. For the assessors, a 4-hour educational program consisting of study

overview, measurement tools, and practice sessions with scenarios will be provided before data collection. All patients in the intervention and control groups will be evaluated with baseline tests before the intervention or observation (T1). At discharge, the second assessment (T2) will be conducted. After discharge, follow-up assessments will be conducted 3 months ± 4 weeks (T3) and 6 months ± 4 weeks (T4) after discharge. A summary of the main measures at the patient level and the corresponding timetable is shown in **Table 3.**

Table 3. Schedule of enrolment, interventions, and assessments

	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
TIMEPOINT	$-t_2$	$-t_1$	t_1	t_2	t_3	t_4
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
CGA based multicomponent intervention			←	→		
ASSESSMENTS:						
[Clinical effectiveness] Primary outcomes					X^a	
[Clinical effectiveness] Secondary outcomes	X^{b-1}		X^{b-2}	X^{b-3}	X^{b-4}	X^a, X^{b-5}
[Economic evaluation]				X^c	X^c	

t1: Baseline (Before intervention measurement); t2: Discharge (After intervention measurement); t3: Follow-up measurement (3 months after discharge); t4: Follow-up measurement (6 months after discharge); Xa: Living at home; X^{b-1}: frailty, X^{b-2}: Quality of life, recognition of advance directive and changes in sarcopenic obesity,

activity of daily living; X^{b-3}; Medication management, length of hospital stay, geriatric syndrome during hospitalisation, readiness for hospital discharge, family interaction, therapeutic alliance, empowerment; X^{b-4}, Quality of life, activity of daily living, overall treatment utility, recognition of advance directive and changes in sarcopenic obesity, health care utilisation, empowerment, frailty; X^{b-5}; overall treatment utility, recognition of advance directive and changes in sarcopenic obesity, health care utilisation, frailty; X^{c}: cost-effectiveness analysis

Data will be recorded in hardcopy at the time of the measurement and will subsequently be entered electronically in iCReaT (http://icreat.nih.go.kr), a web-based clinical research management system developed by Korea National Institute of Health. Automatic checks will be applied when entering the data based on predetermined ranges. Missing data will also be automatically detected, and data query reports will be sent to the local data manager. If any errors are found in the data, the data managers will ask the assessors for correction or clarification. Furthermore, to promote follow-up and retention, assessors will report any issues with the patients. If there is a discontinuation of research participation, a brief short-form report will be generated and submitted. All patients will be assigned a unique research ID, and the research team will train the assessors to secure the research data to maintain its safety. The data collection forms will not contain any identifiable personal information. An electronic password-protected file will be saved on a password-protected computer. The final data set will be retrieved by the iCReaT.

The data monitoring committee (DMC) comprises investigators who are independent of the clinical investigation team and includes a team member who manages the data quality. This committee will meet once when 50% of the planned recruitment has occurred. The datasets that will be generated and/or analysed during the current study are not publicly available but are available from the sponsor on reasonable request.

The data centre of the Korean Cancer Study Group, which is independent of the investigators and the sponsor, will design an electronic case report form (CRF) based on the paper CRF, invented by the clinical investigator and conduct data monitoring through site initiation, routine

monitoring visits, and site close-out visits. If any serious adverse event happens, it will be reviewed by the principal investigator and reported to the Seoul National University Bundang Hospital (SNUBH) Institutional Review Board (IRB). A serious adverse event refers to an intensive care unit admission, death, or other consequences of permanent or significant disability or impairment.

Patient and public involvement

There was no patient or public involvement in the design and conduct of this study.

Sample Size

The sample size is calculated as follows: statistical power is calculated based on the primary clinical outcome, which is being alive and residing at home 3 months after discharge. We assume the clinical effectiveness of the CGA-based multidisciplinary intervention based on the results of a previous study. [21] A total sample of 882 participants will be required. Anticipating a 15% dropout rate, approximately 1,040 patients will be required for this study. The test statistic used is the two-sided Fisher's exact test, with an alpha of 0.05, a probability of 0.01 for beta error (90% power). The power analysis and sample size calculations are performed using PASS 14.0 (NCSS LLC, Kaysville, UT).

Randomisation

This study uses an un-blinded stratified cluster randomised design. The unit of randomisation is the patient. We will conduct systematic randomisation using a random table generated by

one of the researchers who is not involved in collecting the data from participants. The random table is embedded in the iCReaT (http://icreat.nih.go.kr). Random tables have been generated for (1) sub-studies 1 and 2 and (2) sub-study 3. Randomisation will be stratified with (1) sub-study (in sub-studies 1 and 2), (2) institutions, and (3) cancer type (in sub-study 3). Patients will be allocated into the intervention and control groups with a 1:1 ratio. The final dataset is coded for blinding for randomisation, and the analysis will be done with blinded until the end of the effectiveness evaluation.

Statistical Analysis

Both descriptive and analytic statistics will be used. The baseline patient characteristics will be summarised for each group using descriptive statistics. Baseline differences will be evaluated using the independent t-test for continuous variables, and the Pearson chi-square test or Fisher's exact test will be used for dichotomous or categorical variables. Two-sided p-values of <0.05 will be considered statistically significant. Any potential confounding factors of the groups will be considered for inclusion in the multivariable analysis. The main analysis is conducted based on an intention-to-treat principle. For the secondary analysis, we will include the potential confounding pre-randomisation variables as confounders in the regression model to derive the confounder-adjusted intervention effect. To account for the clustered data structure, we will apply a multilevel regression analysis and use a generalised linear mixed-effects model, including fixed factors (time, intervention) and random factors. Two random effects will be included, one at the institutional (cluster) and the other at the patient (individual) level. For each of the aforementioned analyses, to adjust for missing data, we will implement imputation or conduct sensitivity analysis. Sensitivity analyses will also be conducted on the effect of attrition and the inclusion of patients and subgroup analyses to examine the difference

in sub-study or institution.

ETHICS AND DISSEMINATION

This study is registered with the Clinical Research Information Service Registry (trial registration number: KCT0006270). The study is sponsored by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI19C0481, HC20C0086) and centrally managed by staff at SNUBH. The sponsors had no role in the design, methods, participant recruitment, data collection and analysis, or preparation of the article. The protocol was first reviewed and approved by the SNUBH IRB on 26 April 2021. Further protocol revision was followed by final approval on 30 November 2021 for the informed consent form, correction of typographical errors, addition of assessment items and clarification of inclusion criteria (IRB No. B-2104/676-001). The current protocol version is version 1.4. The corresponding author and the researchers of this study will have access to the data set. Further dissemination of the data set can be decided by the corresponding author.

The CGA-based multicomponent intervention may not have positive effects, but the risk of negative effect on patient outcomes is limited. All participants and their guardians (only if the participants lose their ability to make decisions) will sign an informed consent form. After the trial, the data will be analysed, and the study findings will be published in major peer-reviewed journals.

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Author Contributions

JYC, KIK, JYL, IGH, and YGL drafted the manuscript.

JYC, JYL, JYS, COK, KJK, IGH, YGL, SJK, SJY, MGK, JWK, JYK and KIK contributed to the study design, data collection, and critical revision of the manuscript.

JYC, KIK, JYL, IGH, COK, KJK, JYK, SJY and MGK contributed to the study design and critical revision of the manuscript. KIK and JYC contributed to the study concept, study design, data collection, and drafting of the manuscript.

All authors reviewed and approved the manuscript and agree to be accountable for all aspects of the work.

