Pursuing the Triple Aim in Hotspotters: identification and integrated care

protocol Version 4.1, April 2023

PROTOCOL TITLE 'Pursuing the Triple Aim in Hotspotters: identification and integrated care'

Protocol ID	NL78646
Short title	The Hotspotters Project
Version	4.1
Date	04/2023
Coordinating investigator/project leader	*K.A. Leming, MSc, k.a.leming@lumc.nl* *V. Tiemes, MSc, v.tiemes@lumc.nl*
Principal investigator(s) (in Dutch: hoofdonderzoeker/ uitvoerder	*Dr. R.C. Vos, r.c.vos@lumc.nl* *Dr. M.A. Bruijnzeels, m.a.bruijnzeels@lumc.nl*
Sponsor (in Dutch: verrichter/opdrachtgever)	*LUMC afdeling public health and eerstelijnsgeneeskunde (PHEG) campus Den Haag, Turfmarkt 99, 2511 DV, Den Haag* *Tel: 070-8009500*
Subsidising party	Nederlandse organisatie voor gezondheidsonderzoek en zorginnovatie (ZonMw) CZ Menzis
Independent expert (s)	Mw. Dr. Bertien Hart, huisarts en kaderhuisarts diabetes h.e.hart@umcutrecht.nl

PROTOCOL SIGNATURE SHEET

Name	**Signature**	**Date**
Sponsor or legal representative: **Head of Department:**	LUMC *Prof. M. E. Numans,* *afdelingshoofd PHEG*	
Coordinating Investigator/Project leader/Principal Investigator:	Dr. R.C. Vos, Principle investigator, Project leader *r.c.vos@lumc.nl*	

TABLE OF CONTENTS

LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

ABR	**General Assessment and Registration form (ABR form), the application form that is required for submission to the accredited Ethics Committee; in Dutch: Algemeen Beoordelings- en Registratieformulier (ABR-formulier)**
AE	**Adverse Event**
AR	**Adverse Reaction**
CA	**Competent Authority**
CCMO	**Central Committee on Research Involving Human Subjects; in Dutch: Centrale Commissie Mensgebonden Onderzoek**
CV	**Curriculum Vitae**
DSMB	**Data Safety Monitoring Board**
EU	**European Union**
EudraCT	**European drug regulatory affairs Clinical Trials**
GCP	**Good Clinical Practice**
GDPR	**General Data Protection Regulation; in Dutch: Algemene Verordening Gegevensbescherming (AVG)**
IB	**Investigator's Brochure**
IC	**Informed Consent**
IMP	**Investigational Medicinal Product**
IMPD	**Investigational Medicinal Product Dossier**
METC	**Medical research ethics committee (MREC); in Dutch: medisch-ethische toetsingscommissie (METC)**
(S)AE	**(Serious) Adverse Event**
SPC	**Summary of Product Characteristics; in Dutch: officiële productinformatie IB1-tekst**
Sponsor	**The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.**
SUSAR	**Suspected Unexpected Serious Adverse Reaction**
UAVG	**Dutch Act on Implementation of the General Data Protection Regulation; in Dutch: Uitvoeringswet AVG**
WMO	**Medical Research Involving Human Subjects Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen**

SUMMARY

Rationale:
People with complex problems on multiple life domains, so called 'hotspotters', receive fragmented care. This is difficult to manage by patients and care providers, leading to little effect of care and persistent unmet needs. The accumulation and complexity of problems often leads to high medical expenses. Next to their high medical spending levels, hotspotters´ experiences with the healthcare system are low as the healthcare system is not (yet) successful in dealing with their needs. Interventions aimed at the complex situation of hotspotters in our current healthcare system might benefit by applying a Triple Aim approach. This approach aims to simultaneously improve the individual experience of care, reduce the cost of care per capita and improve the health of populations by offering proactive integrated care.

Objective:
Is proactive integrated care costeffective and does it result in better patients experience than usual care after 12 months for patients with problems on multiple life domains?

Main and secundary study parameters:
This study will focus on measuring the changes in the following:
1. Incremental cost-effectiveness from a societal perspective. Information on cost will be based on patient-reported data obtained by questionnaires supplied with data from the GP medical files (*Huisarts informatie system, HIS) and CBSmicrodata*. To assess the effectiveness the EQ-5D-5L will be used for determining quality of life.

The secondary study parameters are:

1. Insight into patients experience of care, quality of life, proactive coping, and self-efficacy. This information will be gathered using interviews, focus groups and questionnaires (SF-12, UPCC, PAM-13 & Self-efficacy and Intentie itemlist).
2. Process evaluation with the involved care professionals, including the integration level of care per GP-practice, the nature of the communication between healthcare provider and patient (HCCQ, OPTION5), and acceptability (AIM), appropriateness (IAM), feasibility (FIM) ,and perceived and experienced effectiveness of the intervention.

Study design:
A stepped-wedge cluster randomised controlled trial (RCT) design will be used
This study will be performed in 20 general practices that do not yet offer proactive integrated care for hotspotters. Data on cost-effectiveness will be quantitatively assessed. Patient experience will be qualitatively assessed through focus groups and quantitative using validated questionnaires. Besides, the process will be both qualitatively and quantitatively evaluated using interviews or focusgroups, observations (audio recording) with care professionals on common themes of process evaluatation and a validated questionnaire.

Study population:
In total 200 hotspotters will be included. Hotspotters are individuals with at least two incidents of acute care utilisation (defined as out-of-office GP consultations, acute psychiatric care, emergency department visits and unplanned admissions) during the past year, and problems on two out of three health domains (chronic somatic, mental and/or social problems) based on diagnosis (coded with the International Classification of Primary Care) or medication

(ATC) coding.

Intervention:
The proactive integrated care intervention that will be used consists of five steps:
1. Active invitation of the patient from the practice.
2. Consult of 45 minutes with a trained Practice Nurse Mental Health Care based on the Positive Health Methodology.
3. Multidisciplinary team meeting based on the spider web with domain specific explanation to create a personalised care plan and assign a care coordinator to each patient.
4. Execution of the personalised care plan and frequent pro-active contact between care coordinator and the patient. In the first 12 weeks there is a minimum of 3 contact moments, however more frequent contact is expected. The proactive nature of this contact is emphasized.
5. Follow-up of the personalised care plan using clinical review and at least one multidisciplinary meeting. If needed, ad hoc additional meetings can be organised.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
Participation in this study is expected to be low risk for the patients. However, both risks and benefits are associated with participation.
Benefits include: Improved knowledge and insight. Participation might lead patients to have a better understanding of the factors that contribute to their overall well-being. This can be achieved with analysing the six life domains of the positive health conversation tool. This insight might result in appropriate interventions that meet the needs of the hotspotters.

