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Hospital at Home care for older patients with cognitive impairment: A protocol for a randomized controlled feasibility trial

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Public title

Hospital at Home care for older patients with cognitive impairment and an acute medical illness

Scientific title

Hospital at Home care for older patients with cognitive impairment: A protocol for a randomized controlled feasibility trial

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Acronym

H@H

Abstract

INTRODUCTION: An acute hospital admission is a stressful life event for older people, particularly for those with cognitive impairment. The hospitalisation is often complicated by hospital-associated geriatric syndromes, including delirium and functional loss, leading to functional decline and nursing home admission. Hospital at Home care aims to avoid hospitalisation-associated adverse outcomes in older patients with cognitive impairment by providing hospital care in the patient's own environment.

METHODS AND ANALYSIS: This randomized, non-blinded feasibility trial aims to assess the feasibility of conducting a randomized controlled trial in terms of the recruitment, use and acceptability of Hospital at Home care for older patients with cognitive impairment. The quality of care will be evaluated and the advantages and disadvantages of the Hospital at Home care program compared to usual hospital care. Eligible patients will be randomized either to Hospital at Home care in their own environment or usual hospital care. The intervention consists of hospital level care provided at patients' homes, including visits from health care professionals, diagnostics (laboratory tests, blood cultures) and treatment. The control group will receive usual hospital care. Measurements will be conducted at baseline, during admission, at discharge and at three and six months after the baseline assessment.

ETHICS AND DISSEMINATION: Institutional ethics approval has been granted. The findings will be disseminated through public lectures, professional and scientific conferences, as well as peer-reviewed journal articles. The study findings will contribute to knowledge on the implementation of Hospital at Home care for older patients with cognitive disorders. The results will be used to inform and support strategies to deliver eligible care to older patients with cognitive impairment.

TRIAL REGISTRATION: This study was registered with the NTR registry (NTR6581) on 26 July 2017.

Keywords: Dementia, Cognition disorders, Central Nervous System Diseases, Aged, Home Care Services; Hospital-Based, Hospitalization, Randomized Controlled Trials, Hospital at Home

Strengths and limitations of this study

- This study addresses patients with cognitive impairment, a population who might benefit most of the Hospital at Home care concept, but is often excluded from participation in scientific research.
- As a feasibility trial does not show effectiveness, it will support the implementation of Hospital at Home care and a future trial
- This study is clinically relevant as it investigates patient centred care instead of hospital centred care

Introduction

Background

An acute hospital admission is a stressful life event, particularly for older people. In addition to the stress of an acute illness, the hospital admission itself contributes to this stress.¹ Older hospitalized patients are often deprived of sleep, and they spend an average of 20 of every 24 hours in bed, they become poorly nourished, and experience sensory deprivation or overstimulation, resulting in confusion.²⁻⁵ These adverse effects of hospitalization contribute to the occurrence of geriatric conditions, such as delirium, functional decline, falls, incontinence, hospital acquired infections and pressure injuries.⁶⁻⁹ Adverse effects of hospitalization occur more easily in older people, particularly in those who are already frail, a growing portion of the worldwide ageing population.^{10,11} Frailty is a state of increased vulnerability to external stressors resulting from aging-associated declines in reserve and function across multiple physiologic systems.¹⁰ Cognitive impairment (i.e., dementia) is an important contributor to frailty in older people.¹² Cognitively impaired older people are more likely to become hospitalised and once admitted, they experience longer stays than their peers without cognitive impairment.¹³⁻¹⁵ The combination of hospitalization and cognitive impairment in older people is associated with further functional and cognitive declines and higher mortality rates, and it leads to more discharges to long-term care facilities.^{16,17} The prevalence and worldwide burden of cognitive impairment will continue to increase as the average life expectancy increases.¹⁸ The total number of people with cognitive impairment is estimated to be 75.6 million in 2030 and will nearly triple in 2050 to 135.5 million.¹⁹ An increase in the number of hospital admissions of older people with cognitive impairment and an increase in number of hospitalisation-associated adverse outcomes are therefore to be expected.

Besides adverse outcomes of hospitalization, many older people and their caregivers do not necessarily desire a hospital admission in case of an acute illness or exacerbation of a chronic illness. Fried et al. (2000) have studied the preferences of community-dwelling persons 65 years of age and

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3 76 older who were hospitalized with a primary diagnosis of congestive heart failure, chronic obstructive
4 77 pulmonary disease or pneumonia. The authors reported that over 50% of older patients preferred to
5 78 receive hospital treatment at home, because they felt that their homes were more comfortable.²⁰ In
6 79 the treatment preferences of seriously ill patients 60 years of age and older, the likelihood of
7 80 cognitive and functional impairment as an adverse outcome of the treatment was weighed in the
8 81 decision-making process. There was a substantial decrease in the number of participants who opted
9 82 for treatment if the likelihood of impairment after treatment was 50% or higher.²¹

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15 84 Hospital at Home care could provide an effective alternative to inpatient care for a select group of
16 85 elderly patients now requiring hospitalisation. Hospital at Home care is coordinated, multidisciplinary
17 86 care in the homes of people who would otherwise be admitted to the hospital. Hospital at home care
18 87 is an accepted alternative to inpatient hospital level care in several countries (e.g., the United States,
19 88 Australia, Italy and the United Kingdom) but not yet in the Netherlands.²² Since the 1990s, Hospital at
20 89 Home has been evaluated in (older) persons with various acute medical conditions, such as heart
21 90 failure, exacerbations in chronic obstructive pulmonary disease (COPD) and infections (e.g., cellulitis,
22 91 pneumonia).²² In a systematic review comparing alternative strategies to inpatient hospitalization,
23 92 lower or equal mortality rates and return hospitalization rates (i.e., subsequent admissions after
24 93 discharge) were found for Hospital at Home care, and there was a positive effect on patient and
25 94 caregiver satisfaction.^{22,23} Only one trial conducted in Italy included 109 patients with cognitive
26 95 impairment (i.e. dementia), Tibaldi et al. reported a positive effect of a Hospital at Home intervention
27 96 on behavioural disturbances and caregiver stress in patients with dementia.²⁴ Whether Hospital at
28 97 Home care provides a suitable alternative with regard to other outcomes as patient satisfaction,
29 98 quality of care, hospitalisation-associated adverse events and costs in older people with cognitive
30 99 impairment remains unclear and further research is needed. Therefore, our primary aim is to
31 100 investigate the feasibility of a Hospital at Home care program for older patients with cognitive
32 101 impairment in terms of the patient recruitment, use and acceptability, and secondly to investigate
33 102 the advantages and disadvantages of Hospital at Home care compared to usual hospital care from
34 103 different perspectives.

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49 105 Objectives of this study are:

- 50 106 1) To assess the participation rate of the Hospital at Home trial among patients 65 years and older
51 107 with cognitive impairment, acute illness, and emergency hospital admission. What are the reasons
52 108 for non-participation?
53 109 2) To assess the differences in the quality of care provided in the Hospital at Home care group and
54 110 the usual hospital care group with regard to geriatric syndromes, institutionalization, mortality, total

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3 111 days with urinary catheter, length of stay (in the hospital or in Hospital at Home care) and
4 112 timing/intensity of the contact with health care professionals.
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6 113 3) To assess the potential advantages and disadvantages of Hospital at Home care and usual hospital
7 114 care for the patients, caregivers and Dutch medical health system.
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115 **Methods and analysis**

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117 **Trial design**

118 The design is a randomized controlled feasibility trial and will utilize a process evaluation. This study
119 will be conducted at the medical emergency department (ED) of the academic hospital of the
120 University Medical Center of Groningen in the Netherlands and will evaluate cognitively impaired
121 older patients who are in need of acute hospital care. Figure 1 shows the trial design summary.
122 Participants will be randomized to either Hospital at Home care or usual hospital care in a 4:1 ratio,
123 respectively. Patients will be randomized using a computerized random number generator
124 (<http://www.randomization.com>), including block randomization.

125 An independent research nurse who is not involved in the patient care will complete the baseline
126 assessment and allocate the participants (using sealed sequenced envelopes) into the Hospital at
127 Home care (intervention) or usual hospital care group (control). The research nurse will not be aware
128 of the randomization method. The participants, health care professionals and research staff will not
129 be blinded to the intervention. The reporting of the design of this trial protocol is in accordance with
130 the SPIRIT 2013 statement for clinical trial protocols.²⁵
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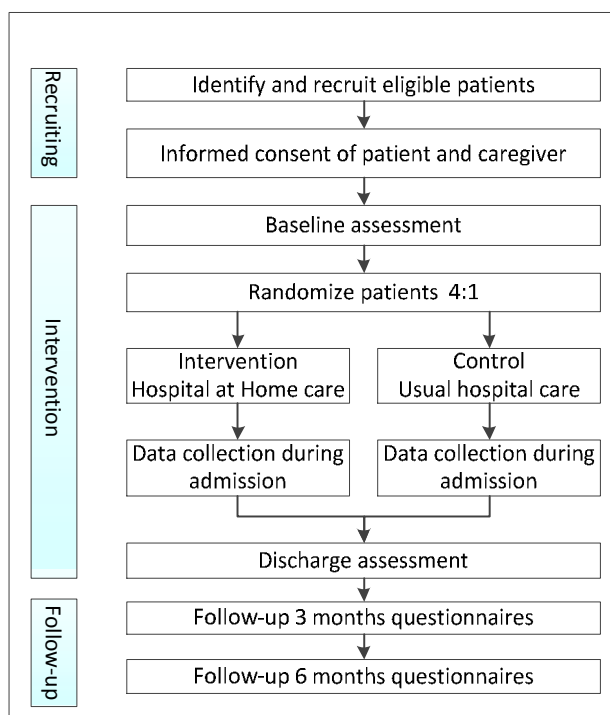
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Figure 1: Flowchart of trial design summary

134 **Study population**

135 Patients 65 years of age and older who are admitted to the medical emergency department (ED) will
 136 be identified by the ED staff as potential eligible patients. Subsequently, the ED staff will inform the
 137 research nurse. The research nurse will complete the eligibility criteria checklist (table 1). The
 138 research nurse will ask the patient and their informal caregiver (i.e., partner, child, relative, friend)
 139 for their willingness to participate in the study and to provide written informed consent. The patient
 140 and informal caregiver will need to both sign the informed consent form before the patient can
 141 participate in the H@H trial.

142 If the participant lacks the capacity to consent (mentally incapacitated), and an informal caregiver
 143 (i.e., partner, child, friend) is present, this informal caregiver will be asked to act as a personal
 144 consultee. The personal consultee will determine whether he or she believes that participation in the
 145 study would be in accordance with the values and interests of the individual and will subsequently
 146 sign the patient's informed consent form.

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148 **Table 1** Patient eligibility criteria for participation in Hospital at Home trial

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> ▪ Age 65 years of age and older ▪ Cognitive impairment, i.e. dementia, delirium or other cause of cognitive impairment, and either: <ul style="list-style-type: none"> ○ previously diagnosed or documented in the medical records or ○ identified by the ED-clinician (e.g., with the 4AT-test and/or Six item cognitive impairment test)²⁶⁻²⁸ ▪ Presented at the ED with a defined acute illness ▪ Required hospital admission, according to the attending ED physician but not expected to require emergency interventions <ul style="list-style-type: none"> ○ Modified Early Warning Score (MEWS) ≤ 2 points²⁹⁻³¹ ▪ Living in hospital's catchment area (< 25 km) ▪ Informal caregiver is present and able to understand and perform instructions and consented to participate in the trial ▪ Home suitable for Hospital at Home care (available informal caregiver, running water, adequate heating, safety)²⁸ 	<ul style="list-style-type: none"> ▪ Previously enrolled ▪ Hospitalized within the seven days preceding ED presentation ▪ Nursing home residents or awaiting a nursing home place on an active waiting list (excluding so-called sleeping waiting list candidates)²⁷ ▪ Additional care needed <ul style="list-style-type: none"> ○ Required surgical assessment ○ Suspected acute coronary syndrome or cardiac arrhythmia³¹ ○ Dialysis dependent patients³¹ ○ Expected terminal events³¹ or in need of diagnostic or palliative care due to oncological or haematological illness

149 ED= Emergency department

150

151 **Sample size of study population**

152 Based on the numbers available from the emergency department (ED) of the University Medical
 153 Center Groningen, the Netherlands, we calculated that an average of 3990 older patients 65 years
 154 and over is admitted to our medical ED each year. The Hospital at Home trial will be introduced
 155 during working hours, which provides an estimated 1900 patients per year. Not all 1900 patients will
 156 be eligible for study inclusion. Based on screening of ED medical records, approximately 15% of the
 157 patients meet the eligibility criteria for Hospital at Home care, resulting in 285 eligible persons per
 158 year. In recent randomized controlled trials (RCTs) of Hospital at Home care in Italy, 54% and 57% of
 159 the eligible patients was willing to participate and gave informed consent.^{32,33} We presume a similar
 160 consent rate of 50%, as described in these previous clinical trials, and expect for 143 patients to be
 161 included.