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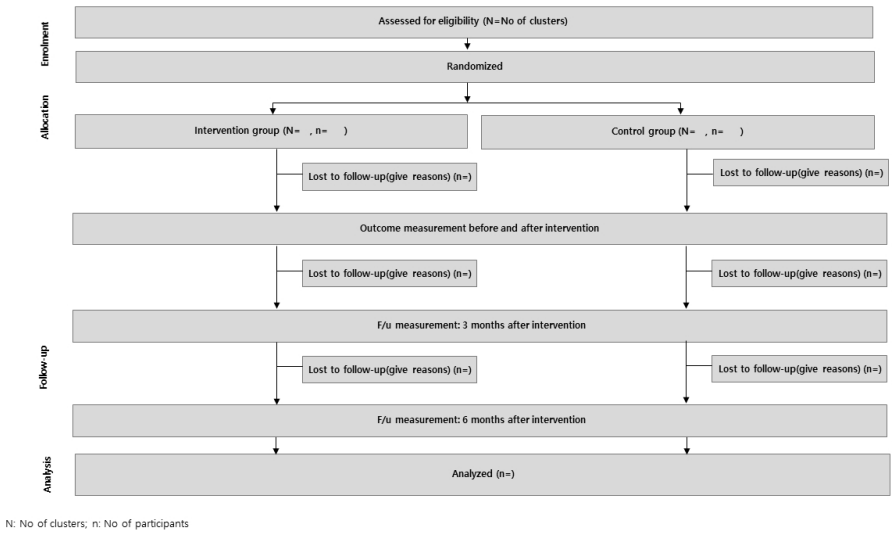

Flow diagram of cluster trial. N, number of clusters; n, number of older patients

338x190mm (96 x 96 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	#3	Date and version identifier	17
Funding	#4	Sources and types of financial, material, and other support	21
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	21
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	21

Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	21
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	14
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	6
Objectives	#7	Specific objectives or hypotheses	6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5-6

Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	NA
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	10

Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	10-12
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	13
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	15
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7-8
Methods: Assignment of interventions (for controlled trials)			

Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7, 15
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7, 15
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	15
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	15
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			

Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	12-15
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11-15
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11-14
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	16
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	16
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	16

Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	14
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	14
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	17
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	14-15
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	17
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to	17

		relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	17
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	17
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	14
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	21
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	16
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in	17

		results databases, or other data sharing arrangements), including any publication restrictions	
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	NA
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Y
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

BMJ Open

COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS): a protocol of pragmatic trials within a cohort

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COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS): a protocol of pragmatic trials within a cohort

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Keywords: Geriatric assessment, Frailty, Multidisciplinary health team, Pragmatic clinical trial

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ABSTRACT

Introduction: There is an increased demand for services for hospitalised older patients with acute medical conditions due to rapidly ageing population. The COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS) study will test the effectiveness of comprehensive geriatric assessment (CGA) and multidisciplinary intervention by comparing it with conventional care among acute hospitalised older adults in Korea.

Methods and analysis: A multicentre trial within a cohort comprising 3 sub-studies (randomised controlled trials) will be conducted. The intervention includes CGA and CGA-based multidisciplinary interventions by physicians (geriatricians, oncologists), nurses, nutritionists, and pharmacists. The multidisciplinary intervention includes nutritional support, medication review and adjustment, rehabilitation, early discharge planning, and prevention of geriatric syndromes (falls, delirium, pressure sore, and urinary retention). The analysis will be based on an intention-to-treat (ITT) principle. The primary outcome is living at home 3 months after discharge. In addition to assessing the economic effects of the intervention, a cost-utility analysis will be conducted.

Ethics and dissemination: The study protocol was reviewed and approved by the ethics committees of Seoul National University Bundang Hospital and each study site. The study findings will be published in peer-reviewed journals. Subgroup and further in-depth analyses will subsequently be published.

Trial Registration Details: This study has been registered at https://cris.nih.go.kr/ (trial registration number: KCT0006270)

Strengths and limitations of this study

- The multicentre trials within the cohort study will evaluate the clinical effectiveness and health outcomes of comprehensive geriatric assessment (CGA) and CGA-based multidisciplinary team intervention for acute hospitalised older patients in various clinical settings.
- The study will compare the CGA and CGA-based multidisciplinary interventions, including nutritional support, medication adjustment, rehabilitation, discharge care plan, geriatric syndrome prevention (falls, delirium, pressure sore, and urinary incontinence), with conventional care.
- This pragmatic study will compare multicomponent intervention by an interdisciplinary team with usual care in various clinical settings; thus, this study's result will confirm the clinical effectiveness of CGA-based multidisciplinary intervention in real-world clinical practice conditions.
- This study will be conducted in Korea, and the findings may not be generalisable to other countries due to the different healthcare systems.

INTRODUCTION

Comprehensive geriatric assessment (CGA) is a multidimensional, interdisciplinary assessment for evaluating older patients' medical, psychological, physical functions and social status. It aims to detect unidentified and potentially reversible problems and develop a coordinated and integrated management plan for treatment and long-term follow-up care.[1] Previous studies have suggested that CGA-based multidisciplinary care is superior to conventional care in reducing the risk of mortality or institutionalisation and improving functional capacity.[2, 3] However, there was a difference in the effect between wards and teams, and no randomised controlled trial has been completed in an acute care setting in Korea.

Geriatric medical professionals and multidisciplinary teams for older inpatient management are rare in Korea (with less than 10 academic hospitals), and detailed protocols vary between institutions. Furthermore, a hospitalist system was introduced in 2016 to improve the quality of in-patient care in Korea.[4] Although CGA-based multidimensional intervention is the accepted gold standard in care for older hospitalised patients with frailty, CGA-based intervention needs to be verified in Korea due to differences in insurance and healthcare systems. The shortage of geriatric consultants or practitioners caring for hospitalised older patients is also one of the biggest problems in other countries. Therefore, it is necessary to validate the effect of CGA-based multidimensional intervention in the setting with or without geriatricians.[5]

Randomised controlled trials (RCTs) are considered the gold standard for generating high-quality evidence for the efficacy of an intervention. However, RCT design is sometimes criticised due to its limited external validity, resulting from difficulties and restricted environments in patient recruitment. Consequently, pragmatic trials, aiming to guide decision-

making in clinical practice, were proposed.[6] As an implementation of both pragmatic trials and RCT concepts, trials within cohorts (TwiCs) enable researchers to conduct several randomised trials using conventional care comparators within a cohort.[6]

The COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS) was set up according to the TwiCs design. COMPASS aims to compare the clinical efficacies of CGA-based multidisciplinary team intervention and conventional care for pre-frail or frail older patients hospitalized in an acute care setting. COMPASS study targeted multiple domains; medical optimization for multi-morbidity, early mobilisation or physical rehabilitation to reduce functional decline, prevention of geriatric syndromes, medication management, nutritional intervention and discharge planning to prevent readmission.

We hypothesised that the CGA-based multidisciplinary team intervention increases the likelihood that patients will be living at home 3 months after discharge (primary outcome). Reduction in the total number of medications or inappropriate medications, length of hospital stay, re-admission, all-cause mortality, quality of life, length of days living at home, geriatric syndrome incidence during hospitalisation, emergency department visits, functional status, cost-utility analysis, and other indicators will be assessed as secondary outcomes.

METHODS AND ANALYSIS

Trial design

The COMPASS study will adopt the TwiCs design with 3 RCT sub-studies. Each sub-study will recruit patients from institutions (COMPASS-ER: 2 hospitals, COMPASS-IN: 2 hospitals,

COMPASS-ONCO: 5 hospitals). COMPASS-ER compares the effect of a proactive multidisciplinary team intervention model based on the CGA to that of conventional treatment for patients admitted through the emergency department. COMPASS-IN compares the geriatrician-led care (multidisciplinary team intervention model based on the CGA) to the hospitalist-led care (conventional treatment) for hospitalised older patients. COMPASS-ONCO compares the effect of an oncologist-led multidisciplinary team intervention based on the CGA to that of conventional treatment for older cancer patients without the involvement of geriatricians. The patients will be randomised into the intervention or control groups in a 1:1 ratio. Randomisation will be performed through a web-based system according to the pre-embedded, computer-generated, permuted blocks with stratification. Allocation concealment will be secured by preventing researchers from assigning groups using the central system. The recruitment of participants started on 2 November 2021. This study will follow the Consolidation Standards of Reporting Trials (CONSORT) **(Figure 1)**.[7]

Participants and Setting

The study participants are hospitalised older patients with acute medical problems. The inclusion criteria are as follows: (1) 65 years of age or older, (2) pre-frail or frail status assessed by Korean version of the Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight scale (K-FRAIL) questionnaire,[8] (3) having two or more of the following diseases; hypertension, diabetes, ischemic heart disease, chronic lung disease, arthritis, stroke, depression, chronic kidney disease, and dementia, (4) living at home for more than 3 months before hospitalisation, (5) (for COMPASS-ONCO only) subject to conventional primary chemotherapy because local treatment for curative purposes (such as surgery, concurrent chemo-radiotherapy, and radiation

therapy) is ineligible (stage 3 or higher), and (6) (for COMPASS-ONCO only) histologically confirmed cancer (gastric adenocarcinoma, colorectal adenocarcinoma, non-small cell and small cell lung cancer, pancreatic adenocarcinoma, or biliary adenocarcinoma).

