BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034742
Article Type:	Protocol
Date Submitted by the Author:	03-Oct-2019
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Keywords:	Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, GERIATRIC MEDICINE

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Implementation of a strategy involving a multidisciplinary mobile unit team to prevent hospital admission in nursing home residents: protocol of a quasi-experimental study (MMU-1 Study)

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Word count: 3165

Abstract: 300; **Tables**: 1; **Figures**: 2; **References**: 18

Running Title: Multidisciplinary mobile unit intervention for nursing homes

ABSTRACT

Introduction- Nursing home residents represent a particularly vulnerable population experiencing high risk of unplanned hospital admissions, but few interventions have proved effective in reducing this risk. The aim of this research will be to verify the effects of a hospital-based multidisciplinary mobile unit (MMU) team intervention delivering urgent care to nursing home residents directly at their bedside.

Methods and analysis- Four nursing homes based in the Parma province, in Northern Italy, will be involved in this prospective, pragmatic, multicenter, 18-month quasi-experimental study (sequential design with two cohorts). The residents of two nursing homes will receive the MMU team care intervention. In case of urgent care needs, the nursing home physician will contact the hospital physician responsible for the MMU team by phone. The case will be triaged as a) manageable by phone advice, b) requiring urgent assessment by the MMU team or c) requiring immediate ED referral. MMU team is composed of one senior physician and one Emergency-Medicine resident chosen within the staff of Internal Medicine and Critical Subacute Care Unit of Parma University-Hospital, usually with different specialty background, and equipped with portable ultrasound, set of drugs and devices useful in urgency. The MMU visits patients in nursing homes, with the mission of stabilizing clinical conditions and avoiding hospital admission. The residents of the other two nursing homes will receive usual care, i.e. ED referral in every case of urgency. Study endpoints include unplanned hospital admissions (primary), crude all-cause mortality, hospital mortality, length of stay and healthcare-related costs (secondary).

Ethics and dissemination- The study protocol was approved by the Ethics Committee of Area Vasta Emilia Nord. Informed consent will be collected from patients or their legal representatives. The results will be actively disseminated through peer-reviewed journals and conference presentations, in compliance with the Italian law.

Registration ID- ClinicalTrials.gov NCT 04085679

Key words: multimorbidity; geriatrics; hospitalization; multidisciplinary care; hospital-community partnership

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ✓ This study will explore the effectiveness of a complex intervention focused on the avoidance of hospital admissions for nursing home residents, with a strong hospital-community partnership.
- ✓ The study intervention consists in bringing specialist hospital care directly at the bedside of nursing home residents, an innovative approach not previously described in the scientific literature.
- ✓ The intervention has been developed considering the organization of Italian healthcare system, but is reproducible and applicable in other settings.
- ✓ Due to ethical concerns and complex nature of the intervention, randomization of participants is not possible.

INTRODUCTION

The increasing clinical complexity of older medical patients in industrialized countries, due to multimorbidity, polypharmacy, frailty, disability and social hardship, is challenging for health care systems.[1 2] Firstly, these patients are often admitted to Emergency Departments (EDs), accounting for 12 to 24% of all ED visits.[3] However, their complex needs are often poorly met in this setting, where the busy, overcrowded environment does not always allow a careful evaluation of the multi-faceted clinical problems of elderly patients.[4-6] These difficulties not only contribute to ED overcrowding, but they may also lead to inaccurate diagnoses and unrecognized or untreated health problems.[7] Older patients furthermore have an up to 5-times-higher risk of ward admission, irrespective of the severity of the clinical problem.[3 5 8] Once admitted, they are far more likely to stay in hospital for more than two weeks[6] and are at much greater risk of experiencing complications related to hospital admission.[9]

These issues are especially relevant for residents of nursing homes, who exhibit a particularly high risk of hospitalization (greater than 20% per year)[10] and are at high risk of complications during hospitalization, due to frailty, multimorbidity and the possible presence of cognitive impairment.

In the light of these considerations, a number of approaches have been developed designed to reduce the risk of hospitalization in nursing home residents. These are summarized in the very recent systematic review by Santosaputri et al,[11] which includes quantitative comparative studies of all designs aiming to determine the efficacy of interventions provided by a health professional specializing in geriatric medicine. Sixteen studies were eligible, of which 6 randomized controlled trials, involving an estimated total of over 7400 patients. The authors of the review categorized 14 intervention programs into three primary approaches (two did not fit in any category):

- Prevention approach (nine studies): Interventions applied in the nursing home to prevent hospitalization of residents, in most cases involving care provided by nurses, physicians, and sometimes allied health personnel. The majority of interventions involved either direct review of patients, telephone (or telemedicine) support, or comprehensive geriatric assessment.
- Emergency department-based hospital avoidance (three studies): interventions targeting nursing home residents presenting to the ED to facilitate early discharge and avoid hospitalization. Programs of this type involved care provided by nursing staff (e.g. intravenous therapy, wound care, catheter management).

- Post-hospital supported discharge (two studies): Interventions designed to support residents following hospital admission. One of the studies evaluated the efficacy of geriatrician and nurse review in the facility and the development of a comprehensive tailored care plan following hospital admission; the other assessed the efficacy of a tailor-made intervention compared to a standardized rehabilitation program following admission due to hip fracture.

Although the majority of the studies reported reductions in hospitalizations (in the form of either ED presentations or hospital admissions), only six obtained statistically significant findings, of which none were RCTs. Unfortunately, the quality of evidence was considered low to moderate, therefore the authors emphasize the need for further, well-designed studies to identify which interventions are effective in reducing hospitalization in the older residents.

At our institution, different projects have been carried out for many years to improve care of the elderly, primarily targeting hospital organization, with the main objective to reduce unnecessary, avoidable length of stay (LOS).[12-14] These efforts benefit in-hospital patients, but are not designed to prevent hospitalizations. Based on literature evidence, and drawing on our long-time experience with elderly care, we hypothesize that a complex intervention delivered in nursing homes, where vulnerable high-risk patients live, involving direct patient care by hospital medical staff with geriatric expertise, may reduce hospitalization of residents.

METHODS AND ANALYSIS

Study setting

The study is based in the University Hospital of Parma, which has a catchment area of more than 400,000 inhabitants, of whom 22.3% is over 65 years old. It provides the only Emergency service of the district, and it ranks fourth in Italy by number of ED visits (yearly average of over 110,000). The average admission rate of the adult ED population is 18%, of which 65% concern people older than 65.

In the last two decades, the University Hospital of Parma has implemented several innovative initiatives to manage the hospital flow of frail multimorbid patients and their complex needs. These initiatives included bed management to avoid "bed-blockers",[12] physician accountability for the discharge process,[13] and creation of a dedicated hospital unit, organized by intensity of care to anticipate the needs of these patients preserving high performance indices.[14] This unit, called Internal Medicine and Critical Subacute Care Unit, performs over

3,500 urgent admissions of frail multimorbid elderly patients per year, with an average length of stay that in 30% of cases is lower than 3 days.[14]

Nursing homes participating to the study are public facilities which ensure the presence of nursing staff 24 hours a day and of a physician at least 4 hours a day (high-intensity care facilities). The possible role of distance to the hospital is considered by including in each group one nursing home located next to the hospital and one located >5 km of distance.

The participating nursing homes are the following:

- C.R.A. "I Tigli" C/O Comprensorio di Villa Parma, Piazzale Fiume 5, Parma (intervention group)
- C.R.A. "Casa degli Anziani", Via Aldo Moro 2, Collecchio (intervention group)
- C.R.A. "Le Tamerici" C/O Comprensorio di Villa Parma, Piazzale Fiume 5, Parma (control group)
- C.R.A. "Ines Ubaldi", Via Ravenna 4, Parma (control group)

This study follows a multimethod approach, based on the MRC framework for developing and evaluating complex interventions,[15] including the development, feasibility assessment, and evaluation phases.

Development of the intervention

First, the different types of approaches reported in the literature, described above, were considered. The "prevention approach", interventions conducted in nursing homes, was chosen as the most suitable strategy to integrate the hospital's organizational model already in place, as it can target both hospitalization rates and ED overcrowding, allowing to intervene before the person accesses the hospital.

Available evidence also prompted us to opt for a multicomponent approach. In fact, data from qualitative interviews reveal that the decision to transfer residents to hospital may be influenced by different factors, such as staffing and skill mix in the nursing homes, treatment options available in the facility, end-of-life decision-making, and communication and bureaucratic requirements. This multifactorial association means that a multicomponent intervention is likely to be more effective than a single-component intervention.[16]

The choice of employing a mobile geriatric specialist service was supported by the positive results obtained by the two controlled studies which examined similar interventions.[17 18] Schippinger et al evaluated a service where a physician did regular and on-call visits intended to provide services otherwise associated with hospitalization.[17] Dìaz-Gegùndez et al evaluated an ambulant team with a nurse and a physician, doing comprehensive geriatric assessments of residents as well as reviewing medications and providing support to

staff.[18] Our intervention does not involve a nurse, unlike the Dìaz-Gegùndez study, because in the participating facilities nursing staff is available 24 hours a day. Unlike the experience of Schippinger et al, moreover, we chose not to perform periodic visits on site, since routine clinical management and scheduled follow-up is already performed by nursing home physicians.

Finally, medical hospital staff was preferred to community geriatricians, on the assumption that older patients may feel more comfortable being handled by physicians who may have already cared for them at the hospital. Moreover, hospital staff enables direct patient referral to the ward. Finally, this allows the use of diagnostic technologies available at the hospital, which can be used immediately without the need for hospital admission.

Description of the intervention

The model hinges on the strong collaboration between hospital and nursing home staff to provide residents with patient-centered care. It entails a multicomponent intervention which is integrated in standard care and comprises three steps: 1) MMU team activation, 2) on site visit by a team of physicians with geriatric expertise, 3) interdisciplinary care planning (Figure 1).

Step 1: MMU team activation

Patient selection is necessary to ensure that available resources are used for patients who may really benefit. To this end, the nursing home physician contacts by phone the "flow manager", a skilled internist with strong clinical expertise, organizational attitude and managerial training, during the 8 a.m.-6 p.m. time frame, Monday to Friday. The phone consultation is reported on a form containing the description of the patient's clinical condition and a summary of the conversation. The form also indicates which decision was reached among the following 6 not mutually exclusive options:

a) The patient can be managed by nursing home staff, therapeutic advice is provided by phone
b) Remote reassessment is scheduled after a number of hours agreed upon by the team
c) The MMU team is dispatched for evaluation, treatment and stabilization on site
d) A significant change in vital parameters is observed which requires immediate activation of emergency services
e) Direct hospital admission is considered necessary
f) Ambulatory outpatient visits or tests are planned

Step 2: on site visit by a team of physicians with geriatric expertise

Visits at the nursing home are performed by two members of the MMU team: an expert hospital physician chosen on a case-by-case basis among the clinical staff of the Internal Medicine and Critical Subacute Care Unit, which comprises internists, gastroenterologists, geriatricians, specialists in clinical nutrition, depending on the disease or clinical problem that must be treated, and a specifically trained resident in Emergency Medicine.

The team is provided with a car to reach the nursing homes, a portable ultrasound system, and an essential set of drugs and medical devices useful in an emergency setting. The ultrasound system is equipped with three probes (convex, linear, and phased-array) for performing thoraco-pulmonary, cardiac, vascular, abdominal and soft tissue ultrasound, when required. Available drugs include those that can be administered intravenously for treating urgent conditions (e.g. loop diuretics, steroids, fluids, antibiotics). Devices include central and peripheral venous lines, naso-gastric and rectal tubes and bladder catheters. Blood tests can also be performed. Table 1 shows possible clinical scenarios which may require MMU team activation, and possible decisions.

Step 3: interdisciplinary care planning

Based on the results of the visit and of any performed investigations, the MMU team formulates personalized advice and referrals, and discusses these with the nursing home physician. If stabilization on site is not deemed possible, the MMU team plans a direct admission to the Internal Medicine and Critical Subacute Care Unit, thus avoiding ED access. The planning and the final outcome of the intervention are recorded in the second part of the form.

Feasibility assessment

A pilot phase of 5 months (December 2018-April 2019) was conducted in two nursing homes in order to look at feasibility of the MMU care Model described above. Before the intervention was introduced, meetings were held with nursing home staff to agree on activation modalities.

In this period, 99 phone calls were received, of which 84 required MMU team onsite visits, and 15 were managed with remote consultancy. Of the latter, 3 required direct admission after remote phone consultancy.

Only 4 of the 84 patients visited onsite required direct admission. One patient was sent to the ED for massive intestinal bleeding (Figure 2).

This phase demonstrated the feasibility of the intervention, and did not highlight any need for modifications.

Evaluation phase

Aim and objectives

The study aim is to verify the effects of the implementation of the MMU care model tested in the pilot phase. Primary objective is to verify reduction of unplanned hospitalization rates in the nursing homes of the intervention group compared to the nursing homes in the control group. Secondary objectives are to measure the effects of the intervention in terms of mortality, health service use, and costs.

Study Design

This study is a prospective, pragmatic, multicenter, quasi-experimental study (sequential design with two cohorts), in which usual nursing home care is compared to care provided by applying the MMU model.

Study Population

All residents of the participating nursing homes are eligible, regardless of their clinical status. Residents who do not provide informed consent will be excluded.

Usual Care

Patients in the control cohort receive usual care, which means the actions to take are decided by the nursing home staff. Generally, this implies that patients who are clinically unstable, or require urgent instrumental tests, will be sent to the ED.

Measures: Baseline variables

Demographic data on gender and age are collected by chart review.

Measures: Outcome variables

The primary outcome is hospitalization rate, considering at the numerator all unplanned admissions occurred during a 1-year period, and at the denominator the sum of the person-time of the at risk population (days of stay at the nursing home). For the intervention group, the numerator corresponds to options d) and e) defined in "Step 1: MMU team activation".

The secondary outcomes are the following*:*

- Crude all-cause Death Rate (CDR): the number of deaths *during a* 1-year period on person-time of the at risk population
- Hospital Mortality rate: the frequency of patients who die while in the hospital (death rate/1000)
- Length of stay (LOS): the duration of a single episode of hospitalization. Inpatient days are calculated by subtracting day of admission from day of discharge.
- Adverse events or complications: frequency of events occurred within 48 hours from MMU team activation and subsequent patient stabilization, for which hospital access becomes necessary.
- Costs analysis, comparing the cost differences in the two groups

Data Collection

Patient demographic and clinical characteristics are collected at baseline to describe the study population and determine factors associated with hospital rate. Participants' files and electronic data are stored securely at the study site (e.g. locked area, password protected hard- and software). Data integrity will be scrutinized with several strategies (e.g. valid values, range checks, consistency checks). Patient data are only identifiable with the unique participant's number. Personal information will be collected and saved in a separate file (on a different server) which can only be accessed by the Principal Investigator (PI). This information will be used by the PI to retrieve data on any hospital admissions (length of stay, in-hospital death …) from administrative databases (discharge summaries, ED data, Death Registry). Residents' identification data will be deleted once the study is completed, making the dataset anonymous. All study protocol authors will have access to the anonymous dataset.

Cost analysis

We will identify the changes in net costs associated with one-year exposure to the intervention, consisting in the induced costs due to incremental resource inputs for carrying out the intervention and hospital health

service utilization costs. Staffing costs will be calculated considering the time spent by the professionals involved in the intervention. Non-staff running costs include expenses of MMU staff travelling to and from the nursing home. The health service utilization costs will be identified based on the Diagnosis Related Group (DRG) system.

Study duration

Overall expected duration is 18 months, with study initiation presumably in November 2019 and completion in April 2021.

Statistical Methodology

Sample size calculation

The number of subjects to include was estimated using the findings of Diaz-Gegundez et al [Diaz 2011], who performed a large quasi-experimental trial. Thus, considering 56 cases vs 32 cases per 100 residents, and using a 2-sided, large-samples z-test of the Poisson incidence rate difference at a significance level of 0.05, and with a power of 0.90, overall 338 residents should be enrolled.

Statistical analysis plan

Descriptive statistics will be used to summarize patient populations and will be presented as means and standard deviations (SD) when normally distributed, or as medians and interquartile ranges (IQR).