162 **Study procedures**

163 After (written) informed consent is obtained, the participants will complete two brief cognitive tests,
 164 and the participant and caregiver will complete the baseline assessment. Subsequently,
 165 randomization takes place to either (a) the Hospital at Home care-intervention, translocation of care
 166 from the hospital to a participants' home or (b) the control group, usual hospital care. All care will be
 167 delivered according to hospital protocols, current regulations and guidelines and, if needed,

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3 168 described in the standard operating procedures (SOPs). If no informed consent is given by either the
4 169 patient or the caregiver, the reasons for non-participation, date of birth, sex of the patient and the
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6 170 relationship between patient and caregiver will be reported.
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8 171 **Intervention**

9 172 **Hospital at Home care**

10 173 Hospital at Home care will be delivered by a multidisciplinary team consisting of a physician, nurse
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12 174 and physiotherapist. Depending on the participants' needs, other disciplines (e.g., a dietician,
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14 175 occupational therapist or social services) can be involved in the Hospital at Home care. The day-to-
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16 176 day care will be provided by the nurse and physician visiting the participant. The Hospital at Home
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18 177 care team works under the responsibility of the medical specialist in the hospital, and 24/7
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20 178 consultation of the expertise and services of the hospital is part of the protocol.
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23 180 The participants allocated to Hospital at Home care will receive hospital level care in their own
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25 181 homes. After a stay of one night in the hospital, while the Hospital at Home care arrangements are
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27 182 being made, the participant will be transferred home and receive Hospital at Home care. The
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29 183 Hospital at Home nurse is responsible for the day-to-day care and will be present upon arrival of the
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31 184 participant at his/her residence. Hospital at Home care is described in the care protocols including
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33 185 SOPs and could include intravenous therapy (e.g., antibiotics, fluid, and/or diuretics), oxygen therapy,
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35 186 and/or nebulizer, indwelling urine catheter or a nasopharyngeal food tube. After the care intake and
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37 187 a period of direct nursing supervision, the participant will receive intermittent nursing visits daily
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39 188 (starting with 3x/day). The Hospital at Home physician will make a home visit every day (excl.
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41 189 weekends). The Hospital at Home physician and nurse will be available for emergency visits. The
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43 190 participant will receive a medical alert device in the house, with a 24/7 connection to an on-call
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45 191 service. Alert instructions will be explained to the participant and caregiver. A physiotherapist will
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47 192 visit the participant at home to evaluate any problems with balance and/or walking and immobility.
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49 193 The Hospital at Home team works under the supervision of the hospital medical specialist. Daily
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51 194 screenings and measurements will be recorded in a Hospital at Home record, which stays with the
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53 195 participant. Diagnostic procedures and therapeutics that cannot wait and are not available at home,
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55 196 such as endoscopy or CT-scan, will be arranged through brief visits to the hospital. The participant
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57 197 will be 'admitted' to the Hospital at Home care for as long as indicated.
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59 198 *Discharge from Hospital at Home*

60 199 If the participant recovers to such an extent that hospital level care is no longer needed, the
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201 200 participant will be discharged from the Hospital at Home care program, similar to the discharge
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203 201 procedure when the participant would receive usual hospital care. Hospital at Home care will end

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3 202 with discharge planning with the participant, family, Hospital at Home physician and nurse. The
4 203 discharge plan includes follow-up appointments (e.g., at the hospital or general practitioner),
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6 204 information on medication, warning signs and symptoms and an on-going management plan. All
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8 205 hospital-related care equipment will be removed from the participants' house, and arrangements
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10 206 with homecare agencies and/or paramedical staff will be reviewed and adjusted to the current
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12 207 situation.

13 208 **Hospital care as usual**

14 209 Participants allocated to the control arm will be admitted to a hospital ward and receive usual
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16 210 hospital care. After admission and intake on the ward, the participant will receive intermittent visits
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18 211 from the ward nurse multiple times a day. The ward physician will visit once every day (excl.
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20 212 weekends), with extra visits provided if needed. An emergency alert device, through which nurses
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22 213 and physician can be contacted, will be placed next to the bed. A physiotherapist will visit the
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24 214 participant at the ward to address problems with balance and/or walking and immobility. Depending
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26 215 on the participants' needs, other disciplines (e.g., a dietician, occupational therapist or social
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28 216 services) can be involved in the hospital care. The medical record is the hospital record and
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30 217 additional H@H research forms will be added to this record for research purposes. The participant
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32 218 will be admitted to the hospital for as long as indicated.

33 219 34 220 *Hospital discharge*

35 221 If the participant recovers to such an extent that hospital level care is no longer needed, the
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37 222 participant will be discharged from the hospital after discharge planning with the participant, family,
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39 223 physician and nurse. The discharge plan includes follow-up appointments (e.g., at the hospital or
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41 224 general practitioner), information on medication, warning signs and symptoms and an on-going
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43 225 management plan. Arrangements with homecare agencies and/or paramedical staff will be reviewed
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45 226 and adjusted to the current situation.

46 227 47 228 **Follow-up**

48 229 At three and six months following randomization, all participants will be contacted for an interview
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50 230 by telephone³⁴ or a face-to-face interview, if needed. The participants will be allowed to receive
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52 231 support with these questions from their relatives or informal caregivers. An interview will require a
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54 232 maximum of 30 minutes. In case of institutionalization or mortality, this event will be recorded.
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56 233 Additionally, information on hospital readmission and length of stay will be collected from the
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58 234 hospital administration system and health insurers. Mortality and nursing home placements will be
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60 235 collected from registries from the general practitioner and municipalities.

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Timing of measurements and outcome measures

Data will be collected at baseline at the emergency department, during admission (in Hospital at Home or hospital), at discharge and at three and six months following randomization, plus or minus two weeks. An overview of the timing of measurements and outcome measures are shown in Table 2.

Feasibility

For the participation rates, the proportion of participants per step will be calculated. The reasons for non-participation and data concerning the characteristics of non-participants will be collected. We consider the participation rate feasible when it is similar to the participation rate as is described in previous RCTs and around 50% of the eligible patients will consent to participate.^{32,33} Quality of care will be measured by collecting data on patient, institutionalization (e.g., to the hospital or nursing home), mortality, ADL-functioning, prevalence of hospitalisation-associated geriatric syndromes, the length of stay in the hospital or Hospital at Home care program and contact with health care professionals. The study is considered feasible if the quality of care of Hospital at Home care on these measurements is non- inferior to usual hospital care.

255 **Table 2** Overview of the content and description of outcome measures and timing of measurements

	Description and instrument	Timing of measurements					
		screening	baseline	daily	discharge	3 months	6 months
Degree of illness based on physiological parameters	Vital signs alarm score; Modified Early Warning Score, ³⁵	R					
Cognitive impairment	4AT-test for delirium* Six item cognitive impairment test for cognitive impairment*, ^{26,36}	R					
Socio-demographics	Date of birth, nationality, household composition, marital status, highest level of education		R				
Health status	Charlson co-morbidity index*, ³⁷		R				
Identifying at-risk patients	Safety management system patient screening (VMS), ³⁸		R				
Functional status	Activities of daily living, modified Katz-ADL index score, ³⁹		R		R	R	R
Health status	EQ-5d-5l*, ⁴⁰		R		R	R	R
(Health-related) quality of life, well-being	Icepap capability measure for Older people (ICECAP-O)* ⁴¹		R		R	R	R
Caregiver burden	Self-rated burden scale*, caregiver strain index*, ^{42,43}		C		C	C	C
Medical consumption	Imta Medical Consumption Questionnaire (imcq)*, ⁴⁴		P,C			P,C	P,C
Hospitalisation-associated geriatric syndromes	Infections, falls, pressure injuries, in case of delirium; delirium observation scale score (DOSS) ⁴⁵ and use of physical or chemical restraints, total days with a urinary catheter			N			
Nutrition	Malnutrition Universal Screening Tool (MUST), ⁴⁶ food intake, fluid intake			N			
Pain	Numeric Rating Scale-score (NRS) for pain ⁴⁷			N			
Health perception	(Rotterdam) symptom checklist* ⁴⁸			N			
Immobility	Hierarchical assessment of balance and mobility (HABAM) ⁴⁹			Ph			
Satisfaction with care	Client Satisfaction Questionnaire 8 (CSQ-8)*, care evaluation question*, ^{50,51}				P	P,C	N,D
Mortality	Mortality at 30 days, 3 months and 6 months after baseline*				N	R	R
(Re)admission hospital	Length of stay, readmission rate at 30 days, 3 months and 6 months after baseline*				N	R	R

256 Assessed by: P= Participant, C=Caregiver, N= Nurse, D= Doctor, R= Research nurse, Ph=Physiotherapist.

257 (*)= All assessments marked by an asterisk are extra for trial purposes and are not part of the medical treatment

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259 *Other outcomes measures*

260 Advantages and disadvantages of the Hospital at Home care program will be assessed through
 261 multiple instruments and questionnaires. The instruments are validated and used in community-
 262 dwelling older patients with cognitive disorders. Additional data will be collected on the time spent
 263 at home (home-time); total number of days alive and out of the hospital or a skilled nursing facility in
 264 the 6 months following the randomization at the emergency department,⁵² the number of transfers
 265 (home ↔ hospital) and the number of health care professionals involved.

266 Cost data will be collected, as described by Drummond et al., including the costs to the health care
267 system, patients and families, and other sectors.⁵³ The volume of care use will be extracted from
268 hospital files and combined with the reference cost values, as provided by the cost guidance module
269 of the Dutch National Health Care Institute.⁵⁴

270 **Process evaluation**

271 A process evaluation will be conducted as part of the feasibility study to understand the barriers and
272 facilitators to participate and to gain an understanding of the experiences and perceptions of
273 Hospital at Home care of participants and health care professionals. From all eligible patients who
274 declined to participate, data concerning the patient characteristics and reasons for non-participation
275 will be collected. At the end of the trial, a representative sample of participants and/or their informal
276 caregivers will be invited for an interview to evaluate their experiences receiving Hospital at Home
277 care. The interviewer will not be an active member of the research team or involved in day-to-day
278 care and will explore independently how the participants perceived Hospital at Home care, including
279 the contact with the health professionals and the impact of Hospital at Home care on their lives and
280 their caregivers' personal lives. In case of participant dropout, efforts will be made to obtain an
281 understanding of why the participants did not complete the trial.

282 In addition, a representative sample of health care professionals, consisting of physicians and nurses
283 working in the Emergency Department, physicians and nurses providing the Hospital at Home care,
284 and general practitioners, will be asked to participate in a face-to-face interview. The health care
285 professionals will be asked about their experiences and opinions about the H@H-trial and Hospital at
286 Home care. All interviews will be transcribed verbatim, and a framework analysis will be used as the
287 method of qualitative data analysis.⁵⁵

288 **Data management**

289 All data will be entered in an electronic trial-specific database, with the participants identified by a
290 unique trial number. Confidentiality of participant information will be maintained throughout the
291 trial. Information can only be traced to the participants by designated researchers. The database will
292 be stored and maintained by Castor Electronic Data Capture, compliant with GCP guidelines and the
293 European Data Protection Directive (Castor Electronic Data Capture, Ciwit BV, Amsterdam, the
294 Netherlands, 2017). Data will be stored for a maximum period of 15 years after the study has ended,
295 according to Dutch law.⁵⁶

296 **Statistical analysis**

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298 The participant flow diagram, according to CONSORT guidelines,⁵⁷ will provide a summary of the
299 recruitment and declination rates in percentage (%) at baseline, discharge and three- and six-month
300 follow-ups. Distributions of the data at baseline, discharge and three and six months after
301 randomization will be explored, with unusual values noted and explained. Variables will be
302 summarized as the n (%), mean (standard deviation) or median (interquartile range) for each group,
303 to characterize the sample and search for any imbalances. The percentages, means and standard
304 deviation, and medians and interquartile ranges will be calculated to describe the quality of care and
305 the advantages and disadvantages of Hospital at Home care at baseline, discharge and three- and six-
306 month follow-ups.