A potential risk that should be taken into account is temporary elevated stress. Hotspotters experience a combination of different problems which can make life more complex and challenging. The heightened emphasis, especially in the beginning, on the factors that contribute to their health and social problems could result in higher stress levels in some participants.

1. INTRODUCTION AND RATIONALES

The term 'hotspotters' was first introduced in Gawande's landmark article (Gawande, 2011). He suggested that the accumulation of problems and high hospital costs were concentrated in certain areas (also defined as 'hot spots') in Camden, New Jersey. When looking at medical care data he noticed that there was a small group of people located in these areas, who accounted for most of the medical costs. It was revealed that one per cent of the hundred thousand people who used Camden's medical facilities, accounted for thirty per cent of its costs (Gawande, 2011).

These so called 'hotspotters' are defined as people who have complex problems on multiple life domains, treated with fragmented care which is difficult to manage by patients and care providers, leading to high medical costs, little effect of the care and persistent unmet needs. Next to their high medical spending levels, hotspotters experiences with the healthcare system are low as the healthcare system is not (yet) successful in dealing with their needs. Furthermore, this group places a lot of strain on healthcare professionals as their problems require a multidisciplinary supply of healthcare services, often in combination with social care and welfare (Wammes et al., 2017; Lee, Whitman, Vakharia, Taksler, & Rothberg, 2017). Various studies claim that the current healthcare system produces a lot of waste of resources in the hotspotters group (Lantz, 2020). Due to the lack of coordination and reactive character of the care, many healthcare providers dealing with these patients are confronted with acute situations that could be prevented.

Currently in The Netherlands, the ad hoc care as usual approach is the standard when treating any patient, including hotspotters. This type of care is concentrated around the general practitioner (GP), home care, mental health and social care. Hotspotters' problems have are multidimensional and addressed by an ad hoc network of care providers. A central caregiver or coordinator is often lacking. All these different care providers respond reactively on symptoms and problems presented by the patient, have their own perspective and treat the patient from their own treatment options. The various care providers are not stimulated to work proactively together.

In a pilot study performed in Portland Oregon showed that in patients with overuse and having a chronic condition, mental problems and substance abuse, the spending was at least 4 times higher than in a person with just a chronic condition. After a relatively simple intervention with health resilience workers the median number of ED visits was reduced from annually 9.3 to 6.2 and of hospital admissions from 2.0 to 1.3 (Bisognano & Kenney, 2012). Based on this experience, a pilot was done in 2017 in two healthcare centres in Zoetermeer.

The pilot study in the Netherlands (Zoetermeer) concentrated on a group identified hotspotters. In the two healthcare centres twenty-five hotspotters with multiple problems were enrolled. These 25 patients received an extensive interview based on positive health methodology, followed by welfare-support according to the individual needs. The one year results of the pilot demonstrated that positive health based on the positive health-tool of Machteld Huber improved in the overall group from a mean score of 5.5 (1.5 sd) to 6.7 (1.1 sd) ($t= 7.33$, $p<0.01$), which is 22% (Huber et al., 2011). Due to methodological study design issues (observational data with the regression to the mean effect in a group with extreme health care utilisation) the evidence remains promising, but not convincing. The small

number of RCTs performed showed mixed results (Iovan, Lantz, & Shapiro, 2018; Lantz, 2020; Iovan, Lantz, Allan, & Abir, 2020).

This intervention requires a different organization of care for complex patients. The integrated and proactive nature of the proposed approach for patients identified as hotspotters ensues an improved holistic approach. Since evidence for an integrated and proactive approach for hotspotters is not substantial yet, a proper cost-effectiveness study is needed to provide evidence if the approach is worth the effort.

1. OBJECTIVES

The primary goal of this study is to get insight in the cost-effectiveness after 12 months of working with a proactive, integrated (social) care approach in patients fitting our definition of a hotspotter. A hotspotter is a patient with problems on two out of three health domains (chronic somatic, psychiatric and/or social) and at least 2 acute care activities in the previous 12 months. The medical data from 3 years prior to the start of the study will be used to analyse the costs and utilisation of care. This extended period used for data analysis was deliberately chosen to include a timeframe during and before the SARS-CoV-2 pandemic. Since it is yet unknown how the pandemic and it subsequent measures affected our population and their usage of care.

Hypothesis: We hypothesise that after one year of working with a proactive approach of integrated care to improve the care for patients with problems on two out of three health domains (chronic somatic, psychic and/or social) and at least 2 acute care activities in the previous 12 months will result in reduction in volume and spending of acute care, improvement in experienced health and in patient experience.

Research questions:
Is proactive integrated care costeffective and result in better patients experience than usual care after 12 months for patients with problems on multiple life domains?

Primary outcomes: Incremental cost-effectiveness from a societal perspective. Information on cost will be based on patient-reported data obtained by questionnaires supplied with data from the GP medical files (*Huisarts informatie system, HIS)* and trough CBS microdata. To assess the effectiveness the EQ-5D-5L will be used for determining quality of life.

Secondary outcomes:
Insight into patients experience of care:
Insights into the experiences of care will be gathered during a focus group and information about self-efficay (PAM-13 and SE+IN itemlist), proactive coping (UPCC), and quality of life (SF-12) will be collected using questionnaires (Hibbard, Mahoney, Stockard, & Tusler, 2005; Bode, & de Ridder, 2008; Rurner-Bowker, & Hoque, 2014). A questionnaire on experience of care has been considered, but no validated and appropriate questionnaires for this population are available. Therefore, for insight and rich information on the experienced care the format of a focus group was chosen.

Process evaluation:
A process evaluation of this study will be done simultaneously, as a process evaluation can provide valuable insight on the practicalities of the intervention.This information is useful for

future implementation of this intervention. Data on recruitment and reach of the population will be gathered during the inclusion of patiens in this study. Integration of care will be collacted by using the Integration Meter, patient satisfaction with care using a modified version of the NPS (Reichheld, 2003; Krol et al, 2015), and the nature of the communication between care professional and patient, will be assessed using a HCCQ questionnaire (Jochems, Duivenvoorden, van der Feltz-Cornelis, & van Dam, 2014; Czajkowska, Wang, Hall, Sewitch, & Körner, 2017) and an observation questionnaire (OPTION5) for shared decision making based on audio records. Furthermore, a questionnaire will be used combining the assessment of the acceptability (Acceptability of Intervention Measure - AIM), appropriateness (Intervention Appropriateness Measure - IAM), feasibility (Feasibility of Intervention Measure – FIM), and perceived and experienced effectiveness of the intervention (Weiner, Lewis, & Stanick, 2017) (see F1).