For the primary analysis we will used Poisson regression with robust standard errors (SEs) to evaluate relative differences in hospital rates among our two cohorts while adjusting for demographic characteristics.

Concerning the secondary outcomes, the following analyses will be performed:

- Rates will be compared considering the quotient between the intervention and control groups
- A lognormal model will be used to compare in-hospital LOS.
- Chi square tests will be conducted for categorical data as adverse events or complications
- For costs, we will use the following equations to summarize the annual net costs associated with the implementation of the intervention. Any costs with negative values mean "savings" and any costs with positive values mean "losses". Net costs ˆ A (intervention costs) ± B (Costs for differences in hospital health service utilization) where: A= intervention: staffing costs+intervention: non- staff costs and B=

Costs for differences in inpatient care utilization. Therefore, the net costs arising from one-year implementation of the intervention as compared with the current practice will be obtained, where a negative value of net costs represents "cost-saving" and a positive value represents "not cost-saving"

The demographic and clinical variables which influence the outcome with a p value<0.20 in the univariate analysis will be included in the Poisson regression model.

The analyses will be performed using SAS 8.2 (SAS Institute, Cary, NC, USA) and STATA-SE 11 (Stata Corp LP, College Station, TX, USA).

ETHICS AND DISSEMINATION

The study will be conducted in compliance with the principles of the revision of the Helsinki Declaration and by current legislation on scientific research. The protocol and the patient informed consent form have been approved by the competent Ethics Committee, in accordance with Italian current norms. The study protocol has been registered on ClinicalTrials.gov (NCT 04085679).

This study does not entail any experimental pharmacological treatment, or changes in the diagnostic-therapeutic pathway. Eligible patients will be asked to give consent to handling of their personal data in writing. The consent form will be dated and signed by the patient and by the investigator, authorized according to norms of the local Ethics Committee.

A copy of the signed informed consent form shall be given to the patient, and the original shall be retained by the investigator as part of the study documentation. Informed consent is required for all patients, also in the control group. Inform consents are obtained by nursing home physicians, who are in charge of enrolment. In the case of persons incapable of giving informed consent according to the investigator (such as patients with dementia), consent will be sought from a legal representative.

If a patient wishes to discontinue his/her participation in the study, it is the responsibility of the investigator to ensure that no further data regarding the person's health condition shall be collected. All collected data will be used in the final analysis.

All data collected, handled and stored for the purpose of this study will be kept confidential at any time and will be securely stored, as required in GCP guidelines and in current privacy legislation. All data will be gathered anonymously and handled by the project team in charge of analysis and management.

The Promoter of the study is the University Hospital of Parma, which therefore maintains ownership of data. The Research and Innovation Unit of the University Hospital of Parma is responsible for data management and statistical analysis. Findings will be published under the responsibility of the study's promoter. Authorship will be determined in compliance with International Committee of Medical Journal Editors (ICMJE) recommendations.

Contributors

A.N., B.P., S.L., P.M., E.B., M.F. and T.M. conceptualised the project and designed the intervention. F.D., A.T., P.S., F.P., B.S. and C.C. provided relevant contributions for study conception and design. E.I. gave statistical consult. A.N., C.C., F.D. and A.T. drafted the manuscript. All the authors read and approved the final manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

Patient consent

Not required.

Ethics approval

The study was approved by the competent Ethics Committee (Comitato Etico Area Vasta Emilia Nord), under the ID 846/20197OSS/AOUPR.

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TABLE 1

Overview of possible expected clinical situations for which a Multidisciplinary Mobile Unit consultation may be activated, and possible management.

Clinical situation	Clinical question	Mobile Unit Intervention	Disposition
Dyspnea of unknown origin	Pulmonary? Cardiac? Embolism? Other causes?	Chest and Abdomen Ultrasound. Arterial Gas sample, ECG, intravenous antibiotic administration	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Abdominal pain	Gallbladder stones? Cholecystitis? Renal colic? Diverticular disease? Urinary retention? Faecal impaction? Peritonitis? Ascites? Acute/subacute Hernia?	Abdomen ultrasound, basic blood tests, intravenous antibiotic administration	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Hematuria	UTI? Catheter dysfunction? Bladder polyps? Stones?	Abdomen ultrasound, Bladder lavage, Catheter (re-)positioning, Intravenous antibiotic administration	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Psychomotor agitation in previously stable dementia	Inadequate therapy? Emerging internistic problem? Other	CGA, Neurogeriatric visit, exclusion of internistic emerging problem, ECG, Thoracic&abdominal US	Appropriate diagnosis and treatment on site.
Fever	Origin?	Thoracic&abdominal US, basic blood test	Excluding common differential diagnosis
Absence of peripheral veins for drugs or nutrients infusion	How to find adequate venous access	US guided Central venous catheter or PICC or peripheral access	Securing patient
Monolateral leg edema	DVT? Erysipelas? Trauma?	Venous and soft tissues ultrasound	Appropriate diagnosis and treatment on site.
Terminal illness	Palliation strategy? How to get symptoms relief?	CGA. Multidisciplinary assessment. Positioning of drains (eg abdominal drainage for ascites). Interview with relatives / caregivers and GP for sharing strategies	Appropriate management.
Ultrasound exam in a patient who can be transported with difficulty	GP's question	Abdominal, cardiac, arterial, thyroid, neck ultrasound	Appropriate assessment

ECG = Electrocardiogram; UTI = Urinary Tract Infection; CGA = Comprehensive Geriatric Assessment; US = Ultrasound; PICC = Peripherally-Inserted Central Venous Catheter; DVT = Deep Vein Thrombosis; GP = General Practitioner.

Figure 1. Description of the intervention of MMU Team

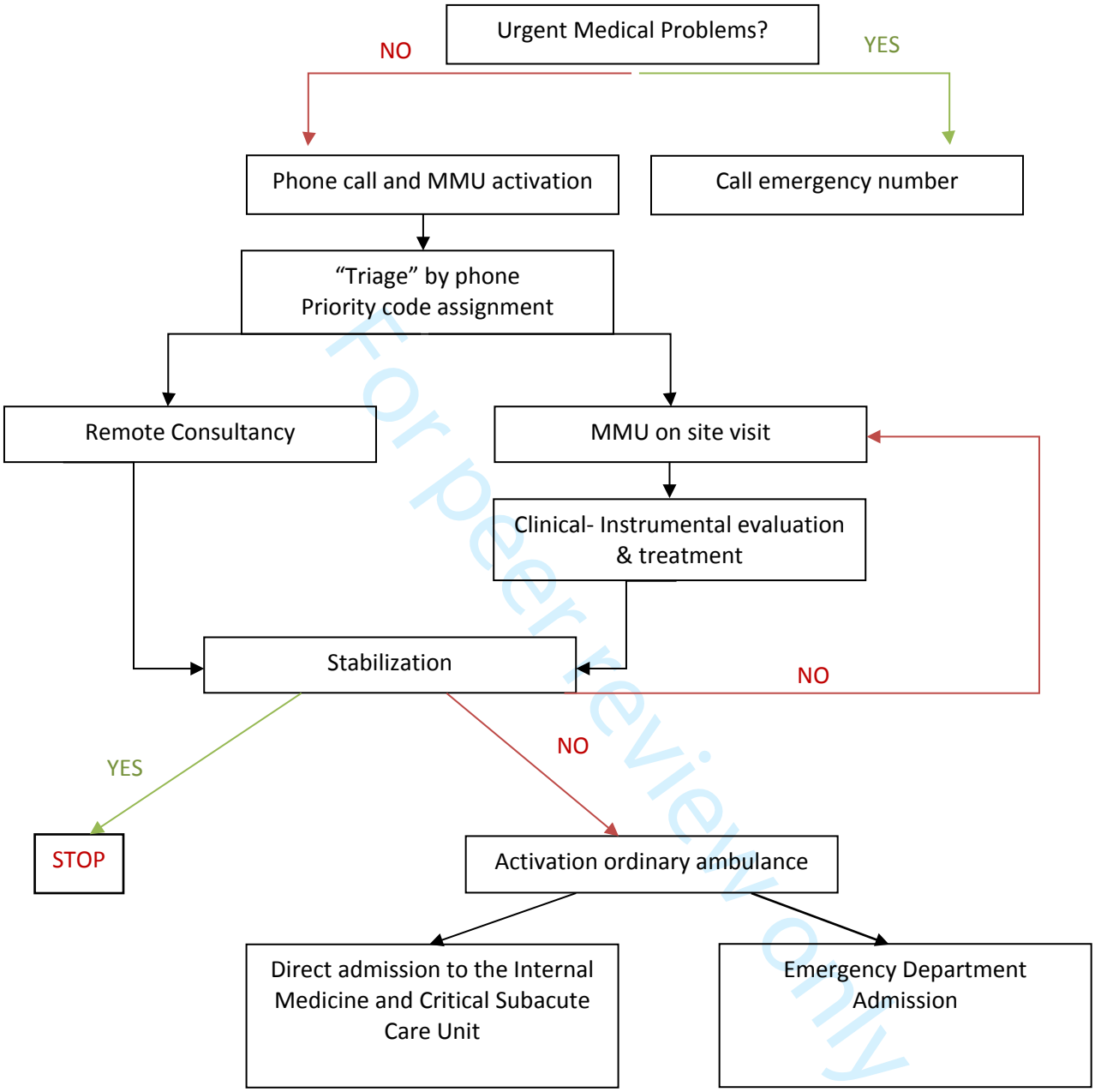
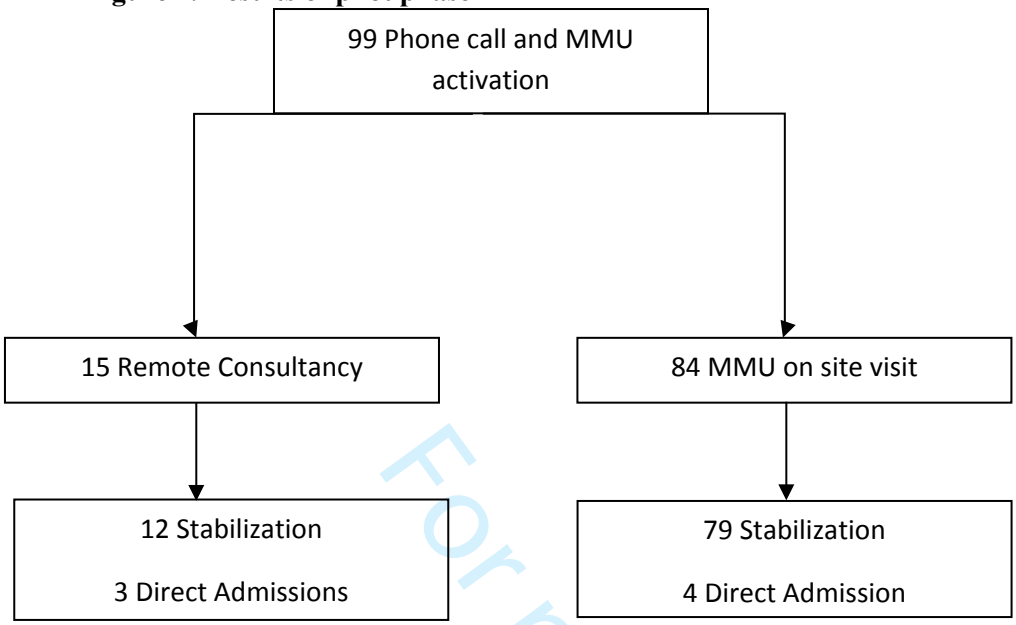
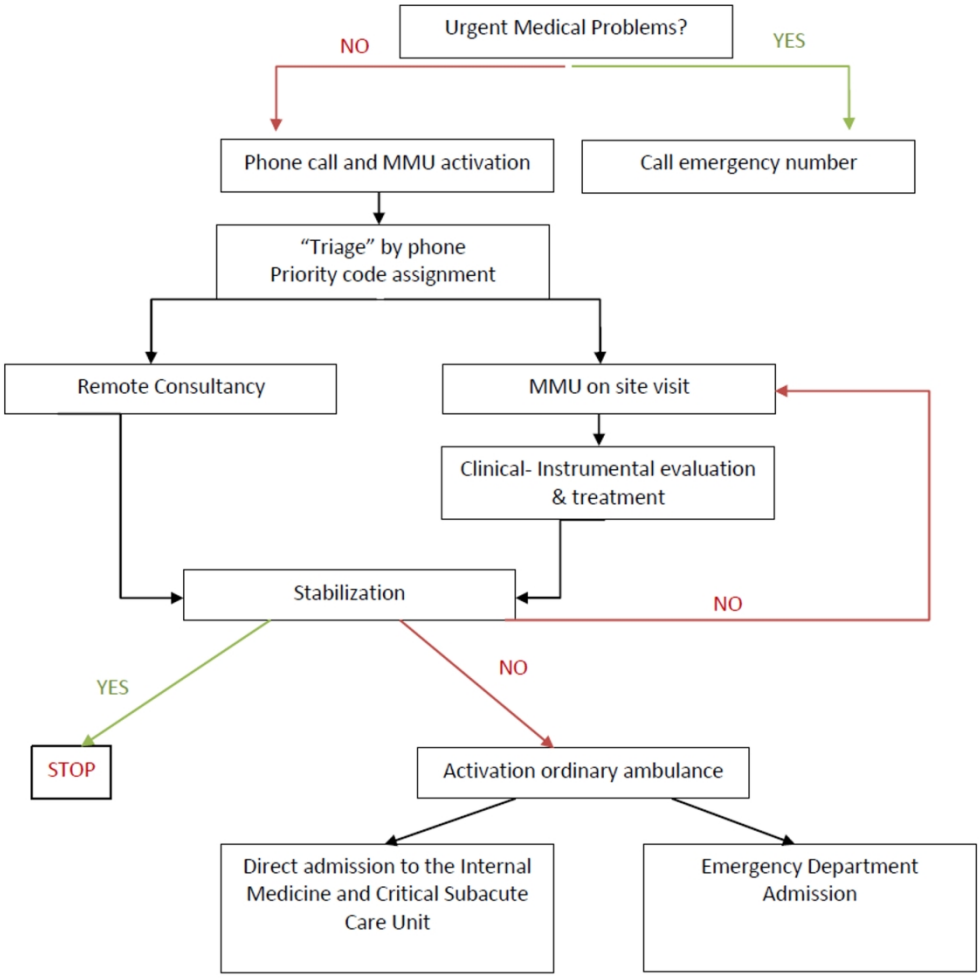


Figure 2. Results of pilot phase





Description of the intervention of MMU Team

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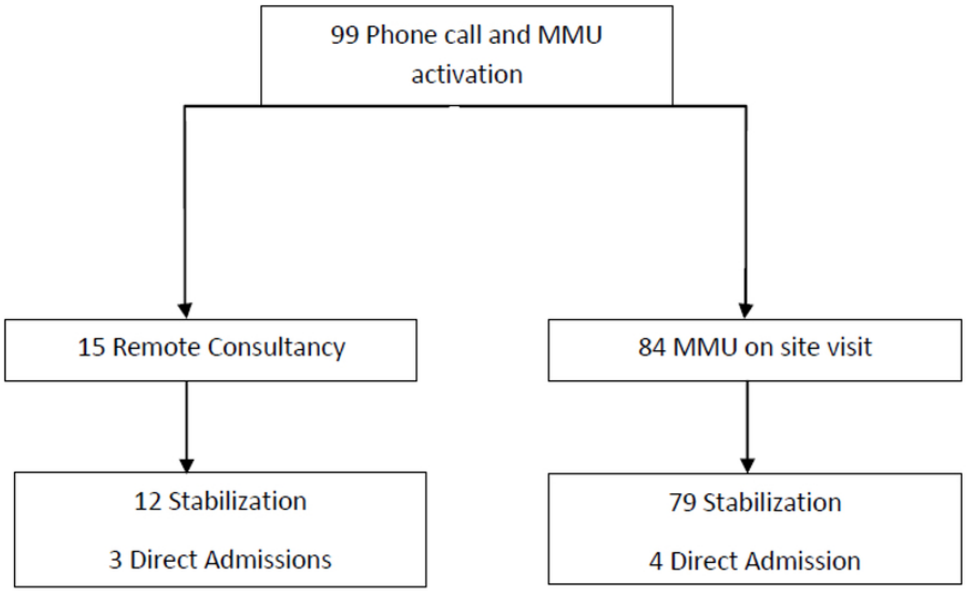

Results fo the pilot phase

76x44mm (300 x 300 DPI)

MMU-1 STUDY PROTOCOL

Implementation of a strategy to prevent hospital admission in nursing home residents: protocol of a quasi-experimental study

Promoter: Azienda Ospedaliero-Universitaria di Parma

Principal Investigator: Prof. Tiziana Meschi, U.O.C. Medicina Interna e Lungodegenza Critica, Dipartimento Medico-Geriatrico-Riabilitativo, Azienda Ospedaliero-Universitaria di Parma

Protocol ID: MMU-1

Version: n.2 of 2/10/2019

ClinicalTrials.org ID: NCT 04085679

BACKGROUND

The increasing clinical complexity of older medical patients in industrialized countries, due to multimorbidity, polypharmacy, frailty, disability and social hardship, is challenging for health care systems [Corazza 2019, Mannucci 2018]. Firstly, these patients are often admitted to Emergency Departments (EDs), accounting for 12 to 24% of all ED visits [Samaras 2010]. However, their complex needs are often poorly met in this setting, where the busy, overcrowded environment does not always allow a careful evaluation of the multi-faceted clinical problems of elderly patients [Aminzadeh 2002, Salvi 2007, Jay 2017]. These difficulties not only contribute to ED overcrowding, but they may also lead to inaccurate diagnoses and unrecognized or untreated health problems [Limpawattana 2016]. Older patients furthermore have an up to 5-times-higher risk of ward admission, irrespective of the severity of the clinical problem [Samaras 2010, Salvi 2007, Roberts 2008]. Once admitted, they are far more likely to stay in hospital for more than two weeks [Jay 2017] and are at much greater risk of experiencing complications related to hospital admission [Buurman 2012].