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308 **Monitoring and participant safety**

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310 Although, the H@H trial is considered to be a low risk trial, the participant safety will be monitored
311 by an independent Data Monitoring Committee (DMC). The DMC will consist of two members: an
312 experienced clinician and an epidemiologist. Members of the DMC are independent of the trial and
313 will discuss each individual participant with serious adverse events. The DMC will receive and review
314 the serious adverse events and evaluate the risk involved with negative outcomes. The DMC is
315 authorized to make recommendations to temporary put on hold or ending the study prematurely
316 when participant safety is an issue, based on their findings. All serious adverse events will be
317 reported to the principal investigator within 24 hours of knowledge of the event and then
318 subsequently reported to the Dutch portal for medical research involving human subjects.

319 **Discussion**

320 Reducing unwanted hospital admissions in older patients with cognitive impairments and facilitating
321 patient-centred care in a patient's preferred location is a goal worthy of pursuing. This goal aligns
322 with the tenet of the current Dutch government and the advice provided by the Dutch Council for the
323 Environment and Infrastructure: to actively promote and enable people to live independently in their
324 own homes for as long as they desire.⁵⁸ Previous trials and a recent review have confirmed that
325 alternative management strategies for low-risk patients with acute medical conditions conventionally
326 treated through hospitalization exist with positive impact on patient satisfaction, are effective and
327 can be safely achieved in lower cost settings.^{22,23,59}

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3 328 Introducing a Hospital at Home care trajectory in the Netherlands is incited by the principles of value-
4 329 based health care: improving the patients experience of care and as a result of this process reducing
5 330 the costs.⁶⁰ All countries with an ageing population experience pressure, in terms of shortage of
6 331 (emergency) hospital beds and rising healthcare costs. Hospital at Home care could be shown
7 332 beneficial in facilitating higher valued care for patients and their caregivers without additional costs.
8 333 Benefit should be measured in other outcomes than clinical indicators such as mortality. To illustrate,
9 334 one of the outcomes of a future RCT could be the time spent at home. Time spent at home has been
10 335 defined as the total number of days alive and out of the hospital or a skilled nursing facility in the 6
11 336 months after hospital admission.⁵² It has been used as a primary outcome in a follow-up study of
12 337 older patients with acute hospital admissions, and has been demonstrated to be of more importance
13 338 in older patients.⁶¹⁻⁶³ Evaluation of time spent a home in this feasibility study could support
14 339 estimating a sample size based on a patient-relevant outcome in a future RCT.

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18 340 This study will be the first to investigate the feasibility of providing acute hospital care at home for
19 341 older patients with cognitive impairment in the Netherlands. Studying Hospital at Home care and
20 342 identifying the barriers and facilitators will support the implementation of Hospital at Home care and
21 343 break new ground for a future RCT investigating the (cost-)effectiveness.

344 **Ethics and Dissemination**

345 This study was approved by the Medical Research Ethics Committee of the University Medical Center
346 Groningen in April 2017, reference number: 2016.686 The trial will be conducted in accordance with
347 the Declaration of Helsinki 1996, principles of good clinical practice and the University Medical
348 Center of Groningen Research Code. Any protocol amendments will be submitted to the ethics
349 committee. A register of the protocol amendments will be available in the study protocol.

350 The results of the trial will be reported according to the CONSORT guidelines and will contribute to
351 knowledge of the implementation of Hospital at Home care and patient-centred acute care for older
352 patients with cognitive impairment. The study will also contribute to the knowledge of the
353 transmurial cooperation and costs of providing care, in terms of the translocation of hospital care to
354 home. Regularly updates will be published on the study website and in newsletters. Conferences and
355 meetings will be held for all involved health care professionals. Participants who requested
356 information on the study will be sent a lay summary. A publication policy will be agreed upon with
357 co-applicants. The study findings will be published in relevant peer-reviewed journals.

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369

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379

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387

388 **Competing interests** All authors have declared that they have no competing interests

389

390 **Ethics approval** for this study has been obtained from the Medical Research Ethics Committee of the University
391 Medical Center Groningen April 2017 (ref: 2016.686).

392

393 **Recruitment status** is pending; participants are not yet being recruited or enrolled. Anticipated date of
394 enrolment of the first participant is December 2017.

395

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404 Abbreviations

405 ADL: Activities of Daily Living

406 CT: Computer Tomography

407 DMC: Data Monitoring Committee

408 ED: Emergency Department

409 H@H: Hospital at Home

410 RCT: Randomized Controlled Trial

411 UMCG: University Medical Center Groningen

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on 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	1
	2b	All items from the World Health Organization Trial Registration Data Set	1, 3, 4, 5, 6, 8, 9, 13, 14
Protocol version	3	Date and version identifier	all
Funding	4	Sources and types of financial, material, and other support	14
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	14
	5b	Name and contact information for the trial sponsor	14
	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	14
	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)	n/a

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1				
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3	Introduction			
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5	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	3
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8		6b	Explanation for choice of comparators	3
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10	Objectives	7	Specific objectives or hypotheses	3
11				
12	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, noninferiority, exploratory)	4
13				
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15	Methods: Participants, interventions, and outcomes			
16				
17	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	4
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19				
20	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)	6
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23	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7, 8
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26		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)	7, 8
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29		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	n/a
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32		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9, 10
33				
34	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	9, 10
35				
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39	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)	10
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2	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	6
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5	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5
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7				

Methods: Assignment of interventions (for controlled trials)

Allocation:

11	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	4
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17	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	4
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21	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
22				
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24	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	4
25				
26				
27		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
28				
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Methods: Data collection, management, and analysis

33	Data collection methods	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	9, 10, 11
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38		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11
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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

Statistical methods 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

20b Methods for any additional analyses (eg, subgroup and adjusted analyses) n/a

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

Methods: Monitoring

Data monitoring 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 12

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 12

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 12

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

Ethics and dissemination

Research ethics approval 24 Plans for seeking research ethics committee/institutional review board (REC/IRB) approval 12

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

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2				
3	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	5
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5				
6		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
7				
8	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	10
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11	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
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14	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	10
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17	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	Available on request
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20	Dissemination policy	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	12
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23		31b	Authorship eligibility guidelines and any intended use of professional writers	13
24				
25		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
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29	Appendices			
30				
31	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Available on request
32				
33				
34	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
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37 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items.
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Hospital at Home care for older patients with cognitive impairment: A protocol for a randomized controlled feasibility trial

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Public title

Hospital at Home care for older patients with cognitive impairment and an acute medical illness

Scientific title

Hospital at Home care for older patients with cognitive impairment: A protocol for a randomized controlled feasibility trial

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Acronym

H@H

Abstract

INTRODUCTION: An acute hospital admission is a stressful life event for older people, particularly for those with cognitive impairment. The hospitalisation is often complicated by hospital-associated geriatric syndromes, including delirium and functional loss, leading to functional decline and nursing home admission. Hospital at Home care aims to avoid hospitalisation-associated adverse outcomes in older patients with cognitive impairment by providing hospital care in the patient's own environment.

METHODS AND ANALYSIS: This randomized, non-blinded feasibility trial aims to assess the feasibility of conducting a randomized controlled trial in terms of the recruitment, use and acceptability of Hospital at Home care for older patients with cognitive impairment. The quality of care will be evaluated and the advantages and disadvantages of the Hospital at Home care program compared to usual hospital care. Eligible patients will be randomized either to Hospital at Home care in their own environment or usual hospital care. The intervention consists of hospital level care provided at patients' homes, including visits from health care professionals, diagnostics (laboratory tests, blood cultures) and treatment. The control group will receive usual hospital care. Measurements will be conducted at baseline, during admission, at discharge and at three and six months after the baseline assessment.

ETHICS AND DISSEMINATION: Institutional ethics approval has been granted. The findings will be disseminated through public lectures, professional and scientific conferences, as well as peer-reviewed journal articles. The study findings will contribute to knowledge on the implementation of Hospital at Home care for older patients with cognitive disorders. The results will be used to inform and support strategies to deliver eligible care to older patients with cognitive impairment.

TRIAL REGISTRATION: This study was registered with the NTR registry (NTR6581) on 26 July 2017.

Keywords: Dementia, Cognition disorders, Central Nervous System Diseases, Aged, Home Care Services; Hospital-Based, Hospitalization, Randomized Controlled Trials, Hospital at Home

Strengths and limitations of this study

- This study addresses the feasibility of Hospital at Home care in patients with cognitive impairment, a patient population that is often excluded from participation in scientific research
- A process evaluation facilitates the investigation of factors that influence the experiences and perceptions of all persons involved in Hospital at Home care
- Stakeholders were involved in the development of the design of the study which will support the implementation of Hospital at Home care and a future trial
- Because of a limited sample size due to the study being centered on feasibility, results will not show effectiveness of Hospital at Home care compared to usual hospital care.

Introduction

Background

An acute hospital admission is a stressful life event, particularly for older people. In addition to the stress of an acute illness, the hospital admission itself contributes to this stress.¹ Older hospitalized patients are often deprived of sleep, and they spend an average of 20 of every 24 hours in bed, they become poorly nourished, and experience sensory deprivation or overstimulation, resulting in confusion.²⁻⁵ These adverse effects of hospitalization contribute to the occurrence of geriatric conditions, such as delirium, functional decline, falls, incontinence, hospital acquired infections and pressure injuries.⁶⁻⁹ Adverse effects of hospitalization occur more easily in older people, particularly in those who are already frail, a growing portion of the worldwide ageing population.^{10,11} Frailty is a state of increased vulnerability to external stressors resulting from aging-associated declines in reserve and function across multiple physiologic systems.¹⁰ Cognitive impairment (i.e., dementia) is an important contributor to frailty in older people.¹² Cognitively impaired older people are more likely to become hospitalised and once admitted, they experience longer stays than their peers without cognitive impairment.¹³⁻¹⁵ The combination of hospitalization and cognitive impairment in older people is associated with further functional and cognitive declines and higher mortality rates, and it leads to more discharges to long-term care facilities.^{16,17} The prevalence and worldwide burden of cognitive impairment will continue to increase as the average life expectancy increases.¹⁸ The total number of people with cognitive impairment is estimated to be 75.6 million in 2030 and will nearly triple in 2050 to 135.5 million.¹⁹ An increase in the number of hospital admissions of older people with cognitive impairment and an increase in number of hospitalisation-associated adverse outcomes are therefore to be expected.

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2
3 75 Besides adverse outcomes of hospitalization, many older people and their caregivers do not
4 76 necessarily desire a hospital admission in case of an acute illness or exacerbation of a chronic illness.
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6 77 Fried et al. (2000) have studied the preferences of community-dwelling persons 65 years of age and
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8 78 older who were hospitalized with a primary diagnosis of congestive heart failure, chronic obstructive
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10 79 pulmonary disease or pneumonia. The authors reported that over 50% of older patients preferred to
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12 80 receive hospital treatment at home, because they felt that their homes were more comfortable.²⁰ In
13
14 81 the treatment preferences of seriously ill patients 60 years of age and older, the likelihood of
15
16 82 cognitive and functional impairment as an adverse outcome of the treatment was weighed in the
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18 83 decision-making process. There was a substantial decrease in the number of participants who opted
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20 84 for treatment if the likelihood of impairment after treatment was 50% or higher.²¹

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22 85
23 86 Hospital at Home care could provide an effective alternative to inpatient care for a select group of
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25 87 elderly patients now requiring hospitalisation. Hospital at Home care is coordinated, multidisciplinary
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27 88 care in the homes of people who would otherwise be admitted to the hospital. Hospital at Home
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29 89 care is an accepted alternative to inpatient hospital level care in several countries (e.g., the United
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31 90 States, Australia, Italy and the United Kingdom) but not yet in the Netherlands.²² Since the 1990s,
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33 91 Hospital at Home has been evaluated in (older) persons with various acute medical conditions, such
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35 92 as heart failure, exacerbations in chronic obstructive pulmonary disease (COPD) and infections (e.g.,
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37 93 cellulitis, pneumonia).²² In systematic reviews comparing alternative strategies to inpatient
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39 94 hospitalization, lower or equal mortality rates and return hospitalization rates (i.e., subsequent
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41 95 admissions after discharge) were found for Hospital at Home care, there was a lower incidence of
42
43 96 delirium, and there was a positive effect on patient and caregiver satisfaction.²²⁻²⁴ Only one
44
45 97 completed trial conducted in Italy included 109 patients with cognitive impairment (i.e. dementia),
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47 98 Tibaldi et al. reported a positive effect of a Hospital at Home intervention on behavioural
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49 99 disturbances and caregiver stress in patients with dementia.²⁵ Results of a still on-going trial including
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51 100 people with i.a. cognitive impairment in the United Kingdom, will follow in the near future.²⁶

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53 101 Whether Hospital at Home care provides a suitable alternative with regard to other outcomes as
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55 102 patient satisfaction, quality of care, hospitalisation-associated adverse events and costs in older
56
57 103 people with cognitive impairment remains unclear and further research is needed. Therefore, our
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59 104 primary aim is to investigate the feasibility of a Hospital at Home care program for older patients
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105 with cognitive impairment in terms of the patient recruitment, use and acceptability, and secondly to
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107 investigate the advantages and disadvantages of Hospital at Home care compared to usual hospital
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109 care from different perspectives.