Through focusgroups with the involved care professionals the following themes of process evaluation will be discussed:
- Fidelity (the extend to which the intervention is executed conform protocol)
- Dose delivered (the extend in which the intervention is offered)
- Dose received (the extend in which the patient received the offered care)
- Context (other factors not related to this protocol that might have an influence on the outcomes)
- Satisfaction (the extend to which the care providers are satisfied with the intervention and procedures)

3. STUDY DESIGN

We will use a stepped-wedge randomised controlled trial (RCT) design (Hemming, Haines, Chilton, Girling ,& Lilford, 2015). This design involves random and sequential crossover of groups from control to intervention until all groups are exposed to the intervention. A stepped wedge cluster RCT is especially useful when the intervention is thought to do more good than harm (i.e.,when there is no equipoise). In that situation, it is unethical to withhold or withdraw the intervention from a proportion of the subjects as would occur in a parallel group or classic cluster RCT. Besides, it may be impossible to implement the intervention in half of all clusters simultaneously because of practical, logistical, or financial reasons, which is also the case in the current study with regard to the practical and logistical reasons. Then, the stepwise treatment implementation
of the stepped wedge design offers a solution. Since all patients included in this study will be offered the intervention, which may contribute to limiting lost to follow-up

The personalized approach, local collaborations with the social domain and organizational differences between general practices will result in nuanced differences in how our intervention will be applied. Besides, training the Positive Health methodology and the enhanced collaboration between domains most likely effects patients not-offered the intervention as well. Randomisation will therefore be done by cluster.

This study will be performed in 20 general practices. Each practice will form one cluster. We aim to include an average of 10 patients per cluster. A GP or POH-GGZ can only participate in one cluster. The terms GP practice and cluster will be used alternatively and exchangeable form this point on, both referring to the given description.

Each participating patient starts with a control period and will cross-over to the intervention period. The control period varies between 2 to 8 months. All patients from a GP practice cross-over at the same moment. Therefore the GP-practices are randomized into one of four groups.

All clusters start to collect control data at the same time (t=0). The 20 clusters will be divided into four groups evenly and each group will be randomly assigned one of four time points at which they will start to implement the proactive integrated care intervention. The first switch will be after 2 months (t=2). Every subsequent 2 months a next group of general practices will switch to the intervention mode until all groups have started the intervention. All groups will continue with the intervention as described in this protocol for a total of 12 months. After the 12 months of intervention, care will be delivered as usual. There is no objection if care providers and patients wish to maintain certain aspects of the intervention. All measurements and timepoints after the switch to the intervention falls under the intervention period. The total duration of this study comprises 22 months. This results in varying control period ranging from 2 to 8 months. The total of intervention and follow-up period vary from 14 to 20 months. This time table is summarized in the following chart.
In order to achieve more accurate answers from patients and in turn more reliable results, a member of the research team will administer the SF-12, and questionnaires on proactive coping (UPCC), and self-efficacy (PAM-13 and SE+IN) during a face to face interview, as these might require extra guidance when filling in. This will be done at three time points for each group (before the start of the intervention, at the end of the intervention, and two months after the intervention has ended).

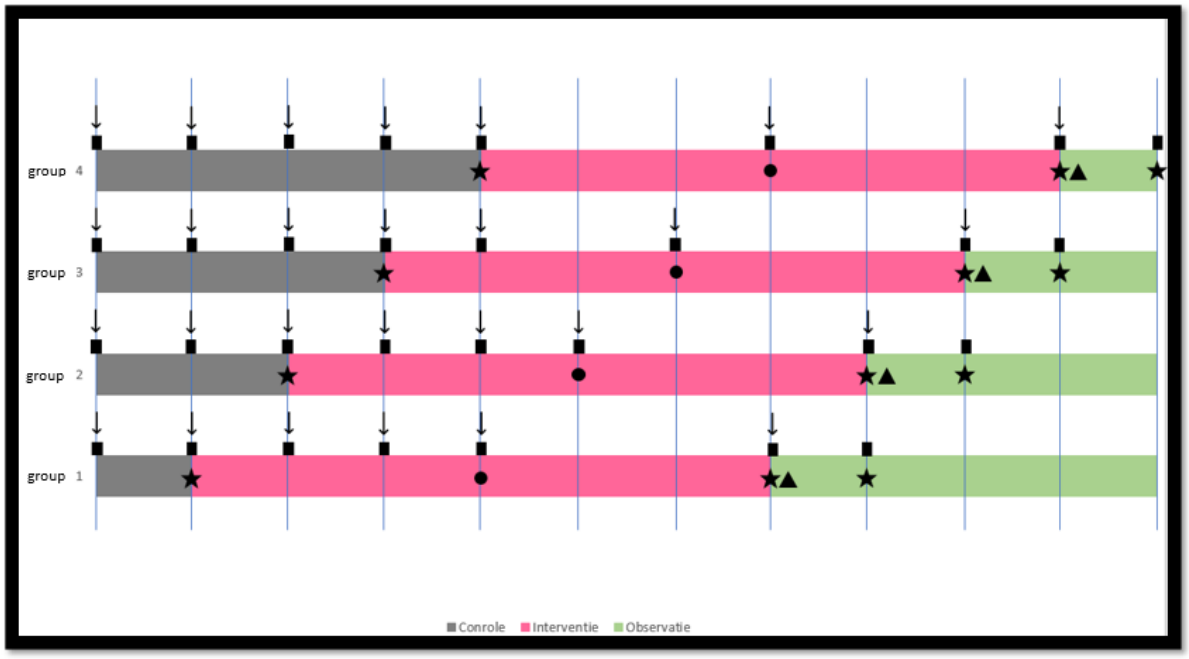

Figure 1. This figure depicts the time schedule of this study. The EQ-5D-5L is administered 7 or 8 times, depending on cluster, and is depicted as a square. The Care and Work questionnaire is depicted with an arrow. The questionnaires PAM, SE+IN, SF-12 and UPCC are administered thrice: at the start and end of intervention and two months after endig the intervention (star). The dot represents the HCCQ and adapted NPS at 6 months after the start of the intervention. Focus groups (triangle) are organised per cluster, after finishing the intervention.

4. STUDY POPULATION

4.1 Population (base)

The population consists of individuals that are registered patients at one of the participating GP practices and have at least two incidents of acute care utilisation during the past year. These individuals also have active problems on two of three domains (somatic, mental and/or social problems) based on diagnosis (coded with the International Classification of Primary Care) or medication (ATC) coding. The patients will be identified by analysing data from GP's electronic medical records from the participating GP practises.

An algorithm and the general practitioner both identify eligible patients. This results in two separate, possible overlapping, lists. The general practitioner makes an assessment of possible suitable patients. This list will be checked for in- and exclusion criteria. A combination of the *Adjusted Clinical care Groups*, a risk stratification tool, and a specifically designed algorithm (Girwar, Fiocco, Sutch, Numans, & Bruijnzeels, 2021; Girwar et al., 2022). -- that predicts high acute care utilisation in patients with problems on multiple life domains-- are used to identify eligible patients from routine care data. The 60 highest scoring patients are screened for the inclusion criteria. After that, the GP checks exclusion criteria. In order to run these tools a pseudonymised extraction of HIS-data will be done, including needed data on age, sex, ICPC-, and ATC-codes and number of recent GP-visits. The data-extraction will be performed in two modes depending on whether the GP practice is affiliated within a regional GP network. In practices that are not affiliated, the extraction will be performed in the GP practice using a standalone computer. In practices that are affiliated data extraction will be performed via a thrusted third party (ELAN or RadboudUMC).