These issues are especially relevant for residents of nursing homes, who exhibit a particularly high risk of hospitalization (greater than 20% per year [Wyman 2010] and are at high risk of complications during hospitalization, due to frailty, multimorbidity and the possible presence of cognitive impairment.

In the light of these considerations, a number of approaches have been developed designed to reduce the risk of hospitalization in nursing home residents. These are summarized in the very recent systematic review by Santosaputri et al [Santosaputri 2019], which includes quantitative comparative studies of all designs aiming to determine the efficacy of interventions provided by a health professional specializing in geriatric medicine. 16 studies were eligible, of which 6 randomized controlled trials, involving an estimated total of over 7400 patients. The authors of the review categorized 14 intervention programs into three primary approaches (two did not fit in any category):

- Prevention approach (nine studies): Interventions applied in the nursing home to prevent hospitalization of residents, in most cases involving care provided by nurses, physicians, and sometimes allied health personnel. The majority of interventions involved either direct review of patients, telephone (or telemedicine) support, or comprehensive geriatric assessment.
- Emergency department-based hospital avoidance (three studies): interventions targeting nursing home residents presenting to the ED to facilitate early discharge and avoid hospitalization. Programs of this type involved care provided by nursing staff (e.g. intravenous therapy, wound care, catheter management).
- Post-hospital supported discharge (two studies): Interventions designed to support residents following hospital admission. One of the studies evaluated the efficacy of geriatrician and nurse review in the facility and the development of a comprehensive tailored care plan following hospital admission; the other assessed the efficacy of a tailor-made intervention compared to a standardized rehabilitation program following admission due to hip fracture.

Although the majority of the studies reported reductions in hospitalizations (in the form of either ED presentations or hospital admissions), only six obtained statistically significant findings, of which none were RCTs. Unfortunately, the quality of evidence was considered low to moderate, therefore the authors emphasize the need for further, well-designed studies to identify which interventions are effective in reducing hospitalization in the older residents.

At our institution, for many years different projects have been carried out to improve care of the elderly, primarily targeting hospital organization, with the main objective to reduce unnecessary, avoidable length of stay (LOS) [Meschi 2012, Caminiti 2013, Meschi 2016]. These efforts benefit in-hospital patients, but are not designed to prevent hospitalizations. Based on literature evidence, and drawing on our long-time experience with elderly care, we hypothesize that a complex intervention delivered in nursing homes, where vulnerable high-risk patients live, involving direct patient care by hospital medical staff with geriatric expertise, may reduce hospitalization of residents.

METHODS

The study is based in the University Hospital of Parma, which has a catchment area of more than 400,000 inhabitants, of whom 22.3% is over 65 years old. It provides the only Emergency service of the district, and it ranks fourth in Italy by number of ED visits (yearly average of over 110,000). The average admission rate of the adult ED population is 18%, of which 65% concern people older than 65.

In the last two decades, the University Hospital of Parma has implemented several innovative initiatives to manage the hospital flow of frail multimorbid patients and their complex needs. These initiatives included bed management to avoid "bed-blockers" [Meschi 2012], physician accountability for the discharge process [Caminiti 2013], and creation of a dedicated hospital unit, organized by intensity of care to anticipate the needs of these patients preserving high performance indices [Meschi 2016]. This unit, called Internal Medicine and Critical Subacute Care Unit, performs over 3,500 urgent admissions of frail multimorbid elderly patients per year, with an average length of stay that in 30% of cases is lower than 3 days [Meschi 2016].

Participating nursing homes are public facilities which ensure the presence of nursing staff 24 hours a day and of a physician at least 4 hours a day (high-intensity care facilities). The possible role of distance to the hospital is considered by including in each group one nursing home located next to the hospital and one located >5 km of distance.

The participating nursing homes are the following:

- C.R.A. "I Tigli" C/O Comprensorio di Villa Parma, Piazzale Fiume 5, Parma (intervention group)
- C.R.A. "Casa degli Anziani", Via Aldo Moro 2, Collecchio (intervention group)
- C.R.A. "Le Tamerici" C/O Comprensorio di Villa Parma, Piazzale Fiume 5, Parma (control group)
- C.R.A. "Ines Ubaldi", Via Ravenna 4, Parma (control group)

This study follows a multimethod approach, based on the MRC framework for developing and evaluating complex interventions [Craig 2008], including the development, feasibility assessment, and evaluation phases.

1. *Development of the intervention*

First, the different types of approaches reported in the literature, described above, were considered. The "prevention approach", interventions conducted in nursing homes, was chosen as the most suitable strategy to integrate the hospital's organizational model already in place, as it can target both hospitalization rates and ED overcrowding, allowing to intervene before the person accesses the hospital.

Available evidence also prompted us to opt for a multicomponent approach. In fact, data from qualitative interviews reveal that the decision to transfer residents to hospital may be influenced by different factors, such as staffing and skill mix in the nursing homes, treatment options available in the facility, end-of-life decision-making, and communication and bureaucratic requirements. This multifactorial association means that a multicomponent intervention is likely to be more effective than a single-component intervention [Arendts 2010].

The choice of employing a mobile geriatric specialist service was supported by the positive results obtained by the two controlled studies which examined similar interventions [Schippinger 2012, Dìaz-Gegùndez 2011]. Schippinger et al [Schippinger 2012] evaluated a service where a physician did regular and on-call visits intended to provide services otherwise associated with hospitalization. Dìaz-Gegùndez et al [Dìaz-Gegùndez 2011] evaluated an ambulant team with a nurse and a physician, doing comprehensive geriatric assessments of residents as well as reviewing medications and providing support to staff. Our intervention does not involve a nurse, unlike the Dìaz-Gegùndez study, because in the participating facilities nursing staff is available 24 hours a day. Unlike the experience of Schippinger et al, moreover, we chose not to perform periodic visits on site, since routine clinical management and scheduled follow-up is already performed by nursing home physicians.

Finally, medical hospital staff was preferred to community geriatricians, on the assumption that older patients may feel more comfortable being handled by physicians who may have already cared for them at the hospital. Moreover,

hospital staff enables direct patient referral to the ward. Finally, this allows the use of diagnostic technologies available at the hospital, which can be used immediately without the need for hospital admission.

The MMU care model intervention

The model hinges on the strong collaboration between hospital and nursing home staff to provide residents with patient-centered care. It entails a multicomponent intervention which is integrated in standard care and comprises three steps: 1) MMU team activation, 2) on site visit by a team of physicians with geriatric expertise, 3) interdisciplinary care planning (Figure 1).

Step 1: MMU team activation

Patient selection is necessary to ensure that available resources are used for patients who may really benefit. To this end, the nursing home physician contacts by phone the "flow manager", a skilled internist with strong clinical expertise, organizational attitude and managerial training, during the 8 a.m.-6 p.m. time frame, Monday to Friday. The phone consultation is reported on a form containing the description of the patient's clinical condition and a summary of the conversation. The form also indicates which decision was reached among the following 6 not mutually exclusive options:

a) The patient can be managed by nursing home staff, therapeutic advice is provided by phone
b) Remote reassessment is scheduled after a number of hours agreed upon by the team
c) The MMU team is dispatched for evaluation, treatment and stabilization on site
d) A significant change in vital parameters is observed which requires immediate activation of emergency services
e) Direct hospital admission is considered necessary
f) Ambulatory outpatient visits or tests are planned

Step 2: on site visit by a team of physicians with geriatric expertise

Visits at the nursing home are performed by two members of the MMU team: an expert hospital physician chosen on a case-by-case basis among the clinical staff of the Internal Medicine and Critical Subacute Care Unit, which comprises internists, gastroenterologists, geriatricians, specialists in clinical nutrition, depending on the disease or clinical problem that must be treated, and a specifically trained resident in Emergency Medicine.

The team is provided with a car to reach the nursing homes, a portable ultrasound system, and an essential set of drugs and medical devices useful in an emergency setting. The ultrasound system is equipped with three probes (convex, linear, and phased-array) for performing thoraco-pulmonary, cardiac, vascular, abdominal and soft tissue ultrasound, when required. Available drugs include those that can be administered intravenously for treating urgent conditions (e.g. loop diuretics, steroids, fluids, antibiotics). Devices include central and peripheral venous lines, naso-gastric and rectal tubes and bladder catheters. Blood tests can also be performed.

Table 1 shows possible clinical scenarios which may require MMU team activation, and possible decisions.

Step 3: interdisciplinary care planning

Based on the results of the visit and of any performed investigations, the MMU team formulates personalized advice and referrals, and discusses these with the nursing home physician. If stabilization on site is not deemed possible, the MMU team plans a direct admission to the Internal Medicine and Critical Subacute Care Unit, thus avoiding ED access. The planning and the final outcome of the intervention are recorded in the second part of the form.

2. *Feasibility assessment*

A pilot phase of 5 months (December 2018-April 2019) was conducted in two nursing homes in order to look at feasibility of the MMU care Model described above. Before the intervention was introduced, meetings were held with nursing home staff to agree on activation modalities.

In this period, 99 phone calls were received, of which 84 required MMU team onsite visits, and 15 were managed with remote consultancy. Of the latter, 3 required direct admission after remote phone consultancy. Only 4 of the 84 patients visited onsite required direct admission. One patient was sent to the ED for massive intestinal bleeding (Figure 2).

This phase demonstrated the feasibility of the intervention, and did not highlight any need for modifications.

3. *Evaluation phase*

Aim and objectives

The study aim is to verify the effects of the implementation of the MMU care model tested in the pilot phase.

Primary objective is to verify reduction of unplanned hospitalization rates in the nursing homes of the intervention group compared to the nursing homes in the control group. Secondary objectives are to measure the effects of the intervention in terms of mortality, health service use, and costs.

Study Design

This study is a prospective, pragmatic, multicenter, quasi-experimental study (sequential design with two cohorts), in which usual nursing home care is compared to care provided by applying the MMU model.

Study Population

All residents of the participating nursing homes are eligible, regardless of their clinical status. Residents who do not provide informed consent will be excluded.

Usual Care

Patients in the control cohort receive usual care, which means the actions to take are decided by the nursing home staff. Generally, this implies that patients who are clinically unstable, or require urgent instrumental tests, will be sent to the ED.

Measures

Baseline variables

Demographic data on gender and age are collected by chart review.

Outcome variables

The primary outcome is hospitalization rate, considering at the numerator all unplanned admissions occurred during a 1-year period, and at the denominator the sum of the person-time of the at risk population (days of stay at the nursing home). For the intervention group, the numerator corresponds to options d) and e) defined in "Step 1: MMU team activation".

Secondary outcomes*:*

- Crude all-cause Death Rate (CDR): the number of deaths *during a* 1-year period on person-time of the at risk population
- Hospital Mortality rate: the frequency of patients who die while in the hospital (death rate/1000)

- Length of stay (LOS): the duration of a single episode of hospitalization. Inpatient days are calculated by subtracting day of admission from day of discharge.
- Adverse events or complications: frequency of events occurred within 48 hours from MMU team activation and subsequent patient stabilization, for which hospital access becomes necessary.
- Costs analysis, comparing the cost differences in the two groups

Data Collection

Patient demographic and clinical characteristics are collected at baseline to describe the study population and determine factors associated with hospital rate. Participants' files and electronic data are stored securely at the study site (e.g. locked area, password protected hard- and software). Data integrity will be scrutinized with several strategies (e.g. valid values, range checks, consistency checks). Patient data are only identifiable with the unique participant's number. Personal information will be collected and saved in a separate file (on a different server) which can only be accessed by the Principal Investigator (PI). This information will be used by the PI to retrieve data on any hospital admissions (length of stay, in-hospital death …) from administrative databases (discharge summaries, ED data, Death Registry). Residents' identification data will be deleted once the study is completed, making the dataset anonymous. All study protocol authors will have access to the anonymous dataset.

Cost analysis

We will identify the changes in net costs associated with one-year exposure to the intervention, consisting in the induced costs due to incremental resource inputs for carrying out the intervention and hospital health service utilization costs. Staffing costs will be calculated considering the time spent by the professionals involved in the intervention. Non-staff running costs include expenses of MMU staff travelling to and from the nursing home. The health service utilization costs will be identified based on the Diagnosis Related Group (DRG) system.

Statistical Methodology

Sample size calculation

The number of subjects to include was estimated using the findings of Diaz-Gegundez et al [Diaz 2011], who performed a large quasi-experimental trial. Thus, considering 56 cases vs 32 cases per 100 residents, and using a 2-sided, large-samples z-test of the Poisson incidence rate difference at a significance level of 0.05, and with a power of 0.90, overall 338 residents should be enrolled.

Statistical analysis

Descriptive statistics will be used to summarize patient populations and will be presented as means and standard deviations (SD) when normally distributed, or as medians and interquartile ranges (IQR).

For the primary analysis we will used Poisson regression with robust standard errors (SEs) to evaluate relative differences in hospital rates among our two cohorts while adjusting for demographic characteristics.

Concerning the secondary outcomes, the following analyses will be performed:

- Rates will be compared considering the quotient between the intervention and control groups
- A lognormal model will be used to compare in-hospital LOS.
- Chi square tests will be conducted for categorical data as adverse events or complications
- For costs, we will use the following equations to summarize the annual net costs associated with the implementation of the intervention. Any costs with negative values mean "savings" and any costs with positive values mean "losses". Net costs ˆ A…(intervention costs) +‡ B (Costs for differences in hospital health service utilization) where: A= intervention: staffing costs+intervention: non- staff costs and B= Costs

for differences in inpatient care utilization. Therefore, the net costs arising from one-year implementation of the intervention as compared with the current practice will be obtained, where a negative value of net costs represents "cost-saving" and a positive value represents "not cost-saving"

The demographic and clinical variables which influence the outcome with a p value<0.20 in the univariate analysis will be included in the Poisson regression model.
The analyses will be performed using SAS 8.2 (SAS Institute, Cary, NC, USA) and STATA-SE 11 (Stata Corp LP, College Station, TX, USA).

Data monitoring

Since this is a non-profit study promoted by the University Hospital of Parma, study monitoring is in charge of trained staff of the hospital's Research and Innovation Unit, as set forth in current legislation (Ministerial Decrees 211/2003 and 15/11/2011).

Ethical and regulatory aspects

The study will be conducted in compliance with the principles of the revision of the Helsinki Declaration and by current legislation on scientific research.
The protocol and the patient informed consent form will be submitted to the competent Ethics Committee for approval, in accordance with Italian current norms. The study will be initiated prior authorization from the legal representative of the center in which it is conducted.

Informed consent

This study does not entail any experimental pharmacological treatment, or changes in the diagnostic-therapeutic pathway. Eligible patients will be asked to give consent to handling of their personal data in writing. The consent form will be dated and signed by the patient and by the investigator, authorized according to norms of the local Ethics Committee.
A copy of the signed informed consent form shall be given to the patient, and the original shall be retained by the investigator as part of the study documentation. Informed consent is required for all patients, also in the control group. Inform consents are obtained by nursing home physicians, who are in charge of enrolment. In the case of persons incapable of giving informed consent according to the investigator (such as patients with dementia), consent will be sought from a legal representative.
If a patient wishes to discontinue his/her participation in the study, it is the responsibility of the investigator to ensure that no further data regarding the person's health condition shall be collected. All collected data will be used in the final analysis.

Confidentiality

All data collected, handled and stored for the purpose of this study will be kept confidential at any time and will be securely stored, as required in GCP guidelines and in current privacy legislation. All data will be gathered anonymously and handled by the project team in charge of analysis and management.

Patients will only be identifiable by the clinical staff of the center where the patient was recruited. All data collected anonymously will be checked and analyzed at the Research and Innovation Unit of the University Hospital of Parma, responsible for the analysis and correct keeping of the archive.

Study organization and responsibilities

Scientific Committee (SC)

It performs overall study supervision and strategic control through periodic meetings, in which the coordination team informs the Committee on the project's progress, on any observed problems, and on possible solutions. It is responsible to decide whether a process should be halted or modified. It ensures that results are published on peer-reviewed journals within one year after study completion.

Principal Investigator (PI)

The PI is responsible for the protection of patients' rights and for the integrity of the research. The PI must keep an updated list of appropriately qualified professionals, to whom he can delegate important activities relating to the study, and for whom he must provide the necessary training. The PI shall ensure that no deviations from the protocol occur, and that the protocol is not modified in any way without prior documented Ethics Committee review and approval. Before study initiation, the PI must obtain authorization from the Managing Director of the University Hospital of Parma to conduct the trial in compliance with the protocol.

The PI must guarantee precision, completeness, readability and timeliness of data reported in the collection forms (CRFs) and in all required reports. Data reported in the eCRF, retrieved from original documents, must agree with those indicated in the reports; any discrepancies shall be verified and explained.

The PI will prepare a folder (Investigator's File, IF) containing: all study documentation approved by the Ethics Committee, including amendments and minutes, signed agreements, curricula vitae of the PI and other investigators/delegates, register of enrolled subjects, list of subject identification codes.

The PI is responsible for the retention of documents essential to the conduction of the clinical trial in the Investigator's Study File, for the time required by relevant legislation, and must adopt all necessary measures to prevent the accidental or premature destruction of these documents.

At study completion, the PI shall immediately inform the institutions involved in the trial and the competent Ethics Committee, providing them a detailed report on conduction and results.

Clinical Investigators (CIs)

They are the physicians comprising the MMU and those working in participating nursing homes. The latter perform patient screening and enrolment, and are in charge of the informed consent obtainment process. The informed consent must be acquired and documented in accordance with current applicable norms and must adhere to GCP and ethical principles rooted in the Helsinki Declaration. Patients shall be provided with exhaustive information on all aspects relating to the study, including modalities and duration, and collection of necessary data.

Trial Statistician (TS)

The TS develops the eCRF equipped with automatic checks and tracking of corrections made by the user and user identification, ensuring the presence of strictly necessary variables. The TS conducts statistical analyses required to verify study end points, after checking for data quality (quality assurance and quality control) and after defining the Statistical Analysis Plan (SAP). The TS prepares the tables and graphs needed to summarize and publish results, and contributes to the drafting of the paper, by providing indications concerning analysis interpretation, and the presence of any biases and methodological limitations.

Retaining of original documents

The medical staff of the nursing homes shall retain the original copies of the informed consents, dated and signed by the patient and the physician. MMU medical staff will be responsible for storing the case report forms of each enrolled patient.

Publication policy

The Promoter of the study is the University Hospital of Parma, which therefore maintains ownership of data. The Research and Innovation Unit is responsible for data management and statistical analysis. Findings will be published under the responsibility of the study's SC and prior verification of the Promoter (according to Ministerial Decree 17/12/2004).

Authorship will be determined by unanimous consensus of the SC, in compliance with International Committee of Medical Journal Editors (ICMJE) recommendations, which indicate the following four criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or revising it critically for important intellectual content; AND
3. Final approval of the version to be published; AND
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Individual researchers wishing to perform additional analyses to include in publications or conference presentations shall submit a request to the SC, for evaluation and authorization. A copy of any presentation, manuscript or abstract must be sent to the SC before dissemination.

Protocol modifications

All amendments made to the protocol shall be submitted to the AVEN Ethics Committee. Amendments shall not be implemented without prior ethical approval. Modifications to the protocol which only concern administrative or logistical aspects of the study will need to be communicated to the Ethics Committee. Any violations of the protocol shall be reflected in the data reported in the eCRF and in the original documents, and original documents shall describe such violations, as well as the circumstances that made them necessary.

Study duration

Overall expected duration is 18 months, with study initiation presumably in November 2019 and completion in April 2021.

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TABLE 1

Overview of possible expected clinical situations for which a Multidisciplinary Mobile Unit consultation may be activated, and possible management.

Clinical situation	Clinical question	Mobile Unit Intervention	Disposition
Dyspnea of unknown origin	Pulmonary? Cardiac? Embolism? Other causes?	Chest and Abdomen Ultrasound. Arterial Gas sample, ECG	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Abdominal pain	Gallbladder stones? Cholecystitis? Renal colic? Diverticular disease? Urinary retention? Faecal impaction? Peritonitis? Ascites? Acute/subacute Hernia?	Abdomen ultrasound, basic blood tests	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Hematuria	UTI? Catheter dysfunction? Bladder polyps? Stones?	Abdomen ultrasound, Bladder lavage, Catheter (re-)positioning	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Psychomotor agitation in previously stable dementia	Inadequate therapy? Emerging internistic problem? Other	CGA, Neurogeriatric visit, exclusion of internistic emerging problem, ECG, Thoracic&abdominal US	Appropriate diagnosis and treatment on site.
Fever	Origin?	Thoracic&abdominal US, basic blood test	Excluding common differential diagnosis
Absence of peripheral veins for drugs or nutrients infusion	How to find adequate venous access	US guided Central venous catheter or PICC or peripheral access	Securing patient
Monolateral leg edema	DVT? Erysipelas? Trauma?	Venous and soft tissues ultrasound	Appropriate diagnosis and treatment on site.

Terminal illness	Palliation strategy? How to get symptoms relief?	CGA. Multidisciplinary assessment. Positioning of drains (eg abdominal drainage for ascites). Interview with relatives / caregivers and GP for sharing strategies	Appropriate management.
Ultrasound exam in a patient who can be transported with difficulty	GP's question	Abdominal, cardiac, arterial, thyroid, neck ultrasound	Appropriate assessment

ECG = Electrocardiogram; UTI = Urinary Tract Infection; CGA = Comprehensive Geriatric Assessment; US = Ultrasound; PICC = Peripherally-Inserted Central Venous Catheter; DVT = Deep Vein Thrombosis; GP = General Practitioner.

Figure 1. Description of the intervention of MMU Team

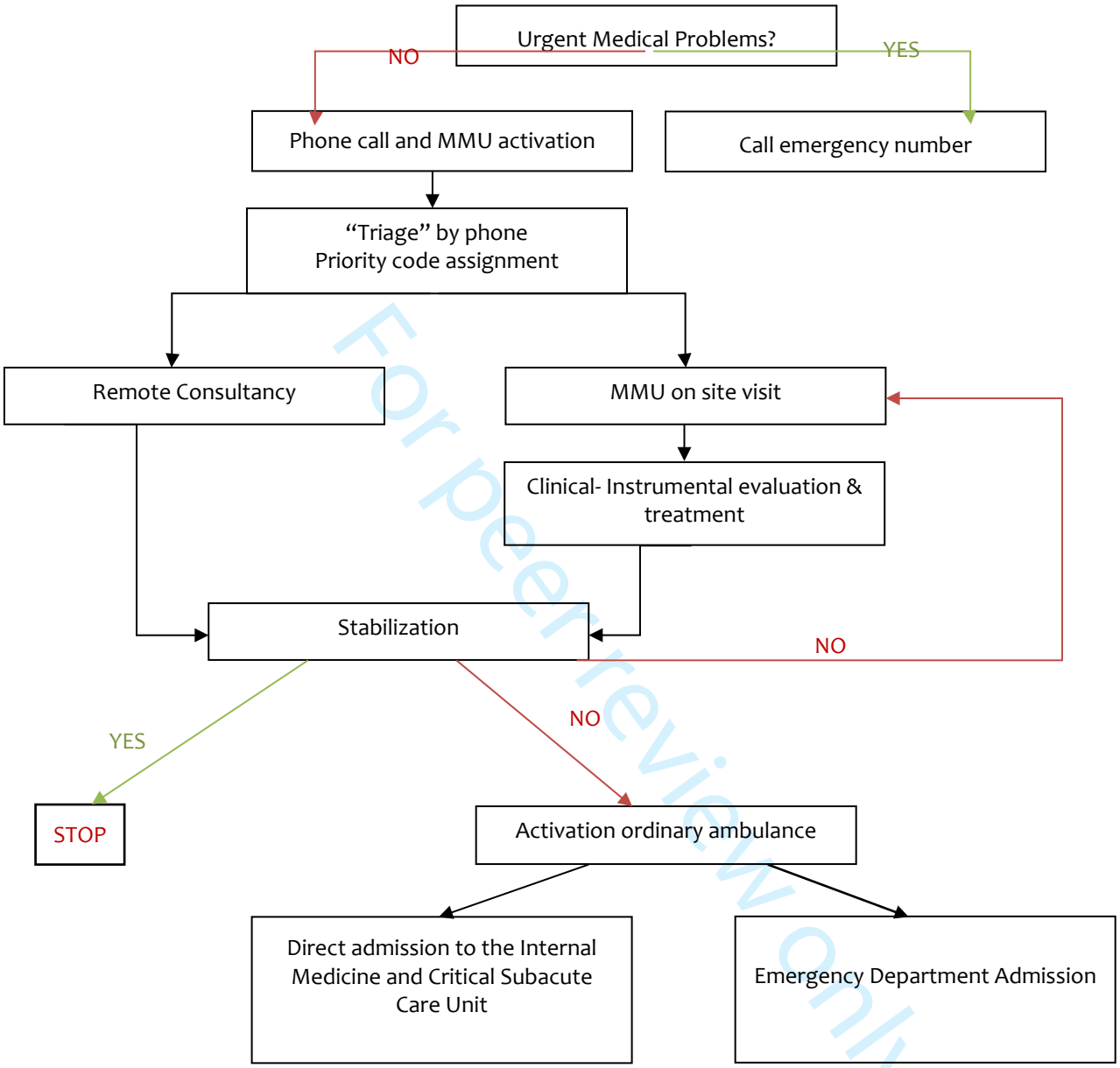
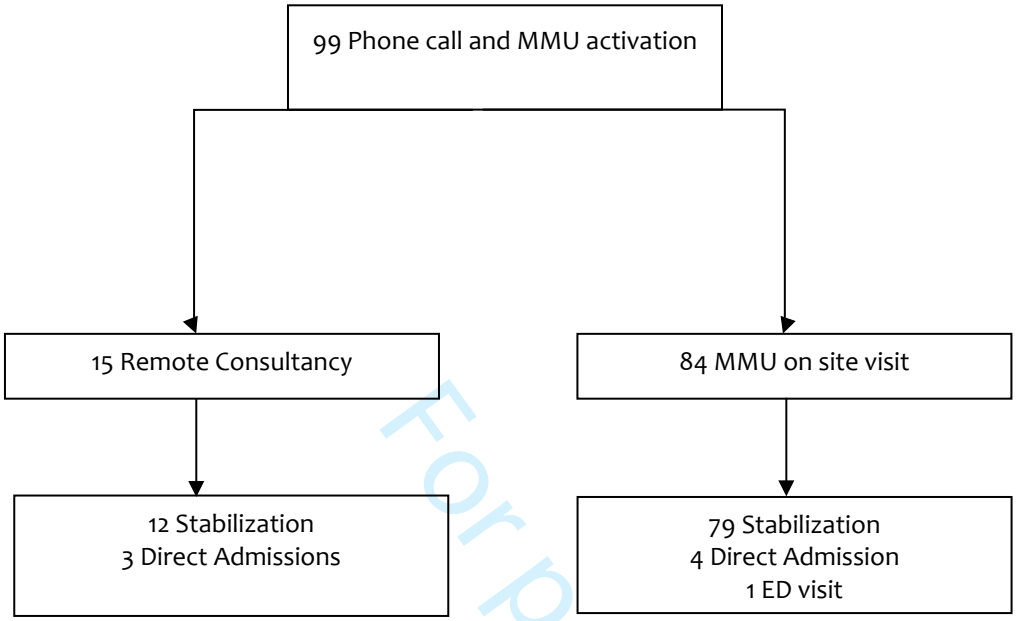


Figure 2. Results of pilot phase



Parma, 25/7/2019

Undersigned,

The Principal Investigator
Prof. Tiziana Meschi

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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		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	2, end of abstract
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	Supplemental Material
Funding	#4	Sources and types of financial, material, and other support	14
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 14
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	N/A (page 14)
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	N/A (page 13)

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)	13
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	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5
Objectives	#7	Specific objectives or hypotheses	6, 9
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)	9-10
Methods:			
Participants,			

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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	6
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)	10
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9, 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)	N/A (complex intervention on organization of care)
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	N/A (the intervention concerns organization of care in nursing homes)

Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7-10
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
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)	11
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	11
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	N/A (all residents in participating nursing homes will be

			eligible for the study)
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	N/A (quasi-experimental study design on organization of care)
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	N/A (quasi-experimental study design on organization of care)
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A (quasi-experimental study design on organization of care)

Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A (quasi-experimental study design on organization of care)
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	N/A (quasi-experimental study design on organization of care)
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	10-11

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	N/A (quasi-experimental study design on organization of care)
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, 13
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	12
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
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)	N/A due to particular study design
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	13
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	13
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	N/A due to particular study design
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A due to particular study design
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	12-13

Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	12-13 + supplemental material
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	12-13 + supplemental material
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	12-13 + supplemental material
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	12-13 + supplemental material
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	14
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	12-13 + supplemental material

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	N/A due to particular study design
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 results databases, or other data sharing arrangements), including any publication restrictions	13 + supplemental material
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	Supplemental material
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Supplemental material
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Supplemental material
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	N/A due to study design

NOTE: The original protocol approved by the competent Ethics Committee (in English language) has been uploaded as Supplemental Material.

BMJ Open

Implementation of a strategy involving a multidisciplinary mobile unit team to prevent hospital admission in nursing home residents: protocol of a quasi-experimental study (MMU-1 Study)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034742.R1
Article Type:	Protocol
Date Submitted by the Author:	20-Dec-2019
Complete List of Authors:	Nouvenne, Antonio; Azienda Ospedaliero-Universitaria di Parma, Geriatric-Rehabilitation Department Caminiti, Caterina; Azienda Ospedaliero-Universitaria di Parma, Research and Innovation Unit Diodati, Francesca; Azienda Ospedaliero-Universitaria di Parma, Research and Innovation Unit Iezzi, Elisa; Azienda Ospedaliero-Universitaria di Parma, Research and Innovation Unit Prati, Beatrice; Azienda Ospedaliero-Universitaria di Parma, Geriatric-Rehabilitation Department Lucertini, Stefano; Azienda Unità Sanitaria Locale di Parma, Primary Care Department Schianchi, Paolo; Azienda Unità Sanitaria Locale di Parma, Primary Care Department Pascale, Federica; Azienda Unità Sanitaria Locale di Parma, Primary Care Department Starcich, Bruno; Azienda Unità Sanitaria Locale di Parma, Primary Care Department Manotti, Pietro; Azienda Ospedaliero-Universitaria di Parma, Medical Direction Brianti, Ettore; Azienda Ospedaliero-Universitaria di Parma, Medical Direction Fabi, Massimo; Azienda Ospedaliero-Universitaria di Parma, General Manager Ticinesi, Andrea; Azienda Ospedaliero-Universitaria di Parma, Geriatric-Rehabilitation Department Meschi, Tiziana; Azienda Ospedaliero-Universitaria di Parma, Geriatric-Rehabilitation Department; Università degli studi di Parma, Department of Medicine and Surgery
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	General practice / Family practice, Emergency medicine
Keywords:	Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, GERIATRIC MEDICINE

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Implementation of a strategy involving a multidisciplinary mobile unit team to prevent hospital admission in nursing home residents: protocol of a quasi-experimental study (MMU-1 Study)

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Word count: 3700

Abstract: 299; **Tables**: 1; **Figures**: 2; **References**: 30

Running Title: Multidisciplinary mobile unit intervention for nursing homes

ABSTRACT

Introduction- Nursing home residents represent a particularly vulnerable population experiencing high risk of unplanned hospital admissions, but few interventions have proved effective in reducing this risk. The aim of this research will be to verify the effects of a hospital-based multidisciplinary mobile unit (MMU) team intervention delivering urgent care to nursing home residents directly at their bedside.

Methods and analysis- Four nursing homes based in the Parma province, in Northern Italy, will be involved in this prospective, pragmatic, multicenter, 18-month quasi-experimental study (sequential design with two cohorts). The residents of two nursing homes will receive the MMU team care intervention. In case of urgent care needs, the nursing home physician will contact the hospital physician responsible for the MMU team by phone. The case will be triaged as a) manageable by phone advice, b) requiring urgent assessment by the MMU team or c) requiring immediate ED referral. MMU team is composed of one senior physician and one Emergency-Medicine resident chosen within the staff of Internal Medicine and Critical Subacute Care Unit of Parma University-Hospital, usually with different specialty background, and equipped with portable ultrasound, set of drugs and devices useful in urgency. The MMU visits patients in nursing homes, with the mission to stabilize clinical conditions and avoid hospital admission. Residents of the other two nursing homes will receive usual care, i.e. ED referral in every case of urgency. Study endpoints include unplanned hospital admissions (primary), crude all-cause mortality, hospital mortality, length of stay and healthcare-related costs (secondary).

Ethics and dissemination- The study protocol was approved by the Ethics Committee of Area Vasta Emilia Nord. Informed consent will be collected from patients or their legal representatives. The results will be actively disseminated through peer-reviewed journals and conference presentations, in compliance with the Italian law.

Registration ID- ClinicalTrials.gov NCT 04085679

Key words: multimorbidity; geriatrics; hospitalization; multidisciplinary care; hospital-community partnership

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ✓ This study will explore the effectiveness of a complex intervention focused on the avoidance of hospital admissions for nursing home residents, with a strong hospital-community partnership.
- ✓ The study intervention consists in bringing specialist hospital care directly at the bedside of nursing home residents, an innovative approach not previously described in the scientific literature.
- ✓ The intervention has been developed considering the organization of the Italian healthcare system, but is reproducible and applicable in other settings.
- ✓ Due to ethical concerns and the complex nature of the intervention, randomization of participants is not possible.

INTRODUCTION

The increasing clinical complexity of older medical patients, due to multimorbidity, polypharmacy, frailty, disability and social hardship, is challenging for health care systems.[1 2] These characteristics are emphasized in nursing home residents, who experience a particularly high risk of Emergency Department (ED) visits and hospitalization (greater than 20% per year).[3-8] In the ED, these patients may experience misdiagnoses and undertreatment, due to their clinical complexity and atypical presentation of acute illness, and substantially contribute to the overcrowding phenomenon.[4 5 9-11] Once admitted to wards, they are also far more likely to have long stays (>2 weeks)[9] and experience hospital-related complications.[12]

In the light of these considerations, confirmed by large cohort studies conducted in the United States and Canada,[7 8] a number of approaches have been developed designed to reduce the risk of hospitalization in nursing home residents. These are summarized in the recent systematic review by Santosaputri et al,[13] which includes quantitative comparative studies of all designs aiming to determine the efficacy of interventions provided by a health professional with specialization in geriatric medicine. Sixteen studies were eligible, of which 6 randomized controlled trials, involving an estimated total of over 7400 patients. The authors of the review categorized 14 intervention programs into three primary approaches (two did not fit in any category):

- Prevention approach (nine studies): Interventions applied in the nursing home to prevent hospitalization of residents, in most cases involving care provided by nurses, physicians, and sometimes allied health personnel. The majority of interventions involved either direct review of patients, telephone (or telemedicine) support, or comprehensive geriatric assessment.
- Emergency department-based hospital avoidance (three studies): interventions targeting nursing home residents presenting to the ED to facilitate early discharge and avoid hospitalization. Programs of this type involved care provided by nursing staff (e.g. intravenous therapy, wound care, catheter management).
- Post-hospital supported discharge (two studies): Interventions designed to support residents in the care transition from the hospital to nursing home, to prevent readmissions, including geriatrician and nurse review in the facility and standardized rehabilitation programs.

Although the majority of the studies reported reductions in hospitalizations (in the form of either ED presentations or hospital admissions), only six, with different designs and interventions, obtained statistically significant findings.[14-19] Two of these studies, with a retrospective design, involved delivery of routine care to

nursing home residents by hospital-based nursing staff, with the possibility of obtaining support from a geriatrician in case of urgent situations.[14-15] In another prospective quasi-experimental study, a team including a geriatrician and specialized nurses supported the nursing home physician in delivering routine care and in managing urgent clinical situations.[16] The remaining three studies, all with prospective quasi-experimental design, were more focused on selected clinical scenarios, involving advice and education by ED staff to nursing home personnel after ED admission of residents,[17] hospital nurse visits in the nursing home to implement strategies of delirium prevention,[18] and rehabilitation intervention delivered by a geriatric orthopedic team to residents with hip fracture.[19]

Unfortunately, the quality of evidence was considered low to moderate, therefore further, well-designed studies are needed to identify which interventions are effective in reducing hospitalization in the older residents.[13] The interventions performed in the existing studies were also mainly focused on routine care, while a prompt and correct management of urgent situations and acute/subacute conditions may be of paramount importance for avoiding ED admissions in nursing home residents. Namely, interventions delivering urgent care with a multidisciplinary approach, based not only on geriatric expertise but also on the capacity of performing first line diagnostic examinations, such as ultrasonography, and basic invasive procedures, such as central venous line or nasogastric tube insertion, have a great potential of being successful in reducing ED visits, but have not been adequately investigated to date.

At our institution, different projects have been carried out for many years to improve care of the elderly, primarily targeting hospital organization, with the main objective to reduce unnecessary, avoidable length of stay (LOS).[20-22] These efforts benefit in-hospital patients, but are not designed to prevent hospitalizations. In this framework, based on literature evidence, best current knowledge and long-time experience with elderly care developed at our university-hospital, we hypothesize that a complex intervention delivered in nursing homes, where vulnerable high-risk patients live, involving direct patient care by hospital medical staff with multidisciplinary approach grounded on geriatric expertise, may reduce hospitalization of residents.

METHODS AND ANALYSIS

Study setting

The study is based in the University Hospital of Parma, which has a catchment area of more than 400,000 inhabitants, of whom 22.3% is over 65 years old. It provides the only Emergency service of the district, and it

ranks fourth in Italy by number of ED visits (yearly average of over 110,000). The average admission rate of the adult ED population is 18%, of which 65% concern people older than 65.

In the last two decades, the University Hospital of Parma has implemented several innovative initiatives to manage the hospital flow of frail multimorbid patients and their complex needs. These initiatives included bed management to avoid "bed-blockers",[20] physician accountability for the discharge process,[21] and creation of a dedicated hospital unit, organized by intensity of care to anticipate the needs of these patients preserving high performance indices.[22] The MMU team will be based in this unit, called Internal Medicine and Critical Subacute Care.

Nursing homes participating in the study are public facilities of similar size (90-100 residents) which ensure the presence of nursing staff 24 hours a day and of a physician at least 4 hours a day (high-intensity care facilities), in compliance with the care standards set by the Local Health Authority. No staff member is shared among the participating nursing homes. The possible role of distance to the hospital is considered by including in each group one nursing home located next to the hospital and one located at a distance of >5 km.

The participating nursing homes are the following CRAs (Casa Residenza Anziani):

- C.R.A. "I Tigli" Parma (intervention group)
- C.R.A. "Casa degli Anziani", Collecchio (intervention group)
- C.R.A. "Le Tamerici" Parma (control group)
- C.R.A. "Ines Ubaldi", Parma (control group)

This study follows a multimethod approach, based on the Medical Research Council framework for developing and evaluating complex interventions,[23] including the development, feasibility assessment, and evaluation phases.

Development of the intervention

First, the different types of approaches reported in the literature, described above, were considered.[13] The "prevention approach", interventions conducted in nursing homes, was chosen as the most suitable strategy to integrate the hospital's organizational model already in place, as it can target both hospitalization rates and ED overcrowding, allowing to intervene before the person accesses the hospital.

Available evidence also prompted us to opt for a multicomponent approach. In fact, the current literature, mainly based on qualitative interviews with nursing home staff members in different countries, suggests that

the decision to transfer residents to hospital may be influenced by different factors, such as staffing and skill mix in the nursing homes, treatment options available in the facility, end-of-life decision-making, and communication and bureaucratic requirements.[24] This multifactorial association means that a multicomponent intervention is likely to be more effective than a single-component intervention.[25]

Based on the Schippinger[16] and Diaz-Gegundez[26] studies, we created a mobile physician service. Unlike those studies, we did not involve a nurse, because the participating facilities have nursing staff available 24 hours a day, and we used medical hospital staff because routine clinical management and scheduled follow-up evaluations are already performed by nursing home physicians during their office hours.

Finally, medical hospital staff was preferred to community geriatricians, on the assumption that older patients may feel more comfortable being handled by physicians who may have already cared for them at the hospital. Moreover, hospital staff enables direct patient referral to the ward. Finally, this allows the use of diagnostic technologies available at the hospital, which can be used immediately without the need for hospital admission.

Description of the intervention

The model hinges on the strong collaboration between hospital and nursing home staff to provide residents with patient-centered care. It entails a multicomponent intervention which is integrated in standard care and comprises three steps: 1) MMU team activation, 2) on site visit by a team of physicians with geriatric expertise, 3) interdisciplinary care planning (Figure 1).

Step 1: MMU team activation

Patient selection is necessary to ensure that available resources are used for patients who may really benefit. To this end, the nursing home physician contacts by phone the "flow manager", a skilled internist with strong clinical expertise, organizational attitude and managerial training, during the 8 a.m.-6 p.m. time frame, Monday to Friday. The phone consultation is reported on a form containing the description of the patient's clinical condition and a summary of the conversation. The form also indicates which decision was reached among the following six not mutually exclusive options:

a) The patient can be managed by nursing home staff, therapeutic advice is provided by phone
b) Remote reassessment is scheduled after a number of hours agreed upon by the team
c) The MMU team is dispatched for evaluation, treatment and stabilization on site

d) A significant change in vital parameters is observed which requires immediate activation of emergency services

e) Direct hospital admission is considered necessary

f) Ambulatory outpatient visits or tests are planned

Step 2: on site visit by a team of physicians with geriatric expertise

Visits at the nursing home are performed by two members of the MMU team: an expert hospital physician chosen on a case-by-case basis among the clinical staff of the Internal Medicine and Critical Subacute Care Unit, depending on the disease or clinical problem that must be treated, and a specifically trained resident in Emergency Medicine. The physicians that may be involved in MMU activation include specialists in internal medicine, clinical ultrasonography, gastroenterology, geriatrics or clinical nutrition.

The team is provided with a car to reach the nursing homes, a portable ultrasound system, and an essential set of drugs and medical devices useful in an emergency setting. The ultrasound system is equipped with three probes (convex, linear, and phased-array) for performing thoraco-pulmonary, cardiac, vascular, abdominal and soft tissue ultrasound, when required. Available drugs include those that can be administered intravenously for treating urgent conditions (e.g. loop diuretics, steroids, fluids, antibiotics). Devices include central and peripheral venous lines, naso-gastric and rectal tubes and bladder catheters. Blood tests can also be performed. Table 1 shows possible clinical scenarios which may require MMU team activation, and possible decisions.

Step 3: interdisciplinary care planning

Based on the results of the visit and of any performed investigations, the MMU team formulates personalized advice and referrals, and discusses these with the nursing home physician. If stabilization on site is not deemed possible, the MMU team plans a direct admission to the Internal Medicine and Critical Subacute Care Unit, thus avoiding ED access. The planning and the final outcome of the intervention are recorded in the second part of the form.

Feasibility assessment

A pilot phase of 5 months (December 2018-April 2019) was conducted in two nursing homes in order to look at feasibility of the MMU care Model described above. Before the intervention was introduced, meetings were held with nursing home staff to agree on activation modalities.

In this period, 99 phone calls were received, of which 84 required MMU team onsite visits, and 15 were managed with remote consultancy. Of the latter, 3 required direct admission after remote phone consultancy. Only 4 of the 84 patients visited onsite required direct admission. One patient was sent to the ED for massive intestinal bleeding (Figure 2).

This phase demonstrated the feasibility of the intervention, and did not highlight any need for modifications.

Evaluation phase

Aim and objectives

The study aim is to verify the effects of the implementation of the MMU care model tested in the pilot phase. Primary objective is to verify reduction of unplanned hospitalization rates in the nursing homes of the intervention group compared to the nursing homes in the control group. Secondary objectives are to measure the effects of the intervention in terms of mortality, health service use, and costs.

Study Design

This study is a prospective, pragmatic, cluster-multicenter, quasi-experimental study (sequential design with two cohorts), in which usual nursing home care is compared to care provided by applying the MMU model. The cluster design was selected because the intervention is organizational and requires high involvement of all center staff; therefore, randomizing individual clinicians or patients would entail a high risk of contamination bias. A quasi-randomized design was chosen as it prevents the need to discontinue the intervention conducted in two nursing homes which had participated in the pilot phase, and would thus be more acceptable by staff. Furthermore, quasi-experiments do not imply the selection effects and "artificiality" of randomized trials, and are thus more suitable for studies on intervention implementation in real life, enabling a high degree of external validity.[27]

A stepped-wedge design would have been desirable, enabling all participating nursing homes to receive the intervention, but was deemed unfeasible because it entails a larger sample size and study duration; furthermore,

the currently available technical and human resources would not be sufficient to sustain MMU intervention delivery in more than two nursing homes at the same time.

Study Population

All residents of the participating nursing homes are eligible, regardless of their clinical status. Informed consent will be collected from patients or their proxies/legal representatives, according to the European Union law. Refusal to provide informed consent, either by patients or legal representatives, will imply study exclusion.

Usual Care

Patients in the control cohort receive usual care, which means the actions to take are decided by the nursing home staff. Generally, this implies that patients who are clinically unstable, or require urgent instrumental tests, will be sent to the ED.

Measures: Baseline variables

Demographic data on gender and age are collected by chart review.

Measures: Outcome variables

The primary outcome is hospitalization rate, considering at the numerator all unplanned admissions occurred during a 1-year period, and at the denominator the sum of the person-time of the at risk population (days of stay at the nursing home). For the intervention group, the numerator corresponds to options d) and e) defined in "Step 1: MMU team activation".

The secondary outcomes are the following*:*

- Crude all-cause Death Rate (CDR): the number of deaths during 1-year period on person-time of the at risk population
- Hospital Mortality rate: the frequency of patients who die while in the hospital (death rate/1000)
- Length of stay (LOS): the duration of a single episode of hospitalization. Inpatient days are calculated by subtracting day of admission from day of discharge.

- Adverse events or complications: frequency of events with novel unexpected worsening of clinical conditions occurring within 48 hours from MMU team activation, for which hospital access becomes necessary.
- Costs analysis, comparing the cost differences in the two groups

Data Collection

Patient demographic and clinical characteristics will be collected at baseline from nursing home clinical records to describe the study population and determine hospital admission rate. For participants in the control group, only data on age, sex, timing of admission and discharge in nursing home will be collected. For those in the intervention group, additional data on any MMU activation (reasons, timing, intervention, procedures and outcomes) will be collected with a specific Case Report Form (CRF).

Participants' files and electronic data will be stored securely at the study site (e.g. locked area, password protected hard- and software). Data integrity will be scrutinized with several strategies (e.g. valid values, range checks, consistency checks). Patient data will be only identifiable with the unique participant's number. Personal information will be collected and saved in a separate file (on a different server) which can only be accessed by the Principal Investigator (PI). For the primary outcome, information will be obtained using administrative databases of the hospital and nursing homes. For secondary outcomes the following data sources will be used: validated regional death registry to determine CDR; electronic discharge summaries to calculate hospital mortality rate and LOS; electronic ED registry to detect adverse events or complications; hospital administrative database and CRF for the cost analysis. Residents' identification data will be deleted once the study is completed, making the dataset anonymous. All study protocol authors will have access to the anonymous dataset.

Study duration

Overall expected duration is 18 months, with study initiation presumably in November 2019 and completion in April 2021.

Statistical Methodology

Sample size calculation

The number of subjects to include was estimated using the findings of Diaz-Gegundez et al, who performed a large quasi-experimental trial.[26] Thus, considering 56 cases vs 32 cases per 100 residents, and using a 2-sided, large-samples z-test of the Poisson incidence rate difference at a significance level of 0.05, and with a power of 0.90, overall 338 residents should be enrolled. Since each of the participating nursing homes has between 90 and 100 residents, the study appears as feasible.

Statistical analysis plan

Descriptive statistics will be used to summarize patient populations and will be presented as means and standard deviations (SD) when normally distributed, or as medians and interquartile ranges (IQR).

For the primary analysis we will used Poisson regression with robust standard errors (SEs) to evaluate relative differences in hospital rates among our two cohorts while adjusting for demographic characteristics.

Concerning the secondary outcomes, the following analyses will be performed:

- Rates will be compared considering the quotient between the intervention and control groups
- A lognormal model will be used to compare in-hospital LOS.
- Chi square tests will be conducted for categorical data as adverse events or complications

The demographic and clinical variables which influence the outcome with a p value<0.20 in the univariate analysis will be included in the Poisson regression model.

Finally, cost analysis will be performed. We will identify the changes in net costs associated with one-year exposure to the intervention, consisting in the induced costs due to incremental resource inputs for carrying out the intervention and hospital health service utilization costs. Staffing costs will be calculated considering the time spent by the professionals involved in the intervention. Non-staff running costs include expenses of MMU staff travelling to and from the nursing home. The health service utilization costs will be identified based on the standard regional tariffs assigned to each admission according to the Diagnosis Related Group (DRG) system. We will use the following equations to summarize the annual net costs associated with the implementation of the intervention. Any costs with negative values mean "savings" and any costs with positive values mean "losses". Net costs ˆ A (intervention costs) ± B (Costs for differences in hospital health service utilization) where: A= intervention: staffing costs+intervention: non- staff costs and B= Costs for differences in inpatient care utilization. Therefore, the net costs arising from one-year implementation of the intervention

as compared with the current practice will be obtained, where a negative value of net costs represents "cost-saving" and a positive value represents "not cost-saving"

The analyses will be performed using SAS 8.2 (SAS Institute, Cary, NC, USA) and STATA-SE 11 (Stata Corp LP, College Station, TX, USA).

ETHICS AND DISSEMINATION

The study will be conducted in compliance with the principles of the revision of the Helsinki Declaration and by current legislation on scientific research. All participants or their legal representatives will sign informed consent form. This study does not entail any experimental pharmacological treatment, or changes in the diagnostic-therapeutic pathway. Eligible patients, or their legal representatives, will be also asked to give written consent to handling of their personal data. If a patient wishes to discontinue his/her participation in the study, it is the responsibility of the investigator to ensure that no further data regarding the person's health condition shall be collected. All collected data will be used in the final analysis.

All data collected, handled and stored for the purpose of this study will be kept confidential at any time and will be securely stored, as required in GCP guidelines and in current privacy legislation.

DISCUSSION

The MMU-1 Study will represent one of the first attempts to prevent hospital admissions of nursing home residents by using a multicomponent complex intervention with a strong multidisciplinary approach. Most of previous studies in this field were in fact focused on geriatric routine care, nurse counselling and education, but did not deliver diagnostic and therapeutic interventions at the bedside in case of urgent needs.[13-19,26] The multidisciplinary skills of MMU-1 staff, that may involve expert physicians with different skills and background depending on the clinical problem of patients, represents a novelty at the current literature state-of-the-art and has a great potential of being successful in preventing hospital admission, considering the high clinical complexity of nursing home residents. The use of bedside ultrasound equipment also represents a high value added to the care of these patients, allowing to reach a high diagnostic accuracy and to perform invasive procedures without moving patients to the hospital.[28-29] The use of bedside ultrasonography in geriatrics is becoming increasingly popular but is generally unavailable in nursing homes.[28-29] When integrated with an accurate physical examination, bedside ultrasonography can dramatically improve the diagnostic process,[30]

especially in geriatric multimorbid patients where severity of symptoms, cognitive impairment and mobility-limitations may reduce the accuracy of traditional imaging.[28-29]

Finally, the MMU-1 intervention is not fixed into a rigid algorithm, but different kinds of consultancy can be made according to the clinical situation of each patient (Figure 1). This circumstance represents an advancement with respect of other interventions previously described in the literature,[13] and an effort towards personalization of geriatric care.

Some limitations of this study should be considered. First, we acknowledge that the stepped wedge cluster randomized design would represent the best design for testing the effects of a novel care model implemented in multiple nursing homes. However, as described above, this was not feasible due to practical and economic barriers. It is also noteworthy that most of the existing studies included in the Santosaputri review[13] adopted a quasi-experimental design, because, in research on complex care interventions, methodological soundness must always face practical considerations on feasibility.[27]

In conclusion, if the results of this study suggest benefits for patients and the health care system, future investigations with sounder methodology should be implemented to assess a large-scale application of the proposed care model.

Contributors

A.N., B.P., S.L., P.M., E.B., M.F. and T.M. conceptualised the project and designed the intervention. F.D., A.T., P.S., F.P., B.S. and C.C. provided relevant contributions for study conception and design. E.I. gave statistical consult. A.N., C.C., F.D. and A.T. drafted the manuscript. All the authors read and approved the final manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

Patient consent

Not required.

Ethics approval

The study was approved by the competent Ethics Committee (Comitato Etico Area Vasta Emilia Nord), under the ID 846/2019/OSS/AOUPR.

Patient and public involvement

No patient involved.

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TABLE 1

Overview of possible expected clinical situations for which a Multidisciplinary Mobile Unit consultation may be activated, and possible management.

Clinical situation	Clinical question	Mobile Unit Intervention	Disposition
Dyspnea of unknown origin	Pulmonary? Cardiac? Embolism? Other causes?	Chest and Abdomen Ultrasound. Arterial Gas sample, ECG, intravenous antibiotic administration	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Abdominal pain	Gallbladder stones? Cholecystitis? Renal colic? Diverticular disease? Urinary retention? Faecal impaction? Peritonitis? Ascites? Acute/subacute Hernia?	Abdomen ultrasound, basic blood tests, intravenous antibiotic administration	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Hematuria	UTI? Catheter dysfunction? Bladder polyps? Stones?	Abdomen ultrasound, Bladder lavage, Catheter (re-)positioning, Intravenous antibiotic administration	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Psychomotor agitation in previously stable dementia	Inadequate therapy? Emerging internistic problem? Other	CGA, Neurogeriatric visit, exclusion of internistic emerging problem, ECG, Thoracic&abdominal US	Appropriate diagnosis and treatment on site.
Fever	Origin?	Thoracic&abdominal US, basic blood test	Excluding common differential diagnosis
Absence of peripheral veins for drugs or nutrients infusion	How to find adequate venous access	US guided Central venous catheter or PICC or peripheral access	Securing patient
Monolateral leg edema	DVT? Erysipelas? Trauma?	Venous and soft tissues ultrasound	Appropriate diagnosis and treatment on site.
Terminal illness	Palliation strategy? How to get symptoms relief?	CGA. Multidisciplinary assessment. Positioning of drains (eg abdominal drainage for ascites). Interview with relatives / caregivers and GP for sharing strategies	Appropriate management.
Ultrasound exam in a patient who can be transported with difficulty	GP's question	Abdominal, cardiac, arterial, thyroid, neck ultrasound	Appropriate assessment

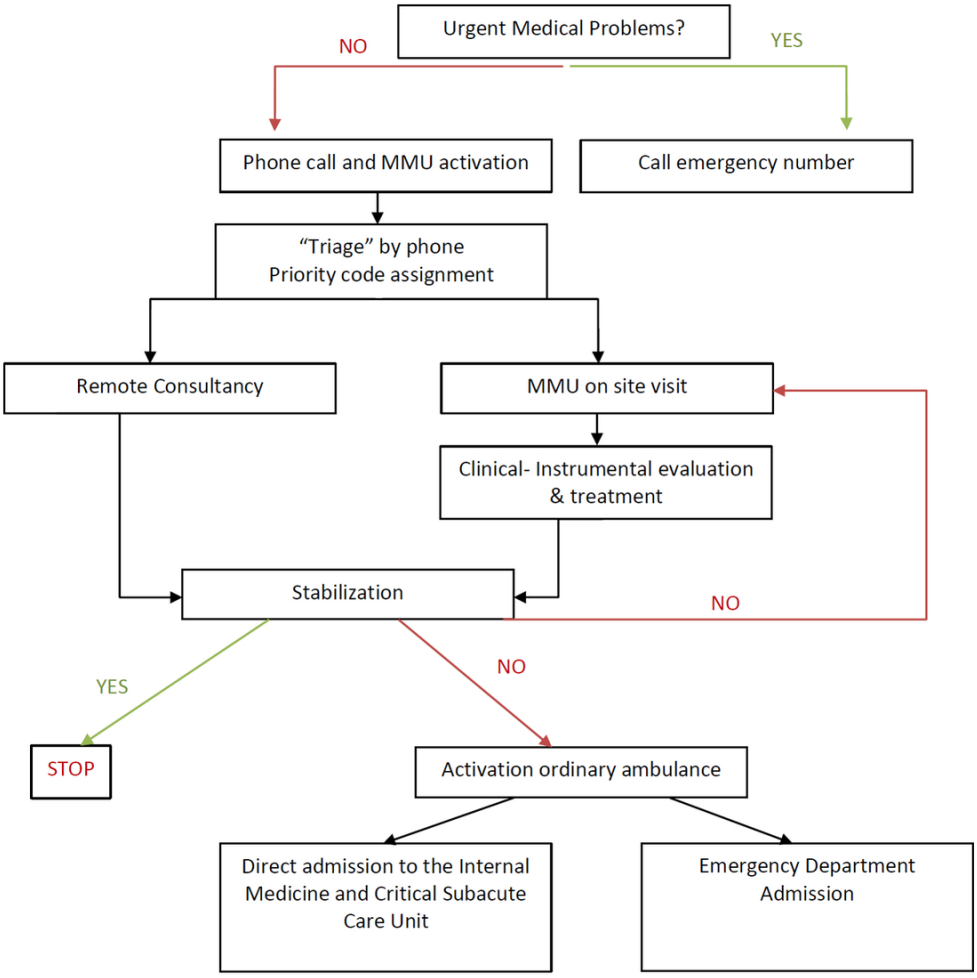
ECG = Electrocardiogram; UTI = Urinary Tract Infection; CGA = Comprehensive Geriatric Assessment; US = Ultrasound; PICC = Peripherally-Inserted Central Venous Catheter; DVT = Deep Vein Thrombosis; GP = General Practitioner.

FIGURE 1

Description of the intervention of MMU Team.

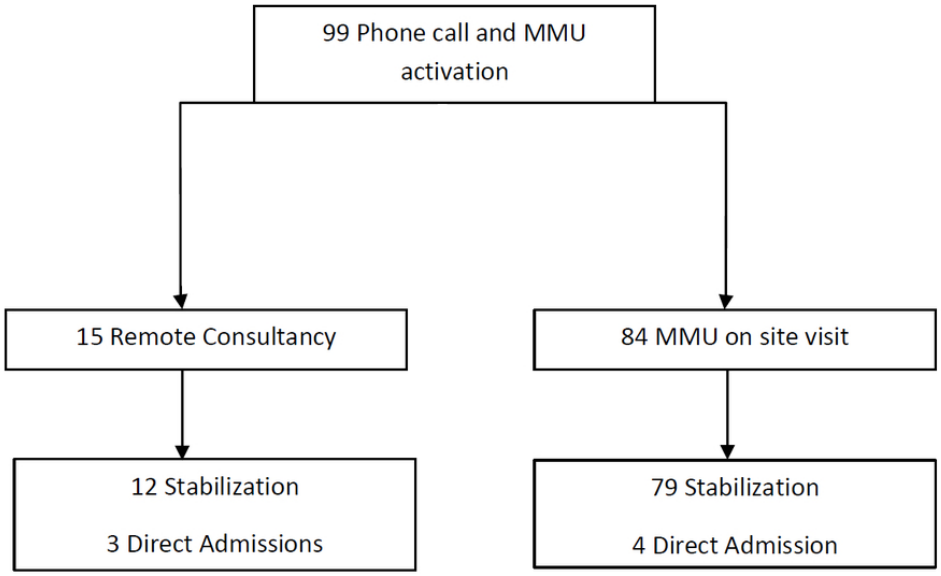
FIGURE 2

Results of pilot phase.



Description of the intervention of MMU Team

95x95mm (300 x 300 DPI)



Results of pilot phase

78x48mm (300 x 300 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

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		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	2, end of abstract
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	Supplemental Material
Funding	#4	Sources and types of financial, material, and other support	14
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 14
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	N/A (page 14)
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	N/A (page 13)

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)	13
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	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5
Objectives	#7	Specific objectives or hypotheses	6, 9
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)	9-10
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	6
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)	10
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9, 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)	N/A (complex intervention on organization of care)
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	N/A (the intervention concerns organization of care in nursing homes)

Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7-10
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
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)	11
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	11
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	N/A (all residents in participating nursing homes will be

			eligible for the study)
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	N/A (quasi-experimental study design on organization of care)
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	N/A (quasi-experimental study design on organization of care)
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A (quasi-experimental study design on organization of care)

Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A (quasi-experimental study design on organization of care)
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	N/A (quasi-experimental study design on organization of care)
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	10-11

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	N/A (quasi-experimental study design on organization of care)
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, 13
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	12
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
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)	N/A due to particular study design
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	13
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	13
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	N/A due to particular study design
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A due to particular study design
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	12-13

Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	12-13 + supplemental material
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	12-13 + supplemental material
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	12-13 + supplemental material
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	12-13 + supplemental material
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	14
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	12-13 + supplemental material

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	N/A due to particular study design
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 results databases, or other data sharing arrangements), including any publication restrictions	13 + supplemental material
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	Supplemental material
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Supplemental material
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Supplemental material
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	N/A due to study design

NOTE: The original protocol approved by the competent Ethics Committee (in English language) has been uploaded as Supplemental Material.

BMJ Open

Implementation of a strategy involving a multidisciplinary mobile unit team to prevent hospital admission in nursing home residents: protocol of a quasi-experimental study (MMU-1 Study)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034742.R2
Article Type:	Protocol
Date Submitted by the Author:	28-Jan-2020
Complete List of Authors:	Nouvenne, Antonio; Azienda Ospedaliero-Universitaria di Parma, Geriatric-Rehabilitation Department Caminiti, Caterina; Azienda Ospedaliero-Universitaria di Parma, Research and Innovation Unit Diodati, Francesca; Azienda Ospedaliero-Universitaria di Parma, Research and Innovation Unit Iezzi, Elisa; Azienda Ospedaliero-Universitaria di Parma, Research and Innovation Unit Prati, Beatrice; Azienda Ospedaliero-Universitaria di Parma, Geriatric-Rehabilitation Department Lucertini, Stefano; Azienda Unità Sanitaria Locale di Parma, Primary Care Department Schianchi, Paolo; Azienda Unità Sanitaria Locale di Parma, Primary Care Department Pascale, Federica; Azienda Unità Sanitaria Locale di Parma, Primary Care Department Starcich, Bruno; Azienda Unità Sanitaria Locale di Parma, Primary Care Department Manotti, Pietro; Azienda Ospedaliero-Universitaria di Parma, Medical Direction Brianti, Ettore; Azienda Ospedaliero-Universitaria di Parma, Medical Direction Fabi, Massimo; Azienda Ospedaliero-Universitaria di Parma, General Manager Ticinesi, Andrea; Azienda Ospedaliero-Universitaria di Parma, Geriatric-Rehabilitation Department Meschi, Tiziana; Azienda Ospedaliero-Universitaria di Parma, Geriatric-Rehabilitation Department; Università degli studi di Parma, Department of Medicine and Surgery
Primary Subject Heading:	Geriatric medicine
Secondary Subject Heading:	General practice / Family practice, Emergency medicine
Keywords:	Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, GERIATRIC MEDICINE

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Implementation of a strategy involving a multidisciplinary mobile unit team to prevent hospital admission in nursing home residents: protocol of a quasi-experimental study (MMU-1 Study)

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Word count: 3732

Abstract: 300; **Tables**: 1; **Figures**: 2; **References**: 31

Running Title: Multidisciplinary mobile unit intervention for nursing homes

ABSTRACT

Introduction- Nursing home residents represent a particularly vulnerable population experiencing high risk of unplanned hospital admissions, but few interventions have proved effective in reducing this risk. The aim of this research will be to verify the effects of a hospital-based multidisciplinary mobile unit (MMU) team intervention delivering urgent care to nursing home residents directly at their bedside.

Methods and analysis- Four nursing homes based in the Parma province, in Northern Italy, will be involved in this prospective, pragmatic, multicenter, 18-month quasi-experimental study (sequential design with two cohorts). The residents of two nursing homes will receive the MMU team care intervention. In case of urgent care needs, the nursing home physician will contact the hospital physician responsible for the MMU team by phone. The case will be triaged as a) manageable by phone advice, b) requiring urgent assessment by the MMU team or c) requiring immediate ED referral. MMU team is composed of one senior physician and one Emergency-Medicine resident chosen within the staff of Internal Medicine and Critical Subacute Care Unit of Parma University-Hospital, usually with different specialty background, and equipped with portable ultrasound, set of drugs and devices useful in urgency. The MMU visits patients in nursing homes, with the mission to stabilize clinical conditions and avoid hospital admission. Residents of the other two nursing homes will receive usual care, i.e. ED referral in every case of urgency. Study endpoints include unplanned hospital admissions (primary), crude all-cause mortality, hospital mortality, length of stay and healthcare-related costs (secondary).

Ethics and dissemination- The study protocol was approved by the Ethics Committee of Area Vasta Emilia Nord (Emilia-Romagna region). Informed consent will be collected from patients or legal representatives. The results will be actively disseminated through peer-reviewed journals and conference presentations, in compliance with the Italian law.

Registration ID- ClinicalTrials.gov NCT 04085679

Key words: multimorbidity; geriatrics; hospitalization; multidisciplinary care; hospital-community partnership

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ✓ This study will explore the effectiveness of a complex intervention focused on the avoidance of hospital admissions for nursing home residents, with a strong hospital-community partnership.
- ✓ The study intervention consists in bringing specialist hospital care directly at the bedside of nursing home residents, an innovative approach not previously described in the scientific literature.
- ✓ The intervention has been developed considering the organization of the Italian healthcare system, but is reproducible and applicable in other settings.
- ✓ Due to ethical concerns and the complex nature of the intervention, individual randomization of participants is not possible.
- ✓ The quasi-experimental design of the study allows an optimal compromise between soundness and feasibility, facilitating the transferability of results into clinical practice.

INTRODUCTION

The increasing clinical complexity of older medical patients, due to multimorbidity, polypharmacy, frailty, disability and social hardship, is challenging for health care systems.[1 2] These characteristics are emphasized in nursing home residents, who experience a particularly high risk of Emergency Department (ED) visits and hospitalization (greater than 20% per year).[3-8] In the ED, these patients may experience misdiagnoses and undertreatment, due to their complexity and atypical presentation of acute illness, and contribute to the overcrowding phenomenon.[4 5 9-11] Once admitted to wards, they are also more likely to have long stays (>2 weeks)[9] and experience hospital-related complications.[12] Additionally, when they are discharged back to nursing homes, they may experience further adverse events related to care transitions.[6 12]

In the light of these considerations, confirmed by large cohort studies conducted in the United States and Canada,[7 8] a number of approaches have been developed to reduce the risk of hospitalization in nursing home residents. These are summarized in the systematic review by Santosaputri et al,[13] which includes quantitative comparative studies of all designs aiming to determine the efficacy of interventions provided by geriatric health professionals. Sixteen studies were eligible, of which 6 randomized controlled trials, involving an estimated total of over 7400 patients. The authors of the review categorized 14 intervention programs into three primary approaches (two did not fit in any category):

- Prevention approach (nine studies): Interventions (such as direct review of patients, telemedicine, comprehensive geriatric assessment) delivered in the nursing home by nurses, physicians, and sometimes allied health personnel to prevent hospitalization of residents
- Emergency department-based hospital avoidance (three studies): interventions provided by nursing staff (such as wound care or catheter management) targeting nursing home residents during ED visits
- Post-hospital supported discharge (two studies): Interventions designed to support residents in the care transition from the hospital to nursing home, including geriatrician and nurse review in the facility and standardized rehabilitation programs.

Although the majority of the studies reported reductions in hospitalizations, only six, with different designs and interventions, obtained statistically significant findings.[14-19] Two of these studies, with retrospective design, involved delivery of routine care to nursing home residents by hospital-based nursing staff, with the possibility of obtaining support from a geriatrician in case of urgent situations.[14-15] In another prospective quasi-experimental study, a team including a geriatrician and specialized nurses supported the nursing home

physician in delivering routine care and in managing urgent clinical situations.[16] The remaining three studies, all with prospective quasi-experimental design, were more focused on selected clinical scenarios, involving advice and education by ED staff to nursing home personnel after ED admission of residents,[17] hospital nurse visits in the nursing home to implement strategies of delirium prevention,[18] and rehabilitation intervention delivered by a geriatric orthopedic team to residents with hip fracture.[19]

Unfortunately, the quality of evidence was considered low to moderate, therefore further, well-designed studies are needed to identify which interventions are effective in reducing hospitalization in the older residents.[13] The interventions performed in the existing studies were also mainly focused on routine care, while a prompt and correct management of urgent situations and acute/subacute conditions may be fundamental for avoiding ED admissions in nursing home residents.[7 20] Namely, interventions delivering urgent care with a multidisciplinary approach, based not only on geriatric expertise but also on the capacity of performing first line diagnostic examinations, such as ultrasonography, and basic invasive procedures, such as central venous line or nasogastric tube insertion, have a great potential of being successful in reducing ED visits, but have not been adequately investigated to date.[7 20]

At our institution, different projects have been carried out for many years to improve care of the elderly, primarily targeting hospital organization, with the main objective to reduce unnecessary, avoidable length of stay (LOS).[21-23] These efforts benefit in-hospital patients, but are not designed to prevent hospitalizations. In this framework, based on literature evidence, best current knowledge and long-time experience with elderly care developed at our university-hospital, we hypothesize that a complex intervention delivered in nursing homes, where vulnerable high-risk patients live, involving direct patient care by hospital medical staff with multidisciplinary approach grounded on geriatric expertise, may reduce hospitalization of residents.

METHODS AND ANALYSIS

Study setting

The study is based in the University Hospital of Parma, which has a catchment area of more than 400,000 inhabitants, of whom 22.3% is over 65 years old. It provides the only Emergency service of the district, and it ranks fourth in Italy by number of ED visits (yearly average of over 110,000). The average admission rate of the adult ED population is 18%, of which 65% concern people older than 65.

In the last two decades, the University Hospital of Parma has implemented several innovative initiatives to manage the hospital flow of frail multimorbid patients and their complex needs. These initiatives included bed management to avoid "bed-blockers",[21] physician accountability for the discharge process,[22] and creation of a dedicated hospital unit, organized by intensity of care to anticipate the needs of these patients preserving high performance indices.[23] The Multidisciplinary Mobile Unit (MMU) team will be based in this unit, called Internal Medicine and Critical Subacute Care.

Nursing homes participating in the study are public facilities of similar size (90-100 residents) which ensure the presence of nursing staff 24 hours a day and of a physician at least 4 hours a day (high-intensity care facilities), in compliance with the care standards set by the Local Health Authority. No staff member is shared among the participating nursing homes. The possible role of distance to the hospital is considered by including in each group one nursing home located next to the hospital and one located at a distance of >5 km.

The participating nursing homes are the following CRAs (Casa Residenza Anziani):

- C.R.A. "I Tigli" Parma (intervention group)
- C.R.A. "Casa degli Anziani", Collecchio (intervention group)
- C.R.A. "Le Tamerici" Parma (control group)
- C.R.A. "Ines Ubaldi", Parma (control group)

This study follows a multimethod approach, based on the Medical Research Council framework for developing and evaluating complex interventions,[24] including the development, feasibility assessment, and evaluation phases.

Development of the intervention

First, the different types of approaches reported in the literature, described above, were considered.[13] The "prevention approach", interventions conducted in nursing homes, was chosen as the most suitable strategy to integrate the hospital's organizational model already in place, as it can target both hospitalization rates and ED overcrowding, allowing to intervene before the person accesses the hospital.

Available evidence also prompted us to opt for a multicomponent approach. In fact, the current literature, mainly based on qualitative interviews with nursing home staff members in different countries, suggests that the decision to transfer residents to hospital may be influenced by different factors, such as staffing and skill mix in the nursing homes, treatment options available in the facility, end-of-life decision-making, and

communication and bureaucratic requirements.[25] This multifactorial association means that a multicomponent intervention is likely to be more effective than a single-component intervention.[26]

Based on the Schippinger[16] and Diaz-Gegundez[27] studies, that obtained significant reduction of hospital admissions, we created a mobile physician service. Unlike those studies, we did not involve a nurse, because the participating facilities have nursing staff available 24 hours a day, and we used medical hospital staff because routine clinical management and scheduled follow-up evaluations are already performed by nursing home physicians during their office hours.

Finally, medical hospital staff was preferred to community geriatricians, on the assumption that older patients may feel more comfortable being handled by physicians who may have already cared for them at the hospital. Moreover, hospital staff enables direct patient referral to the ward. Finally, this allows the use of diagnostic technologies available at the hospital, which can be used immediately without the need for hospital admission.

Description of the intervention

The model hinges on the strong collaboration between hospital and nursing home staff to provide residents with patient-centered care. It entails a multicomponent intervention which is integrated in standard care and comprises three steps: 1) MMU team activation, 2) on site visit by a team of physicians with geriatric expertise, 3) interdisciplinary care planning (Figure 1).

Step 1: MMU team activation

Patient selection is necessary to ensure that available resources are used for patients who may really benefit. To this end, the nursing home physician contacts by phone the "flow manager", a skilled internist with strong clinical expertise, organizational attitude and managerial training, during the 8 a.m.-6 p.m. time frame, Monday to Friday. The phone consultation is reported on a form containing the description of the patient's clinical condition and a summary of the conversation. The form also indicates which decision was reached among the following six not mutually exclusive options:

a) The patient can be managed by nursing home staff, therapeutic advice is provided by phone

b) Remote reassessment is scheduled after a number of hours agreed upon by the team

c) The MMU team is dispatched for evaluation, treatment and stabilization on site

d) A significant change in vital parameters is observed which requires immediate activation of emergency services

e) Direct hospital admission is considered necessary

f) Ambulatory outpatient visits or tests are planned

Step 2: on site visit by a team of physicians with geriatric expertise

Visits at the nursing home are performed by two members of the MMU team: an expert hospital physician chosen on a case-by-case basis among the clinical staff of the Internal Medicine and Critical Subacute Care Unit, depending on the disease or clinical problem that must be treated, and a specifically trained resident in Emergency Medicine. The physicians that may be involved in MMU activation include specialists in internal medicine, clinical ultrasonography, gastroenterology, geriatrics or clinical nutrition.

The team is provided with a car to reach the nursing homes, a portable ultrasound system, and an essential set of drugs and medical devices useful in an emergency setting. The ultrasound system is equipped with three probes (convex, linear, and phased-array) for performing thoraco-pulmonary, cardiac, vascular, abdominal and soft tissue ultrasound, when required. Available drugs include those that can be administered intravenously for treating urgent conditions (e.g. loop diuretics, steroids, fluids, antibiotics). Devices include central and peripheral venous lines, naso-gastric and rectal tubes and bladder catheters. Blood tests can also be performed. Table 1 shows possible clinical scenarios which may require MMU team activation, and possible decisions.

Step 3: interdisciplinary care planning

Based on the results of the visit and of any performed investigations, the MMU team formulates personalized advice and referrals, and discusses these with the nursing home physician. If stabilization on site is not deemed possible, the MMU team plans a direct admission to the Internal Medicine and Critical Subacute Care Unit, thus avoiding ED access. The planning and the final outcome of the intervention are recorded in the second part of the form.

Feasibility assessment

A pilot phase of 5 months (December 2018-April 2019) was conducted in the two nursing homes participating to the study as intervention group, in order to look at feasibility of the MMU care Model described above.

Before the intervention was introduced, meetings were held with nursing home staff to agree on activation modalities.

In this period, 99 phone calls were received, of which 84 required MMU team onsite visits, and 15 were managed with remote consultancy. Of the latter, 3 required direct admission after remote phone consultancy. Only 4 of the 84 patients visited onsite required direct admission. One patient was sent to the ED for massive intestinal bleeding (Figure 2).

This phase demonstrated the feasibility of the intervention, and did not highlight any need for modifications.

Evaluation phase (current study)

Aim and objectives

The study aim is to verify the effects of the implementation of the MMU care model tested in the pilot phase. Primary objective is to verify reduction of unplanned hospitalization rates in the nursing homes of the intervention group compared to the nursing homes in the control group. Secondary objectives are to measure the effects of the intervention in terms of crude all-cause mortality, hospital mortality, length of stay and healthcare-related costs.

Study Design

This study is a prospective, pragmatic, cluster-multicenter, quasi-experimental study (sequential design with two cohorts), in which usual nursing home care is compared to care provided by applying the MMU model. The cluster design was selected because the intervention is organizational and requires high involvement of all center staff; therefore, randomizing individual clinicians or patients would entail a high risk of contamination bias. A quasi-randomized design was chosen as it prevents the need to discontinue the intervention conducted in two nursing homes which had participated in the pilot phase, and would thus be more acceptable by staff. Furthermore, quasi-experiments do not imply the selection effects and "artificiality" of randomized trials, and are thus more suitable for studies on intervention implementation in real life, enabling a high degree of external validity.[28]

Study Population

All residents staying in the participating nursing homes at the moment of study initiation or admitted afterwards are eligible for inclusion, regardless of their clinical status. Informed consent will be collected from patients or their proxies/legal representatives, according to the European Union law. Refusal to provide informed consent, either by patients or legal representatives, will imply study exclusion.

Usual Care

Patients in the control cohort receive usual care, which means the actions to take are decided by the nursing home staff. Generally, this implies that patients who are clinically unstable, or require urgent instrumental tests, will be sent to the ED.

Measures: Baseline variables

Demographic data on gender and age are collected by chart review.

Measures: Outcome variables

The primary outcome is hospitalization rate, considering at the numerator all unplanned admissions occurred during a 1-year period, and at the denominator the sum of the person-time of the at risk population (days of stay at the nursing home). For the intervention group, the numerator corresponds to options d) and e) defined in "Step 1: MMU team activation" (activation of Emergency services and direct hospital admission).

The secondary outcomes are the following*:*

- Crude all-cause Death Rate (CDR): the number of deaths during 1-year period on person-time of the at risk population
- Hospital Mortality rate: the frequency of patients who die while in the hospital (death rate/1000)
- Length of stay (LOS): the duration of a single episode of hospitalization. Inpatient days are calculated by subtracting day of admission from day of discharge.
- Adverse events or complications: frequency of events with novel unexpected worsening of clinical conditions, defined as alterations of vital signs, occurring within 48 hours from MMU team activation, for which hospital access becomes necessary.
- Costs analysis, comparing the cost differences in the two groups

Data Collection

Patient demographic and clinical characteristics will be collected at baseline from nursing home clinical records to describe the study population and determine hospital admission rate. For participants in the control group, only data on age, sex, timing of admission and discharge in nursing home will be collected. For those in the intervention group, additional data on any MMU activation (reasons, timing, intervention, procedures and outcomes) will be collected with a specific Case Report Form (CRF).

Participants' files and electronic data will be stored securely at the study site (e.g. locked area, password protected hard- and software). Data integrity will be scrutinized with several strategies (e.g. valid values, range checks, consistency checks). Patient data will be only identifiable with the unique participant's number. Personal information will be collected and saved in a separate file (on a different server) which can only be accessed by the Principal Investigator (PI). For the primary outcome, information will be obtained using administrative databases of the hospital and nursing homes. For secondary outcomes the following data sources will be used: validated regional death registry to determine CDR; electronic discharge summaries to calculate hospital mortality rate and LOS; electronic ED registry to detect adverse events or complications; hospital administrative database and CRF for the cost analysis. Residents' identification data will be deleted once the study is completed, making the dataset anonymous. All study protocol authors will have access to the anonymous dataset.

Study duration

Overall expected duration is 18 months, with study initiation presumably in January 2020 and completion in June 2021.

Statistical Methodology

Sample size calculation

The number of subjects to include was estimated using the findings of Diaz-Gegundez et al, who performed a large quasi-experimental trial.[27] Thus, considering 56 cases vs 32 cases per 100 residents, and using a 2-sided, large-samples z-test of the Poisson incidence rate difference at a significance level of 0.05, and with a power of 0.90, overall 338 residents should be enrolled. Since each of the participating nursing homes has between 90 and 100 residents, the study appears as feasible.

Statistical analysis plan

Descriptive statistics will be used to summarize patient populations and will be presented as means and standard deviations (SD) when normally distributed, or as medians and interquartile ranges (IQR).

For the primary analysis we will used Poisson regression with robust standard errors (SEs) to evaluate relative differences in hospital rates among our two cohorts while adjusting for demographic characteristics.

Concerning the secondary outcomes, the following analyses will be performed:

- Rates will be compared considering the quotient between the intervention and control groups
- A lognormal model will be used to compare in-hospital LOS.
- Chi square tests will be conducted for categorical data as adverse events or complications

The demographic and clinical variables which influence the outcome with a p value<0.20 in the univariate analysis will be included in the Poisson regression model.

Finally, cost analysis will be performed. We will identify the changes in net costs associated with one-year exposure to the intervention, consisting in the induced costs due to incremental resource inputs for carrying out the intervention and hospital health service utilization costs. Staffing costs will be calculated considering the time spent by the professionals involved in the intervention. Non-staff running costs include expenses of MMU staff travelling to and from the nursing home. The health service utilization costs will be identified based on the standard regional tariffs assigned to each admission according to the Diagnosis Related Group (DRG) system. We will use the following equations to summarize the annual net costs associated with the implementation of the intervention. Any costs with negative values mean "savings" and any costs with positive values mean "losses". Net costs ˆ A (intervention costs) ± B (Costs for differences in hospital health service utilization) where: A= intervention: staffing costs+intervention: non- staff costs and B= Costs for differences in inpatient care utilization. Therefore, the net costs arising from one-year implementation of the intervention as compared with the current practice will be obtained, where a negative value of net costs represents "cost-saving" and a positive value represents "not cost-saving"

The analyses will be performed using SAS 8.2 (SAS Institute, Cary, NC, USA) and STATA-SE 11 (Stata Corp LP, College Station, TX, USA).

Patient and public involvement

No patient involved.

ETHICS AND DISSEMINATION

The study will be conducted in compliance with the principles of the revision of the Helsinki Declaration and by current legislation on scientific research. All participants or their legal representatives will sign informed consent form. This study does not entail any experimental pharmacological treatment, or changes in the diagnostic-therapeutic pathway. Eligible patients, or their legal representatives, will be also asked to give written consent to handling of their personal data. If a patient wishes to discontinue his/her participation in the study, it is the responsibility of the investigator to ensure that no further data regarding the person's health condition shall be collected. All collected data will be used in the final analysis.

All data collected, handled and stored for the purpose of this study will be kept confidential at any time and will be securely stored, as required in GCP guidelines and in current privacy legislation.

DISCUSSION

The MMU-1 Study will represent one of the first attempts to prevent hospital admissions of nursing home residents by using a multicomponent complex intervention with a strong multidisciplinary approach. Most of previous studies in this field were in fact focused on geriatric routine care, nurse counselling and education, but did not deliver diagnostic and therapeutic interventions at the bedside in case of urgent needs.[13-19,27] The multidisciplinary skills of MMU-1 staff, that may involve expert physicians with different skills and background depending on the clinical problem of patients, represents a novelty at the current literature state-of-the-art and has a great potential of being successful in preventing hospital admission, considering the high clinical complexity of nursing home residents. The use of bedside ultrasound equipment also represents a high value added to the care of these patients, allowing to reach a high diagnostic accuracy and to perform invasive procedures without moving patients to the hospital.[29-30] The use of bedside ultrasonography in geriatrics is becoming increasingly popular but is generally unavailable in nursing homes.[29-30] When integrated with an accurate physical examination, bedside ultrasonography can dramatically improve the diagnostic process,[31] especially in geriatric multimorbid patients where severity of symptoms, cognitive impairment and mobility-limitations may reduce the accuracy of traditional imaging.[29-30]

Finally, the MMU-1 intervention is not fixed into a rigid algorithm, but different kinds of consultancy can be made according to the clinical situation of each patient (Figure 1). This circumstance represents an advancement with respect of other interventions previously described in the literature,[13] and an effort towards personalization of geriatric care. Even in the two studies by Schippinger[16] and Diaz-Gegundez[27] reporting a significant reduction of hospital admissions, the intervention was rather fixed, centered exclusively on comprehensive geriatric assessment and lacked technological support such as bedside ultrasound.

Some limitations of this study should be considered. First, we acknowledge that the stepped wedge cluster randomized design would represent the best design for testing the effects of a novel care model implemented in multiple nursing homes. However, this was not feasible due to practical and economic barriers. In fact, it entails a larger sample size and study duration, and the currently available technical and human resources would not be sufficient to sustain MMU intervention delivery in more than two nursing homes at the same time. It is also noteworthy that most of the existing studies included in the Santosaputri review[13] adopted a quasi-experimental design, because, in research on complex care interventions, methodological soundness must always face practical considerations on feasibility.[28]

In conclusion, if the results of this study suggest benefits for patients and the health care system, future investigations with sounder methodology should be implemented to assess a large-scale application of the proposed care model.

Contributors

A.N., B.P., S.L., P.M., E.B., M.F. and T.M. conceptualised the project and designed the intervention. F.D., A.T., P.S., F.P., B.S. and C.C. provided relevant contributions for study conception and design. E.I. gave statistical consult. A.N., C.C., F.D. and A.T. drafted the manuscript. All the authors read and approved the final manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

Patient consent

Not required.

Ethics approval

The study was approved by the competent Ethics Committee (Comitato Etico Area Vasta Emilia Nord, Emilia-Romagna region), under the ID 846/2019/OSS/AOUPR.

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TABLE 1

Overview of possible expected clinical situations for which a Multidisciplinary Mobile Unit consultation may be activated, and possible management.

Clinical situation	Clinical question	Mobile Unit Intervention	Disposition
Dyspnea of unknown origin	Pulmonary? Cardiac? Embolism? Other causes?	Chest and Abdomen Ultrasound. Arterial Gas sample, ECG, intravenous antibiotic administration	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Abdominal pain	Gallbladder stones? Cholecystitis? Renal colic? Diverticular disease? Urinary retention? Faecal impaction? Peritonitis? Ascites? Acute/subacute Hernia?	Abdomen ultrasound, basic blood tests, intravenous antibiotic administration	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Hematuria	UTI? Catheter dysfunction? Bladder polyps? Stones?	Abdomen ultrasound, Bladder lavage, Catheter (re-)positioning, Intravenous antibiotic administration	Appropriate diagnosis and treatment on site. Immediate or scheduled admission whenever appropriate
Psychomotor agitation in previously stable dementia	Inadequate therapy? Emerging internistic problem? Other	CGA, Neurogeriatric visit, exclusion of internistic emerging problem, ECG, Thoracic&abdominal US	Appropriate diagnosis and treatment on site.
Fever	Origin?	Thoracic&abdominal US, basic blood test	Excluding common differential diagnosis
Absence of peripheral veins for drugs or nutrients infusion	How to find adequate venous access	US guided Central venous catheter or PICC or peripheral access	Securing patient
Monolateral leg edema	DVT? Erysipelas? Trauma?	Venous and soft tissues ultrasound	Appropriate diagnosis and treatment on site.
Terminal illness	Palliation strategy? How to get symptoms relief?	CGA. Multidisciplinary assessment. Positioning of drains (eg abdominal drainage for ascites). Interview with relatives / caregivers and GP for sharing strategies	Appropriate management.
Ultrasound exam in a patient who can be transported with difficulty	GP's question	Abdominal, cardiac, arterial, thyroid, neck ultrasound	Appropriate assessment

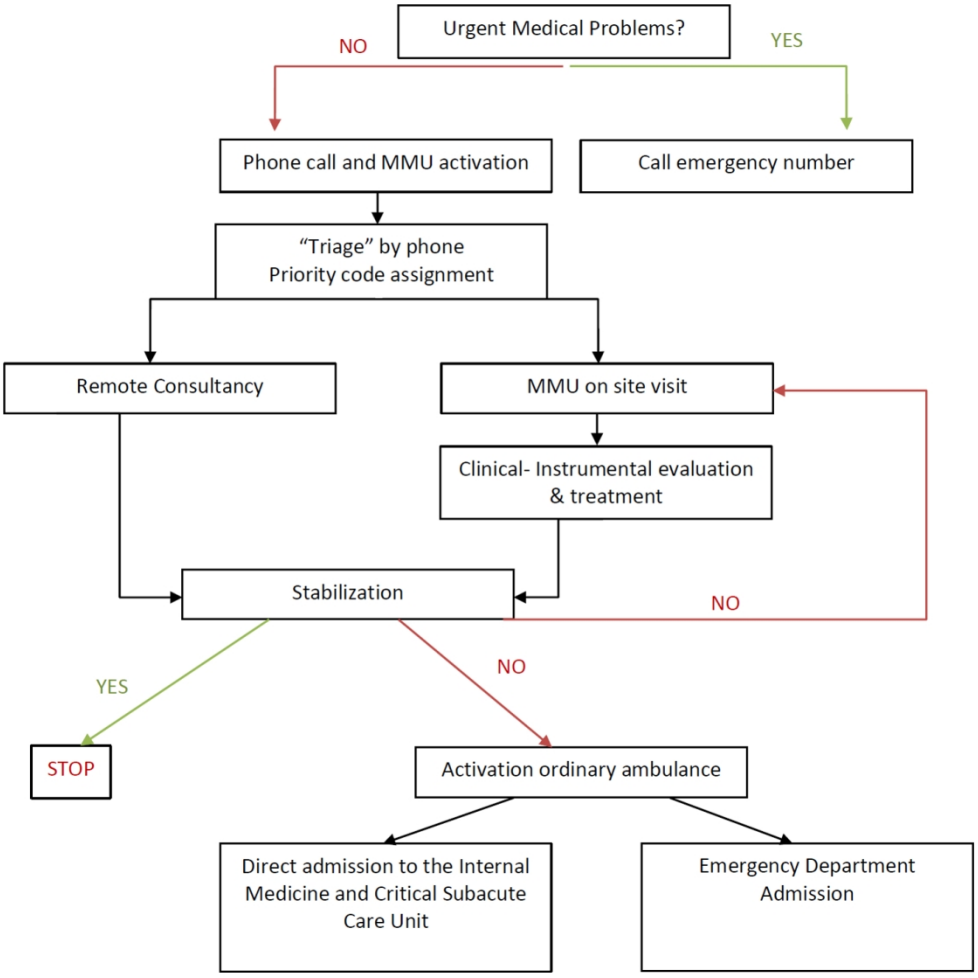
ECG = Electrocardiogram; UTI = Urinary Tract Infection; CGA = Comprehensive Geriatric Assessment; US = Ultrasound; PICC = Peripherally-Inserted Central Venous Catheter; DVT = Deep Vein Thrombosis; GP = General Practitioner.

FIGURE 1

Description of the intervention of MMU Team.

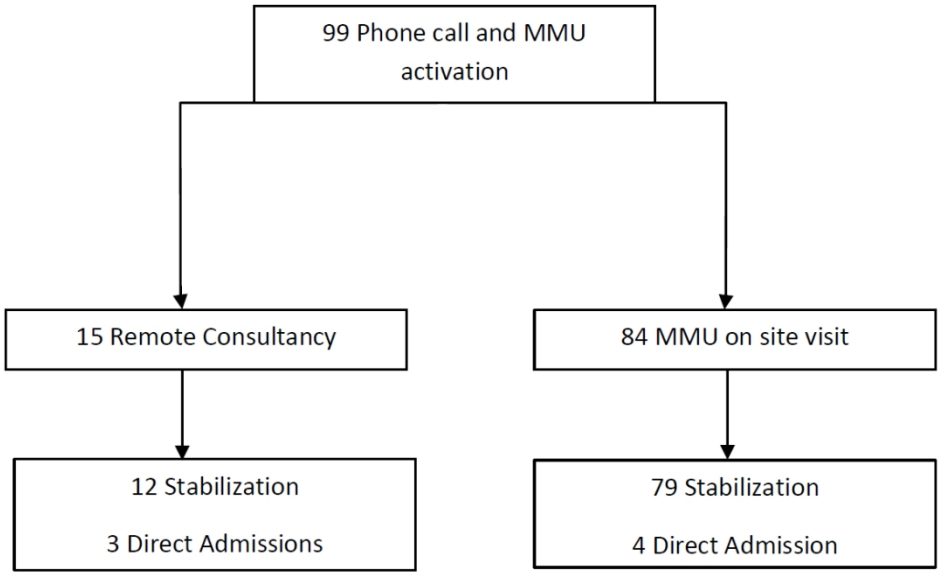
FIGURE 2

Results of pilot phase.



Description of the intervention of MMU Team

95x95mm (400 x 400 DPI)



Results of pilot phase

78x48mm (400 x 400 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		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	2, end of abstract
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	Supplemental Material
Funding	#4	Sources and types of financial, material, and other support	14
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 14
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	N/A (page 14)
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	N/A (page 13)

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)	13
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	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5
Objectives	#7	Specific objectives or hypotheses	6, 9
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)	9-10
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	6
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)	10
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9, 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)	N/A (complex intervention on organization of care)
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	N/A (the intervention concerns organization of care in nursing homes)

Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7-10
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
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)	11
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	11
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	N/A (all residents in participating nursing homes will be

			eligible for the study)
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	N/A (quasi-experimental study design on organization of care)
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	N/A (quasi-experimental study design on organization of care)
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A (quasi-experimental study design on organization of care)

Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A (quasi-experimental study design on organization of care)
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	N/A (quasi-experimental study design on organization of care)
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	10-11

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	N/A (quasi-experimental study design on organization of care)
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, 13
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	12
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
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)	N/A due to particular study design
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	13
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	13
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	N/A due to particular study design
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A due to particular study design
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	12-13

Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	12-13 + supplemental material
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	12-13 + supplemental material
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	12-13 + supplemental material
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	12-13 + supplemental material
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	14
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	12-13 + supplemental material

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	N/A due to particular study design
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 results databases, or other data sharing arrangements), including any publication restrictions	13 + supplemental material
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	Supplemental material
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	Supplemental material
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Supplemental material
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	N/A due to study design

NOTE: The original protocol approved by the competent Ethics Committee (in English language) has been uploaded as Supplemental Material.