The exclusion criteria are as follows: (1) planned hospitalisation in the specialised care unit, such as an intensive care unit and/or acute stroke ward, at the time of admission, (2) terminal status requiring hospice or palliative care, (3) life expectancy of 6 months or less, (4) other severe conditions that limit the participation in the research, (5) (for COMPASS-ONCO only) oral targeted therapy as a palliative first-line chemotherapy, and (6) (for COMPASS-ONCO only) recurrence within 6 months after adjuvant chemotherapy.

Informed consent will be obtained from the patients. At the sponsor's request, consent for third party provision of research data and use of secondary ancillary research will be additionally obtained. Participants were recruited from 2 November 2021, and recruitment will continue until December 2024.

Interventions

The intervention comprises the CGA and CGA-based multidisciplinary interventions. A description of the adapted CGA and multicomponent intervention is shown in **Table 1.**

Table 1. Overview of Comprehensive Geriatric Assessment and Multidisciplinary Team Intervention

Domain	Assessment Tool and Risk Criteria	Assessor/ Provider	Intervention
Nutrition	MNA ≤23 MNA-SF ≤11	Nutritionist APN RN	Dietary change and education (Patient / Caregiver) Oral nutritional supplements Protein/amino acid replacement

			Dysphagia assessment and rehabilitation if needed Tube feeding Dental care
Medication	Potentially inappropriate medication list, Polypharmacy (≥10)	Pharmacist APN RN Physician	Education (Institution / Patient / Caregiver) Medication reconciliation De-prescription
Rehabilitation	TUGT ≥10 seconds Grip strength (<28 kg in male <18 kg in female) ADL/IADL dependency	APN RN Physician	Early ambulation/rehabilitation Transfer to rehabilitation medicine
Discharge care plan		APN RN Physician	Identify decision-makers among family members and preferred discharge location Check financial and social situation Discharge care planning and consultation Consult with hospital transfer centre or home health nursing centre
Geriatric syndrome (Falls, Delirium, Sore, Urinary incontinency)	(Falls) Hendrich II fall risk model ≥5, John's Hopkins fall risk assessment tool ≥14, history of falls, TUGT ≥10 (Delirium) history of delirium, K-MMSE 2 ≤26, age ≥80 (Sore) Braden scale ≤18 (Urinary Incontinence) indwelling urinary catheter	Nutritionist Pharmacist APN RN Physician	(Falls) Fall prevention education handouts for patient and caregiver Early ambulation/exercise Consultation to rehabilitation medicine (Delirium) Non-pharmacological delirium prevention (medical optimisation, pain control, sleep hygiene) De-prescribing for medications that potentially cause delirium (Sore) Nutritional support Frequent positioning and application of pressure relief aids Consultation to Pressure sore management team or plastic surgery (Urinary retention) Identification of urinary retention (infection) Residual urine volume check after catheter removal Education for clean intermittent catheterisation Medication treatment if needed.

Notes: APN = advanced practice nurse; MMSE = Mini-Mental State Examination; MNA = Mini Nutritional Assessment; MNA-SF = Mini Nutritional Assessment Short Form; RN = registered nurse; TUGT = timed up-and-go test.

Comprehensive Geriatric Assessment (CGA)

The CGA includes the collection of information on sociodemographic characteristics,

functional status (Activities of Daily Living [ADL] [9] and Instrumental Activities of Daily Living [IADL] [10]), comorbidities (the Charlson Comorbidity Index [11]), history of falls, delirium and pressure sores, a medication review, grip strength, Timed Up and Go test (TUGT), nutritional status (Mini Nutritional Assessment [MNA] or MNA short form [MNA-SF]),[12] cognitive function (Korean-mini mental state examination 2 [K-MMSE 2]),[13] and mood (Korean Version of Short Form Geriatric Depression Scale [SGDS-K])[14] The CGA will be administered by geriatric advanced practice nurses (APN) or registered nurses (RN) at baseline. The CGA, in our experience, takes approximately 45–60 minutes based on the cooperation of the older patients.

CGA-based multidisciplinary intervention

The standardised geriatric management protocol will be delivered based on the CGA results; the predefined evidence-based intervention is described in **Table 1**. The multidisciplinary intervention team will comprise a geriatrician, nurse, case manager, pharmacist, and nutritionist. Physicians will request consultations with a healthcare professional if it is difficult to assemble a multidisciplinary team with all members. For the COMPASS-ONCO sub-study, the oncologist will be the principal investigator instead of a geriatrician.

RN or APN will monitor whether the individualised intervention plan is properly applied based on the CGA results for the participant randomized to the intervention group. The recommended intervention strategy will be communicated to the multidisciplinary team. The intervention team will implement all recommendations as much as possible to facilitate adherence.

Comparison

Patients in the control group will receive conventional care provided by the study hospital. Since a structured CGA will not be implemented, consultations will be allowed without any restriction if physicians in charge determine that there is a specific problem.

Outcome measures

This study aims to assess the clinical effectiveness and cost-effectiveness of the CGA-based multidisciplinary intervention. The primary outcome is living at home 3 months after discharge. Living at home at 3 months is the odds of participants being alive and in their own home 3 months after discharge. The secondary outcomes are living at home 6 months after discharge, the total number of medications reduced or inappropriate medications at discharge, length of hospital stay, unplanned re-admission, all-cause mortality, and quality of life. In addition length of days living at home, the incidence of geriatric syndromes during hospitalisation, emergency department visits after discharge, functional status at 3 months after discharge, and cost-utility.

In addition to the outcomes measured in the entire COMPASS study, additional outcomes will be measured in the sub-studies. In the COMPASS-IN study, the readiness for hospital discharge,[15] family interaction,[16] a therapeutic alliance between patient and provider,[17] and empowerment [18] will be investigated, and frailty status will be followed-up at 3 and 6 months.[8] In the COMPASS-ONCO study, overall treatment utility, recognition of advance directives, changes in body composition, and validity of anticancer drug toxicity prediction model will also be assessed.[19] Overall treatment utility is a clinical outcome incorporating objective and subjective measures of anticancer efficacy, tolerability and acceptability.[20]

A cost-utility analysis will be conducted. For cost analysis, medical costs and programme operating costs will be assessed. From insurer's perspective, the medical cost is primarily defined that official or direct medical cost, including out-of-pocket expenditures, co-payment from insurance. In addition, we also perform sensitivity analysis considering the perspective of limited healthcare system including long-term care costs and nursing expenses based on the indirect data from the nationally representative data, the Korea Health Panel Survey and the Korean Longitudinal Study of Aging.[21,22] Finally, medical costs will be evaluated based on the difference in the health care expenses between the intervention and control groups. Based on the fee for service reimbursement system, the medical cost can be calculated by adding the costs of all medical treatments, examinations, and other input resources microscopically. The program's cost will be determined using the data of the participating institutions. The duration of participation of the health care professionals in the intervention team will be assessed by medical staff by asking for the additional time used for the intervention. The minute-wise cost of the program will be determined by the wages of the health care professionals and the duration of participation in the intervention team. The index of clinical effectiveness will be used as the reference in the cost-utility analysis. The results will be analysed as incremental cost-utility ratios.