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Objectives of this study are:

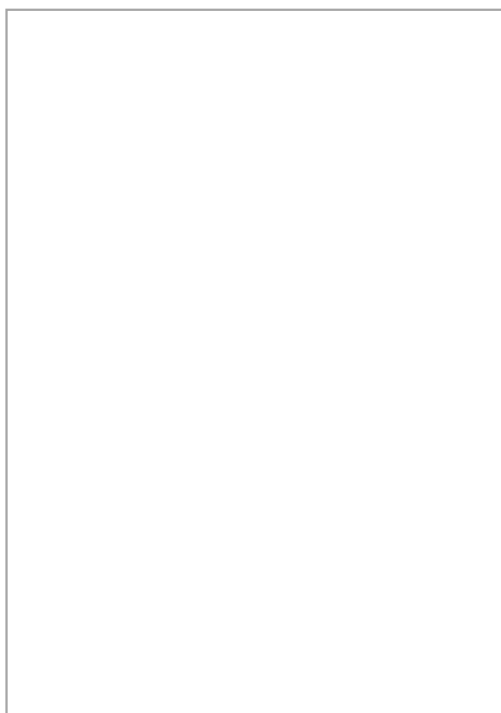
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3 110 1) To assess the participation rate of the Hospital at Home trial among patients 65 years and older
4 111 with cognitive impairment, acute illness, and emergency hospital admission. What are the reasons
5 112 for non-participation?
6
7 113 2) To assess the potential advantages and disadvantages of Hospital at Home care and usual hospital
8 114 care for the patients, caregivers and Dutch medical health system.
9
10 115 3) To assess the feasibility of Hospital at Home care in terms of the quality of care with regard to
11 116 geriatric syndromes, institutionalization, mortality, total days with urinary catheter, length of stay (in
12 117 the hospital or in Hospital at Home care) and timing/intensity of the contact with health care
13
14 118 professionals.

119 **Methods and analysis**

120 **Trial design**

121
122 The design is a randomized controlled feasibility trial and will utilize a process evaluation. This study
123 will be conducted at the medical emergency department (ED) of the academic hospital of the
124 University Medical Center of Groningen in the Netherlands and will evaluate cognitively impaired
125 older patients who are in need of acute hospital care. Figure 1 shows the trial design summary.
126 Participants will be randomized to either Hospital at Home care or usual hospital care in a 4:1 ratio,
127 respectively. Patients will be randomized using a computerized random number generator
128 (<http://www.randomization.com>), including block randomization.
129 An independent research nurse who is not involved in the patient care will complete the baseline
130 assessment and allocate the participants (using sealed sequenced envelopes) into the Hospital at
131 Home care (intervention) or usual hospital care group (control). The research nurse will not be aware
132 of the randomization method. The participants, health care professionals and research staff will not
133 be blinded to the intervention. The reporting of the design of this trial protocol is in accordance with
134 the SPIRIT 2013 statement for clinical trial protocols.²⁷

135



136
137

Figure 1

138 **Study population**

139 Patients 65 years of age and older who are admitted to the medical emergency department (ED) will
140 be identified by the ED staff as potential eligible patients. Subsequently, the ED staff will inform the
141 research nurse. The research nurse will complete the eligibility criteria checklist (table 1). The
142 research nurse will ask the patient and their informal caregiver (i.e., partner, child, relative, friend)
143 for their willingness to participate in the study and to provide written informed consent. The patient
144 and informal caregiver will need to both sign the informed consent form before the patient can
145 participate in the H@H trial.

146 An evaluation to assess the mental capacity is conducted by the involved ED staff in the setting of the
147 emergency department assessment. If the participant lacks the capacity to consent (mentally
148 incapacitated), and an informal caregiver (i.e., partner, child, friend) is present, this informal
149 caregiver will be asked to act as a personal consultee. The personal consultee will determine whether
150 he or she believes that participation in the study would be in accordance with the values and
151 interests of the individual and will subsequently sign the patient's informed consent form.

152

153 **Table 1** Patient eligibility criteria for participation in Hospital at Home trial

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> ▪ Age 65 years of age and older ▪ Cognitive impairment, i.e. dementia, delirium or other cause of cognitive impairment, and either: <ul style="list-style-type: none"> ○ previously diagnosed or documented in the medical records or ○ identified by the ED-clinician (e.g., with the 4AT-test and/or Six item cognitive impairment test)²⁸⁻³⁰ ▪ Presented at the ED with a defined acute illness ▪ Required hospital admission, according to the attending ED physician but not expected to require emergency interventions <ul style="list-style-type: none"> ○ Modified Early Warning Score (MEWS) ≤ 2 points³¹⁻³³ ▪ Living in hospital's catchment area (< 25 km) ▪ Informal caregiver is present and able to understand and perform instructions and consented to participate in the trial ▪ Home suitable for Hospital at Home care (available informal caregiver, running water, adequate heating, safety)³⁰ 	<ul style="list-style-type: none"> ▪ Previously enrolled ▪ Hospitalized within the seven days preceding ED presentation ▪ Nursing home residents or awaiting a nursing home place on an active waiting list (excluding so-called sleeping waiting list candidates)²⁷ ▪ Additional care needed <ul style="list-style-type: none"> ○ Required surgical assessment ○ Suspected acute coronary syndrome or cardiac arrhythmia³¹ ○ Dialysis dependent patients³¹ ○ Expected terminal events³¹ or in need of diagnostic or palliative care due to oncological or haematological illness

154 ED= Emergency department

155

156 **Sample size of study population**

157 Based on the numbers available from the emergency department (ED) of the University Medical
 158 Center Groningen, the Netherlands, we calculated that an average of 3990 older patients 65 years
 159 and over is admitted to our medical ED each year. The Hospital at Home trial will be introduced
 160 during working hours, which provides an estimated 1900 patients per year. Not all 1900 patients will
 161 be eligible for study inclusion. Based on screening of ED medical records, approximately 15% of the
 162 patients meet the eligibility criteria for Hospital at Home care, resulting in 285 eligible persons per
 163 year. In recent randomized controlled trials (RCTs) of Hospital at Home care in Italy, 54% and 57% of
 164 the eligible patients was willing to participate and gave informed consent.^{34,35} We presume a similar
 165 consent rate of 50%, as described in these previous clinical trials, and expect for 143 patients to be
 166 included.

167 **Study procedures**

168 After (written) informed consent is obtained, all participants will complete two brief tests to assess
 169 cognitive impairment, and the participant and caregiver will complete the baseline assessment.
 170 Subsequently, randomization takes place to either (a) the Hospital at Home care-intervention,
 171 translocation of care from the hospital to a participants' home or (b) the control group, usual
 172 hospital care. All care will be delivered according to hospital protocols, current regulations and

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3 173 guidelines and, if needed, described in the standard operating procedures (SOPs). If no informed
4 174 consent is given by either the patient or the caregiver, the reasons for non-participation, date of
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6 175 birth, sex of the patient and the relationship between patient and caregiver will be reported.
7

8 176 **Intervention**

9 177 **Hospital at Home care**

10 178 Hospital at Home care will be delivered by a multidisciplinary team consisting of a physician, nurse,
11
12 179 pharmacist and physiotherapist. Depending on the participants' needs, other disciplines (e.g., a
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14 180 dietician, occupational therapist or social services) can be involved in the Hospital at Home care. The
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16 181 day-to-day care will be provided by the nurse and physician visiting the participant. The Hospital at
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18 182 Home care team works under the responsibility of the medical specialist in the hospital, and 24/7
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20 183 consultation of the expertise and services of the hospital is part of the protocol.
21

22
23 185 The participants allocated to Hospital at Home care will receive hospital level care in their own
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25 186 homes. After a stay of one night in the hospital, while the Hospital at Home care arrangements are
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27 187 being made, the participant will be transferred home and receive Hospital at Home care. The
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29 188 Hospital at Home nurse is responsible for the day-to-day care and will be present upon arrival of the
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31 189 participant at his/her residence. Hospital at Home care is described in the care protocols including
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33 190 SOPs and could include intravenous therapy (e.g., antibiotics, fluid, and/or diuretics), oxygen therapy,
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35 191 and/or nebulizer, indwelling urine catheter or a nasopharyngeal food tube. After the care intake and
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37 192 a period of direct nursing supervision, the participant will receive intermittent nursing visits daily
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39 193 (starting with 3x/day), including weekends and public holidays. The Hospital at Home physician will
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41 194 make a home visit every day (excl. weekends). The Hospital at Home physician and nurse will be
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43 195 available for emergency visits. The participant will receive a medical alert device in the house, with a
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45 196 24/7 connection to an on-call service. Alert instructions will be explained to the participant and
46
47 197 caregiver. A physiotherapist will visit the participant at home to evaluate any problems with balance
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49 198 and/or walking and immobility. The Hospital at Home team works under the supervision of the
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51 199 hospital medical specialist. Daily screenings and measurements will be recorded in a Hospital at
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53 200 Home record, which stays with the participant. Diagnostic procedures and therapeutics that cannot
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55 201 wait and are not available at home, such as endoscopy or CT-scan, will be arranged through brief
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57 202 visits to the hospital. The participant will be 'admitted' to the Hospital at Home care for as long as
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59 203 indicated.

53 204 *Discharge from Hospital at Home*

54 205 If the participant recovers to such an extent that hospital level care is no longer needed, the
55
56 206 participant will be discharged from the Hospital at Home care program, similar to the discharge
57
58

207 procedure when the participant would receive usual hospital care. Hospital at Home care will end
208 with discharge planning with the participant, family, Hospital at Home physician and nurse. The
209 discharge plan includes follow-up appointments (e.g., at the hospital or general practitioner),
210 information on medication, warning signs and symptoms and an on-going management plan. All
211 hospital-related care equipment will be removed from the participants' house, and arrangements
212 with homecare agencies and/or paramedical staff will be reviewed and adjusted to the current
213 situation.

214 **Hospital care as usual**

215 Participants allocated to the control arm will be admitted to a hospital ward and receive usual
216 hospital care. After admission and intake on the ward, the participant will receive intermittent visits
217 from the ward nurse multiple times a day. The ward physician will visit once every day (excl.
218 weekends), with extra visits provided if needed. An emergency alert device, through which nurses
219 and physician can be contacted, will be placed next to the bed. A physiotherapist will visit the
220 participant at the ward to address problems with balance and/or walking and immobility. Depending
221 on the participants' needs, other disciplines (e.g., a dietician, occupational therapist or social
222 services) can be involved in the hospital care. The medical record is the hospital record and
223 additional H@H research forms will be added to this record for research purposes. The participant
224 will be admitted to the hospital for as long as indicated.

225

226 *Hospital discharge*

227 If the participant recovers to such an extent that hospital level care is no longer needed, the
228 participant will be discharged from the hospital after discharge planning with the participant, family,
229 physician and nurse. The discharge plan includes follow-up appointments (e.g., at the hospital or
230 general practitioner), information on medication, warning signs and symptoms and an on-going
231 management plan. Arrangements with homecare agencies and/or paramedical staff will be reviewed
232 and adjusted to the current situation.

233

234 **Follow-up**

235 At three and six months following randomization, all participants will be contacted for an interview
236 by telephone³⁶ or a face-to-face interview, if needed. The participants will be allowed to receive
237 support with these questions from their relatives or informal caregivers. An interview will require a
238 maximum of 30 minutes. In case of institutionalization or mortality, this event will be recorded.
239 Additionally, information on hospital readmission and length of stay will be collected from the

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3 240 hospital administration system and health insurers. Mortality and nursing home placements will be
4 241 collected from registries from the general practitioner and municipalities.

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7 243 **Timing of measurements and outcome measures**

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9 245 Data will be collected at baseline at the emergency department, during admission (in Hospital at
10 246 Home or hospital), at discharge and at three and six months following randomization, plus or minus
11 247 two weeks. An overview of the timing of measurements and outcome measures are shown in Table
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17 250 *Feasibility*

18 251 For the participation rates, the proportion of participants per step will be calculated. The reasons for
19 252 non-participation and data concerning the characteristics of non-participants will be collected. We
20 253 consider the participation rate feasible when it is similar to the participation rate as is described in
21 254 previous RCTs and around 50% of the eligible patients will consent to participate.^{34,35} Quality of care
22 255 will be measured by collecting data on patient, institutionalization (e.g., to the hospital or nursing
23 256 home), mortality, ADL-functioning, prevalence of hospitalisation-associated geriatric syndromes, the
24 257 length of stay in the hospital or Hospital at Home care program and contact with health care
25 258 professionals. The study is considered feasible if the quality of care of Hospital at Home care on these
26 259 measurements is non- inferior to usual hospital care.

