’Evaluation of an integrated care pathway for hospital-at-home treatment of elderly with an acute moderate-severe lower respiratory tract infection or pneumonia’

PROTOCOL TITLE 'Evaluation of an integrated care pathway for hospital-at-home treatment of elderly with an acute moderate-severe lower respiratory tract infection or pneumonia'

Protocol ID	**T22-066**
Short title	**The Hague RTI Care Bridge**
EudraCT number	**Not applicable**
Version	**3**
Date	**04-11-2022**
Coordinating investigator	**Haga Teaching Hospital** Dept. of Internal Medicine Els Borst-Eilersplein 275 2545 AA The Hague, The Netherlands *Rick Roos, MD* r.roos@hagaziekenhuis.nl
Principal investigator	**Haga Teaching Hospital** Dept. of Internal Medicine Els Borst-Eilersplein 275 2545 AA The Hague, The Netherlands *Cees van Nieuwkoop, MD, PhD* c.vannieuwkoop@hagaziekenhuis.nl
Participating centers and co-investigators	**Health Campus Den Haag** Dept. of Public Health and Primary Care Leiden University Medical Centre (LUMC) *Mattijs E. Numans, MD, PhD, Professor* m.e.numans@lumc.nl *Rianne M.C. Pepping, MD* r.m.c.pepping@lumc.nl *Rimke C. Vos, PhD* *r.c.vos@lumc.nl* **Haaglanden Medical Centre** Dept. of Internal Medicine *Sharif M. Pasha, MD, PhD* s.pasha@haaglandenmc.nl Dept. of Emergency Medicine *Susan. M. Mollink, MD* s.mollink@haaglandenmc.nl **HADOKS Den Haag** *Jojanneke Kant, MD* jkant@hadoks.nl

	Florence *Ingrid Kroon, MD* ikroon@hadoks.nl **Haga Teaching Hospital** Dept. of Internal Medicine, section of Geriatrics *Geert Labots, MD* g.labots@hagaziekenhuis.nl *Ali Lahdidioui, MD* a.lahdidioui@hagaziekenhuis.nl Dept. of Pulmonology Johanna M.W. *van den Berg, MD* j.m.w.vandenberg@hagaziekenhuis.nl Dept. of Emergency Medicine *Nikki E. Kolfschoten, MD, PhD* n.kolfschoten@hagaziekenhuis.nl **Leiden University Medical Centre** Dept. of Internal Medicine, section of Gerontology and Geriatrics *Frederiek van den Bos, MD, PhD* f.van_den_bos@lumc.nl
Sponsor	**Haga Teaching Hospital** Dept. of Internal Medicine Els Borst-Eilersplein 275 2545 AA The Hague, The Netherlands
Subsidising party	**ZonMw (program: Right care on the right place; project number 10100032220003)** Laan van Nieuw Oost-Indië 334 2593 CE The Hague, The Netherlands **MenzisFonds (project: Elderly with a respiratory infection/pneumonia: reducing and preventing unnecessary hospitalizations)** Lawickse Allee 130 6709 DZ Wageningen, The Netherlands **Bavo Stichting** Velserweg 20 1942 LD Beverwijk

Independent expert(s)	**Haga Teaching Hospital** Dept. of Intensive Care *Iwan A. Meynaar, MD, PhD* i.meynaar@hagaziekenhuis.nl
Laboratory sites	LabWest
Pharmacy	Pharmacy Lijnbaan (Haaglanden Medical Center) Haga Pharmacy (Haga Teaching Hospital) Emergency Pharmacy (Haga Teaching Hospital)

PROTOCOL SIGNATURE SHEET

Name	Signature	Date
Sponsor or legal representative: **Haga Teaching Hospital**		
Principal Investigator: **C. van Nieuwkoop, MD, PhD**		
Coordinating Investigator: **R. Roos, MD**		

TABLE OF CONTENTS

LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

6-CIT	**6-item Cognitive Impairment Test**
ADL	**Activities of Daily Living**
AE	**Adverse Event**
APOP	**Acute Presenting Older Patient**
AR	**Adverse Reaction**
AVG	**General Data Protection Regulation (GDPR); in Dutch: Algemene Verordening Gegevensbescherming (AVG)**
COPD	**Chronic Obstructive Pulmonary Disease**
COVID-19	**Coronavirus Disease 2019**
CRP	**C-Reactive Protein**
DSMB	**Data Safety Monitoring Board**
ECG	**Electrocardiogram**
ED	**Emergency Department**
eGFR	**Estimated Glomerular Filtration Rate**
EudraCT	**European drug regulatory affairs Clinical Trials**
GA	**Geriatric Assessment**
GP	**General Practitioner**
GPC	**General Practice Centre**
IADL	**Instrumental Activities of Daily Living**
IC	**Informed Consent**
LRTI	**Lower Respiratory Tract Infection**
LSP	**National exchange point; in Dutch: Landelijk Schakelpunt**
METC	**Medical research ethics committee (MREC); in Dutch: Medisch-Ethische Toetsingscommissie (METC)**
NT-proBNP	**N-Terminal pro Brain Natriuretic Peptide**
PCR	**Polymerase-Chain Reaction**
PROMIS	**Patient-Reported Outcomes Measurement Information System**
PSI	**Pneumonia Severity Index**
(S)AE	**(Serious) Adverse Event**
SARS-CoV-2	**Severe Acute Respiratory Syndrome Coronavirus 2**
SPC	**Summary of Product Characteristics**
SPSS	**Statistical Package for the Social Sciences**
SUSAR	**Suspected Unexpected Serious Adverse Reaction**
WMO	**Medical Research Involving Human Subjects Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen**