We will design model of natural history of discharge outcomes in geriatric patients. Then, we will observe type of complications, its duration of state, and its related quality of life. Also, transition probability to each pathway will be calculated with cost. After developing the analytic model, we will set virtual cohort of the aged 65 with 100,000 populations. It is planned to perform 35 annual cycles, to reach 100 years-old, with half-cycle correction with equal weight. Discount rate will be three percent annually. To consolidate the results, we will

consider different discount rates including 0%, and 5 % as sensitivity analyses. (**Table 2**)

Table 2. Outcome variables

Domain	Variable	Source (target population)	Outcome Type	Timeline			
				t_1	t_2	t_3	t_4
Clinical effectiveness							
Living at home		Survey & EMR	Primary & Secondary			X	X
Inappropriate medications		Survey &EMR	Secondary	X	X		
Total number of medications		Survey &EMR	Secondary	X	X		
Length of hospital stay		Survey &EMR	Secondary		X		
Health care utilisation (re-admission and visit to emergency department)		Survey &EMR	Secondary			X	X
Mortality		Survey &EMR	Secondary				X
Quality of Life		Survey using EQ-5D	Secondary	X		X	
Length of days living at home		EMR	Secondary				X
Geriatric syndrome during hospitalisation		Survey &EMR	Secondary		X		
Activities of daily living		Survey &EMR	Secondary	X		X	
Readiness for hospital discharge (Only in COMPASS-IN)		Survey	Secondary		X		
Family interaction (Only in COMPASS-IN)		Survey	Secondary		X		
Therapeutic alliance (Only in COMPASS-IN)		Survey	Secondary		X		
Empowerment (Only in COMPASS-IN)		Survey	Secondary		X	X	
Frailty (Only in COMPASS-IN)		Survey & EMR	Secondary			X	X
Overall treatment utility (Only in COMPASS-ON)		Survey &EMR	Secondary			X	
Recognition of advance directive (Only in COMPASS-ON)		Survey	Secondary		X		
Changes in body composition (Only in COMPASS-ON)		Survey & EMR	Secondary	X		X	X
Economic effectiveness							
Economic evaluation		Survey using EQ-5D, ADL	Secondary	X		X	

t_1: Before intervention measurement (baseline); t_2: After intervention measurement (at discharge); t_3: Follow-up measurement (3 months after discharge); t_4: Follow-up measurement (6 months after discharge); EMR: Electronic medical record; ADL: Activities of Daily Living

Data collection and management

Research assessors registered in this study will collect data according to the standardised protocol. A 4-hour educational program consisting of the study overview, measurement tools, and practice sessions with scenarios will be provided for the assessors before data collection. All patients in the intervention and control groups will be evaluated with baseline tests before intervention or observation (T1). At discharge, the second assessment (T2) will be conducted. Follow-up assessments will be conducted for 3 months ± 4 weeks (T3) and 6 months ± 4 weeks (T4) after discharge. A research assessor will conduct T1 and T2 measurements at hospital before the participants' discharge. After discharge, T3 and T4 measurements will be conducted by face-to-face personal interview at an outpatient clinic. However, a telephone interview will be used if the participants cannot visit the clinic. A summary of the main measures at the patient level and the corresponding timetable is shown in **Table 3.**

Table 3. Schedule of enrolment, interventions, and assessments

	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
TIMEPOINT	$-t_2$	$-t_1$	t_1	t_2	t_3	t_4
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
CGA based multicomponent intervention			←	→		

ASSESSMENTS:						
[Clinical effectiveness] Primary outcomes					X^{a}	
[Clinical effectiveness] Secondary outcomes	X^{b-1}		X^{b-2}	X^{b-3}	X^{b-4}	X^{a}, X^{b-5}
[Economic evaluation]				X^{c}	X^{c}	

t1: Baseline (Before intervention measurement); t2: Discharge (After intervention measurement); t3: Follow-up measurement (3 months after discharge); t4: Follow-up measurement (6 months after discharge); Xa: Living at home; X^{b-1}: frailty, X^{b-2}: Quality of life, *recognition of advance directive and changes in sarcopenic obesity, activity of daily living; X^{b-3}; Medication management, length of hospital stay, geriatric syndrome during hospitalisation, readiness for hospital discharge, family interaction, connectedness, empowerment; X^{b-4}, Quality of life, activity of daily living, *overall treatment utility, *recognition of advance directive and changes in sarcopenic obesity, health care utilisation, empowerment, frailty; X^{b-5}; *overall treatment utility, *recognition of advance directive and changes in sarcopenic obesity, health care utilisation, frailty; X^{c}: cost-effectiveness analysis

Data will be recorded in hardcopy at the time of the measurement and subsequently entered electronically in iCReaT (http://icreat.nih.go.kr), a web-based clinical research management system developed by the Korea National Institute of Health. Automatic checks will be applied when entering the data based on predetermined ranges. Missing data will also be automatically detected, and data query reports will be sent to the local data manager. The data managers will ask the assessors for correction or clarification if any errors are found in the data. Furthermore, to promote follow-up and retention, assessors will report any issues with the patients. A brief short-form report will be generated and submitted if there is a discontinuation of research participation. All patients will be assigned a unique research ID, and the research team will train the assessors to secure the research data to maintain its safety. The data collection forms will not contain any identifiable personal information. An electronic password-protected file will be saved on a password-protected computer. The final data set will be retrieved by the iCReaT.

The data monitoring committee (DMC) comprises investigators independent of the clinical

investigation team and includes a team member who manages the data quality. This committee will meet once when 50% of the planned recruitment has occurred. The datasets that will be generated and/or analysed during the current study are not publicly available but are available from the sponsor on reasonable request.

The data centre of the Korean Cancer Study Group, which is independent of the investigators and sponsor, will design an electronic case report form (CRF) based on the paper CRF, invented by the clinical investigator. Data monitoring will also be conducted through site initiation, routine monitoring, and site close-out visits. The principal investigator will review and report any serious adverse event to the Seoul National University Bundang Hospital (SNUBH) Institutional Review Board (IRB). A serious adverse event refers to an intensive care unit admission, death, or other consequences of permanent or significant disability or impairment.

Patient and public involvement

There was no patient or public involvement in the design and conduct of this study.

Sample size

The sample size is calculated as follows: statistical power is calculated based on the primary clinical outcome (being alive and residing at home 3 months after discharge). We assume the clinical effectiveness of the CGA-based multidisciplinary intervention based on the results of a previous study. [23] A total sample of 882 participants will be required. Approximately 1,040 patients will be required for this study, anticipating a 15% dropout rate. The test statistic used is the two-sided Fisher's Exact Test, with an alpha of 0.05 and a probability of 0.01 for beta

error (90% power). The power analysis and sample size calculations are performed using PASS 14.0 (NCSS LLC, Kaysville, UT).

Randomisation

This study uses a trial within cohorts with an un-blinded stratified randomised design. The unit of randomisation is the patient. We will conduct systematic randomisation using a random table generated by one of the researchers not involved in collecting the data from participants. The random table is embedded in iCReaT (http://icreat.nih.go.kr). Random tables have been generated for (1) sub-studies 1 and 2 and (2) sub-study 3. Randomisation will be stratified with (1) sub-study (in sub-studies 1 and 2), (2) institutions, and (3) cancer type (in sub-study 3). Patients will be allocated into the intervention and control groups with a 1:1 ratio. The final dataset is coded for blinding for randomisation, and the analysis will be done with blinded until the end of the effectiveness evaluation.

Statistical analysis

Both descriptive and inferential statistics will be used. The baseline patient characteristics will be summarised for each group using descriptive statistics. Baseline differences will be evaluated using the independent t-test for continuous variables, and the chi-squared test or Fisher's exact test will be used for dichotomous or categorical variables. Two-sided p-values of <0.05 will be considered statistically significant. Any potential confounding factors of the groups will be considered for inclusion in the multivariable analysis. The main analysis is conducted based on an ITT principle. We will include the potential confounding pre-

randomisation variables as confounders in the regression model for the secondary analysis to derive the confounder-adjusted intervention effect. We will apply a multilevel regression analysis and a generalised linear mixed-effects model, including fixed factors (time, intervention) and random factors to account for the cluster data structure. Two random effects will be included, one at the institutional (cluster) and the other at the patient (individual) level. We will implement imputation or conduct sensitivity analysis to adjust for missing data for each analysis. Sensitivity analyses will also be conducted on the effect of attrition and the inclusion of patients and subgroup analyses to examine the difference in sub-study or institution.

ETHICS AND DISSEMINATION

This study is registered with the Clinical Research Information Service Registry (trial registration number: KCT0006270). The study is sponsored by a grant of Patient-Centered Clinical Research Coordinating Center (PACEN) funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HC20C0086) and centrally managed by staff at SNUBH. The sponsors had no role in the design, methods, participant recruitment, data collection and analysis, or preparation of the article. The protocol was first reviewed and approved by the SNUBH IRB on 26 April 2021. Further protocol revision was followed by final approval on 30 November 2021 for the informed consent form, correction of typographical errors, addition of assessment items and clarification of inclusion criteria. (IRB No. B-2104/676-001). The current protocol version is version 1.4. The corresponding author and the researchers of this study will have access to the data set. Further dissemination of the data set can be decided by the corresponding author.