Patients can be grouped in one of three categories: (1)eligible per GP-list and per algorithm, (2) eligible per GP list and (3) eligible per algorithm. We aim to equally include patients from the GP's selection and the algorithm's. The internal order of these lists are randomised. First, patients who appear on the list of both GP and algorithm are approached for study participation. Then, recruitment alternates between the GP-list and the algorithm list to acquire a 50/50 divide. Inclusion stops when there are no more patients to recruit, or when the GP practice reached their maximum number of inclusions.

4.2 Inclusion criteria

In order to be eligible to participate in this study, the following criteria must be met by the general practice and participating patients.

<u>GP practice:</u>

- There is a POH-GGZ available in the GP practice.
- Planning of a multidisciplinairy meeting (MTM or MDO) is a possibility within the GP practice.
- The GP practice is willing to work and share information with different care professionals in the recurring multidisciplinary meetings, to optimise the results of the intervention.
-

Participants:

- The patients are ≥ 18yrs
- The patients are registered within one of the participating GP practices.
- Patients with at least two acute care encounters in the past 12 months. Acute care encounter is defined as an encounter with out-of-hours GP service, emergency care, acute mental health care or unplanned hospital admittance.
- Patients have problems registered in the GP Information system on at least two out of three of the following domains: somatic, mental or social. Somatic problems is having at least one ICPC code on the problem list. Mental problems is having at least one ICPC code from the “P”-chapter on either the problem list, as a reason for encounter, and/or having medication prescribed related to mental health problems. Social problems is having at least one ICPC code from the “Z”-chapter or as reason for encounter, and/or having medication prescribed related to social problems.

4.3 Exclusion criteria

For this study exclusion criteria are set for GP practices and for participating patients.

Participants:

- The patient is terminal.
- The patient is living in a residential home.
- The patient has dementia or a disability that prevents them from communicating effectively.The patient already has experience with the positive health tool.
- The patient is not competent to make decisions concerning their health. This wil be assessed by the patient’s own general practitioner.
- Veto of the GP

Exclusion criteria for GP practices:

- Veto of GP
- The GP or POH-GGZ is already participating in this study in a different cluster.

4.4 Sample size calculation

Sample size calculation for a stepped wedge cluster RCT is performed using the formule of De Hoop et al (Woertman et al., 2013). The unadjusted sample size for a RCT was established on 380, 190 per arm, based on average one year Health Insurance Act spending of a mean of ca €22.494 (€24.585SD)(source Statistics Netherlands), with 80% power, 5% alpha, 2-sided Equality and 25% decrease. The design effect for this study is 0.54. This is based on 1 baseline measure, 4 steps, and ICC of 0.1, 10 patients per cluster and a lost to follow-up of 20%. This leads to a sample side of 204 patients. Rounded off, we willinclude 200 patients divided over 20 clusters.

TREATMENT OF SUBJECTS

4.5 Investigational treatment

The proactive integrated care intervention that will be used consists of five steps:

1. Active invitation of the patient from the practice

2. Consult of 45 minutes with a trained Practice Nurse Mental Health Care based on the Positive Health Methodology. The outcome of this consultation is a spiderweb with an overview of current health status according to positive health methodology.
3. Multidisciplinary Team meeting (MDO) based on the spider web with the domain specific explanation. In this MDO at least the mental health practice nurse, GP, social worker or community nurse are present. The patient is always invited. The outcome of this meeting is: (1) a personalised care plan; (2) appointment of one care coordinator and (3) a structured follow up plan (frequency and duration) of the progression of this patient's problems.
4. Execution of the personalised care plan. The care coordinator has frequent contact with the patient. A minimum of 3 consultations for the first 12 weeks is set, however more frequent consultation can be expected. The proactive nature of this contact is emphasized. A minimum of 4 consultations between patient an care coordinator is set. These minimum amount of consultation is deliberately set to take frequency of consultation as an outcome parameter. The proactive nature will be strongly endorsed, however implementation may differ according to the needs of each individual patient. Given the complex nature of the population the frequency of contact is expected to be higher in the majority.
5. Follow-up of the personalised care plan. During the regular monthly meetings of the health and social care network the follow-up of the patients will be reviewed. Each patient will be discussed at least two times, but more often if necessary. In case the care plan is not followed correctly or it does not have the desired outcome, the patient and the care network will make the needed adjustments to the care plan.

5. METHODS

5.1 Study parameters/endpoints

5.1.1 Main study parameter/endpoint

The main study parameter is incremental cost-effectiveness. To measure this outcome several data sources will be used and linked at the individual level.

Costs and utilisation of care during the trial

At the start of the study (t=0) and at the end (t=22) data on care usage and costs will be collected. Data on medical and acute care utilization for individual patients will be obtained from HIS and CBS microdata, supplemented with patient reported data. A selection of relevant (potential) costs for this population is made via expert opinion. The patient reported data consist only of data not available in HIS, for which questions were selected from the iPCQ, iMCQ and TiC-P questionnaires (See F1). Items with limited effect on cost of care which were not retrievable from HIS or microdata were excluded (See F1).

These data will be translated into cost using standard cost prices from the Dutch guideline for economic evaluations. The datasets containing coded data will be stored on the I-Drive of the LUMC for a period of 15 years. This drive is secured and only accessible by the researchers. Baseline characteristics from patients as well as information collected from the questionnaires will also be securely stored in an online database, named CASTOR.

Cost and utilisation of care previous to trial

The medical data from 3 years prior to the start of the study will be used to analyse the costs and utilisation of care. This extended period used for data analysation was deliberately chosen to include a timeframe during and before the SARS-CoV-2 pandemic. It is yet unknown how the pandemic and it subsequent measures affected our population and their usage of care.

Data on cost of care and care utilization prior to the start of the trial is retrieved from CBS microdata (Statistics Netherlands). Data from several sources are linked at a personal level by Statistics Netherlands in a secured remoted access environment. Data in the CBS microdata environment is secured by using a linkage key. All data in this environment is pseudonymized and data extraction is checked by Statistics Netherlands on traceability. By doing this, the privacy and linkage on individual level is secured. The proposed linkages in this proposal are in accordance with the General Data Protection Regulation (GDPR), as Statistics Netherlands is allowed by law to link data sets under strict disclosure condition (The European Parliament & the Council of the European Union, 2016).

Quality of life

The EQ-5D-L5 will be used to provide the quality of life measures in this study. This questionnaire is used to define health in terms of 5 dimensions: self-care, usual activities, mobility, anxiety/depression and pain/discomfort. It is also possible to define unique health states with this questionnaire, as each domain has five answer levels ranging from no problems to extreme problems (Versteegh et al., 2016). Besides being short and easy to comprehend, the questionnaireisalso validated. In addition, quality of life will also be assessed by using the validated SF-12 (12-items), including 8 dimensions, namely: bodily

pain, vitality (energy and fatigue), general mental health (psychological distress and well-being), general health perceptions, limitations in physical activities because of health problems, limitations in social activities because of physical or emotional problems, limitations in usual role activities because of emotional problems, and limitations in usual role activities because of physical health problems (Turner-Bowker et al., 2014).

The 'cost and utilization and EQ-5D-L5 questionnaires will be filed in at 7 or 8 different timepoints, which will result in 7 or 8 measurements per participant Participants are asked if they prefer a questionnaire on paper per post or one per email (using Castor). After receiving the questionnaire participants have one week to fill out the questionnaire. If there is no respons, patients are called and offered an interview by phone on the questionnaire. The first interview will be done at the start of the study (t=0) Afterwards information for the questionnaires will be gathered 6 or 7 more times, see figure 1 in §3 study design for an overview and timing of questionnaires. In order to achieve more reliable results, a member of the research team will administer the SF-12 and other secondary study parameter questionnaires that might require extra guidance, during a face to face interview at three time points (before the start of the intervention, at the end of the intervention, and three months after the intervention has ended).

5.1.2 Secondary study parameters: Patient experience of care

The secondary study parameter is insight into the patient experience of care. To assess their experience focus groups will be organized. A questionnaire on experience of care has been considered, but no appropriate and validated quesntiones for this population are avilible. Therefore, the format of a focus group was chosen. Focus groups will be organised at 4 different timepoint (t=14, t=16, t=18 and t=20) and each focus group will consist of 6 to 12 patients. For each timepoint several focus groups will be organised. The exact size of the group and number of organised groups, will dependent on the number of patients that choose to participate. Four main topics will be discussed, namely: care before the new approach, the new approach, the collaboration between the professionals and the experienced effects of the new approach (see F1).

The presence of proactive coping skills will be quantitively measured with the *Utrechtse Proactieve Coping Competentie lijst* (UPCC). This is a 21-item questionnaire that measures self-rated proactive coping competences. The questionnaire has been validated in different adult dutch patient groups. (Bode et al., 2008) (see F1).

Self-efficacy will be measured using two different instruments. The first is the validated Patient activation Measure (PAM-13). This is a 13-item instrument that measures self-reported knowledge, skills and confidence in managing one's health. With this instrument patients can be categorised in four levels of activation (Hibbard et al., 2005). The second questionnaire is the Self-efficacy and Intention itemlist (SE+IN Itemlist). This measures (action and maintenance) self-management self-efficacy, the intention to perform certain self-management behaviors and the presence of certain self-management behaviors. This itemlist was specifically created for this study, as there aren't any questionnaires that are geared towards understanding behavior change in this complex and heterogeneous group of patients. The itemlist consists of 22-items and was created using the Health Action Process

Approach (HAPA) model (to determine to constructs that need to be measured) (Schwarzer, 2016), a combination of literature and conversations with care professionals (to determine relevant self-management behaviors that these patient seem to lack) and other questionnaires with elements of self-management self-efficacy (Ludman et al., 2013; Bodenheimer, Lorig, Holman, & Grumbach, 2002; Lorig, Halsted, & Holman, 2003).

5.1.3 Secondary study parameter: Process evaluation

A process evaluation of this study will be done simultaneously, as a process evaluation can provide valuable insight on the practicalities of the intervention.This information is useful for future implementation of this intervention. Data on recruitment and reach of the population will be gathered during the inclusion of patiens in this study, and on shared decision making will during the intake and MDO.

All involved care professionals in this study will be invited to participate in a focusgroup (see E1 and F1). These focusgroups will be held at four different timepoints (t=14, t=16, t=18 and t=20).Through focusgroups with the involved care professionals the following themes of process evaluation will be discussed:
- Fidelity (the extend to which the intervention is executed conform protocol)
- Dose delivered (the extend in which the intervention is offered)
- Dose received (the extend in which the patient received the offered care)
- Context (other factors not related to this protocol that might have an influence on the outcomes)
- Satisfaction (the extend to which the care providers are satisfied with the intervention and procedures)

During this study information of each GP practice will be gathered on the level of integration of care with the social and mental domain. This will be done using an adapted *integratiemeter* (Broesveld et al., 2016*)*. The level of integration with the social, mental and somatic domain will be determinant based on an (minor) adapted version of the *integratiemeter* from Broesveld et al. (2016*)*. The wording of this questionnaire has been very slightly altered to fit our population (see F1).

Additionally, information about acceptability, feasibility, appropriateness ,and perceived and experienced effectiveness of the intervention will be gathered from care professionals from participating as well as non-participating practices. This will be done before the intervention starts and right after the intervention for each group of GP's. Acceptability, appropriateness, and feasibility will be measured using the The Acceptability of Intervention Measure (AIM), Intervention Appropriateness Measure (IAM), and Feasibility of Intervention Measure (FIM) four-item measures of implementation outcomes that are often considered "leading indicators" of implementation success (Weiner et al., 2017; Proctor et al., 2011).
The FIM, AIM, and IAM have been translated and backtranslated for this study.
Perceived and experienced effectiveness of the intervention will be measured with one item (see F1).

To assess the patients' experiences with the intervention and their care coordinator an adjusted version of the Net Promotor Score (2 item questionnaire) will be administered (Reichheld, 2003). Furthermore, the patients' perceptions of the degree to which their

healthcare provider is autonomy supportive will be assessed using the 6 item Health Care Climate Questionnaire (Jochems et al., 2014; Czaikowska et al., 2017) (see F1). Level of shared decision making will be based on audio recored which will be scored by two independed observers using the validated OPTION5 questionnaire. If a participant is not comfortable with these recordings, the recorings may be skipped without further consequence for study participation.

5.2 Randomisation, blinding and treatment allocation

Randomisation happens twice in this study. First, clusters are randomised evenly into one of four group (see chapter 3), which corresponds with duration of control period. Every 2 months a new group will start with the intervention, until all groups have received the intervention. The first group will start 2 months after the start of the study. A specifically designed randomisation tool using *Microsoft Excel* is used. We randomise clusters *en bloc*.

The second randomisation is to determine the order in which selected patients are approached. While identifying eligible patients, we end with a selection of patients who fall under 1 of 3 categories: (1)eligible per GP-list and per algorithm, (2) eligible per GP list and (3) eligible per algorithm. We aim to equally include patients from the GP's selection and the algorithm's. The internal order of these lists are randomized using a specifically designed randomisation tool using *Microsoft Excel.* First, those who appear on the list of both GP and algorithm are approached for study participation. Then, recruitment alternates between the GP-list and the algorithm list to acquire a 50/50 divide.

5.3 Study procedures

The procedure with patients will go as following:

- An algorithm and the general practitioner both identify eligible patients. This results in two separate, possible overlapping, lists.
- Lists of patients are screened for inclusion criteria.
- GP checks the list of patients, meeting inclusion criteria, for exclusion criteria. Patients can be grouped in one of three categories: (1)eligible per GP-list and per algorithm, (2) eligible per GP list and (3) eligible per algorithm.
- Internal order of these lists are randomised. First, patients who appear on the list of both GP and algorithm are approached for study participation. Then, recruitment alternates between the GP-list and the algorithm list to acquire a 50/50 divide.
- GP practice approached patient and ask permission/ consent for sharing the contact information with the researchers so they give them written and oral information about the study
- Study information is sent per mail.
- Phone call from researcher to answer questions and acquire informed consent.
- Start control period.
- Baseline questionnaire:The 'cost and care utilization' and EQ-5D-5L questionnaires will be sent out to participants to fill in at home.
- Start of intervention period (including intake and MDO's).
- Questionnaires: Repetition of the 'cost and care utilization' and EQ-5D-5L questionnaires according to schedule as depicted in §3 study design (7 or 8 measurements per patient). Furthermore, four questionnaires (SF-12, UPCC, SE+IN

itemlist, and PAM-13) will be repeated three times (before the start of the intervention, at the end of the intervention and 2 months after the intervention has ended). The remaining two questionnaires (HCCQ and adapted NPS) will be administered once (at the end of the 6 month mark of the intervention).
- All participants are invited to join a focus group 12 months after starting the intervention. Patients will first be informed about the focus group though the patient information form. When a group is near the end of the 12-month intervention period, all patients in this group will be approached by the researchers to confirm participation. The goal of the focus group is to obtain insight about the patients' experience with the new approach. Participation is not obligatory.
- As part of process evaluation all involved professionals (GP, POH-GGZ, social workers or other) will be invited to join a focusgroup on their experience with this proactive, integrated care approach and the audio records of the intake and MDO will be scored on the level of shared decision making by two independent observers.
- Collection of data on: medical and acute care 20tilization, medical costs. (beginning and end of study).

<u>The following time investment will be asked from each patient:</u>
- 10 minutes: invitation of the patient by the GP practice and sharing of information about the study with the patient. Permission to send information about the study, will be asked.
- 10 minutes: follow-up with patient about participation in the study. If the patient agrees to participate, an informed consent form will be send out.
- 170 minutes for the questionnaires: this consists of 4 timepoints of EQ-5D-5L and Care and work questionnaire (4x10min = 40min), two timepoints of psychological questionnaires(SF-12, PAM-13, SE+IN) with EQ-5D-5L and care and work (2x40min = 80min), once EQ-5D-5L with Care and Work and evaluative questionnaire (modified NPS, HCCQ) (1x 10min = 10 min) and once psychological questionnaires combined with EQ-5D-5L (1x40min = 40min).
- 45 minutes: first consultation based on the Positive Health Methodology.
- 60 minutes (2x30=60min): all patients are invited and stimulated to join the multidisciplinary meetings. Patients will be discussed at least at least 2 times during the 12 month period. Additional ad hoc meeting is possible if necessary.
- 10-30 minutes (minimum of 4 times, thus combined total of 40-120 minutes): for the extra meetings that patients are going to have with their care coordinator, according to their personal care plan.
- 60 minutes: focus group focused on the patients their experience with the intervention. Each focus group will be 60 minutes and each patient will only be invited once. This will be done after they end the intervention.

	First three month period	**Total 12 months period**	**Total in study period**
POH-GGZ intake	1x45 min	1x 45 min	1x45 minutes
Multidisciplinary meeting	1x30 min	Minimum 2x 30	Minimum 2x 30 minutes
Care coordinator	Minimum of 3x, more frequent contact is	Minimum of 4x in 12 months, however more	Minimum of 4x in 12 months

	possible. Proactive nature of this contact is highlighted.	frequent contact is expected. Proactive nature of contact is highlighted.	
Questionnaires			170 minutes
Focusgroup			1x60 minutes

During the 22 month study period, the following questionnaires will be sent out per mail, but in case of no respons done by interview (see F1):

- EQ-5D-L5 (Versteegh et al., 2016). This will be filled in at a maximum of 8 different timepoints.
- Selected questions from iMCQ, iPCQ and TiC-P. This will also be filled in at a maximum of 7 different timepoints.
- HCCQ and modified NPS (Jochems et al., 2014; Czajkowska et al., 2017; Reichheld, 2003; Krol et al, 2015). This will be filled in at 1 timepoint.

The remaining questionnaires will be filled in during a face to face interview with the researcher or trained intern or research assistant (before the start of the intervention, at the end of the intervention and 2 months after the intervention has ended).

5.4 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons.

5.4.1 Specific criteria for withdrawal

The participating patients have the option to revert back to care as usual, at any given time. The reason for withdrawal will be asked, however patients are not obliged to answer if they do not wish to share the reason.

5.5 Replacement of individual subjects after withdrawal

Patients that chose to withdrawal from the study, will not be replaced.

5.6 Follow-up of subjects withdrawn from treatment

When a participant choses to retract from of the study, data collection for that participant will stop. The data collected until the moment of withdrawal will be used when analysing the data, unless the patient specifically requests otherwise.

5.7 Premature termination of the study

This is not applicable to this study. There are no health risks associated with study.

6. STATISTICAL ANALYSIS

Before analysis, all data will be cleaned improving data quality.

Quantitative data:
We will conduct intention-to-treat and per protocol analysis. We will use multilevel generalized linear models with the patient as the first level to correct for the repeated measures. The GP-practice (or cluster) will be the second level, and the group in which the GP practice is randomized will be the third level. We will adjust for level of integration, neighbourhood,time from start of study (continuous; with an interaction between cluster and time so that each cluster had its own underlying time trend), and total time on the randomised intervention, with time before intervention given as zero (continuous). Based on ICPC-codes used to select eligible patients, we will explore if subgroups can be identified in mainly (chronic) somatic, mainly mental or mainly social problems. Furthermore, analyses/ results will be stratification for sex. The analysis of the implementation will be descriptive.

Cost-effectiveness analysis/budet impact analysis:
The economic evaluation will consist of a trial-based cost-utility analysis (cost per QALY) with a time horizon of one year and a cost-utility analysis with a lifetime horizon (cost per QALY). Both analyses will be performed from a societal perspective. Next to this a Budget Impact Analysis will be performed according to the ISPOR Task Force principles.

Qualitative data:
Qualitative data will be collected through interviews or focus groups with care providers and patients and audiorecording. The interviews and focus groups will be conducted using a topic list based on experience of the pilot (protocol number **NL8223-10216**) and literature, to determine their satisfaction with the new approach.
The collected qualitative data will be analysed using both an inductive and deductive approach. This will be done by first transcribing the data and doing a thematic content analysis. After this, the data will be put into an initial coding book and futher analysed until a final coding book is formed. The deductive analysis will be done using the positive health methodology. We will analyze whether positive health topics and techniques are being discussed and applied, as recommended by the methodology.
The audiotapes will be scored by two independent obesrvers using the validated OPTION5 questionnaire.

6.1 AEs, SAEs and SUSARs

6.1.1 Adverse events (AEs)

Due to the high amount of expected (serious) adverse events caused by treatment of the patients as part of standard care, only study related (S)AE's will be reported immediately. This means all (S)AE's related to participation in this study protocol, meaning from filling in the questionnaires, will be reported. All other (S)AE's will not be reported, as no patient benefit is expected from this.

The sponsor will report the intervention related (S)AEs through the web portal *ToetsingOnline* to the accredited METC that approved the protocol, within 7 days of first knowledge for SAEs that result in death or are life threatening followed by a period of maximum of 8 days to complete the initial preliminary report. All other SAEs will be reported within a period of maximum 15 days after the sponsor has first knowledge of the serious adverse events.

7. ETHICAL CONSIDERATIONS

7.1 Regulation statement

This study will be conducted according to the principles of the Declaration of Helsinki (version 7, oktober 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO) and other guidelines, regulations and Acts.

This study does not invade the physical integrity of participants, but the extra care appointments and the frequent and personal questionnaires can be seen as an additional burden to the participants. Besides, this study investigates the effects of a new intervention. Therefore, we consider this study to be subject of the WMO.

7.2 Recruitment and consent

GP practices

The GP-practices affiliated with RadboudUMC, *SGZ* or affiliated with *Hadoks* will be approached through internal communication. This study is submitted as a single center research in agreement with the METC-LDD on 14-11-2021. The department of Public Health and Primary Care takes responsibility for gathering and storing *onderzoeksverklaring* from each participating GP practice.

Patients

Identification and selection of eligible patients is done as described in chapter 4.1. Patients can be grouped in one of three categories: (1)eligible per GP-list and per algorithm, (2) eligible per GP list and (3) eligible per algorithm. We aim to equally include patients from the GP's selection and the algorithm's. The internal order of these lists are randomised. First, patients who appear on the list of both GP and algorithm are approached for study participation. Then, recruitment alternates between the GP-list and the algorithm list to acquire a 50/50 divide. Invitations stops when there are no more patients to recruit, or when the GP practice reached their maximum number of inclusions.
The GP-practices reaches out to the patient using a script (E3). If patients consent, an information package sent including informed consent forms and a link to an information video. A week later the researchers call to answer questions and to acquire informed consent. In case of consent, patients sign the Patient Informed Consent forms twice and sent both to the researcher. After researcher signs, one copy is stored and one copy is sent back to the patient.

7.3 Benefits and risks assessment, group relatedness

Participation in this study is expected to be low risk for the patients. However, both risks and benefits are associated with participation.

Benefits include: Improved knowledge and insight. Participation might lead patients to have a better understanding of the factors that contribute to their overall well-being. This can be achieved with analysing the six life domains of the positive health conversation tool. This insight might result in appropriate interventions that meet the needs of these patients.

A potential risk that should be taken into account is temporary elevated stress. The patients participating in this study experience a combination of different problems which can make life

more complex and challenging. The heightened emphasis, especially in the beginning, on the factors that contribute to their health and social problems could result in higher stress levels in some participants.

7.4 Incentives (if applicable)

Participating GP-Practices will receive two compensations:
1. An hourly rate for time that the GP and POH-GGZ spend in mutlidisciplinairy meetings. A total amount of 1200 per GP practice is expected, but due to a pending application for financing the exact amount can not yet be stated
2. A small one time fee of 150 euro.

Each participant will receive a 15 euro VVV gift card for participating in the study. They will also be compensated for additional transportation costs from their home to the GP practice.

7.5 Compensation for injury

We ask the METC for dispensation of the insurance obligation, as participation in this study is without extra health risk.

8. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

8.1 Handling and storage of data and documents

Baseline characteristics from patients as well as information collected from the questionnaires will be securely stored in an online database, named CASTOR. Data on care utilisation according to the health Care Act (ZVW) from period before the start of the study, and data on care utilisation according to Social care Act (WMO) is available in the secured data environment from Statistics Netherlands (CBS), a Trusted Third Party (TTP). The dataset on medical care utilization and costs will be linked to Statistics Netherlands within their secured data environment by using a linkage key. By doing this the privacy and linkage on individual level are secured. The proposed linkages in this proposal are in accordance with the General Data Protection Regulation (GDPR) as Statistics Netherlands is allowed by law to link data sets under strict disclosure condition (The European Parliament & the Council of the European Union, 2016). The researchers only have access to patient data that has been securely coded (pseudonymised) by CBS. Datasets that include microdata from CBS will be analysed is a secured CBS environment.

Quantitative data retrieved from HIS will be coded and stored on the I-Drive of the LUMC for a period of 15 years. This drive is secured and only accessible by the researchers.

Audiorecordings are transcribed. Transcirpts will be stored on the secured I-drive of the LUMC for a period of 15 years. After transcription, audiorecordings will be deleted.

8.2 Monitoring and Quality Assurance

Monitoring of the study will be executed by (internal) monitors of the LUMC according to the monitor plan .The study will be conducted as described in this protocol. The principal investigators will be contacted when unforeseen events change the course of this study.

8.3 Amendments

All substantial amendments will be notified to the METC and to the competent authority. Non-substantial amendments will not be notified to the accredited METC and the competent authority, but will be recorded and filed by the sponsor.

8.4 Annual progress report

The sponsor/investigator will submit a summary of the progress of the trial to the accredited METC 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, serious adverse events/ serious adverse reactions, other problems, and amendments.

8.5 Temporary halt and (prematurely) end of study report

The investigator/sponsor will notify the accredited METC of the end of the study within a period of 8 weeks. The end of this study is defined as the last group of patients finish their 12 month intervention period. The sponsor will notify the METC immediately of a temporary halt of the study, including the reason of such an action.

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 accredited METC and the Competent Authority.

8.6 Public disclosure and publication policy

An article containing the research outcomes will published in a peer reviewed journal.

9. REFERENCES

1. Autoriteit persoonsgegevens: https://autoriteitpersoonsgegevens.nl/sites/default/files/atoms/files/gdpr.pdf
2. Berwick, D. M., Nolan, T. W., Whittington, J. (2008). The triple aim: care, health and cost. Health affaires,27, (3).
3. Bisognano M, Kenney C. Pursuing the Triple Aim: Seven Innovators Show the Way to Better Care, Better Health, and Lower Costs. San Francisco: Jossey-Bass Publishers; 2012.
4. Bode C, Thoolen B, de Ridder D. Measuring proactive coping. Psychometric characteristics of the Utrecht Proactive Coping Competence scale (UPCC). Psychologie & Gezondheid. 2008; 36(2); 81–91. https://doi.org/10.1007/BF03077476
5. Bodenheimer T, Lorig K, Holman H, Grumbach K. Patient Self-management of Chronic Disease in Primary Care. *JAMA.* 2002;288(19):2469–2475. doi:10.1001/jama.288.19.2469
6. Boesveld, I.C., Annegarn, A.M.A., IJsseldijk, J.M., VeldHuyzen, D.C., Winkel, L., Annot, F., Bruijnzeels, M. D., Franx, A., & Wiegers, T. A. Geïntegreerde geboortezorg Resultaten van de VSV-Integratiemeter, Nederlands Tijdschrift voor Obstetrie & Gynaecologie vol. 129, december 2016
7. CBS: https://www.cbs.nl/en-gb/corporate/2018/21/cbs-is-ready-for-the-eu-gdpr
8. Gawande A. The Hot Spotters: Can we lower medical costs by giving the neediest patients better care? New York Times, Medical Report. January 24, 2011.
9. Girwar, S.M., Fiocco, M., Sutch, S. P., Numans, M. E., Bruijnzeels, M. A. Assessment of the Adjusted Clinical Groups system in Dutch primary care using electronic health records: a retrospective cross-sectional study, BMC Health Services Research volume 21, Article number: 217 (2021)
10. Girwar et al April 2022*; Identifying 'Hotspotters' Using the Adjusted Clinical Groups Risk Stratification Tool* , accepted in American Journal of Managed Care
11. Hemming K, Haines TP, Chilton PJ, Girling AJ, Lilford RJ. The stepped wedge cluster randomised trial: rationale, design analysis, and reporting. BMJ 2015; 350(1):h391.
12. Hibbard, J. H., Mahoney, E. R., Stockard, J., & Tusler, M. (2005). Development and testing of a short form of the patient activation measure. Health services research, 40(6 Pt 1), 1918–1930. https://doi.org/10.1111/j.1475-6773.2005.00438.x
13. Huber, M., Knottnerus, J.A., Green, L., Horst, H. van der, Jadad, A.J., Kromhout, D., et al. How should we define health? BMJ.2011: 343(4163);235–7.
14. Iovan S, Lantz PM, Shapiro S. "Pay for Success" Projects: Financing Interventions That Address Social Determinants of Health in 20 Countries. AJP. 2018 Nov: 108(11); 1473-1477.
15. Jochems EC, Mulder CL, Duivenvoorden HJ, van der Feltz-Cornelis CM, van Dam A. Measures of Motivation for Psychiatric Treatment Based on Self-Determination Theory: Psychometric Properties in Dutch Psychiatric Outpatients. Assessment. 2014;21(4):494-510. doi:10.1177/1073191113517928
16. Lantz PM. "Super Utilizers" Interventions: What they reveal about evaluation research, wishful thinking, and health equity. Milbank Quarterly 2020; DOI: 10.1111/1468-0009, 12499
17. Lee NS, Whitman N, Vakharia N, Taksler GB, Rothberg MB. High-Cost Patients: Hot-Spotters Don't Explain the Half of It. J Gen Intern Med. 2017 Jan;32(1):28-34.
18. Lorig, K.R., Halsted, P.H., & Holman, R. Self-management education: History, definition, outcomes, and mechanisms, *Annals of Behavioral Medicine*, Volume 26, Issue 1, August 2003, Pages 1–7, https://doi.org/10.1207/S15324796ABM2601_01

19. Ludman, E. J., Peterson, D., Katon, W. J., Lin, E. H., Von Korff, M., Ciechanowski, P., Young, B., & Gensichen, J. (2013). Improving confidence for self care in patients with depression and chronic illnesses. Behavioral medicine (Washington, D.C.), 39(1), 1–6. https://doi.org/10.1080/08964289.2012.708682
20. Pim P Valentijn [1], Sanneke M Schepman, Wilfrid Opheij, Marc A Bruijnzeels Understanding integrated care: a comprehensive conceptual framework based on the integrative functions of primary care Int J Integr Care . 2013 Mar 22;13:e010. doi: 10.5334/ijic.886
21. Proctor E, Silmere H, Raghavan R, Hovmand P, Aarons G, Bunger A, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. Admin Pol Ment Health. 2011;38(2):65–76. doi:10.1007/s10488-010-0319-7.
22. Reichheld FF. The one number you need to grow. Harvard Business Review, 2003; 81: 46–54.
23. Samantha Iovan[1] , Paula M. Lantz[1], Katie Allan[1], and Mahshid Abir, Interventions to Decrease Use in Prehospital and Emergency Care Settings Among Super-Utilizers in the United States: A Systematic Review, Medical Care Research and Review, 2020, Vol. 77(2) 99–111
24. Schwarzer, R. (2016). Health action process approach (HAPA) as a theoretical framework to understand behavior change. *Actualidades en Psicología, 30*(121), 119–130. https://doi.org/10.15517/ap.v30i121.23458
25. Turner-Bowker D., Hogue S.J. (2014) Short Form 12 Health Survey (SF-12). In: Michalos A.C. (eds) *Encyclopedia of Quality of Life and Well-Being Research. Springer*, Dordrecht.
26. Versteegh MM,Vermeulen KM, Evers SMAA, de Wit GA, Prenger R, Stolk EA. Dutch Tariff for the Five-Level Version of EQ-5D. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2016;19:343-52.
27. Wammes JJG, Tanke M, Jonkers W, Westert GP, Van der Wees P, Jeurissen PP. Characteristics and healthcare utilization patterns of high-cost beneficiaries in the Netherlands: a cross-sectional claims database study. BMJ Open. 2017 Nov 12;7(11):e017775.
28. Weiner, B.J., Lewis, C.C., Stanick, C. *et al.* Psychometric assessment of three newly developed implementation outcome measures. *Implementation Sci* **12,** 108 (2017). https://doi.org/10.1186/s13012-017-0635-3
29. Woertman, de Hoop, Moerbeek, Zuidema, Gerritsen and Teerenstra, Stepped wedge designs could reduce the required sample size in cluster randomized trials Journal of Clinical Epidemiology 66 (2013) 752e758
30. Krol, M. W., de Boer, D., Delnoij, D. M., & Rademakers, J. J. (2015). The Net Promoter Score--an asset to patient experience surveys?. *Health expectations : an international journal of public participation in health care and health policy*, *18*(6), 3099−3109. https://doi.org/10.1111/hex.12297