SUMMARY

Rationale: An acute lower respiratory tract infection (LRTI) or pneumonia in (frail) older people is generally characterized by diagnostic uncertainty and high risk of complications and negative outcomes (for example due to overlap with heart failure and chronic obstructive pulmonary disease (COPD)). Besides that, care in the home situation often acutely falls short because of an acute care problem (for example due to falls, decline in activities in daily living (ADL) function or a state of confusion). This often leads to a presentation at the emergency department (ED) with the goal to define the optimal treatment for the (frail) elderly patient. This optimal treatment often consists of a combination of antibiotics/antivirals, oxygen suppletion and/or inhalation medication, optimization of the hemodynamic, physiotherapy and treatment and/or prevention of delirium. In principle, this kind of care and treatment could take place outside the hospital (for example in a patient's home). However hospitalization usually follows because treatment at home is considered irresponsible, inhumane or impossible due to the acute care problem. Hospitalized (frail) elderly are at high risk for complications, like malnutrition, delirium (with the consequence of prescribing sedative medication) and falls/functional decline. These hospitalizations are a consequence of the fact that the healthcare and treatment protocols between the involved regional care partners (for example general practitioners (GPs), hospitals, nursing homes and homecare institutions) are insufficiently coordinated: the lack of diagnostic and treatment possibilities in primary care, the lack of capacity in the nursing homes and homecare, and the presence of financial barriers. In (frail) older people, an acute respiratory infection therefore causes unnecessary or unnecessarily long hospitalizations with high risk of complications, like iatrogenic harm such as delirium. Besides that, these hospitalizations of (frail) older people with acute moderate-severe LRTI or pneumonia, especially in the flu season, also cause hospital capacity problems that may result in postponing other necessary treatments.
Recently, an integrated care pathway has been developed with the aim to treat patients with a moderate-severe LRTI or pneumonia outside the hospital setting based on a hospital-at-home setting. The implementation of this regional care pathway 'The Hague RTI Care Bridge' supports GPs in the diagnostics, the treatment and the organisation of care for (frail) older people with an acute moderate-severe LRTI or pneumonia. There are three patient paths imbedded in the care pathway with one of them being a hospital-at-home track in which patients will receive antibiotics/antivirals and when clinically indicated oxygen suppletion, inhalation medication and/or homecare. The second patient path is an adjusted visit to the ED with a priority assessment and the third is an admittance to a readily available recovery bed in a nursing home. Clear collaboration agreements are made between involved regional

care partners. In the hospital-at-home track, patients and caregivers receive a monitoring kit (including a pulsoximeter and thermometer) to evaluate the vital signs. These will be written down onto a registration form three times a day, and discussed with the treating physician. The care pathway supports patients and caregivers to keep control over their own care process by home monitoring.

Objective: The objective is to evaluate the implementation of this multidisciplinary developed regional care pathway for (frail) older people with an acute moderate-severe LRTI or pneumonia, to thereby optimize the regional coordination of care and prevent unnecessary hospitalizations.

Study design: Prospective observational study.

Study population: (Frail) older people (age ≥ 65 years) with an acute moderate-severe LRTI or pneumonia treated outside the hospital versus those (partially) treated in the hospital.

Main study parameters/endpoints: The primary study outcome is to determine the feasibility of the care pathway, which is defined as the percentage of patients included in the care pathway that were not admitted to the hospital (treated outside the hospital). Secondary outcomes are the practical applicability (defined as the percentage of patients that can be included in the care pathway and that are actually included), the total amount of days of bedridden status or hospitalization, the sleep quantity in the first two days after inclusion and on the seventh day, the sleep quality on the seventh day after inclusion and at 30 days, functional outcome (KATZ-15 and current living situation) and quality of life (EQ-5D-5L) at 30 days, 6 and 12 months, the safety of the care pathway (30-day, 6 month and 12 month mortality) and complications in the first 30 days (readmissions, delirium, falls). Furthermore, the satisfaction of patients/caregivers and professionals with the given care will be evaluated. If possible, cost savings and logistical impact on hospital bed capacities will be evaluated.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: As this is an observational study evaluating the feasibility and the satisfaction of a regional care pathway in common practice, there are no specific benefits nor risks to be expected from participation in the study. Patients receive standard care according to the care pathway or the hospital guidelines. However, participation in the study will cost the patients (2-2.5 hours), caregivers (5-35 minutes) and treating physicians (5-35 minutes) extra time compared to not participating in the study.

1. INTRODUCTION AND RATIONALE

An acute lower respiratory tract infection (LRTI) or pneumonia in (frail) older people is generally characterized by diagnostic uncertainty and a high risk of complications and negative outcomes (for example due to overlap with heart failure and chronic obstructive pulmonary disease (COPD))[1-2]. Besides that, care in the home situation often acutely falls short because of an acute care problem (for example due to falls, decline in activities in daily living (ADL) function or a state of confusion). This often leads to a presentation at the emergency department (ED) with the goal to define the optimal treatment for the (frail) elderly patient. This optimal treatment often consists of a combination of antibiotics/antivirals, oxygen suppletion and/or inhalation medication, optimization of the hemodynamic, physiotherapy and treatment and/or prevention of delirium. In principle, this kind of care and treatment could take place outside the hospital (for example in a patient's home); however hospitalization usually follows because treatment at home is considered irresponsible, inhumane or impossible due to the acute care problem[3-6]. Hospitalized (frail) elderly are at high risk for complications, like malnutrition, delirium (with the consequence of prescribing sedative medication) and falls/ functional decline. These hospitalizations are a consequence of the fact that the healthcare and treatment protocols between the involved regional care partners (for example general practitioners (GPs), hospitals, nursing homes and homecare institutions) are insufficiently coordinated, the lack of diagnostic and treatment possibilities in primary care, the lack of capacity in the nursing homes and homecare, and the presence of financial barriers[7-11]. In (frail) older people, an acute moderate-severe LRTI or pneumonia therefore often causes unnecessary or unnecessarily long hospitalizations with high risk of complications, like iatrogenic harm such as delirium[12-14]. Besides that, these hospitalizations of (frail) older people with acute moderate-severe LRTI or pneumonia, especially in the flu season, also cause hospital capacity problems that may result in postponing other necessary treatments. Therefore, the regional care pathway 'The Hague RTI Care Bridge' is developed multidisciplinary to support GPs in the diagnostics, the treatment and the organisation of care for (frail) elder people (age ≥ 65 years) with an acute moderate-severe LRTI or pneumonia[15]. In this care pathway, three patient paths are imbedded with one of them being a hospital-at-home track in which patients will receive antibiotics/antivirals and when clinically indicated oxygen suppletion, inhalation medication and/or homecare. The second patient path is an adjusted visit to the ED with a priority assessment and the third path is an admittance to a readily available recovery bed in a nursing home. Clear collaboration agreements are made between involved regional care partners. In the hospital-at-home track, patients and caregivers receive a monitoring kit (including a pulsoximeter and thermometer) to evaluate the vital signs. These will be written down onto a registration form three times a day, and

discussed with the treating physician as well as whether the patient went out of bed that day and/or whether the patient has fallen. The care pathway supports patients/caregivers to keep control by home monitoring. In this observational study, the implementation of this care path will be evaluated. During this 12 months project, it is hypothesized that at least 50% of the (frail) elderly patients with an acute moderate-severe LRTI or pneumonia will not be admitted to the hospital (completely treated outside the hospital (at home or in the nursing home)) after inclusion in the care pathway by the GP or treating physician at the ED.