The CGA-based multicomponent intervention may not have positive effects, but the risk

of negative effects on patient outcomes is limited. All participants and their guardians (only if the participants lose their ability to make decisions) will sign an informed consent form. After the trial, the data will be analysed, and the study findings will be published in major peer-reviewed journals.

DISCUSSION

To the best of our knowledge, this is the first pragmatic multicentre trial focusing on CGA and multidisciplinary intervention for hospitalised older patients in various healthcare settings of Korea. This individualized geriatric intervention seems to be a promising approach for maintaining functional status and staying in their home instead of institutionalisation. Our study design is similar to that of real clinical settings, considering the difference in the availability of medical resources between medical centres. This type of trial design could provide more meaningful information on which healthcare decision-making could be based.

Despite the strength of our study, the pragmatic trials within cohort design present some inherent limitations. First, heterogeneity between sub-study and institutions is inevitable because multicentre three sub-study will be conducted. Even though we will adjust potential confounding pre-randomisation variables as confounders in the regression model to derive the confounder-adjusted intervention effect, there may be confounding factors that could not been measured. Second, a pragmatic trial design designed to show the real-world effectiveness of the intervention in broad patient groups may improve external validity. However, internal validity is less likely to be guaranteed than traditional RCT design.

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Author Contributions

JYC, KIK, JYL, IGH, JYS and YGL drafted the manuscript.

JYC, JYL, JYS, COK, KJK, IGH, YGL, SJK, SJY, MGK, JWK, SH, JHK and KIK contributed to the study design, data collection, and critical revision of the manuscript.

JYC, KIK, JYL, IGH, COK, KJK, JYK, SJY, SH and MGK contributed to the study design and critical revision of the manuscript. KIK, JYL, IGH and JYC contributed to the study concept.

All authors reviewed and approved the manuscript and agree to be accountable for all aspects of the work.

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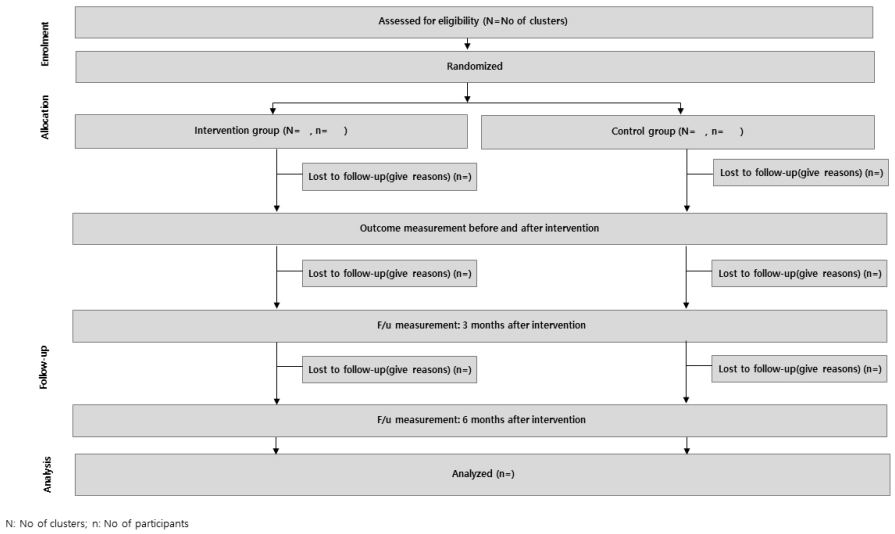
Patient consent for publication: Not required



Flow diagram of cluster trial. N, number of clusters; n, number of older patients

338x190mm (96 x 96 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	#3	Date and version identifier	18
Funding	#4	Sources and types of financial, material, and other support	23
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	23
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	23

Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	18
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	16
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-6
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	6
Objectives	#7	Specific objectives or hypotheses	6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5-7

Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7-8
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	NA
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	10

Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-13
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	14-15
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	16-17
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7-8
Methods: Assignment of interventions (for controlled trials)			

Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7, 17
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7, 17
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	17
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	17
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			

Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	14-17
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10-17
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	14-16
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17-18
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	17-18
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	17-18

Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	16
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	16
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	16
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	14-16
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	18
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to	18

		relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	19
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	19
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	23
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15-16
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in	19

		results databases, or other data sharing arrangements), including any publication restrictions	
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	NA
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Y
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

BMJ Open

COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS): a protocol of pragmatic trials within a cohort

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Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	Health services research
Keywords:	GERIATRIC MEDICINE, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Change management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS): a protocol of pragmatic trials within a cohort

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Keywords: Geriatric assessment, Frailty, Multidisciplinary health team, Pragmatic clinical trial

Word count: 3102

ABSTRACT

Introduction: There is an increased demand for services for hospitalised older patients with acute medical conditions due to rapidly ageing population. The COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS) study will test the effectiveness of comprehensive geriatric assessment (CGA) and multidisciplinary intervention by comparing it with conventional care among acute hospitalised older adults in Korea.

Methods and analysis: A multicentre trial within a cohort comprising 3 sub-studies (randomised controlled trials) will be conducted. The intervention includes CGA and CGA-based multidisciplinary interventions by physicians (geriatricians, oncologists), nurses, nutritionists, and pharmacists. The multidisciplinary intervention includes nutritional support, medication review and adjustment, rehabilitation, early discharge planning, and prevention of geriatric syndromes (falls, delirium, pressure sore, and urinary retention). The analysis will be based on an intention-to-treat (ITT) principle. The primary outcome is living at home 3 months after discharge. In addition to assessing the economic effects of the intervention, a cost-utility analysis will be conducted.

Ethics and dissemination: The study protocol was reviewed and approved by the ethics committees of Seoul National University Bundang Hospital and each study site. The study findings will be published in peer-reviewed journals. Subgroup and further in-depth analyses will subsequently be published.

Trial Registration Details: This study has been registered at https://cris.nih.go.kr/ (trial registration number: KCT0006270)

Strengths and limitations of this study

- The multicentre trials within the cohort study will evaluate the clinical effectiveness and health outcomes of comprehensive geriatric assessment (CGA) and CGA-based multidisciplinary team intervention for acute hospitalised older patients in various clinical settings.
- The study will compare clinical effectiveness of the CGA and CGA-based multidisciplinary interventions, including nutritional support, medication adjustment, rehabilitation, discharge care plan, geriatric syndrome prevention (falls, delirium, pressure sore, and urinary incontinence), with conventional care.
- This pragmatic study will compare multicomponent intervention by an interdisciplinary team with usual care in various clinical settings; thus, this study's result will confirm the clinical effectiveness of CGA-based multidisciplinary intervention in real-world clinical practice conditions.
- This pragmatic trials within cohort design has inevitable limitation of heterogeneity between sub-study and institutions despite we will adjust potential confounding pre-randomisation variables.
- This study will be conducted in Korea, and the findings may not be generalisable to other countries due to the different healthcare systems.

INTRODUCTION

Comprehensive geriatric assessment (CGA) is a multidimensional, interdisciplinary assessment for evaluating older patients' medical, psychological, physical functions and social status. It aims to detect unidentified and potentially reversible problems and develop a coordinated and integrated management plan for treatment and long-term follow-up care.[1] Previous studies have suggested that CGA-based multidisciplinary care is superior to conventional care in reducing the risk of mortality or institutionalisation and improving functional capacity.[2, 3] However, there was a difference in the effect between wards and teams, and no randomised controlled trial has been completed in an acute care setting in Korea.