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261 **Table 2** Overview of the content and description of outcome measures and timing of measurements

Description and instrument		Timing of measurements					
		screening	baseline	admission	discharge	3 months	6 months
Degree of illness based on physiological parameters	Vital signs alarm score; Modified Early Warning Score, ³⁷	R					
Cognitive impairment	4AT-test for delirium* Six item cognitive impairment test for cognitive impairment*, ^{28,38}	R					
Socio-demographics	Date of birth, nationality, household composition, marital status, highest level of education		R				
Health status	Charlson co-morbidity index*, ³⁹		R				
Identifying at-risk patients	Safety management system patient screening (VMS), ⁴⁰		R				
Functional status	Activities of daily living, modified Katz-ADL index score, ⁴¹		R		R	R	R
Health status	EQ-5d-5l*, ⁴²		R		R	R	R
(Health-related) quality of life, well-being	Icepap capability measure for Older people (ICECAP-O)* ⁴³		R		R	R	R
Caregiver burden	Self-rated burden scale*, caregiver strain index*, ^{44,45}		C		C	C	C
Medical consumption	Imta Medical Consumption Questionnaire (imcq)*, ⁴⁶		P,C			P,C	P,C
Hospitalisation-associated geriatric syndromes	Infections, falls, pressure injuries, in case of delirium; delirium observation scale score (DOSS) ⁴⁷ and use of physical or chemical restraints, total days with a urinary catheter			N			
Nutrition	Malnutrition Universal Screening Tool (MUST), ⁴⁸		N				
	Food intake, fluid intake			N			
Pain	Numeric Rating Scale-score (NRS) for pain ⁴⁹			N			
Health perception	(Rotterdam) symptom checklist* ⁵⁰			N			
Immobility	Hierarchical assessment of balance and mobility (HABAM) ⁵¹			Ph			
Satisfaction with care	Client Satisfaction Questionnaire 8 (CSQ-8)*, care evaluation question*, ^{52,53}				P	P,C	N,D
Mortality	Mortality at 30 days, 3 months and 6 months after baseline*				N	R	R
(Re)admission hospital	Length of stay, readmission rate at 30 days, 3 months and 6 months after baseline*				N	R	R

262 Assessed by: P= Participant, C=Caregiver, N= Nurse, D= Doctor, R= Research nurse, Ph=Physiotherapist.

263 (*)= All assessments marked by an asterisk are extra for trial purposes and are not part of the medical treatment

264

265 *Other outcomes measures*

266 Advantages and disadvantages of the Hospital at Home care program will be assessed through
 267 multiple instruments and questionnaires. The instruments are validated and used in community-
 268 dwelling older patients with cognitive disorders. Additional data will be collected on the time spent
 269 at home (home-time); total number of days alive and out of the hospital or a skilled nursing facility in
 270 the 6 months following the randomization at the emergency department,⁵⁴ the number of transfers
 271 (home ↔ hospital) and the number of health care professionals involved.

272 Cost data will be collected, as described by Drummond et al., including the costs to the health care
273 system, patients and families, and other sectors.⁵⁵ The volume of care use will be extracted from
274 hospital files and combined with the reference cost values, as provided by the cost guidance module
275 of the Dutch National Health Care Institute.⁵⁶

276 **Process evaluation**

277 A process evaluation will be conducted as part of the feasibility study to understand the barriers and
278 facilitators to participate and to gain an understanding of the experiences and perceptions of
279 Hospital at Home care of participants and health care professionals. From all eligible patients who
280 declined to participate, data concerning the patient characteristics and reasons for non-participation
281 will be collected. At the end of the trial, a representative sample of participants and/or their informal
282 caregivers will be invited for an interview to evaluate their experiences receiving Hospital at Home
283 care. The interviewer will not be a an active member of the research team or involved in day-to-day
284 care and will explore independently how the participants perceived Hospital at Home care, including
285 the contact with the health professionals and the impact of Hospital at Home care on their lives and
286 their caregivers' personal lives. In case of participant dropout, efforts will be made to obtain an
287 understanding of why the participants did not complete the trial.

288 In addition, a representative sample of health care professionals, consisting of physicians and nurses
289 working in the Emergency Department, physicians and nurses providing the Hospital at Home care,
290 and general practitioners, will be asked to participate in a face-to-face interview. The health care
291 professionals will be asked about their experiences and opinions about the H@H-trial and Hospital at
292 Home care. All interviews will be transcribed verbatim, and a framework analysis will be used as the
293 method of qualitative data analysis.⁵⁷

294 **Data management**

295 All data will be entered in an electronic trial-specific database, with the participants identified by a
296 unique trial number. Confidentiality of participant information will be maintained throughout the
297 trial. Information can only be traced to the participants by designated researchers. The database will
298 be stored and maintained by Castor Electronic Data Capture, compliant with GCP guidelines and the
299 European Data Protection Directive (Castor Electronic Data Capture, Ciwit BV, Amsterdam, the
300 Netherlands, 2017). Data will be stored for a maximum period of 15 years after the study has ended,
301 according to Dutch law.⁵⁸

302 **Statistical analysis**

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304 The participant flow diagram, according to CONSORT guidelines,⁵⁹ will provide a summary of the
305 recruitment and declination rates in percentage (%) at baseline, discharge and three- and six-month
306 follow-ups. Distributions of the data at baseline, discharge and three and six months after
307 randomization will be explored, with unusual values noted and explained. Variables will be
308 summarized as the n (%), mean (standard deviation) or median (interquartile range) for each group,
309 to characterize the sample and search for any imbalances. The percentages, means and standard
310 deviation, and medians and interquartile ranges will be calculated to describe the quality of care and
311 the advantages and disadvantages of Hospital at Home care at baseline, discharge and three- and six-
312 month follow-ups.

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314 **Monitoring and participant safety**

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316 Although, the H@H trial is considered to be a low risk trial, the participant safety will be monitored
317 by an independent Data Monitoring Committee (DMC). The DMC will consist of two members: an
318 experienced clinician and an epidemiologist. Members of the DMC are independent of the trial and
319 will discuss each individual participant with serious adverse events. The DMC will receive and review
320 the serious adverse events and evaluate the risk involved with negative outcomes. The DMC is
321 authorized to make recommendations to temporary put on hold or ending the study prematurely
322 when participant safety is an issue, based on their findings. All serious adverse events will be
323 reported to the principal investigator within 24 hours of knowledge of the event and then
324 subsequently reported to the Dutch portal for medical research involving human subjects.

325 **Discussion**

326 Reducing unwanted hospital admissions in older patients with cognitive impairments and facilitating
327 patient-centred care in a patient's preferred location is a goal worthy of pursuing. This goal aligns
328 with the tenet of the current Dutch government and the advice provided by the Dutch Council for the
329 Environment and Infrastructure: to actively promote and enable people to live independently in their
330 own homes for as long as they desire.⁶⁰ Previous trials and a recent review have confirmed that
331 alternative management strategies for low-risk patients with acute medical conditions conventionally
332 treated through hospitalization exist with positive impact on patient satisfaction, are effective and
333 can be safely achieved in lower cost settings.^{22,23,61}

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3 334 Introducing a Hospital at Home care trajectory in the Netherlands is incited by the principles of value-
4 335 based health care: improving the patients experience of care and as a result of this process reducing
5 336 the costs.⁶² All countries with an ageing population experience pressure, in terms of shortage of
6 337 (emergency) hospital beds and rising healthcare costs. Hospital at Home care could be shown
7 338 beneficial in facilitating higher valued care for patients and their caregivers without additional costs.
8 339 Benefit should be measured in other outcomes than clinical indicators such as mortality. To illustrate,
9 340 one of the outcomes of a future RCT could be the time spent at home. Time spent at home has been
10 341 defined as the total number of days alive and out of the hospital or a skilled nursing facility in the 6
11 342 months after hospital admission.⁵⁴ It has been used as a primary outcome in a follow-up study of
12 343 older patients with acute hospital admissions, and has been demonstrated to be of more importance
13 344 in older patients.⁶³⁻⁶⁵ Evaluation of time spent a home in this feasibility study could support
14 345 estimating a sample size based on a patient-relevant outcome in a future RCT.

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18 346 This study will be the first to investigate the feasibility of providing acute hospital care at home for
19 347 older patients with cognitive impairment in the Netherlands. Studying Hospital at Home care and
20 348 identifying the barriers and facilitators will support the implementation of Hospital at Home care and
21 349 break new ground for a future RCT investigating the (cost-)effectiveness.

30 350 **Ethics and Dissemination**

31
32 351 This study was approved by the Medical Research Ethics Committee of the University Medical Center
33 352 Groningen in April 2017, reference number: 2016.686 The trial will be conducted in accordance with
34 353 the Declaration of Helsinki 1996, principles of good clinical practice and the University Medical
35 354 Center of Groningen Research Code. Any protocol amendments will be submitted to the ethics
36 355 committee. A register of the protocol amendments will be available in the study protocol.

37 356 The results of the trial will be reported according to the CONSORT guidelines and will contribute to
38 357 knowledge of the implementation of Hospital at Home care and patient-centred acute care for older
39 358 patients with cognitive impairment. The study will also contribute to the knowledge of the
40 359 transmurial cooperation and costs of providing care, in terms of the translocation of hospital care to
41 360 home. Regularly updates will be published on the study website and in newsletters. Conferences and
42 361 meetings will be held for all involved health care professionals. Participants who requested
43 362 information on the study will be sent a lay summary. A publication policy will be agreed upon with
44 363 co-applicants. The study findings will be published in relevant peer-reviewed journals.

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30 393

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32 395

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34 397 Medical Center Groningen April 2017 (ref: 2016.686).

35 398

36 399 **Recruitment status** is pending; participants are not yet being recruited or enrolled. Anticipated date of
37 400 enrolment of the first participant is December 2017.

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47 410 **Abbreviations**

48 411 ADL: Activities of Daily Living

49 412 CT: Computer Tomography

50 413 DMC: Data Monitoring Committee

51 414 ED: Emergency Department

52 415 H@H: Hospital at Home

53 416 RCT: Randomized Controlled Trial

54 417 UMCG: University Medical Center Groningen

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571 Figure Legends

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573 Figure 1: Flowchart of trial design summary

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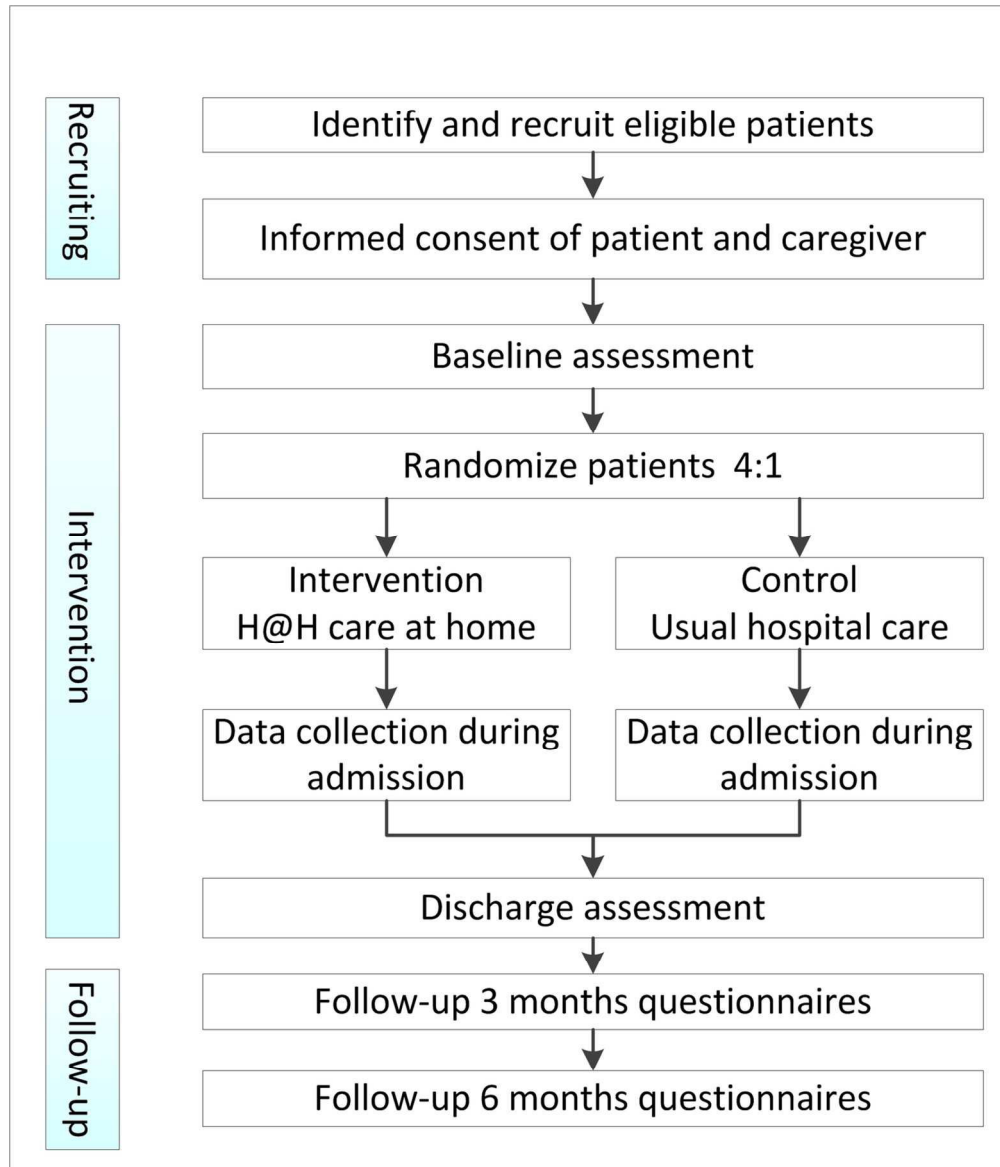


Figure 1: Flowchart of trial design summary

127x148mm (300 x 300 DPI)



STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on 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	1
	2b	All items from the World Health Organization Trial Registration Data Set	1, 3, 4, 5, 6, 8, 9, 13, 14
Protocol version	3	Date and version identifier	all
Funding	4	Sources and types of financial, material, and other support	14
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	14
	5b	Name and contact information for the trial sponsor	14
	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	14
	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)	n/a

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	3
	6b	Explanation for choice of comparators	3
Objectives	7	Specific objectives or hypotheses	3
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, noninferiority, exploratory)	4

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	4
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)	6
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7, 8
	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)	7, 8
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	n/a
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9, 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	9, 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)	10

1				
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3	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	6
4				
5	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5
6				
7				
8	Methods: Assignment of interventions (for controlled trials)			
9				
10	Allocation:			
11				
12	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	4
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17	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	4
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21	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
22				
23				
24	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	4
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27		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
28				
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31	Methods: Data collection, management, and analysis			
32				
33	Data collection methods	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	9, 10, 11
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38		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11
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3	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
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7	Statistical methods	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
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10		20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	n/a
11				
12		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
13				
14				
15	Methods: Monitoring			
16				
17	Data monitoring	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	12
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22		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	12
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25	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	12
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28	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
29				
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32	Ethics and dissemination			
33				
34	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	12
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37	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
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3	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	5
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6		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
7				
8	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	10
9				
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11	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
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14	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	10
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17	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	Available on request
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20	Dissemination policy	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	12
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25		31b	Authorship eligibility guidelines and any intended use of professional writers	13
26				
27		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
28				
29	Appendices			
30				
31	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Available on request
32				
33				
34	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
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*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by/3.0/)" license.

BMJ Open

Hospital at Home care for older patients with cognitive impairment: A protocol for a randomized controlled feasibility trial

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Primary Subject Heading:	Geriatric medicine
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Keywords:	Dementia < NEUROLOGY, Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, GERIATRIC MEDICINE, Delirium & cognitive disorders < PSYCHIATRY, INTERNAL MEDICINE

SCHOLARONE™
Manuscripts

Public title

Hospital at Home care for older patients with cognitive impairment and an acute medical illness

Scientific title

Hospital at Home care for older patients with cognitive impairment: A protocol for a randomized controlled feasibility trial

Acronym

H@H

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Keywords: Dementia, Cognition disorders, Aged, Home Care Services; Hospital-Based, Hospital at Home

Word count: 3985

Abstract

INTRODUCTION: An acute hospital admission is a stressful life event for older people, particularly for those with cognitive impairment. The hospitalisation is often complicated by hospital-associated geriatric syndromes, including delirium and functional loss, leading to functional decline and nursing home admission. Hospital at Home care aims to avoid hospitalisation-associated adverse outcomes in older patients with cognitive impairment by providing hospital care in the patient's own environment.

METHODS AND ANALYSIS: This randomized, non-blinded feasibility trial aims to assess the feasibility of conducting a randomized controlled trial in terms of the recruitment, use and acceptability of Hospital at Home care for older patients with cognitive impairment. The quality of care will be evaluated and the advantages and disadvantages of the Hospital at Home care program compared to usual hospital care. Eligible patients will be randomized either to Hospital at Home care in their own environment or usual hospital care. The intervention consists of hospital level care provided at patients' homes, including visits from health care professionals, diagnostics (laboratory tests, blood cultures) and treatment. The control group will receive usual hospital care. Measurements will be conducted at baseline, during admission, at discharge and at three and six months after the baseline assessment.

ETHICS AND DISSEMINATION: Institutional ethics approval has been granted. The findings will be disseminated through public lectures, professional and scientific conferences, as well as peer-reviewed journal articles. The study findings will contribute to knowledge on the implementation of Hospital at Home care for older patients with cognitive disorders. The results will be used to inform and support strategies to deliver eligible care to older patients with cognitive impairment.

TRIAL REGISTRATION: This study was registered with the NTR registry (NTR6581) on 26 July 2017.

58

Strengths and limitations of this study

- This study addresses the feasibility of Hospital at Home care in patients with cognitive impairment, a patient population that is often excluded from participation in scientific research
- A process evaluation facilitates the investigation of factors that influence the experiences and perceptions of all persons involved in Hospital at Home care
- Stakeholders were involved in the development of the design of the study which will support the implementation of Hospital at Home care and a future trial
- Because of a limited sample size due to the study being centered on feasibility, results will not show effectiveness of Hospital at Home care compared to usual hospital care.

Introduction

Background

An acute hospital admission is a stressful life event, particularly for older people. In addition to the stress of an acute illness, the hospital admission itself contributes to this stress.¹ Older hospitalized patients are often deprived of sleep, and they spend an average of 20 of every 24 hours in bed, they become poorly nourished, and experience sensory deprivation or overstimulation, resulting in confusion.²⁻⁵ These adverse effects of hospitalization contribute to the occurrence of geriatric conditions, such as delirium, functional decline, falls, incontinence, hospital acquired infections and pressure injuries.⁶⁻⁹ Adverse effects of hospitalization occur more easily in older people, particularly in those who are already frail, a growing portion of the worldwide ageing population.^{10,11} Frailty is a state of increased vulnerability to external stressors resulting from aging-associated declines in reserve and function across multiple physiologic systems.¹⁰ Cognitive impairment (i.e., dementia) is an important contributor to frailty in older people.¹² Cognitively impaired older people are more likely to become hospitalised and once admitted, they experience longer stays than their peers without cognitive impairment.¹³⁻¹⁵ The combination of hospitalization and cognitive impairment in older people is associated with further functional and cognitive declines and higher mortality rates, and it leads to more discharges to long-term care facilities.^{16,17} The prevalence and worldwide burden of cognitive impairment will continue to increase as the average life expectancy increases.¹⁸ The total number of people with cognitive impairment is estimated to be 75.6 million in 2030 and will nearly triple in 2050 to 135.5 million.¹⁹ An increase in the number of hospital admissions of older people with cognitive impairment and an increase in number of hospitalisation-associated adverse outcomes are therefore to be expected.

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3 92 Besides adverse outcomes of hospitalization, many older people and their caregivers do not
4 93 necessarily desire a hospital admission in case of an acute illness or exacerbation of a chronic illness.
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6 94 Fried et al. (2000) have studied the preferences of community-dwelling persons 65 years of age and
7
8 95 older who were hospitalized with a primary diagnosis of congestive heart failure, chronic obstructive
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10 96 pulmonary disease or pneumonia. The authors reported that over 50% of older patients preferred to
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12 97 receive hospital treatment at home, because they felt that their homes were more comfortable.²⁰ In
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14 98 the treatment preferences of seriously ill patients 60 years of age and older, the likelihood of
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16 99 cognitive and functional impairment as an adverse outcome of the treatment was weighed in the
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18 100 decision-making process. There was a substantial decrease in the number of participants who opted
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20 101 for treatment if the likelihood of impairment after treatment was 50% or higher.²¹

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22 102
23 103 Hospital at Home care could provide an effective alternative to inpatient care for a select group of
24
25 104 elderly patients now requiring hospitalisation. Hospital at Home care is coordinated, multidisciplinary
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27 105 care in the homes of people who would otherwise be admitted to the hospital. Hospital at Home
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29 106 care is an accepted alternative to inpatient hospital level care in several countries (e.g., the United
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31 107 States, Australia, Italy and the United Kingdom) but not yet in the Netherlands.²² Since the 1990s,
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33 108 Hospital at Home has been evaluated in (older) persons with various acute medical conditions, such
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35 109 as heart failure, exacerbations in chronic obstructive pulmonary disease (COPD) and infections (e.g.,
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37 110 cellulitis, pneumonia).²² In systematic reviews comparing alternative strategies to inpatient
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39 111 hospitalization, lower or equal mortality rates and return hospitalization rates (i.e., subsequent
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41 112 admissions after discharge) were found for Hospital at Home care, there was a lower incidence of
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43 113 delirium, and there was a positive effect on patient and caregiver satisfaction.²²⁻²⁴ Only one
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45 114 completed trial conducted in Italy included 109 patients with cognitive impairment (i.e. dementia),
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47 115 Tibaldi et al. reported a positive effect of a Hospital at Home intervention on behavioural
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49 116 disturbances and caregiver stress in patients with dementia.²⁵ Results of a still on-going trial including
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51 117 people with i.a. cognitive impairment in the United Kingdom, will follow in the near future.²⁶

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53 118 Whether Hospital at Home care provides a suitable alternative with regard to other outcomes as
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55 119 patient satisfaction, quality of care, hospitalisation-associated adverse events and costs in older
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57 120 people with cognitive impairment remains unclear and further research is needed. Therefore, our
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59 121 primary aim is to investigate the feasibility of a Hospital at Home care program for older patients
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122 with cognitive impairment in terms of the patient recruitment, use and acceptability, and secondly to
123 investigate the advantages and disadvantages of Hospital at Home care compared to usual hospital
124 care from different perspectives.

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126 Objectives of this study are:

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3 127 1) To assess the participation rate of the Hospital at Home trial among patients 65 years and older
4 128 with cognitive impairment, acute illness, and emergency hospital admission. What are the reasons
5
6 129 for non-participation?
7
8 130 2) To assess the potential advantages and disadvantages of Hospital at Home care and usual hospital
9 131 care for the patients, caregivers and Dutch medical health system.
10
11 132 3) To assess the feasibility of Hospital at Home care in terms of the quality of care with regard to
12 133 geriatric syndromes, institutionalization, mortality, total days with urinary catheter, length of stay (in
13 134 the hospital or in Hospital at Home care) and timing/intensity of the contact with health care
14
15 135 professionals.

18 136 **Methods and analysis**

20 137 **Trial design**

21 138
22 139 The design is a randomized controlled feasibility trial and will utilize a process evaluation. This study
23 140 will be conducted at the medical emergency department (ED) of the academic hospital of the
24 141 University Medical Center of Groningen in the Netherlands and will evaluate cognitively impaired
25 142 older patients who are in need of acute hospital care. Figure 1 shows the trial design summary.
26 143 Participants will be randomized to either Hospital at Home care or usual hospital care in a 4:1 ratio,
27 144 respectively. Patients will be randomized using a computerized random number generator
28 145 (<http://www.randomization.com>), including block randomization.
29 146 An independent research nurse who is not involved in the patient care will complete the baseline
30 147 assessment and allocate the participants (using sealed sequenced envelopes) into the Hospital at
31 148 Home care (intervention) or usual hospital care group (control). The research nurse will not be aware
32 149 of the randomization method. The participants, health care professionals and research staff will not
33 150 be blinded to the intervention. The reporting of the design of this trial protocol is in accordance with
34 151 the SPIRIT 2013 statement for clinical trial protocols.²⁷
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154 **Figure 1**155 **Study population**

156 Patients 65 years of age and older who are admitted to the medical emergency department (ED) will
157 be identified by the ED staff as potential eligible patients. Subsequently, the ED staff will inform the
158 research nurse. The research nurse will complete the eligibility criteria checklist (table 1). The
159 research nurse will ask the patient and their informal caregiver (i.e., partner, child, relative, friend)
160 for their willingness to participate in the study and to provide written informed consent. The patient
161 and informal caregiver will need to both sign the informed consent form before the patient can
162 participate in the H@H trial.

163 An evaluation to assess the mental capacity is conducted by the involved ED staff in the setting of the
164 emergency department assessment. If the participant lacks the capacity to consent (mentally
165 incapacitated), and an informal caregiver (i.e., partner, child, friend) is present, this informal
166 caregiver will be asked to act as a personal consultee. The personal consultee will determine whether
167 he or she believes that participation in the study would be in accordance with the values and
168 interests of the individual and will subsequently sign the patient's informed consent form.

169

view only

170 **Table 1** Patient eligibility criteria for participation in Hospital at Home trial

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> ▪ Age 65 years of age and older ▪ Cognitive impairment, i.e. dementia, delirium or other cause of cognitive impairment, and either: <ul style="list-style-type: none"> ○ previously diagnosed or documented in the medical records or ○ identified by the ED-clinician (e.g., with the 4AT-test and/or Six item cognitive impairment test)²⁸⁻³⁰ ▪ Presented at the ED with a defined acute illness ▪ Required hospital admission, according to the attending ED physician but not expected to require emergency interventions <ul style="list-style-type: none"> ○ Modified Early Warning Score (MEWS) ≤ 2 points³¹⁻³³ ▪ Living in hospital's catchment area (< 25 km) ▪ Informal caregiver is present and able to understand and perform instructions and consented to participate in the trial ▪ Home suitable for Hospital at Home care (available informal caregiver, running water, adequate heating, safety)³⁰ 	<ul style="list-style-type: none"> ▪ Previously enrolled ▪ Hospitalized within the seven days preceding ED presentation ▪ Nursing home residents or awaiting a nursing home place on an active waiting list (excluding so-called sleeping waiting list candidates)²⁷ ▪ Additional care needed <ul style="list-style-type: none"> ○ Required surgical assessment ○ Suspected acute coronary syndrome or cardiac arrhythmia³¹ ○ Dialysis dependent patients³¹ ○ Expected terminal events³¹ or in need of diagnostic or palliative care due to oncological or haematological illness

171 ED= Emergency department

172 **Sample size of study population**

173 Based on the numbers available from the emergency department (ED) of the University Medical
 174 Center Groningen, the Netherlands, we calculated that an average of 3990 older patients 65 years
 175 and over is admitted to our medical ED each year. The Hospital at Home trial will be introduced
 176 during working hours, which provides an estimated 1900 patients per year. Not all 1900 patients will
 177 be eligible for study inclusion. Based on screening of ED medical records, approximately 15% of the
 178 patients meet the eligibility criteria for Hospital at Home care, resulting in 285 eligible persons per
 179 year. In recent randomized controlled trials (RCTs) of Hospital at Home care in Italy, 54% and 57% of
 180 the eligible patients was willing to participate and gave informed consent.^{34,35} We presume a similar
 181 consent rate of 50%, as described in these previous clinical trials, and expect for 143 patients to be
 182 included.
 183

184 **Study procedures**

185 After (written) informed consent is obtained, all participants will complete two brief tests to assess
 186 cognitive impairment, and the participant and caregiver will complete the baseline assessment.
 187 Subsequently, randomization takes place to either (a) the Hospital at Home care-intervention,
 188 translocation of care from the hospital to a participants' home or (b) the control group, usual
 189 hospital care. All care will be delivered according to hospital protocols, current regulations and

190 guidelines and, if needed, described in the standard operating procedures (SOPs). If no informed
191 consent is given by either the patient or the caregiver, the reasons for non-participation, date of
192 birth, sex of the patient and the relationship between patient and caregiver will be reported.

193 **Intervention**

194 **Hospital at Home care**

195 Hospital at Home care will be delivered by a multidisciplinary team consisting of a physician, nurse,
196 pharmacist and physiotherapist. Depending on the participants' needs, other disciplines (e.g., a
197 dietician, occupational therapist or social services) can be involved in the Hospital at Home care. The
198 day-to-day care will be provided by the nurse and physician visiting the participant. The Hospital at
199 Home care team works under the responsibility of the medical specialist in the hospital, and 24/7
200 consultation of the expertise and services of the hospital is part of the protocol.

201
202 The participants allocated to Hospital at Home care will receive hospital level care in their own
203 homes. After a stay of one night in the hospital, while the Hospital at Home care arrangements are
204 being made, the participant will be transferred home and receive Hospital at Home care. The
205 Hospital at Home nurse is responsible for the day-to-day care and will be present upon arrival of the
206 participant at his/her residence. Hospital at Home care is described in the care protocols including
207 SOPs and could include intravenous therapy (e.g., antibiotics, fluid, and/or diuretics), oxygen therapy,
208 and/or nebulizer, indwelling urine catheter or a nasopharyngeal food tube. After the care intake and
209 a period of direct nursing supervision, the participant will receive intermittent nursing visits daily
210 (starting with 3x/day), including weekends and public holidays. The Hospital at Home physician will
211 make a home visit every day (excl. weekends). The Hospital at Home physician and nurse will be
212 available for emergency visits. The participant will receive a medical alert device in the house, with a
213 24/7 connection to an on-call service. Alert instructions will be explained to the participant and
214 caregiver. A physiotherapist will visit the participant at home to evaluate any problems with balance
215 and/or walking and immobility. The Hospital at Home team works under the supervision of the
216 hospital medical specialist. Daily screenings and measurements will be recorded in a Hospital at
217 Home record, which stays with the participant. Diagnostic procedures and therapeutics that cannot
218 wait and are not available at home, such as endoscopy or CT-scan, will be arranged through brief
219 visits to the hospital. The participant will be 'admitted' to the Hospital at Home care for as long as
220 indicated.

221 *Discharge from Hospital at Home*

222 If the participant recovers to such an extent that hospital level care is no longer needed, the
223 participant will be discharged from the Hospital at Home care program, similar to the discharge

224 procedure when the participant would receive usual hospital care. Hospital at Home care will end
225 with discharge planning with the participant, family, Hospital at Home physician and nurse. The
226 discharge plan includes follow-up appointments (e.g., at the hospital or general practitioner),
227 information on medication, warning signs and symptoms and an on-going management plan. All
228 hospital-related care equipment will be removed from the participants' house, and arrangements
229 with homecare agencies and/or paramedical staff will be reviewed and adjusted to the current
230 situation.

231 **Hospital care as usual**

232 Participants allocated to the control arm will be admitted to a hospital ward and receive usual
233 hospital care. After admission and intake on the ward, the participant will receive intermittent visits
234 from the ward nurse multiple times a day. The ward physician will visit once every day (excl.
235 weekends), with extra visits provided if needed. An emergency alert device, through which nurses
236 and physician can be contacted, will be placed next to the bed. A physiotherapist will visit the
237 participant at the ward to address problems with balance and/or walking and immobility. Depending
238 on the participants' needs, other disciplines (e.g., a dietician, occupational therapist or social
239 services) can be involved in the hospital care. The medical record is the hospital record and
240 additional H@H research forms will be added to this record for research purposes. The participant
241 will be admitted to the hospital for as long as indicated.

242

243 *Hospital discharge*

244 If the participant recovers to such an extent that hospital level care is no longer needed, the
245 participant will be discharged from the hospital after discharge planning with the participant, family,
246 physician and nurse. The discharge plan includes follow-up appointments (e.g., at the hospital or
247 general practitioner), information on medication, warning signs and symptoms and an on-going
248 management plan. Arrangements with homecare agencies and/or paramedical staff will be reviewed
249 and adjusted to the current situation.

250

251 **Follow-up**

252 At three and six months following randomization, all participants will be contacted for an interview
253 by telephone³⁶ or a face-to-face interview, if needed. The participants will be allowed to receive
254 support with these questions from their relatives or informal caregivers. An interview will require a
255 maximum of 30 minutes. In case of institutionalization or mortality, this event will be recorded.
256 Additionally, information on hospital readmission and length of stay will be collected from the

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3 257 hospital administration system and health insurers. Mortality and nursing home placements will be
4 258 collected from registries from the general practitioner and municipalities.

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7 260 **Timing of measurements and outcome measures**

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9 262 Data will be collected at baseline at the emergency department, during admission (in Hospital at
10 263 Home or hospital), at discharge and at three and six months following randomization, plus or minus
11 264 two weeks. An overview of the timing of measurements and outcome measures are shown in Table
12 265 2.

13 266

14 267 *Feasibility*

15 268 For the participation rates, the proportion of participants per step will be calculated. The reasons for
16 269 non-participation and data concerning the characteristics of non-participants will be collected. We
17 270 consider the participation rate feasible when it is similar to the participation rate as is described in
18 271 previous RCTs and around 50% of the eligible patients will consent to participate.^{34,35} Quality of care
19 272 will be measured by collecting data on patient, institutionalization (e.g., to the hospital or nursing
20 273 home), mortality, ADL-functioning, prevalence of hospitalisation-associated geriatric syndromes, the
21 274 length of stay in the hospital or Hospital at Home care program and contact with health care
22 275 professionals. The study is considered feasible if the quality of care of Hospital at Home care on these
23 276 measurements is non- inferior to usual hospital care.

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278 **Table 2** Overview of the content and description of outcome measures and timing of measurements

Description and instrument		Timing of measurements					
		screening	baseline	admission	discharge	3 months	6 months
Degree of illness based on physiological parameters	Vital signs alarm score; Modified Early Warning Score, ³⁷	R					
Cognitive impairment	4AT-test for delirium* Six item cognitive impairment test for cognitive impairment*, ^{28,38}	R					
Socio-demographics	Date of birth, nationality, household composition, marital status, highest level of education		R				
Health status	Charlson co-morbidity index*, ³⁹		R				
Identifying at-risk patients	Safety management system patient screening (VMS), ⁴⁰		R				
Functional status	Activities of daily living, modified Katz-ADL index score, ⁴¹		R		R	R	R
Health status	EQ-5d-5l*, ⁴²		R		R	R	R
(Health-related) quality of life, well-being	Icepap capability measure for Older people (ICECAP-O)* ⁴³		R		R	R	R
Caregiver burden	Self-rated burden scale*, caregiver strain index*, ^{44,45}		C		C	C	C
Medical consumption	Imta Medical Consumption Questionnaire (imcq)*, ⁴⁶		P,C			P,C	P,C
Hospitalisation-associated geriatric syndromes	Infections, falls, pressure injuries, in case of delirium; delirium observation scale score (DOSS) ⁴⁷ and use of physical or chemical restraints, total days with a urinary catheter			N			
Nutrition	Malnutrition Universal Screening Tool (MUST), ⁴⁸		N				
	Food intake, fluid intake			N			
Pain	Numeric Rating Scale-score (NRS) for pain ⁴⁹			N			
Health perception	(Rotterdam) symptom checklist* ⁵⁰			N			
Immobility	Hierarchical assessment of balance and mobility (HABAM) ⁵¹			Ph			
Satisfaction with care	Client Satisfaction Questionnaire 8 (CSQ-8)*, care evaluation question*, ^{52,53}				P	P,C	N,D
Mortality	Mortality at 30 days, 3 months and 6 months after baseline*				N	R	R
(Re)admission hospital	Length of stay, readmission rate at 30 days, 3 months and 6 months after baseline*				N	R	R

279 Assessed by: P= Participant, C=Caregiver, N= Nurse, D= Doctor, R= Research nurse, Ph=Physiotherapist.

280 (*)= All assessments marked by an asterisk are extra for trial purposes and are not part of the medical treatment

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282 *Other outcomes measures*

283 Advantages and disadvantages of the Hospital at Home care program will be assessed through
 284 multiple instruments and questionnaires. The instruments are validated and used in community-
 285 dwelling older patients with cognitive disorders. Additional data will be collected on the time spent
 286 at home (home-time); total number of days alive and out of the hospital or a skilled nursing facility in
 287 the 6 months following the randomization at the emergency department,⁵⁴ the number of transfers
 288 (home ↔ hospital) and the number of health care professionals involved.

289 Cost data will be collected, as described by Drummond et al., including the costs to the health care
290 system, patients and families, and other sectors.⁵⁵ The volume of care use will be extracted from
291 hospital files and combined with the reference cost values, as provided by the cost guidance module
292 of the Dutch National Health Care Institute.⁵⁶

293 **Process evaluation**

294 A process evaluation will be conducted as part of the feasibility study to understand the barriers and
295 facilitators to participate and to gain an understanding of the experiences and perceptions of
296 Hospital at Home care of participants and health care professionals. From all eligible patients who
297 declined to participate, data concerning the patient characteristics and reasons for non-participation
298 will be collected. At the end of the trial, a representative sample of participants and/or their informal
299 caregivers will be invited for an interview to evaluate their experiences receiving Hospital at Home
300 care. The interviewer will not be a an active member of the research team or involved in day-to-day
301 care and will explore independently how the participants perceived Hospital at Home care, including
302 the contact with the health professionals and the impact of Hospital at Home care on their lives and
303 their caregivers' personal lives. In case of participant dropout, efforts will be made to obtain an
304 understanding of why the participants did not complete the trial.

305 In addition, a representative sample of health care professionals, consisting of physicians and nurses
306 working in the Emergency Department, physicians and nurses providing the Hospital at Home care,
307 and general practitioners, will be asked to participate in a face-to-face interview. The health care
308 professionals will be asked about their experiences and opinions about the H@H-trial and Hospital at
309 Home care. All interviews will be transcribed verbatim, and a framework analysis will be used as the
310 method of qualitative data analysis.⁵⁷

311 **Data management**

312 All data will be entered in an electronic trial-specific database, with the participants identified by a
313 unique trial number. Confidentiality of participant information will be maintained throughout the
314 trial. Information can only be traced to the participants by designated researchers. The database will
315 be stored and maintained by Castor Electronic Data Capture, compliant with GCP guidelines and the
316 European Data Protection Directive (Castor Electronic Data Capture, Ciwit BV, Amsterdam, the
317 Netherlands, 2017). Data will be stored for a maximum period of 15 years after the study has ended,
318 according to Dutch law.⁵⁸

319 **Statistical analysis**

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321 The participant flow diagram, according to CONSORT guidelines,⁵⁹ will provide a summary of the
322 recruitment and declination rates in percentage (%) at baseline, discharge and three- and six-month
323 follow-ups. Distributions of the data at baseline, discharge and three and six months after
324 randomization will be explored, with unusual values noted and explained. Variables will be
325 summarized as the n (%), mean (standard deviation) or median (interquartile range) for each group,
326 to characterize the sample and search for any imbalances. The percentages, means and standard
327 deviation, and medians and interquartile ranges will be calculated to describe the quality of care and
328 the advantages and disadvantages of Hospital at Home care at baseline, discharge and three- and six-
329 month follow-ups.

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331 **Monitoring and participant safety**

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333 Although, the H@H trial is considered to be a low risk trial, the participant safety will be monitored
334 by an independent Data Monitoring Committee (DMC). The DMC will consist of two members: an
335 experienced clinician and an epidemiologist. Members of the DMC are independent of the trial and
336 will discuss each individual participant with serious adverse events. The DMC will receive and review
337 the serious adverse events and evaluate the risk involved with negative outcomes. The DMC is
338 authorized to make recommendations to temporary put on hold or ending the study prematurely
339 when participant safety is an issue, based on their findings. All serious adverse events will be
340 reported to the principal investigator within 24 hours of knowledge of the event and then
341 subsequently reported to the Dutch portal for medical research involving human subjects.

342 **Discussion**

343 Reducing unwanted hospital admissions in older patients with cognitive impairments and facilitating
344 patient-centred care in a patient's preferred location is a goal worthy of pursuing. This goal aligns
345 with the tenet of the current Dutch government and the advice provided by the Dutch Council for the
346 Environment and Infrastructure: to actively promote and enable people to live independently in their
347 own homes for as long as they desire.⁶⁰ Previous trials and a recent review have confirmed that
348 alternative management strategies for low-risk patients with acute medical conditions conventionally
349 treated through hospitalization exist with positive impact on patient satisfaction, are effective and
350 can be safely achieved in lower cost settings.^{22,23,61}

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3 351 Introducing a Hospital at Home care trajectory in the Netherlands is incited by the principles of value-
4 352 based health care: improving the patients experience of care and as a result of this process reducing
5 353 the costs.⁶² All countries with an ageing population experience pressure, in terms of shortage of
6 354 (emergency) hospital beds and rising healthcare costs. Hospital at Home care could be shown
7 355 beneficial in facilitating higher valued care for patients and their caregivers without additional costs.
8 356 Benefit should be measured in other outcomes than clinical indicators such as mortality. To illustrate,
9 357 one of the outcomes of a future RCT could be the time spent at home. Time spent at home has been
10 358 defined as the total number of days alive and out of the hospital or a skilled nursing facility in the 6
11 359 months after hospital admission.⁵⁴ It has been used as a primary outcome in a follow-up study of
12 360 older patients with acute hospital admissions, and has been demonstrated to be of more importance
13 361 in older patients.⁶³⁻⁶⁵ Evaluation of time spent a home in this feasibility study could support
14 362 estimating a sample size based on a patient-relevant outcome in a future RCT.

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17 363 This study will be the first to investigate the feasibility of providing acute hospital care at home for
18 364 older patients with cognitive impairment in the Netherlands. Studying Hospital at Home care and
19 365 identifying the barriers and facilitators will support the implementation of Hospital at Home care and
20 366 break new ground for a future RCT investigating the (cost-)effectiveness.

21 22 23 24 25 26 27 28 29 30 367 **Ethics and Dissemination**

31
32 368 This study was approved by the Medical Research Ethics Committee of the University Medical Center
33 369 Groningen in April 2017, reference number: 2016.686 The trial will be conducted in accordance with
34 370 the Declaration of Helsinki 1996, principles of good clinical practice and the University Medical
35 371 Center of Groningen Research Code. Any protocol amendments will be submitted to the ethics
36 372 committee. A register of the protocol amendments will be available in the study protocol.

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38 373 The results of the trial will be reported according to the CONSORT guidelines and will contribute to
39 374 knowledge of the implementation of Hospital at Home care and patient-centred acute care for older
40 375 patients with cognitive impairment. The study will also contribute to the knowledge of the
41 376 transmurial cooperation and costs of providing care, in terms of the translocation of hospital care to
42 377 home. Regularly updates will be published on the study website and in newsletters. Conferences and
43 378 meetings will be held for all involved health care professionals. Participants who requested
44 379 information on the study will be sent a lay summary. A publication policy will be agreed upon with
45 380 co-applicants. The study findings will be published in relevant peer-reviewed journals.

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 403

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 405

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 408

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 411

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417 Abbreviations

418 ADL: Activities of Daily Living
 419 CT: Computer Tomography
 420 DMC: Data Monitoring Committee
 421 ED: Emergency Department
 422 H@H: Hospital at Home
 423 RCT: Randomized Controlled Trial
 424 UMCG: University Medical Center Groningen
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578 Figure Legends

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580 Figure 1: Flowchart of trial design summary

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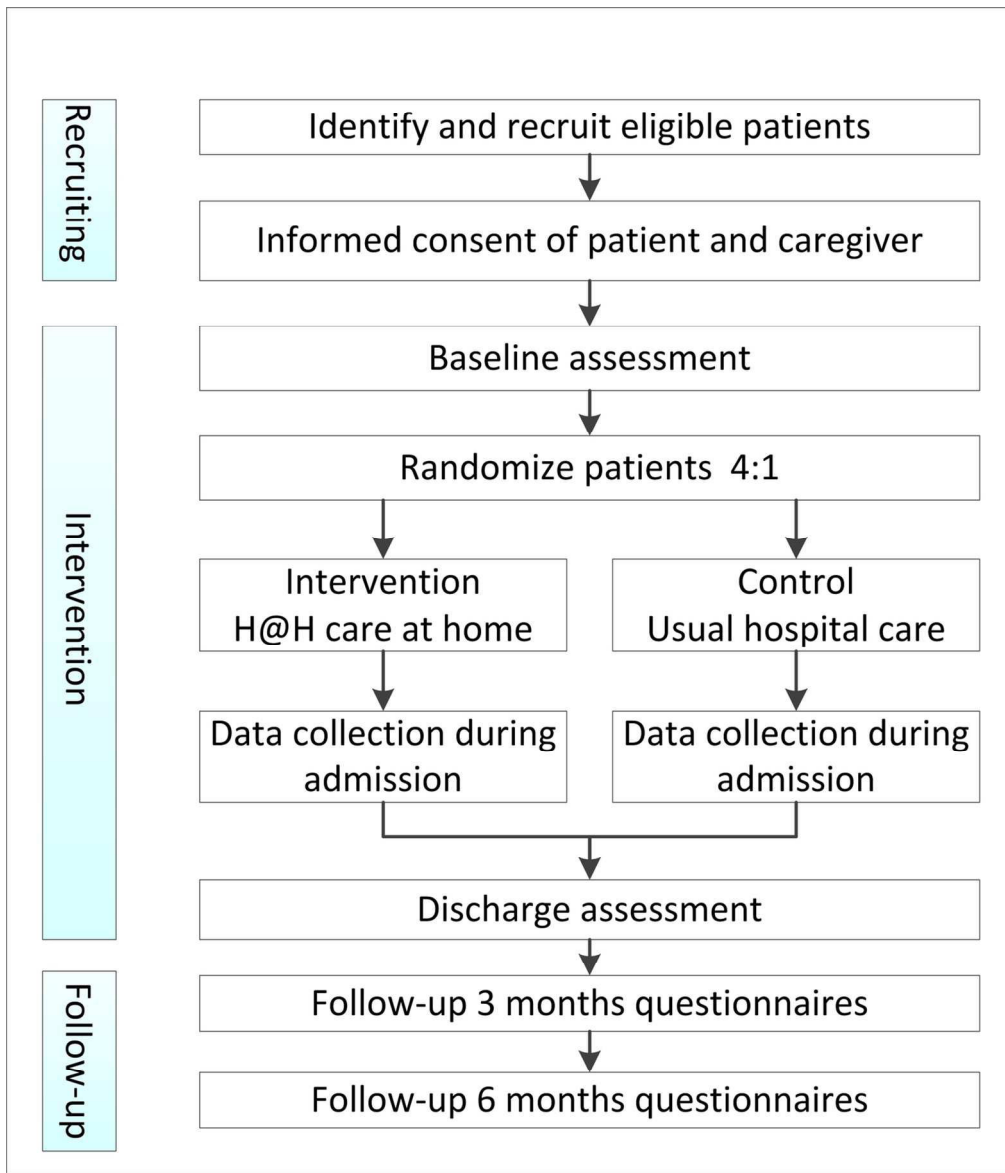


Figure 1: Flowchart of trial design summary

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on 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	1
	2b	All items from the World Health Organization Trial Registration Data Set	1, 3, 4, 5, 6, 8, 9, 13, 14
Protocol version	3	Date and version identifier	all
Funding	4	Sources and types of financial, material, and other support	14
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	14
	5b	Name and contact information for the trial sponsor	14
	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	14
	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)	n/a

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1				
2				
3	Introduction			
4				
5	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	3
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7				
8		6b	Explanation for choice of comparators	3
9				
10	Objectives	7	Specific objectives or hypotheses	3
11				
12	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, noninferiority, exploratory)	4
13				
14				
15	Methods: Participants, interventions, and outcomes			
16				
17	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	4
18				
19				
20	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)	6
21				
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23	Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7, 8
24				
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26		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)	7, 8
27				
28				
29		11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	n/a
30				
31				
32		11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9, 10
33				
34	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	9, 10
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39	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)	10
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2	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	6
3				
4				
5	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	5
6				
7				

Methods: Assignment of interventions (for controlled trials)

Allocation:

11	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	4
12				
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17	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	4
18				
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21	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
22				
23				
24	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	4
25				
26				
27		17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
28				
29				
30				

Methods: Data collection, management, and analysis

33	Data collection methods	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	9, 10, 11
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38		18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	11
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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

Statistical methods 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

20b Methods for any additional analyses (eg, subgroup and adjusted analyses) n/a

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

Methods: Monitoring

Data monitoring 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 12

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 12

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 12

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

Ethics and dissemination

Research ethics approval 24 Plans for seeking research ethics committee/institutional review board (REC/IRB) approval 12

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

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2				
3	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	5
4				
5				
6		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
7				
8	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	10
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11	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
12				
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14	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	10
15				
16				
17	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	Available on request
18				
19				
20	Dissemination policy	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	12
21				
22				
23		31b	Authorship eligibility guidelines and any intended use of professional writers	13
24				
25		31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
26				
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29	Appendices			
30				
31	Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Available on request
32				
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34	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
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37 *It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items.
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