2. OBJECTIVES

Primary Objective: To determine the feasibility of the care pathway, which is defined as the percentage of patients included in the care pathway that were not admitted to the hospital (treated outside the hospital).

Secondary Objectives: To determine the practical applicability of the care pathway (defined as the percentage of patients that can be included in the care pathway and that are actually included), the safety of the care pathway (mortality at 30 days, 6 months and 12 months), complications within the first 30 days (readmissions, delirium, falls), the satisfaction of patients/caregivers and professionals with the care pathway, the total number of days of bedridden status or hospitalization, the sleep quantity in the first two days after inclusion and on the seventh day, the sleep quality on the seventh day and at 30 days, and functional outcome (KATZ-15 and current living situation) and quality of life (EQ-5D-5L) at 30 days, 6 and 12 months. If possible, cost savings and logistical impact on the hospital bed capacities will be evaluated.

3. STUDY DESIGN

The design of the study is a prospective observational study, which will be performed in the Haaglanden area in the Netherlands, consisting of the municipalities of The Hague, Wassenaar, Rijswijk and Voorburg/Leidschendam. The inclusion for this study will be during 12 months from November 14, 2022 until November 13, 2023, thereby including the 2022-2023 winter season / flu season. During this period, the results will be evaluated for the benefit of interim adjustments.

The setting of the study will be mostly in primary care. Based on the care pathway 'The Haque RTI Care Bridge', GPs have three options for the treatment of (frail) older people with a clinical diagnosis of an acute moderate-severe LRTI or pneumonia:

1. Hospital-at-home.
2. Referral to the ED with a priority assessment.
3. Admittance to a recovery bed in a nursing home.

The hospital-at-home treatment can only be started on weekdays (Monday-Friday) during office hours (08.00-18.00) due to practicalities (absence of own GPs during evenings and nights). The admittance to a recovery bed in a nursing home can only be done on weekdays and weekend days from 08.00-20.00. Patients who present at their GP and/or on the ED with a LRTI/pneumonia when the care pathway is active are eligible to be treated according to the care pathway. Patients who are hospitalized subsequently to the priority assessment ED-visit will not be treated following the care pathway, and therefore not be included in the study.

<u>Control group</u>
Patients who fulfill the inclusion criteria and do not meet the exclusion criteria of the care pathway, and are admitted to the hospital on weekdays outside office hours (18.00-08.00) and on weekend days due to the inactivity of the care pathway or unavailability of the recovery bed in a nursing home, will serve as a control group.

4. STUDY POPULATION

4.1 Population (base)

The study population consists of older people (age ≥ 65 years) who present at their GP or on the ED with the clinical diagnosis of an acute moderate-severe LRTI or pneumonia. These older patients with a moderate-severe LRTI or pneumonia will be the main population in this study. The caregivers and treating physicians of these patients will also be asked to participate in this study to evaluate their satisfaction about the given care.

In the Netherlands, >35.000 adults are admitted to the hospital annually with an acute LRTI or pneumonia. In the region of The Hague, this concerns around 1.500-2.000 hospital admissions annually. The Hague has approximately 540.000 citizens, of which about 59.000 are 65 years or older. In 2018, 29.732 patients aged 65 years or older presented at the EDs of the Haga Teaching Hospital and the Haaglanden Medical Centre.

4.2 Inclusion criteria

To be eligible to participate in this study, a patient must meet all following criteria:

- age ≥ 65 years
- clinical diagnosis of an acute moderate-severe* LRTI or pneumonia
- written informed consent (IC) for participation in the study
- oxygen saturation ≥92% with max 5 litres O_2** and a respiratory frequency ≤24/minute

*: moderate-severe is defined by a Pneumonia Severity Index (PSI) class ≥ 3 or a CURB-65 ≥ 2[16-17]

** = or adjusted oxygen saturation cut-offs for the patient as clinically indicated (for example for patients with COPD) by the treating physician (GP or ED-physician)

To be eligible to participate in this study, a caregiver must meet all following criteria:

- age ≥ 18 years
- caregiver of a patient included in the study
- written IC for participation in the study

To be eligible to participate in this study, a physician must meet all following criteria:

- physician of a patient included in the study at the main location of treatment:
    - hospital-at-home: general practitioner
    - nursing home: specialist in elderly care medicine
    - hospital (control group): ward doctor
- physician should have treated the patient at least ≥ 2 (consecutive) days
- written IC for participation in the study

4.3 Exclusion criteria

A potential patient who meets any of the following criteria will not be able to participate:

- patients receiving chemotherapy (< 2 months before presentation)
- patients with active hematologic malignancy
- immunocompromised patients (for example solid organ transplants)
- severe dementia (clinical dementia rating scale sum of boxes (CDR-SOB) score 16-18)[18]

4.4 Sample size calculation

As this is a feasibility and qualitative study, a formal sample size calculation is not possible. We aim to include ±100 (frail) elderly patients, together with their ±100 caregivers and their ±100 treating physicians. In case a patient is included in the study and his/her caregiver and/or treating physician does not want to participate in study, the patient will stay included in the study and no extra patients will be included. Ideally, 50 patients will be treated at home or in a nursing home and 50 patients will be treated in the hospital (control group).

5. TREATMENT OF SUBJECTS

5.1 Investigational product/treatment

Patients will be managed according to the multidisciplinary developed care pathway 'The Hague RTI Care Bridge'. The first procedure in this pathway is the assessment of the patient by the GP. The GP performs a physical examination including vital signs (heart frequency, blood pressure, respiratory frequency, oxygen saturation, and body temperature), a check for the presence of a confused state according to current delirium guidelines and a standard diagnostics package as defined in the care pathway: nasopharyngeal swab for detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza by polymerase-chain reaction (PCR) and an adjusted acute presenting older patient (APOP) screener[19-20]. Next, the GP will evaluate whether the criteria for hospital-at-home treatment are fulfilled and wished upon by the patient and caregiver, or whether additional assessment on the ED or admission to a nursing home is needed.