Geriatric medical professionals and multidisciplinary teams for older inpatient management are rare in Korea (with less than 10 academic hospitals), and detailed protocols vary between institutions. Furthermore, a hospitalist system was introduced in 2016 to improve the quality of in-patient care in Korea.[4] Although CGA-based multidimensional intervention is the accepted gold standard in care for older hospitalised patients with frailty, CGA-based intervention needs to be verified in Korea due to differences in insurance and healthcare systems. The shortage of geriatric consultants or practitioners caring for hospitalised older patients is also one of the biggest problems in other countries. Therefore, it is necessary to validate the effect of CGA-based multidimensional intervention in the setting with or without geriatricians.[5]

Randomised controlled trials (RCTs) are considered the gold standard for generating high-quality evidence for the efficacy of an intervention. However, RCT design is sometimes criticised due to its limited external validity, resulting from difficulties and restricted environments in patient recruitment. Consequently, pragmatic trials, aiming to guide decision-

making in clinical practice, were proposed.[6] As an implementation of both pragmatic trials and RCT concepts, trials within cohorts (TwiCs) enable researchers to conduct several randomised trials using conventional care comparators within a cohort.[6]

The COMPrehensive geriatric AsseSSment and multidisciplinary team intervention for hospitalised older adults (COMPASS) was set up according to the TwiCs design. COMPASS aims to compare the clinical efficacies of CGA-based multidisciplinary team intervention and conventional care for pre-frail or frail older patients hospitalized in an acute care setting. COMPASS study targeted multiple domains; medical optimization for multi-morbidity, early mobilisation or physical rehabilitation to reduce functional decline, prevention of geriatric syndromes, medication management, nutritional intervention and discharge planning to prevent readmission.

We hypothesised that the CGA-based multidisciplinary team intervention increases the likelihood that patients will be living at home 3 months after discharge (primary outcome). Reduction in the total number of medications or inappropriate medications, length of hospital stay, re-admission, all-cause mortality, quality of life, length of days living at home, geriatric syndrome incidence during hospitalisation, emergency department visits, functional status, cost-utility analysis, and other indicators will be assessed as secondary outcomes.

METHODS AND ANALYSIS

Trial design

The COMPASS study will adopt the TwiCs design with 3 RCT sub-studies. Each sub-study will recruit patients from institutions (COMPASS-ER: 2 hospitals, COMPASS-IN: 2 hospitals,

COMPASS-ONCO: 5 hospitals). COMPASS-ER compares the effect of a proactive multidisciplinary team intervention model based on the CGA to that of conventional treatment for patients admitted through the emergency department. COMPASS-IN compares the geriatrician-led care (multidisciplinary team intervention model based on the CGA) to the hospitalist-led care (conventional treatment) for hospitalised older patients. COMPASS-ONCO compares the effect of an oncologist-led multidisciplinary team intervention based on the CGA to that of conventional treatment for older cancer patients without the involvement of geriatricians. The patients will be randomised into the intervention or control groups in a 1:1 ratio. Randomisation will be performed through a web-based system according to the pre-embedded, computer-generated, permuted blocks with stratification. Allocation concealment will be secured by preventing researchers from assigning groups using the central system. The recruitment of participants started on 2 November 2021. This study will follow the Consolidation Standards of Reporting Trials (CONSORT) **(Figure 1)**.[7]

Participants and Setting

The study participants are hospitalised older patients with acute medical problems. The inclusion criteria are as follows: (1) 65 years of age or older, (2) pre-frail or frail status assessed by Korean version of the Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight scale (K-FRAIL) questionnaire,[8] (3) having two or more of the following diseases; hypertension, diabetes, ischemic heart disease, chronic lung disease, arthritis, stroke, depression, chronic kidney disease, and dementia, (4) living at home for more than 3 months before hospitalisation, (5) (for COMPASS-ONCO only) subject to conventional primary chemotherapy because local treatment for curative purposes (such as surgery, concurrent chemo-radiotherapy, and radiation

therapy) is ineligible (stage 3 or higher), and (6) (for COMPASS-ONCO only) histologically confirmed cancer (gastric adenocarcinoma, colorectal adenocarcinoma, non-small cell and small cell lung cancer, pancreatic adenocarcinoma, or biliary adenocarcinoma).

The exclusion criteria are as follows: (1) planned hospitalisation in the specialised care unit, such as an intensive care unit and/or acute stroke ward, at the time of admission, (2) terminal status requiring hospice or palliative care, (3) life expectancy of 6 months or less, (4) other severe conditions that limit the participation in the research, (5) (for COMPASS-ONCO only) oral targeted therapy as a palliative first-line chemotherapy, and (6) (for COMPASS-ONCO only) recurrence within 6 months after adjuvant chemotherapy.

Informed consent will be obtained from the patients. At the sponsor's request, consent for third party provision of research data and use of secondary ancillary research will be additionally obtained. Participants were recruited from 2 November 2021, and recruitment will continue until December 2024.

Interventions

The intervention comprises the CGA and CGA-based multidisciplinary interventions. A description of the adapted CGA and multicomponent intervention is shown in **Table 1.**

Table 1. Overview of Comprehensive Geriatric Assessment and Multidisciplinary Team Intervention

Domain	Assessment Tool and Risk Criteria	Assessor/ Provider	Intervention
Nutrition	MNA ≤23 MNA-SF ≤11	Nutritionist APN RN	Dietary change and education (Patient / Caregiver) Oral nutritional supplements Protein/amino acid replacement

			Dysphagia assessment and rehabilitation if needed Tube feeding Dental care
Medication	Potentially inappropriate medication list, Polypharmacy (≥10)	Pharmacist APN RN Physician	Education (Institution / Patient / Caregiver) Medication reconciliation De-prescription
Rehabilitation	TUGT ≥10 seconds Grip strength (<28 kg in male <18 kg in female) ADL/IADL dependency	APN RN Physician	Early ambulation/rehabilitation Transfer to rehabilitation medicine
Discharge care plan		APN RN Physician	Identify decision-makers among family members and preferred discharge location Check financial and social situation Discharge care planning and consultation Consult with hospital transfer centre or home health nursing centre
Geriatric syndrome (Falls, Delirium, Sore, Urinary incontinency)	(Falls) Hendrich II fall risk model ≥5, John's Hopkins fall risk assessment tool ≥14, history of falls, TUGT ≥10 (Delirium) history of delirium, K-MMSE 2 ≤26, age ≥80 (Sore) Braden scale ≤18 (Urinary Incontinence) indwelling urinary catheter	Nutritionist Pharmacist APN RN Physician	(Falls) Fall prevention education handouts for patient and caregiver Early ambulation/exercise Consultation to rehabilitation medicine (Delirium) Non-pharmacological delirium prevention (medical optimisation, pain control, sleep hygiene) De-prescribing for medications that potentially cause delirium (Sore) Nutritional support Frequent positioning and application of pressure relief aids Consultation to Pressure sore management team or plastic surgery (Urinary retention) Identification of urinary retention (infection) Residual urine volume check after catheter removal Education for clean intermittent catheterisation Medication treatment if needed.

Notes: APN = advanced practice nurse; MMSE = Mini-Mental State Examination; MNA = Mini Nutritional Assessment; MNA-SF = Mini Nutritional Assessment Short Form; RN = registered nurse; TUGT = timed up-and-go test.

Comprehensive Geriatric Assessment (CGA)

The CGA includes the collection of information on sociodemographic characteristics,

functional status (Activities of Daily Living [ADL] [9] and Instrumental Activities of Daily Living [IADL] [10]), comorbidities (the Charlson Comorbidity Index [11]), history of falls, delirium and pressure sores, a medication review, grip strength, Timed Up and Go test (TUGT), nutritional status (Mini Nutritional Assessment [MNA] or MNA short form [MNA-SF]),[12] cognitive function (Korean-mini mental state examination 2 [K-MMSE 2]),[13] and mood (Korean Version of Short Form Geriatric Depression Scale [SGDS-K])[14] The CGA will be administered by geriatric advanced practice nurses (APN) or registered nurses (RN) at baseline. The CGA, in our experience, takes approximately 45–60 minutes based on the cooperation of the older patients.

CGA-based multidisciplinary intervention

The standardised geriatric management protocol will be delivered based on the CGA results; the predefined evidence-based intervention is described in **Table 1**. The multidisciplinary intervention team will comprise a geriatrician, nurse, case manager, pharmacist, and nutritionist. Physicians will request consultations with a healthcare professional if it is difficult to assemble a multidisciplinary team with all members. For the COMPASS-ONCO sub-study, the oncologist will be the principal investigator instead of a geriatrician.

RN or APN will monitor whether the individualised intervention plan is properly applied based on the CGA results for the participant randomized to the intervention group. The recommended intervention strategy will be communicated to the multidisciplinary team. The intervention team will implement all recommendations as much as possible to facilitate adherence.

Comparison

Patients in the control group will receive conventional care provided by the study hospital. Since a structured CGA will not be implemented, consultations will be allowed without any restriction if physicians in charge determine that there is a specific problem.

Outcome measures

This study aims to assess the clinical effectiveness and cost-effectiveness of the CGA-based multidisciplinary intervention. The primary outcome is living at home 3 months after discharge. Living at home at 3 months is the odds of participants being alive and in their own home 3 months after discharge. The secondary outcomes are living at home 6 months after discharge, the total number of medications reduced or inappropriate medications at discharge, length of hospital stay, unplanned re-admission, all-cause mortality, and quality of life. In addition, length of days living at home, the incidence of geriatric syndromes during hospitalisation, emergency department visits after discharge, functional status at 3 months after discharge, and cost-utility. Quality of life will be assessed by Korean version of EuroQol- 5 Dimension and functional status will be measured by ADL.[15]

In addition to the outcomes measured in the entire COMPASS study, additional outcomes will be measured in the sub-studies. In the COMPASS-IN study, the readiness for hospital discharge,[16] family interaction,[17] a therapeutic alliance between patient and provider,[18] and empowerment [19] will be investigated, and frailty status will be followed-up at 3 and 6 months.[8] In the COMPASS-ONCO study, overall treatment utility, recognition of advance directives, changes in body composition, and validity of anticancer drug toxicity prediction

model will also be assessed.[20] Overall treatment utility is a clinical outcome incorporating objective and subjective measures of anticancer efficacy, tolerability and acceptability.[21]

A cost-utility analysis will be conducted. For cost analysis, medical costs and programme operating costs will be assessed. From insurer's perspective, the medical cost is primarily defined that official or direct medical cost, including out-of-pocket expenditures, co-payment from insurance. In addition, we also perform sensitivity analysis considering the perspective of limited healthcare system including long-term care costs and nursing expenses based on the indirect data from the nationally representative data, the Korea Health Panel Survey and the Korean Longitudinal Study of Aging.[22,23] Finally, medical costs will be evaluated based on the difference in the health care expenses between the intervention and control groups. Based on the fee for service reimbursement system, the medical cost can be calculated by adding the costs of all medical treatments, examinations, and other input resources microscopically. The program's cost will be determined using the data of the participating institutions. The duration of participation of the health care professionals in the intervention team will be assessed by medical staff by asking for the additional time used for the intervention. The minute-wise cost of the program will be determined by the wages of the health care professionals and the duration of participation in the intervention team. The index of clinical effectiveness will be used as the reference in the cost-utility analysis. The results will be analysed as incremental cost-utility ratios.

We will design model of natural history of discharge outcomes in geriatric patients. Then, we will observe type of complications, its duration of state, and its related quality of life. Also, transition probability to each pathway will be calculated with cost. After developing the analytic model, we will set virtual cohort of the aged 65 with 100,000 populations. It is planned

to perform 35 annual cycles, to reach 100 years-old, with half-cycle correction with equal weight. Discount rate will be three percent annually. To consolidate the results, we will consider different discount rates including 0%, and 5 % as sensitivity analyses. (**Table 2**)

Table 2. Outcome variables

Domain	Variable	Source (target population)	Outcome Type	Timeline			
				t_1	t_2	t_3	t_4
Clinical effectiveness							
Living at home		Survey & EMR	Primary & Secondary			X	X
Inappropriate medications		Survey &EMR	Secondary	X	X		
Total number of medications		Survey &EMR	Secondary	X	X		
Length of hospital stay		Survey &EMR	Secondary		X		
Health care utilisation (re-admission and visit to emergency department)		Survey &EMR	Secondary			X	X
Mortality		Survey &EMR	Secondary				X
Quality of Life		Survey using EQ-5D	Secondary	X		X	
Length of days living at home		EMR	Secondary				X
Geriatric syndrome during hospitalisation		Survey &EMR	Secondary		X		
Activities of daily living		Survey &EMR	Secondary	X		X	
Readiness for hospital discharge (Only in COMPASS-IN)		Survey	Secondary		X		
Family interaction (Only in COMPASS-IN)		Survey	Secondary		X		
Therapeutic alliance (Only in COMPASS-IN)		Survey	Secondary		X		
Empowerment (Only in COMPASS-IN)		Survey	Secondary		X	X	
Frailty (Only in COMPASS-IN)		Survey & EMR	Secondary			X	X
Overall treatment utility (Only in COMPASS-ON)		Survey &EMR	Secondary			X	
Recognition of advance directive (Only in COMPASS-ON)		Survey	Secondary		X		
Changes in body composition (Only in COMPASS-ON)		Survey & EMR	Secondary	X		X	X
Economic effectiveness							
Economic evaluation		Survey using EQ-5D, ADL	Secondary	X		X	

t_1: Before intervention measurement (baseline); t_2: After intervention measurement (at discharge); t_3: Follow-up measurement (3 months after discharge); t_4: Follow-up measurement (6 months after discharge); EMR: Electronic medical record; ADL: Activities of Daily Living

Data collection and management

Research assessors registered in this study will collect data according to the standardised protocol. A 4-hour educational program consisting of the study overview, measurement tools, and practice sessions with scenarios will be provided for the assessors before data collection. All patients in the intervention and control groups will be evaluated with baseline tests before intervention or observation (T1). At discharge, the second assessment (T2) will be conducted. Follow-up assessments will be conducted for 3 months ± 4 weeks (T3) and 6 months ± 4 weeks (T4) after discharge. A research assessor will conduct T1 and T2 measurements at hospital before the participants' discharge. After discharge, T3 and T4 measurements will be conducted by face-to-face personal interview at an outpatient clinic. However, a telephone interview will be used if the participants cannot visit the clinic. A summary of the main measures at the patient level and the corresponding timetable is shown in **Table 3.**

Table 3. Schedule of enrolment, interventions, and assessments

	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
TIMEPOINT	$-t_2$	$-t_1$	t_1	t_2	t_3	t_4
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
CGA based multicomponent intervention			←	→		

ASSESSMENTS:						
[Clinical effectiveness] Primary outcomes					X^{a}	
[Clinical effectiveness] Secondary outcomes	X^{b-1}		X^{b-2}	X^{b-3}	X^{b-4}	X^{a}, X^{b-5}
[Economic evaluation]				X^{c}	X^{c}	

t1: Baseline (Before intervention measurement); t2: Discharge (After intervention measurement); t3: Follow-up measurement (3 months after discharge); t4: Follow-up measurement (6 months after discharge); Xa: Living at home; X^{b-1}: frailty, X^{b-2}: Quality of life, *recognition of advance directive and changes in sarcopenic obesity, activity of daily living; X^{b-3}; Medication management, length of hospital stay, geriatric syndrome during hospitalisation, readiness for hospital discharge, family interaction, connectedness, empowerment; X^{b-4}, Quality of life, activity of daily living, *overall treatment utility, *recognition of advance directive and changes in sarcopenic obesity, health care utilisation, empowerment, frailty; X^{b-5}; *overall treatment utility, *recognition of advance directive and changes in sarcopenic obesity, health care utilisation, frailty; X^{c}: cost-effectiveness analysis

Data will be recorded in hardcopy at the time of the measurement and subsequently entered electronically in iCReaT (http://icreat.nih.go.kr), a web-based clinical research management system developed by the Korea National Institute of Health. Automatic checks will be applied when entering the data based on predetermined ranges. Missing data will also be automatically detected, and data query reports will be sent to the local data manager. The data managers will ask the assessors for correction or clarification if any errors are found in the data. Furthermore, to promote follow-up and retention, assessors will report any issues with the patients. A brief short-form report will be generated and submitted if there is a discontinuation of research participation. All patients will be assigned a unique research ID, and the research team will train the assessors to secure the research data to maintain its safety. The data collection forms will not contain any identifiable personal information. An electronic password-protected file will be saved on a password-protected computer. The final data set will be retrieved by the iCReaT.

The data monitoring committee (DMC) comprises investigators independent of the clinical

investigation team and includes a team member who manages the data quality. This committee will meet once when 50% of the planned recruitment has occurred. The datasets that will be generated and/or analysed during the current study are not publicly available but are available from the sponsor on reasonable request.