Main criteria for hospital-at-home treatment:

- the patient has an acute moderate-severe LRTI or pneumonia
- the patient/caregiver are motivated and able to learn
- unplanned care is not expected
- an individual care plan and registration form are present
- adequate homecare has been deployed if necessary
- the patient/caregiver can open the door or the patient has a key box at the front door
- the patient/caregiver/homecare can do checks and are able to use the monitoring kit
- the GP is the care director and agrees and knows the method of monitoring
- oxygen saturation ≥92% with max 5 litres O2 and respiratory frequency ≤24/minute*

* = or adjusted oxygen saturation cut-offs for the patient as clinically indicated (for example for patients with COPD) by the treating physician (GP or ED-physician)

First treatment option: hospital-at-home

If the GP aims to treat the patient at home, the following treatment options are available following the current national primary care guidelines[21]. In case of bacterial pneumonia, the first choice is amoxicillin, which can be switched in case of insufficient improvement after two days in no severely ill patients to doxycycline or another antibiotic. The second choice (in case of hypersensitivity) is doxycycline. An alternative treatment is moxifloxacin, which can be started after consultation of an internist or pulmonologist. In case of (or suspicion of) aspiration, amoxicillin/clavulanic acid is the first choice and clindamycin the

second choice (in case of hypersensitivity). An additional treatment option for patients with unreliable oral intake or patients where there is little supervision on the intake is ceftriaxone intramuscular once a day for a total of five days, which will be administered by a specialist nurse from the homecare organisation.

In case of a coronavirus disease 2019 (COVID-19) infection, the patients will be treated at home following the current national primary care guidelines[22]. In case of an influenza infection, the patients will be treated according to the current national primary guidelines with oseltamivir or baloxavir[23]. In the treatment with oseltamivir, attention should be payed to the kidney function.

If patients sound bronchospastic during pulmonary auscultation, the start of inhalation medication can be considered in the form of fenoterol/ipratropium (50/20) per doses aerosol with spacer, consisting of two inhalations at a time with a maximum of eight per day. In patients with underlying obstructive pulmonary disease (asthma/COPD) and/or clinical signs of bronchospasm, it can be considered to start prednisolone 40mg once a day for five days.

Patients requiring oxygen suppletion can receive oxygen suppletion (maximum of 5 litres) at home. The GP can order the oxygen by phone (delivery time within a few hours) and individual target values will be noted on the individual care plan of the patient by the treating physician. Reduction of the oxygen suppletion takes place based on the individual target values in consultation with the GP.

Every patient included for the hospital-at-home treatment according to the care pathway will be registered at the homecare contact centre. The GP will inform them about the therapy of choice, the use of oxygen suppletion (if indicated), the need to start homecare and the individual care plan. Besides that, the GP will give the patient a printed version of the individual care plan to keep at home. The homecare organisation makes sure that a nurse will visit the patient within four hours of registration. To this visit, the nurse will bring a printed version of the registration form, a monitoring kit (including a pulsoximeter and a thermometer) and will administer the first dose of ceftriaxone intramuscular if needed.

During the visit, the nurse will instruct the patient and caregiver about the use of the monitoring kit and the registration form. They will discuss the individual care plan and explain how to contact the homecare contact centre, and answers additional questions. In case inhalation medication is prescribed, instructions on the use will be given. In case

intramuscular ceftriaxone is prescribed, the first gift will be given during this visit and the nurse will also visit the patient daily to administer the other doses of ceftriaxone. The nurse will also evaluate whether there is need for homecare, if not already started.

The GP will have contact at least once a day with the patient/caregiver or the nurse of the homecare. This contact will preferably be by video call, but at least by phone. Patients will be asked to write the vital signs down on the registration form three times a day to discuss them with their treating GP together with whether the patient went out of bed that day and whether the patient has fallen. A fall is defined as an event that results in a person coming to rest inadvertently on the ground or floor or other lower level. In case of doubt, the GP will visit the patient. To guarantee a safety net 24 hours a day, the GP will inform the general practice centre (GPC) about the patient being in the care pathway. Besides that, the GP will ask the patient to give permission to open their national exchange point (LSP) to guarantee that the GPC will also have all patient information after office hours if needed. The GP will also make explicit arrangements about the continuation of care after office hours, like for example a contact moment during weekend days.

<u>Second treatment option: assessment at ED</u>

In case the GP decides further assessment on the ED is clinically indicated, the GP will consult an internist or pulmonologist and refer the patient to the ED via a special template. The ED will try to assess the patient with priority. At the ED, a diagnostics package which is predefined in the care pathway will be used consisting of: laboratory tests (blood count including differentiation, CRP, sodium, potassium, creatinine, urea, and optional are d-dimer and N-terminal pro brain natriuretic peptide (NT-proBNP)), clinical prediction scores (PSI score or CURB-65 score, and APOP-score), nasopharyngeal swab for a PCR on respiratory pathogens, chest imaging (X-ray and/or CT-scan) and an electrocardiogram (ECG).

In case the patient will start with antibiotic therapy, the first gift will be given intravenously at the ED before discharge to home. In case of a confirmed influenza infection, the patient will start with oseltamivir or baloxavir. The treating physician at the ED will draft the individual care plan before discharge to home. In case of discharge to home, the treating physician will contact the homecare contact centre and register the patient. The treating physician will also call the GP during office hours. On discharge, the patients will get a printed version of their individual care plan and their discharge letter.

Third treatment option: admittance to a recovery bed

If the GP or the treating physician on the ED decides treatment in a nursing home is favourable, they will contact the specialist elderly care medicine in case direct placement on a recovery bed is required. The participating nursing homes will always have one recovery bed available for patients included in the care pathway. Criteria for such a recovery bed are that the patient requires temporarily intensive multidisciplinary recovery care, the patient will go back to the own living environment within a maximum of 14 days, and the patient does not require admission on a closed (psychiatric) department. The individual care plan and the discharge letter will be sent to the nursing home and printed versions will also be given with the patient to the nursing home.

5.2 Use of co-intervention

Not applicable.

5.3 Escape medication

Not applicable.

6. INVESTIGATIONAL PRODUCT

Not applicable. The treatment as described in the regional care pathway is considered the golden standard.

7. NON-INVESTIGATIONAL PRODUCT

Not applicable. The pulsoximeter and thermometer as described in the regional care pathway are considered the golden standard.

8. METHODS

8.1 Study parameters/endpoints

8.1.1 Main study parameter/endpoint

The main study endpoint is to determine the feasibility of the care pathway, which is defined as the percentage of patients included in the care pathway that were not admitted to the hospital (treated outside the hospital).

8.1.2 Secondary study parameters/endpoints

The secondary study endpoints are to determine the clinical outcomes of the implementation of the care pathway. This includes:

- Practical applicability of the care pathway (defined as the percentage of patients that can be included in the care pathway, and are actually included)
- Mortality at 30 days, 6 and 12 months
- Complications within the first 30 days (readmissions, delirium, falls)
- Satisfaction of patients, their caregivers and treating physicians by questionnaires with a 5-point or 10-point Likert scale (and semi-structured in-depth interviews in the first 10 patients and their caregivers/physicians with the hospital-at-home treatment)
- Days of bedridden status or hospitalization
- Sleep quantity in the first two days after inclusion and on the seventh day as assessed by the core Consensus Sleep Diary[24]
- Sleep quality on the seventh day after inclusion and at 30 days assessed by the Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance short form 8b[25-26]
- Functional outcome at 30 days, 6 and 12 months as assessed by KATZ-15 (including the KATZ-ADL and Lawton instrumental ADL (IADL))[27-29] and current living situation
- Quality of life at 30 days, 6 and 12 months as assessed by EQ-5D-5L[30-31]

If possible, cost savings and logistical impact on the hospital bed capacities will be evaluated. Cost savings will be roughly estimated using the length of the use of care (hospital/nursing home admission or homecare) and the average care costs per day for care in the hospital, care in a nursing home or homecare. We aim to evaluate the logistical impact on the hospital bed capacities by simulating a scenario in which the patients who were treated at home or the nursing home would have been admitted to the hospital at the time of care pathway inclusion. If this analysis is possible, it will be possible to make a rough estimation of the logistical impact on the hospital bed capacities.

8.1.3 Other study

Not applicable.

8.2 Randomisation, blinding and treatment allocation

Not applicable.

8.3 Study procedures

If the GP decides to treat the patient at home according to the care pathway, the GP will perform a physical examination, measure the vital parameters (heart rate, blood pressure, respiratory rate, oxygen saturation and temperature) and will perform the standard diagnostics package: nasopharyngeal swab (SARS-CoV-2 and influenza) and adjusted APOP-screening. The GP will inform the patient (and representative (e.g. in case of incapacity due to dementia/delirium)) about the study and ask for oral informed consent (IC) to collect data for scientific purposes. If the patient or representative (on behalf of the patient) agrees to participate in the study, the GP will hand over the patient information letter and inform the research personnel about the patient. Within 1 workday, a research team member will visit the patient (and representative if applicable) at home to provide written IC and collect data.
If the patient refuses to participate in this study, no research data will be collected and the patient will be managed according to the regional care pathway anyway.

When the GP decides to refer the patient to the ED for additional assessment, a predefined diagnostics package will be performed on the ED: laboratory tests (blood cell count including differentiation, CRP, sodium/potassium, glucose, kidney function (creatinine/urea), and optional are d-dimer and NT-proBNP), chest imaging (X-ray or CT-scan), and an ECG. All of the data above will be collected on the ED for patients included in the control group. The treating physician on the ED will inform the patient (and representative if applicable) about the study (including handing over the patient information letter) upon inclusion in the care pathway (hospital-at-home treatment or

admission nursing home) or upon hospitalization for patients eligible for the control group, and will ask the patient (or representative if applicable) for oral IC to participate in the study.

Most patients included in the care pathway and in the control group will receive some form of antimicrobial therapy. For the patients in the hospital-at-home track, the nurse from the homecare institution will also check at the explanatory visit (<4 hours after inclusion) whether patients already received their first dose of antimicrobial therapy, otherwise the patients will receive their first dose of antimicrobial therapy by the nurse. The patients/caregivers/nurses in the hospital-at-home track will be checking the vital parameters of the patient at least three times a day and write them down on the given registration form to discuss them with the treating GP together with whether the patient went out of bed that day and whether the patient has fallen. The GPs (hospital-at-home) and specialists in elderly care medicine (admittance on a recovery bed in a nursing home) will collect information regarding illness duration during their follow-up, thereby providing information about mortality, complications (delirium, falls, readmissions) and percentage of complete treatments at home or the nursing home.

One of the research team members will visit the patient at home or in the nursing home on the first day after inclusion in the care pathway and in the hospital when included in the control group. During this visit, patients (and their representatives if applicable) will be able to ask additional questions about the patient information letter and the study. If a patient (or representative on behalf of the patient) agrees to participate in the study, he/she will be asked to give written IC for participation in the study. In case a representative has given written IC for an incapacitated patient (e.g. in case of delirium), and the patient's medical condition improves over time, the patient will be asked for written IC when the patient is considered competent again. During this visit (+/- 1 hour), baseline information will be collected from the patients that gave written informed consent. This baseline information will include demographic information (including ethnicity/religion) and a geriatric assessment (GA). Ethnicity and religion of patients are included in the baseline information as the Haaglanden area has a multicultural society and these factors may influence a patient's care system and thereby the choice for the current treatment location. Dementia research has shown that a considerable amount of the people with a migration background make limited use of professional homecare, and the care is often taken over by family members[32-33], A GA is an evidence-based way of describing different domains that are associated with ageing in the older population

and focuses on older adults their functional, psychosocial and medical capacities. As our study population consists of patients who are in a vulnerable phase of life, we want to keep the study load as low as possible. The following tests will be included in the GA: the Charlson Comorbidity Index[34], G-8 screening tool[35], 6-item cognitive impairment test (6-CIT)[36], KATZ-15, living situation and last quality of life (EQ-5D-5L) one week prior to the onset of disease. During this visit, patients will also be given a core Consensus Sleep Diary to fill in on the two upcoming days and on the seventh day after inclusion. Patients will also be given a PROMIS Sleep Disturbance short form 8b to fill in on the seventh day after inclusion. Homecare nurses will collect the registration and sleep quality/quantity forms at their last patient visit (after a patient is released from the pathway) together with the monitoring kits. After this first visit, the research team member who visited the patient will also contact their caregiver and treating physician to ask for written informed consent for participation in the study.

With the first ten patients included in the hospital-at-home group of the care pathway, a semi-structured in-depth interview (+/- 30 minutes) will be held on voluntary basis with the patient within three weeks after inclusion in the care pathway. If these 10 patients agree to participate in the interview, their caregivers and their treating GPs will also be asked if they agree to undergo a similar interview to collect information about their experiences with the care pathway. The interview of the patient and their caregiver can take place simultaneously, while the interview with the GP will take place separately. The framework that is used to develop the interview guide is the Consolidated Framework for Implementation Research (https://cfirguide.org/), which provides a framework of constructs that have been associated with effective implementation[37-39]. There are five different domains with corresponding example questions. These questions will be adapted and tailored to the intervention program. The information collected during these interviews will be used to adjust the care pathway based on the experiences of patients, caregivers and GPs with the hospital-at-home treatment.

At 30 days, all patients (both patients included in the care pathway and in the control group) will receive a phone call (+/- 30 minutes) from one of the research members in which they will be asked about their sleep quality (PROMIS Sleep Disturbance short form 8b), their functional status (KATZ-15 and current living situation (at home with or without homecare, or in a nursing home)), their quality of life (EQ-5D-5L), the development of complications (for example readmissions, falls and delirium) and their satisfaction with the given care/treatment. The questions to evaluate satisfaction are

based on the Consumer Quality Index, Patient Reported Outcome Measures and other research evaluating home treatment of patients, and adjusted if applicable[40-41].

At 30 days, all participating caregivers and treating physicians (GPs, specialists in elderly care medicine and ward doctors in the hospitals) will receive a short phone call (+/- 5 minutes) from one of the research members in which they will be asked about their satisfaction with the given care/treatment. During this call, the treating physicians will also be asked about the development of complications (for example readmissions, falls and delirium).

At 6 and 12 months, all patients (both patients included in the care pathway and in the control group) will receive a phone call (+/- 15 minutes) from one of the research members in which they will be asked about their functional status (KATZ-15 and current living situation (at home with or without homecare, or in a nursing home)) and quality of life (EQ-5D-5L).

Patients can choose whether the questionnaires at 30 days, 6 months and 12 months will be either sent by post or email, or will be performed by telephone to maximize follow-up response rates. The research group has longstanding experience in performing questionnaires by telephone, and this has proven to be feasible and has been validated in previous studies[42].

8.4 Withdrawal of individual subjects

All patients and representatives can withdraw their consent for the study at any time if they wish to do so without any consequences.

8.4.1 Specific criteria for withdrawal (if applicable)

Not applicable.

8.5 Replacement of individual subjects after withdrawal

The individual subjects will not be replaced after withdrawal.

8.6 Follow-up of subjects withdrawn from treatment

The follow-up of the individual subjects withdrawn from treatment will be stopped.

8.7 Premature termination of the study

Not applicable

9. SAFETY REPORTING

Not applicable.

10. STATISTICAL ANALYSIS

10.1 Primary study parameter(s)

Feasibility is defined as the percentage of the patients included in the pathway that were not admitted to the hospital (treated outside the hospital). This will be quantitative data. Categorical variables will be presented as proportions. The quantitative data will be analysed by the use of Statistical Package for the Social Sciences (SPSS).

10.2 Secondary study parameter(s)

The secondary outcomes are the practical applicability of the care pathway (defined as the percentage of patients that can be included in the care pathway and that are actually included), mortality, complications within the first 30 days (readmissions, delirium, falls), the satisfaction of patients/caregivers and professionals with the given care, the total amount of days of bedridden status or hospitalization, the sleep quantity and quality, the functional outcome and the quality of life. These outcomes will be mixed methods. Some of the outcomes will be clinical outcomes (quality of life, mortality, functionality) while others will be non-clinical outcomes (practical applicability, cost savings, logistical impact).

Categorical variables will be presented as proportions. Differences between groups will be tested with Chi square tests and multivariate logistic regression models. Continuous data (scale questions) will be presented as means (standard deviations) for normally distributed data or medians (interquartile ranges) for not-normally distributed data. Differences between groups will be tested with independent t-tests or one way ANOVA's (normal distribution) or Mann-Whitney U or Kruskal Wallis tests (no normal distribution) depending on the amount of groups to be compared per analysis and by multivariate linear regression models. All tests of significance will be at two-tailed 0.05 level. The 95% confidence intervals will be used to assess presence/absence of associations. The quantitative data will be analysed with SPSS.

All interviews will be recorded, transcribed and hereafter then coded with the program Atlas.ti. Version 9.0. The recordings of the interviews will be saved in a secured folder on the network of the coordinating hospital and will be deleted after transcription of the interview has been performed in the coordinating hospital. The transcriptions of the interviews will be saved on the network of the coordinating hospital. We will apply a thematic content analysis to identify and categorize recurrent themes and key elements in the interviews about the experiences with the hospital-at-home treatment from the first 10 patients included in the hospital-at-home group, their caregivers and their treating GPs.

By selecting the participants in this way, the interviews will be taken without purposive sampling.

10.3 Other study parameters
Not applicable.

10.4 Interim analysis
Not applicable.

11. ETHICAL CONSIDERATIONS

11.1 Regulation statement

This study will be conducted according to the principles of the Declaration of Helsinki (2013) and the General Data Protection Regulation (AVG). The Medical Research Ethics Committee Leiden Den Haag Delft has evaluated the research protocol and confirmed that de the Medical Research Involving Human Subjects Act (Dutch abbreviation: WMO) does not apply to this study.

11.2 Recruitment and consent

The treating physician (GPs and/or ED-physicians) will inform patients (and their representatives if applicable) about the care pathway during their visit. The treating physician will orally explain the purpose and the methodology of the care pathway; patients (and representatives) will also receive a patient information letter about the study. Sufficient time will be given for consideration before patients (or representatives) will be asked if they want to participate in the study. If they want to participate, their oral informed consent for the use of their data will be asked. During the visit by the research team on the first day after inclusion, patients (and their representatives if applicable) will be able to ask additional questions after which they will be asked for written informed consent for the use of their data. After patients (or their representatives) gave written informed consent, their caregivers and treating physicians (GPs, specialists in elderly care medicine) will also be approached to participate in the study and asked to give written informed consent for the study.

The treating ED-physician or ward doctor will orally inform the hospitalized patients (and their representatives if applicable) about the purpose and methodology of the study; they will also receive a patient information letter about the study. Sufficient time will be given for consideration before patients (or representatives) will be asked if they want to participate in the study. If they want to participate, their oral informed consent will be asked. During the visit by the research team on the first day after inclusion, patients (and representatives if applicable) will be able to ask additional questions and will be asked for written informed consent for the use of their data. After patients gave written informed consent, their caregivers and treating physicians (ward doctors) will also be approached to participate in the study and asked to give written informed consent for the study.

In case a representative has given written IC for an incapacitated patient (e.g. in case of delirium), and the patient's medical condition improves over time, the patient will be asked for written IC when the patient is considered competent again.

All patients and representatives will be informed that they can withdraw their consent at any time if they wish to do so without any consequences.

11.3 Objection by minors or incapacitated subjects
Not applicable.

11.4 Benefits and risks assessment, group relatedness
As this is an observational study evaluating the feasibility and satisfaction of a regional care pathway in common practice, there are no specific benefits nor risks to be expected. The patients included in the study will have a PSI score of three or higher, which means they have a mortality risk of 0.9%-27.0% (average 30-day mortality 10%) within 30 days depending on the height of the score[16]. Therefore, the baseline mortality risk of all patients in the study is relatively high, regardless of treatment location (either at home, a nursing home or in the hospital). The hospital-at-home treatment may have a higher risk when a patient deteriorates since the monitoring might be less strict than during a hospitalization. However, earlier studies have shown that patients with higher PSI-scores can safely be treated at home[3-6].

In the care pathway, all patients and their caregivers in the hospital-at-home group will be provided with a monitoring kit (including a thermometer and pulsoximeter), and will be instructed by a nurse from the homecare organization how to monitor the vital signs at home, thereby stimulating autonomy of the patients and caregivers. The homecare contact centre is 24 hours a day reachable by phone. This way, the risk of hospital-at-home treatment is reduced and a safety net is implemented in case of clinical deterioration. The benefit of treatment at home for patients is prevention of unnecessary and unnecessary long hospitalizations with unnecessary risks of iatrogenic harm. Therefore, it is expected that patients will be better off at home than in the hospital. It is good to realize that the patients prognosis depends on the underlying medical condition of the patient and the specific treatment (which is the same at home as in the hospital) and not on the degree of monitoring.

11.5 Compensation for injury
Not applicable.

11.6 Incentives
Not applicable as patients will not receive compensation for participating in the study.

12. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

12.1 Handling and storage of data and documents

The written IC forms will be safely stored at the research department in the coordinating hospital (Haga Teaching Hospital). Data will be stored using Castor EDC through direct data entry by either the coordinating investigator, the (principal) investigators or the research nurses. The data will be coded in the coordinating hospital.

Every participant will get a unique study code, which will not contain any personal details. The code will be made up from three separate parts:

- abbreviation of location:
    - Haga Teaching Hospital: HAG
    - Haaglanden Medical Centrum: HMC
    - GP: HA
    - nursing home: VPH
- type of study participant:
    - patient: PA
    - caregiver: MA
    - treating physician: BA
- number of the study participant at the location:
    - starting with number 1 and adding up with each entry
    - patients, their caregivers and treating physicians have the same number

For example, the third patient at the GP will receive code GP-PA-3, while their caregiver will receive code GP-MA-3 and their treating physician will receive the code GP-BA-3. The numbers for the patients will be arranged by the order of the study visit in case two patients are included in the same location on the same day. Age will be represented in years. Therefore, the data will not be traceable to the individual patient. A SPSS file will be extracted from Castor EDC and will therefore not contain names, birth dates and patient numbers. The key of the code will be stored on a secured drive in the coordinating hospital. After the collection of all data, a combined (coded) database will be stored at a secured drive at the coordinating hospital. The data will be stored for a period of 15 years. The coded database will only be shared with other researchers upon reasonable request after publication of the results. The shared database will only contain the coded individual level data that underlies the results in the publication the researcher is referring to.

12.2 Monitoring and Quality Assurance

Monitoring will be performed by the Haga science bureau. In addition to the at the monitoring, work group meetings will take place, which will be periodic evaluations by

workgroup members (including patients/citizens) each time five patients have been treated at home according to the care pathway. During these meetings, the workgroup is expected to draw conclusions about whether possible adjustments or improvements to the care pathway are needed. Hereby, particular attention is paid to the feasibility, practical applicability and safety of the care pathway and the satisfaction of patients, caregivers and professionals.

12.3 Amendments

Amendments are changes made to the research/protocol after a favourable opinion has been given. All amendments will be notified to the Haga science bureau that gave a favourable opinion.

12.4 Annual progress report

The investigator will submit a summary of the progress of the trial to the Haga science bureau once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial, and amendments.

12.5 Temporary halt and (prematurely) end of study report

The investigator/sponsor will notify the Haga science bureau of the end of the study within a period of 8 weeks. The end of the study is defined as the last contact moment with the last patient.

Within one year after the end of the study, the investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the Haga science bureau.

12.6 Public disclosure and publication policy

The study will be registered at ISRCTN registry (www.isrctn.com). The results will be published in a peer-reviewed journal. The principal investigators will be responsible for the publication of the study results. The study results will be disclosed unreservedly. The principles of generally accepted specifications of authorship shall be followed in the appointing of authors and co-authors. All contributors of the final article will have an opportunity for evaluation of the final text before submission to a peer-reviewed journal.

13. STRUCTURED RISK ANALYSIS

13.1 Potential issues of concern

Not applicable.

13.2 Synthesis

In paragraph 11.4 in this study protocol, a benefits and risks assessment of this study is performed. All antimicrobial therapy in the care path are registered products and already part of the national guidelines for the treatment of LRTI or pneumonia. Therefore, there are no expected risks due to the therapy for subjects participating in study compared to the risks in normal clinical practice. For this study, paragraph 13.1 is therefore not applicable and additional safety measurements are not indicated.

14. REFERENCES

1. Mahler DA. Evaluation of Dyspnea in the Elderly. *Clin Geriatr Med.* 2017;33(4):503-521.
2. Pedersen F, Mehlsen J, Raymond I, Atar D, Skjoldborg US, Hildebrandt PR. Evaluation of dyspnoea in a sample of elderly subjects recruited from general practice. *Int J Clin Pract.* 2007;61(9):1481-1491.
3. Shepperd S, Butler C, Cradduck-Bamford A, et al. Is comprehensive geriatric assessment admission avoidance hospital at home an alternative to hospital admission for older persons?: a randomized trial. *Ann Intern Med.* 2021;174:889-898.
4. Federman AD, Soones T, DeCherrie LV, Leff B, Siu AL. Association of a Bundled Hospital-at-Home and 30-Day Postacute Transitional Care Program With Clinical Outcomes and Patient Experiences. *JAMA Intern Med.* 2018;178(8):1033-1040.
5. Gonçalves-Bradley DC, Iliffe S, Doll HA, et al. Early discharge hospital at home. *Cochrane Database Syst Rev*. 2017;6(6):CD000356.
6. Marrie TJ, Huang JQ. Admission is not always necessary for patients with community-acquired pneumonia in risk classes IV and V diagnosed in the emergency room. *Can Respir J*. 2007;14(4):212-216.
7. Challis D, Hughes J, Xie C, Jolley D. An examination of factors influencing delayed discharge of older people from hospital. *Int J Geriatr Psychiatry*. 2014;29(2):160-168.
8. Cadel L, Guilcher SJT, Kokorelias KM, et al. Initiatives for improving delayed discharge from a hospital setting: a scoping review. *BMJ Open.* 2021;11(2):e044291.
9. Gonçalves-Bradley DC, Lannin NA, Clemson L, Cameron ID, Shepperd S. Discharge planning from hospital. *Cochrane Database Syst Rev*. 2022;2(2):CD000313.
10. Hesselink G, Schoonhoven L, Barach P, et al. Improving patient handovers from hospital to primary care: a systematic review. *Ann Intern Med.* 2012;157(6):417-428.
11. van Seben R, Reichardt LA, Essink DR, van Munster BC, Bosch JA, Buurman BM. 'I feel worn out, as if I neglected myself': older patients' perspectives on post-hospital symptoms after acute hospitalization. *Gerontologist.* 2019;59(2):315-326.
12. Boyd CM, Landefeld CS, Counsell SR, et al. Recovery of activities of daily living in older adults after hospitalization for acute medical illness. *J Am Geriatr Soc.* 2008;56(12):2171-2179.
13. Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. *Age Ageing.* 2006;35(4):350-364.
14. Tsiompanou E, Lucas C, Stroud M. Overfeeding and overhydration in elderly medical patients: lessons from the Liverpool Care Pathway. *Clin Med (Lond).* 2013;13(3):248-251.
15. ZonMw. Project: Ouderen met luchtweginfectie/pneumonie: terugdringen en voorkómen van onnodige ziekenhuisopnamen. Available from: https://www.zonmw.nl/nl/onderzoek-resultaten/geestelijke-gezondheid-ggz/programmas/project-detail/juiste-zorg-op-de-juiste-plek/ouderen-met-luchtweginfectiepneumonie-terugdringen-en-voorkomen-van-onnodige-ziekenhuisopnamen/ [Accessed 23rd June 2022]
16. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med*. 1997;336(4):243-250.
17. Lim WS, van der Eerden MM, Laing R, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax*. 2003;58(5):377-382.

18. O'Bryant SE, Waring SC, Cullum CM, et al. Staging dementia using Clinical Dementia Rating Scale Sum of Boxes scores: a Texas Alzheimer's research consortium study. *Arch Neurol*. 2008;65(8):1091-1095.
19. Nederlands Huisartsen Genootschap. NHG-standaard: Delier, last updated May 2020. [Internet]. Available from: https://richtlijnen.nhg.org/standaarden/delier#volledige-tekst [Accessed 9th May 2022].
20. de Gelder J, Lucke JA, Blomaard LC, et al. Optimization of the APOP-screener to predict functional decline or mortality in older emergency department patients: Cross-validation in four prospective cohorts. *Exp Gerontol.* 2018;110:253-259.
21. Nederlands Huisartsen Genootschap. NHG-standaard: Acuut hoesten, last updated May 2020. [Internet]. Available from: https://richtlijnen.nhg.org/standaarden/acuut-hoesten#volledige-tekst [Accessed 9th May 2022].
22. Nederlands Huisartsen Genootschap. NHG-standaard: COVID-19, last updated April 2022. [Internet]. Available from: https://richtlijnen.nhg.org/standaarden/covid-19#volledige-tekst [Accessed 9th May 2022].
23. Federatie Medisch Specialisten. Richtlijn: Behandeling influenza, last updated: July 2021. [Internet]. Available from: https://richtlijnendatabase.nl/richtlijn/behandeling_influenza/startpagina_-_behandeling_influenza.html [Accessed 2nd June 2022].
24. Carney CE, Buysse DJ, Ancoli-Israel S, et al. The consensus sleep diary: standardizing prospective sleep self-monitoring. *Sleep*. 2012;35(2):287-302.
25. Yu L, Buysse DJ, Germain A, et al. Development of short forms from the PROMIS™ sleep disturbance and Sleep-Related Impairment item banks. *Behav Sleep Med*. 2011;10(1):6-24.
26. Terwee CB, Roorda LD, de Vet HC, et al. Dutch-Flemish translation of 17 item banks from the patient-reported outcomes measurement information system (PROMIS). *Qual Life Res*. 2014;23(6):1733-1741.
27. Laan W, Zuithoff NP, Drubbel I, et al. Validity and reliability of the Katz-15 scale to measure unfavorable health outcomes in community-dwelling older people. *J Nutr Health Aging*. 2014;18(9):848-854.
28. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The Index of the ADL: a standardized measure of biological and psychosocial function. *JAMA.* 1963;185:914-919.
29. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist*. 1969;9(3):179-186.
30. EuroQol Group. EuroQol--a new facility for the measurement of health-related quality of life. *Health Policy*. 1990;16(3):199-208.
31. Lamers LM, McDonnell J, Stalmeier PF, Krabbe PF, Busschbach JJ. The Dutch tariff: results and arguments for an effective design for national EQ-5D valuation studies. *Health Econ*. 2006;15(10):1121-1132.
32. Duran-Giraç G, Uysal-Bozkir Ö, Uittenbroek R, van Hout H, Broese van Groenou MI. Accessibility of health care experienced by persons with dementia from ethnic minority groups and formal and informal caregivers: A scoping review of European literature. *Dementia (London)*. 2022;21(2):677-700.
33. Hootsen MM, Rozema N, van Grondelle NJ. Onderzoeksrapport 'Zorgen voor je ouders is een manier van leven'. *Pharos*. 2013.

34. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383.
35. Bellera CA, Rainfray M, Mathoulin-Pélissier S, et al. Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. *Ann Oncol*. 2012;23(8):2166-2172.
36. Brooke P, Bullock R. Validation of a 6 item cognitive impairment test with a view to primary care usage. *Int J Geriatr Psychiatry*. 1999;14(11):936-940.
37. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci*. 2009;4:50.
38. Kirk MA, Kelley C, Yankey N, Birken SA, Abadie B, Damschroder L. A systematic review of the use of the Consolidated Framework for Implementation Research. *Implement Sci*. 2016;11:72.
39. Sarkies M, Long JC, Pomare C, et al. Avoiding unnecessary hospitalisation for patients with chronic conditions: a systematic review of implementation determinants for hospital avoidance programmes. *Implement Sci*. 2020;15(1):91.
40. Zorginstituut Nederland. Overzicht van alle CQI- en PREM-vragenlijsten, last updated March 18, 2019. Available from: https://www.zorginzicht.nl/ontwikkeltools/ontwikkelen/overzicht-van-alle-cqi--en-prem-vragenlijsten (Accessed 20th of September 2022)
41. Dirikgil E, Brons K, Duindam M, et al. COVID-box Experiences of Patients and Health Care Professionals (COVID-box Project): Single-Center, Retrospective, Observational Study. *JMIR Form Res*. 2022;6(7):e38263.
42. van Holstein Y, van Deudekom FJ, Trompet S, et al. Design and rationale of a routine clinical care pathway and prospective cohort study in older patients needing intensive treatment. *BMC Geriatr*. 2021;21(1):29.