The data centre of the Korean Cancer Study Group, which is independent of the investigators and sponsor, will design an electronic case report form (CRF) based on the paper CRF, invented by the clinical investigator. Data monitoring will also be conducted through site initiation, routine monitoring, and site close-out visits. The principal investigator will review and report any serious adverse event to the Seoul National University Bundang Hospital (SNUBH) Institutional Review Board (IRB). A serious adverse event refers to an intensive care unit admission, death, or other consequences of permanent or significant disability or impairment.

Patient and public involvement

There was no patient or public involvement in the design and conduct of this study.

Sample size

The sample size is calculated as follows: statistical power is calculated based on the primary clinical outcome (being alive and residing at home 3 months after discharge). We assume the clinical effectiveness of the CGA-based multidisciplinary intervention based on the results of a previous study. [24] A total sample of 882 participants will be required. Approximately 1,040 patients will be required for this study, anticipating a 15% dropout rate. The test statistic used is the two-sided Fisher's Exact Test, with an alpha of 0.05 and a probability of 0.01 for beta

error (90% power). The power analysis and sample size calculations are performed using PASS 14.0 (NCSS LLC, Kaysville, UT).

Randomisation

This study uses a trial within cohorts with an un-blinded stratified randomised design. The unit of randomisation is the patient. We will conduct systematic randomisation using a random table generated by one of the researchers not involved in collecting the data from participants. The random table is embedded in iCReaT (http://icreat.nih.go.kr). Random tables have been generated for (1) sub-studies 1 and 2 and (2) sub-study 3. Randomisation will be stratified with (1) sub-study (in sub-studies 1 and 2), (2) institutions, and (3) cancer type (in sub-study 3). Patients will be allocated into the intervention and control groups with a 1:1 ratio. The final dataset is coded for blinding for randomisation, and the analysis will be done with blinded until the end of the effectiveness evaluation.

Statistical analysis

Both descriptive and inferential statistics will be used. The baseline patient characteristics will be summarised for each group using descriptive statistics. Baseline differences will be evaluated using the independent t-test for continuous variables, and the chi-squared test or Fisher's exact test will be used for dichotomous or categorical variables. Two-sided p-values of <0.05 will be considered statistically significant. Any potential confounding factors of the groups will be considered for inclusion in the multivariable analysis. The main analysis is conducted based on an ITT principle. We will include the potential confounding pre-

randomisation variables as confounders in the regression model for the secondary analysis to derive the confounder-adjusted intervention effect. We will apply a multilevel regression analysis and a generalised linear mixed-effects model, including fixed factors (time, intervention) and random factors to account for the cluster data structure. Two random effects will be included, one at the institutional (cluster) and the other at the patient (individual) level. We will implement imputation or conduct sensitivity analysis to adjust for missing data for each analysis. Sensitivity analyses will also be conducted on the effect of attrition and the inclusion of patients and subgroup analyses to examine the difference in sub-study or institution.

ETHICS AND DISSEMINATION

This study is registered with the Clinical Research Information Service Registry (trial registration number: KCT0006270). The study is sponsored by a grant of Patient-Centered Clinical Research Coordinating Center (PACEN) funded by the Ministry of Health & Welfare, Republic of Korea (Grant number: HC20C0086) and centrally managed by staff at SNUBH. The sponsors had no role in the design, methods, participant recruitment, data collection and analysis, or preparation of the article. The protocol was first reviewed and approved by the SNUBH IRB on 26 April 2021. Further protocol revision was followed by final approval on 30 November 2021 for the informed consent form, correction of typographical errors, addition of assessment items and clarification of inclusion criteria. (IRB No. B-2104/676-001). The current protocol version is version 1.4. The corresponding author and the researchers of this study will have access to the data set. Further dissemination of the data set can be decided by the corresponding author.

The CGA-based multicomponent intervention may not have positive effects, but the risk

of negative effects on patient outcomes is limited. All participants and their guardians (only if the participants lose their ability to make decisions) will sign an informed consent form. After the trial, the data will be analysed, and the study findings will be published in major peer-reviewed journals.

DISCUSSION

To the best of our knowledge, this is the first pragmatic multicentre trial focusing on CGA and multidisciplinary intervention for hospitalised older patients in various healthcare settings of Korea. This individualized geriatric intervention seems to be a promising approach for maintaining functional status and staying in their home instead of institutionalisation. Our study design is similar to that of real clinical settings, considering the difference in the availability of medical resources between medical centres. This type of trial design could provide more meaningful information on which healthcare decision-making could be based.

Despite the strength of our study, the pragmatic trials within cohort design present some inherent limitations. First, heterogeneity between sub-study and institutions is inevitable because multicentre three sub-study will be conducted. Even though we will adjust potential confounding pre-randomisation variables as confounders in the regression model to derive the confounder-adjusted intervention effect, there may be confounding factors that could not been measured. Second, a pragmatic trial design designed to show the real-world effectiveness of the intervention in broad patient groups may improve external validity. However, internal validity is less likely to be guaranteed than traditional RCT design.

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Figure Legend

Figure 1. Flow diagram of inclusion and randomization of study participants.

N: Number of clusters, n: Number of patients

Author Contributions

JYC, KIK, JYL, IGH, JYS and YGL drafted the manuscript.

JYC, JYL, JYS, COK, KJK, IGH, YGL, SJK, SJY, MGK, JWK, SH, JHK and KIK contributed to the study design, data collection, and critical revision of the manuscript.

JYC, KIK, JYL, IGH, COK, KJK, JYK, SJY, SH and MGK contributed to the study design and critical revision of the manuscript. KIK, JYL, IGH and JYC contributed to the study concept.

All authors reviewed and approved the manuscript and agree to be accountable for all aspects of the work.

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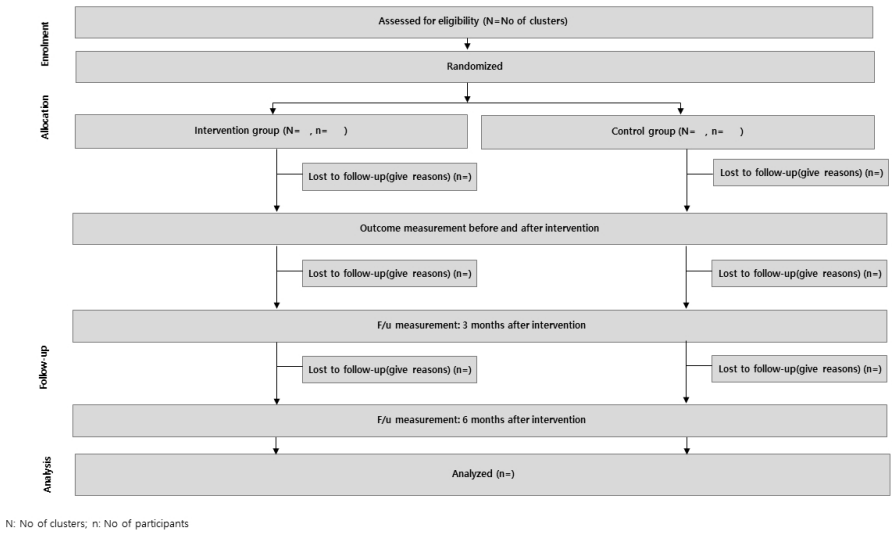

Flow diagram of inclusion and randomization of study participants
N: Number of clusters, n: Number of patients

338x190mm (96 x 96 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	#3	Date and version identifier	18
Funding	#4	Sources and types of financial, material, and other support	23
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	23
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	23

Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	18
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	16
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	5-6
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	6
Objectives	#7	Specific objectives or hypotheses	6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5-7

Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7-8
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	7-8
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8-10
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	NA
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	10

Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-13
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	14-15
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	16-17
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7-8
Methods: Assignment of interventions (for controlled trials)			

Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	7, 17
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	7, 17
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	17
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	17
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			

Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	14-17
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	10-17
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	14-16
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	17-18
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	17-18
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	17-18

Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	16
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	16
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	16
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	14-16
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	18
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to	18

		relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	19
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	19
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	15
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	23
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	15-16
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in	19

		results databases, or other data sharing arrangements), including any publication restrictions	
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	NA
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Y
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA