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Study protocol for a randomized controlled trial

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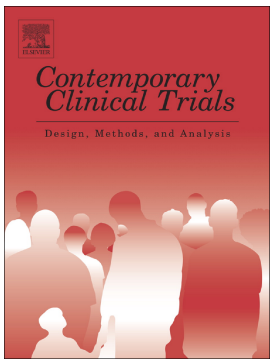

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Proactive health support (PaHS) - telephone-based self-management support for persons at risk of hospital admission: study protocol for a randomized controlled trial

Kirstine Skov Benthien, MSc, PhD[1], kirstine.skov.benthien@regionh.dk
Knud Rasmussen, MD, DMSc[2], kra@regionsjaelland.dk
Camilla Palmhøj Nielsen, MSc, PhD[3], camilla.palmhoj@rm.dk
Louise Hjarnaa, MSc, MPH[1], louise.hjarnaa@regionh.dk
Maja Kjær Rasmussen, MSc[4], maja.kjaer.rasmussen@rsyd.dk
Kristian Kidholm, MSc, PhD[4], kristian.kidholm@rsyd.dk
Berit Kjærside Nielsen, MSc, PhD[3], beritnie@rm.dk
Nina Konstantin Nissen, MSc, PhD[3], niniss@rm.dk
Mia Fredens, MSc[3], mia.fredens@rm.dk
Susanne Winther, MSc, PhD[5], susanne.winther@rn.dk
Mette Grønkjær, MSc, PhD[5,6], mette.groenkjaer@rn.dk
Ulla Toft, MSc, PhD[1], ulla.toft@regionh.dk

1. Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark
2. Production, Research and Innovation, Region Zealand, Sorø, Denmark
3. DEFACTUM - Social & Health Services and Labour Market, Aarhus, Denmark
4. Centre for Innovative Medical Technology, Odense University Hospital, Denmark
5. Clinical Nursing Research Unit, Aalborg University Hospital, Denmark
6. Department of Clinical Medicine, Aalborg University, Denmark

Contact author:
Kirstine Skov Benthien, PhD.
Center for Clinical Research and Prevention
Bispebjerg and Frederiksberg Hospital
Nordre Fasanvej 57
2000 Frederiksberg
Denmark
Phone: +45 38 16 30 63
E-mail: kirstine.skov.benthien@regionh.dk

Abstract

Background

A small proportion of patients account for most of the healthcare costs. Previous studies of supportive interventions have several methodological limitations and results are mixed. This article describes the protocol for Proactive Health Support: a national randomized controlled trial of telephone-based self-management support (ClinicalTrials.gov, NCT03628469). The main aim of the intervention is to reduce hospital admissions and improve quality of life at six months.

Methods

A sample size of 4400 is needed and individuals with the highest risk of hospital admission in Denmark are invited by electronic communication and telephone to participate in a 1:1 randomized controlled trial. The intervention group receives one face-to-face start-up session followed by telephone sessions about individual goals regarding participants' knowledge, coping and need of healthcare. Quality of life was assessed with the mental health composite score of the SF-36v2 questionnaire. Primary analyses are done using the intention-to-treat principle.

Discussion

The trial has been approved by The Regional Committee on Health Research Ethics (SJ-677). Intervention nurses do not assume clinical responsibility for the participants and the intervention is an addition to the general healthcare services. The intervention is complex due to challenging skills and behaviors required by nurses, individual tailoring of the intervention, and interacting intervention components. The study therefore includes process evaluation. The research program comprises: 1. Development initiation, 2. Intervention effect, 3. Cost-effectiveness, 4.

Organizational implementation, and 5. Participants' experiences. Inclusion to the trial began April 9th, 2018, was completed July 1st, 2019 and follow-up will be completed February 1st, 2020.

Keywords

Hospital admissions, High-cost, Health-related quality of life, Randomized controlled trial

List of abbreviations

PaHS: Proactive health support

RCT: Randomized controlled trial

HRQoL: Health-related quality of life

SF36: Short Form 36

heiQ: Health education impact questionnaire

QALY: Quality-adjusted life years

ICER: Incremental cost-effectiveness ratio

Background

A small proportion of mostly multimorbid and older patients stand out in healthcare systems around the Western world by being major hospital users.(1, 2). Multimorbidity may create an amplifying effect on the burden experienced by these patients as demonstrated in models of allostatic load.(3, 4) A substantial proportion of healthcare expenses is concentrated in this small segment of patients. For example, the top 5% of high-cost users in Ontario account for nearly 70% of healthcare costs(5), the top 5% high-cost users in the US Veterans system account for 47% of the total costs(6), and the 10% high-cost Medicare beneficiaries account for 74% of Medicare spending.(7) A high number of preventable hospital admissions in these burdened patients may imply inadequate care and treatment. The definition of preventable hospital admissions varies and, accordingly, the estimated proportion varies from 5-79%.(8) In Denmark, it is estimated that 66 hospital admissions per 1000 elderly can be prevented each year.(9)

Several intervention studies have targeted high-risk and high-cost populations to potentially prevent hospital admissions and to improve patient-reported outcomes.(10-16) Supportive interventions range from case management with coordination of healthcare services to coaching and self-management support aimed at changing patients' behavior within the healthcare system. The results of supportive intervention studies are mixed with small positive effects on self-reported health status and patient satisfaction but no convincing effect on reducing the use of healthcare services.(10-16) The mixed results may be ascribed to variable content and potency of interventions or to methodological issues described in the following.

Among several studies without positive effects, four trials focusing on telephone-based patient support have shown promising results. In a randomized quality-improvement trial of usual versus

enhanced telephone care-management (n=174,120) in the USA (2010), Wennberg et al. demonstrated that the enhanced support led to a 3.6% reduction in medical and pharmacy costs.(14) In Sweden, two trials (2013 and 2015) of telephone-based case-management demonstrated a reduction in visits to emergency departments and hospital admissions (n=286, n=12,181).(11, 12) In 2016, Härter et al. presented a pragmatic Randomized Controlled Trial (RCT) of telephone coaching in Germany (n=10,815) that demonstrated a reduced risk of death for multimorbid and heart failure patients, but also an overall increased number of hospital admissions in patients with chronic diseases.(15)

These four trials depart from international standards for design of RCTs (17) by waving informed consent(14) or seeking informed consent after randomization.(11, 12, 15) This raises the question if the favorable outcomes of these trials are evoked by unmeasured confounding differences between intervention and control groups; particularly when intervention decliners are allocated to the control group.(12) Only one of these studies included patient-reported outcomes (12), and the study design could not secure baseline assessment before randomization. In summary, the need for interventions that identify and support individuals at high risk of hospital admissions is strong, as is the need for robust RCTs to assess the efficacy of these interventions. Consequently, The Danish Ministry of Finance prioritized funding to Proactive Health Support (PaHS). This article describes the protocol for PaHS - a randomized controlled trial of telephone-based self-management support (ClinicalTrials.gov: NCT03628469). The primary aim of the intervention is to reduce hospital admissions and improve health-related quality of life (HRQoL) in individuals with a high risk of hospital admission.

Methods and analysis

Design

This study is an open label RCT with a 1:1 allocation ratio of PaHS versus usual care. The trial was preceded by a development period beginning in the Region Zealand - one of the five Danish regions to develop the PaHS intervention and the algorithm for identifying participants at risk of hospital admission. The development period progressed to the other four regions in Denmark (the Capital, Northern Denmark, Central Denmark and Southern Denmark) and lasted eight months to further develop and ensure regional implementation of the intervention. A national program management was established, and the intervention was developed in cooperation with a consultant agency. The development phase has been described in detail elsewhere.(18) The development phase ended when inclusion to the RCT began on April 9th, 2018 in four regions and April 30th, 2018 in the Region Zealand. Inclusion was completed between November 1st, 2018 and July 1st, 2019. Follow-up will be completed February 1st, 2020. The protocol is dated March 7th, 2018.

Setting and usual care

The Danish healthcare system has tax-financed universal coverage for the 5.8M inhabitants. The hospitals are reimbursed for their activities through Diagnosis-Related Groups(19) and general practitioners act as gatekeepers to hospital-based services. The Danish healthcare system is divided in five geographical regions adhering to the same national clinical standards. The five regions differ in organization, population size (0.6-1.8 M) and life expectancy (80.1-81.5 years).(20)

Participant selection – The PaHS prediction model

The PaHS prediction model selected individuals from the entire Danish population between 18 and 120 years of age, who met inclusion criteria in one of the three groups described under primary screening in table 1. The PaHS prediction model involved three steps that were performed each time a new list of potential participants was generated: 1. Selection of individuals meeting the inclusion criteria defined in table 1, 2. Identification of hospital contact patterns 12-24 months before the prediction period through generalized linear models, 3. Application of the regression coefficients from step two on the hospital contact pattern 12-0 months before the predicted period to calculate the risk of acute hospital admission in the following three months. The PaHS prediction model drew upon information from the Danish National Patient Register about age, gender, diagnoses, type of contact (inpatient/outpatient, acute/planned), length of contact, medical specialty, municipality, cost and procedures performed. The PaHS prediction model was applied in each region with minor variations due to data structure and access to statistics software. The Central Denmark Region managed data with SQL and performed the statistical analyses with Python, applying a random forest algorithm. The other regions performed the analyses with SAS 9.3 or 9.4. A full description of the PaHS prediction model will be presented in another article investigating receiver operating curves, sensitivity, specificity, positive and negative predictive value.

Table 1. Inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
Primary screening - PaHS Prediction model	• Persons with a hospital contact within the last year caused by ≥ 1 of the following diagnoses: heart diseases (DI110, DI130, DI132, DI50), connective tissue diseases (DD86, DM05, DM06, DM08, DM09, DM30, DM31, DM32, DM33, DM34, DM35, DM36), pulmonary diseases (DJ40, DJ41, DJ42, DJ43, DJ44, DJ45, DJ46, DJ47, DJ60, DJ61, , DJ62, DJ63, DJ64, DJ65, DJ66, DJ67, DJ684, DJ701, DJ703, DJ841, DJ842, DJ843, DJ848, DJ849, DJ920, DJ961, DJ982, DJ983) or diabetes (DE10, DE11, DE14) and ≥ one unplanned hospital contact* within 12 months Or • Persons with ≥ three unplanned hospital contacts* in the last six months Or • Persons ≥ 65 years with a preventable hospital admission (predefined diagnoses: dehydration, constipation, lower respiratory tract infections, urinary tract infections, gastroenteritis, fractures, nutrition deficiency anaemia, social causes and pressure ulcers) or a readmission (within 30 days)	• Selected psychiatric diagnoses: substance abuse disorder (DF1), schizophrenia (DF2) or dementia (DF00, DF01, DF02, DF03, DF051) • Metastatic cancer (DC77, DC78, DC79, DC80) • Assisted living facility
Secondary individual screening performed by PaHS nurses		• Documented terminal illness or life expectancy < one year • Assessment of dementia • Major surgery planned within 6 months • Hearing impairment • Not speaking Danish • Cognitive impairment • Substance abuse that impairs adherence • No telephone • Receiving similar trial intervention • Other (E.g. Intervention not suitable or participant unable to come to start-up session)
• A hospital contact is defined by outpatient as well as inpatient contacts		

The PaHS prediction model calculated individuals' risk of a hospital admission within the following three months and each region invited participants with the highest risk for individual screening for possible participation in the PaHS RCT. Each month a new list with ranked risk scores was generated and invitations were drawn from the top of the list (highest risk). The monthly number of participant invitations was based on PaHS nursing capacity and continued until the calculated sample size was reached.

Inclusion procedure

Invitation letters were sent to the potential participants identified in the PaHS prediction model using e-Boks (a secure personal site for electronic mail from government and municipalities, including the healthcare system). Two percent of Danish citizens have been exempted from using e-Boks and were therefore sent a postal letter. Invited participants who did not respond were sent a reminder. In case they still did not respond, PaHS nurses attempted telephone contact twice.

When the potential participant had been contacted, PaHS nurses performed a secondary individual screening for exclusion criteria not identified in the PaHS prediction model (Table 1). The secondary manual screening was preliminarily done by telephone. Potentially eligible participants were invited to a personal meeting with the PaHS nurse where the secondary manual screening was completed by participant interview and review of patient records. Eligible participants were informed about the purpose of PaHS, project design, intervention, anonymity and that project participation was voluntary. Before randomization, the participants gave written, informed consent and completed an online baseline questionnaire about Health-related quality of life (SF-36v2) (21) and Health Education Impact Questionnaire (heiQ).(22) .

Randomization

The randomization was stratified by the risk scores of the PaHS prediction model in three strata: <15%, 15-25% and >25% risk. The randomization was generated by an html-file on the PC of each PaHS nurse with cookies securing equal distribution of control and intervention group for the nurses and thereby region. Participants were randomized in blocks of 4, 6 and 8 that were concealed to the users.

PaHS intervention

The PaHS intervention was performed by registered nurses with several years of clinical experience who were trained for PaHS. In Denmark, nursing education is a bachelors' degree. PaHS is an addition to usual care and PaHS nurses do not assume clinical responsibility for the participants and decisions about hospital admissions belong to a physician.

The purpose of the intervention was to enhance participants' self-management strategies and thereby enable them to cope with illness in their daily life and prevent progression of illness. Self-management support was defined as: "… *the systematic provision of education and supportive interventions to increase patients' skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support*."(23)

Box 1. PaHS intervention

Structure

- Face-to-face start-up session with needs assessment and relationship building
- Telephone-based follow-up sessions
- Lasts 6-9 months

Tools

- Development of one or more personal goals
- Assessment of risk of hospitalization at each session

PaHS nurses' roles

- Caregiver
- Coach
- Healthcare professional

Content

- Knowledge about disease and treatment
- Coping and strategies
- Self-help
- Need for healthcare services

PaHS emphasized supporting and empowering participants to make the necessary contacts to healthcare professionals, social services and relevant non-governmental organizations. If a participant was unable to do so, the PaHS nurse might contact other healthcare professionals on the participant's behalf. Coordination of healthcare services such as managing handover between healthcare providers and medical specialties was outside the scope of the intervention.

The intervention was described in two practice guides: one for the Region Zealand and one for the other four regions. The practice guides describe the workflow processes and intervention methods. The intervention was adapted to individual participants' needs and therefore flexible rather than firmly manualized. The practice guides are summarized in the following and the main components of the PaHS intervention are listed in Box 1.

The start-up session focused on building a relationship with the participant and gaining knowledge about the participant's needs within the four central areas of the intervention: 1. Knowledge about disease and treatment, 2. Coping and strategies in case of worsening condition, 3. Self-help behavior and 4. Involvement of healthcare providers and healthcare services already in place. Participant's needs were explored within each of the four areas to support the development of one or more personal goals. Goal development entailed identifying a problem, setting a goal, deciding actions to reach the goal and continuous appraisal of progress and goal achievement. The goals varied and could involve improving dietary habits, increasing physical activity, emotional coping with illness, improving medication adherence, pharmaceutical and non-pharmaceutical pain management, gaining knowledge about disease and treatment, or learning to improve communication with healthcare providers and so forth. At every follow-up session, the goals were

addressed and adapted or concluded if relevant. The PaHS nurse might help the participant prepare questions and clarify priorities before consultations with general practitioners and other healthcare providers. At the end of each session the PaHS nurse made a case-by-case appraisal of the participant's risk of being hospitalized in three levels of risk: green(low), yellow(medium) and red (high) to determine the time interval to the next session. The risk was assessed by reviewing the previously described four central areas of the intervention (knowledge, coping, strategies and healthcare) and identifying unresolved problems and unmet needs. The risk appraisal was based on a collective view of all four areas. However, should the assessment reveal severe problems in one of the areas, the overall risk would be judged high. Higher risk meant shorter interval between sessions. PaHS nurses could reschedule sessions in case of illness and participants could contact PaHS nurses to reschedule sessions during regular office hours specified regionally.

The PaHS nurses accessed patient records during screening for inclusion only and the participant was the only source of further information. The PaHS nurses alternated between three roles: 1. The caregiver, focusing on active listening(24), comfort and empathy, 2. The coach, promoting patient reflection and supporting progress in self-management strategies, and 3. The healthcare professional, sharing knowledge and giving advice about disease, treatment and self-monitoring of symptoms. Four specific communication methods described in the course-textbook(25) were emphasized in promoting patient reflection and supporting progress in self-management strategies and achieving personal goals: 1. The gamemaster technique, which is inspired by the theory of 'Coordinated Management of Meaning' by W. Barnett Pearce.(25, 26) The gamemaster technique is a type of metacommunication that entails facilitating a contract about the conversation and thereby changing the "game" of the conversation rather than merely playing it. 2. Karl Tomms 'Interventive Interviewing' approach which includes four types of questions: lineal,

circular, strategic or reflexive depending on the underlying assumptions.(25, 27) 3. Identification of significant keywords and curiously exploring their meaning. 4. The core skill in 'Motivational Interviewing' developed by William R. Miller and Stephen Rollnick(25, 28) that entails asking participants to rate the importance of behavior change and their confidence in ability to change on a scale of 1-10. This skill is called 'lift' as it focuses on moving higher up the scale.

In four of five Regions, PaHS nurses participated in the same standardized introduction program, which supported fidelity and adherence to the intervention and included a textbook about systemic coaching.(25) Furthermore, PaHS nurses participated in group supervision, individual supervision and peer-to-peer supervision. Data-driven quality improvement included monitoring inclusion and review of completed interventions and reasons of intervention termination. The purpose was to support PaHS nurses' focus on the participants' progress.

The following standards for the intervention were applied:

- The planned maximum case load for each PaHS nurse should be 60 participants at any time.
- Participants should be contacted within one week of accepting the invitation to the information meeting.
- Participants should be assigned one PaHS nurse that provides the intervention.
- The start-up session is planned to last 1 hour.
- Follow-up telephone sessions are planned to last 15 minutes each.
- The first follow-up telephone session should be offered within one week of the start-up session.

- PaHS nurses should have at least two months of training with the intervention before accepting participants in the PaHS RCT.

Region Zealand, where the development phase was initiated, used a practice guide with some differences to that of the other four regions. In Zealand,

- Introduction was not standardized but adapted to the training needs of the PaHS nurses on the principles for situated learning as proposed by Lave & Wenger(24) after the PaHS nurses have gained experience with the intervention.
- Supervision took place in group and peer-to-peer - not individually.
- Project data were documented in a separate database.
- The practice guide was continuously developed during the RCT.
- The start-up session was planned to last 1.5 hours and follow-up sessions 15-30 minutes.
- Participants were offered transportation to the start-up session.
- Follow-up sessions might include review of hospital records after any hospital admission to identify measures of preventing subsequent admissions.
- The intervention included the structure, tools and content described in box 1 but not the three roles. Instead, there were three positions in communication: personal support, exploring new insights, and finding solutions.
- The practice guide included a section about life crisis and suicide prevention.

In all regions, participants could withdraw consent at any time, and PaHS nurses could terminate the intervention if the participant became too ill, did not cooperate, could not be contacted, did not benefit from the intervention or completed the personal goals. Participants receiving at least two follow-up sessions within two months of the start-up session were classified as having

received the PaHS intervention per protocol unless the intervention was terminated because of lack of cooperation or benefit from the intervention. The intervention was planned to last 6-9 months.

Data

The PaHS RCT data were reported to and stored according to the requirements of the Danish Data Protection Agency (VD-2018-322) that ensures adherence to the General Data Protection Regulation.

The primary and secondary outcomes are listed in table 2. The two primary outcomes are analyzed separately, and the intervention is perceived as successful if either one is affected.

Table 2. Outcomes

Primary outcomes	• Rate of hospital admissions (≥ 24 hours) within 6 months after randomization. • Health-related quality of life (HRQoL) - Short-Form Health Survey 36 version 2 (SF-36v2) mental health component summary score at 6 months follow-up.(21)
Secondary outcomes at 3, 6 and 12 months	
• Patient-reported outcomes	• HRQoL: SF-36v2, all subscales and physical and mental health component summary scores • Health Education Impact Questionnaire (heiQ), all subscales (22)
• Healthcare	• Number and rate of hospital admissions (≥ 24 hours) within 3 and 12 months after randomization. • Hospital days. • Preventable hospital admissions. • Readmissions. • Outpatient visits. • Contact with out-of-hours medical services. • Use of primary care (general physician, psychologists etc.). • Use of municipal rehabilitation. • Use of district nursing services. • Use of prescription medication.
• Costs	• Costs of hospital admission • Costs of outpatient consultations • Costs of out-of-hours medical services • Costs of primary care use • Costs of municipal rehabilitation • Total costs per patient • Incremental cost-effectiveness (ICER, cost per quality-adjusted life year gained).
• Survival after 12 months. This endpoint is included for outcome assessment as well as safety.	

The following variables are collected from registers: Age, gender, marital status, employment status, level of education and diagnoses. Information about demographics will be retrieved from The Civil Registration System.(29) Diagnoses and use of healthcare resources will be retrieved from The Danish National Patient Registry(30) and The Danish National Health Insurance Service Registry.(31) Use of prescription medicine will be retrieved from the Danish National Prescription Registry. Patient-reported outcomes are collected through questionnaires, which are administered online by e-Boks or telephone-interviews according to participants' preferences and access to personal computer. Reminders are sent after one week and two attempts of telephone contact are made in case of no response. Data from all sources is gathered at Statistics Denmark and managed by Center for Clinical Research and Prevention, Bispebjerg and Frederiksberg hospital, Copenhagen, Denmark. The data is combined using the participants' unique civil registration numbers, which are subsequently anonymized. Table 3 gives an overview of the timeline and procedures inspired by the SPIRIT 2013 statement.(32)

Table 3. SPIRIT figure of study period

			Post-allocation			Close-out
Timepoint	**Enrolment**		**Start-up**	**3 months**	**6 months**	**12 months**
Enrolment						
- Eligibility screening	X					
- Informed consent	X					
Interventions						
- Intervention group	Usual care		Needs assessment, goals	Follow-up sessions + usual care		
- Control group	Usual care		Usual care			
Assessments						
- Demographics and diagnoses	X					
- SF-36v2	X			x	x	x
- HeiQ	X			x	x	x
- Use of healthcare resources				x	x	x
- Costs				x	x	x
- Survival						x

Allocation

Data for process evaluation includes timing, length and number of follow-up sessions, completion, and withdrawal from intervention. These data are documented in an electronic project record by PaHS nurses.

Analyses

The sample size calculation was based on a historic cohort from 2013 in the Danish National Patient Register resembling the population included in the development period. Sample size was based on a two-sided T-test, a significance level of 5%, 80% power and was performed for the two co-primary outcomes: hospital admissions and HRQoL. For HRQoL, the minimal group size needed to detect a 5% difference in the SF-36v2 Mental Health Composite Score (standard deviation 10)

between the control and intervention group is 400. Expecting a 10% dropout rate, the planned inclusion is 880 participants. To enable investigation of regional differences in intervention effect on HRQoL, each of the five Danish regions will include 880 participants totaling 4400 nationwide. For hospital admissions, 2000 in each group is needed to detect a difference of 5% in the 44.4% with ≥ one acute hospital admission, of 4% in the 21.8% with ≥ two acute hospital admissions and 3% in the 11.4% with ≥ three acute hospital admissions; also totaling 4400 nationwide. Thus, the study is designed to compare the regions by effects on HRQoL but not by hospital admissions.

The primary analyses will be based on the intention-to-treat principle modified by excluding participants who withdrew consent. The use of healthcare resources including hospital admissions will be analyzed with Poisson regression. Patient-reported outcomes will be analyzed with generalized linear mixed models with autocorrelation and assuming that missing data is related to the previously observed values of same items or covariates (missing at random). Questionnaires with >5 logical errors in SF36 will be excluded from analysis. Secondary analyses are per-protocol. Sensitivity analyses will be adjusted for baseline variables (demographics, diagnoses and patient-reported outcomes). Survival analysis will be performed with Cox regression. Analyses will be performed for each of the five Regions, all five regions combined, and Region Zealand compared to the other four Regions. Effects are considered statistically significant at the 5%-level, whereas a minimally important difference is considered one half standard deviation.(33)

Mean resource utilization, costs of healthcare utilization and quality adjusted life-years (QALYs) will be compared between the intervention and control groups. The differences in mean costs and QALYs between groups will be calculated using regression analysis regressing individual QALYs and costs against allocation in the trial controlling for other factors. The skewness in cost data will be

accounted for with generalized linear models. The differences in costs across regions will be analyzed with mixed effects models. The incremental cost-effectiveness ratio will be determined based on incremental costs and the effects of PaHS in comparison with usual care. The robustness of the ICER will be assessed by non-parametric bootstrapping to quantify the uncertainty around the ICER.

In support of a potential future implementation of the intervention, response to intervention analyses will be performed on the outcomes hospital admissions and physical and mental health component summary scores of SF36v2 after 6 months. The following variables will be tested for interaction with the intervention: Progress in health education impact (heiQ from baseline to 6 months), baseline physical and mental health component summary measures of SF-36v2, number of diagnoses, 3 most prevalent diagnoses, age, sex, level of education, marital status, predicted risk score, region and number of telephone counseling sessions.

Discussion

The five Danish regions differ in population composition and organization of usual care, which may impact intervention efficacy. Furthermore, some regional variation occurred during the development phase despite efforts to ensure homogeneity. The Region Zealand intervention differs from the other four regions and the PaHS prediction model in the Central Denmark Region used a different algorithm due to lack of access to the statistics program of the prediction model (SAS). The inclusion criteria specified in Table 1 is the same with either prediction model. Therefore, any variation might be in the risk scores and their ranking. The regional differences and their potential consequences will be investigated further, including the association between risk score and intervention effect.

Hypothetically, the intervention may reduce the number of admissions by supporting participants in identifying and resolving health issues before they become unmanageable at home. Intervention effect may be mediated by improving participants' behavior, skills, and attitudes in self-monitoring and health service navigation as measured by heiQ. Intervention effect on HRQoL may be instigated directly by caregiving for and empowering participants, indirectly through supporting participants in reaching out to needed health services, or by PaHS nurses occasionally contacting other healthcare providers directly on participants' behalf. Furthermore, any reduction in use of healthcare resources may involve an increase in contacts elsewhere in the healthcare system. Any shift in use of healthcare resources will be included in the cost-effectiveness analyses. This intervention has all the features of a complex intervention defined by the Medical Research Council guidance including difficult behaviors required by participants and nurses delivering the intervention, individual tailoring of the intervention, interacting intervention components, and multiple outcomes.(34) Due to intervention complexity and possible interaction between the components in the intervention, the dynamics of potential effects cannot be fully elucidated. Therefore, the processes of intervention effects will be investigated by assessing multiple outcomes and performing response to intervention analyses. Furthermore, multiple process evaluations are nested within the trial. To this end, the PaHS research program comprises five work packages:

1. Preliminary development of intervention and PaHS prediction model.

2. Intervention effect and validation of the PaHS prediction model. Focus is on the intervention effect on patient-reported and healthcare outcomes described in table 2.

3. Cost-effectiveness. Focus is on the intervention effect on cost outcomes and cost-effectiveness described in table 2.

4. Organizational implementation. The assumption is that the effect of PaHS depends on how the internal organization and execution of the intervention is developed as well as how the interaction with the environment unfolds.(35)

5. The participants' experiences and perspectives of the intervention are investigated with observations and interviews. Focus is on the development of a relationship between participants and PaHS nurses and how this may may contribute to strengthening participants' competencies towards better quality of life, coping and developing self-management strategies.

The work packages provide different perspectives to illuminate the complex intervention processes, mechanisms and effects. According to the PRECIS-2 tool(36), the PaHS intervention may be considered very pragmatic in most domains except the domain recruitment. The proactive patient contact for study recruitment had ethics committee approval and would require additional adaptation before an implementation to standard care.

Declarations

Ethics approval and consent to participate

The PaHS RCT is carried out in accordance with the Helsinki Declaration and has been approved by The Regional Committee on Health Research Ethics (SJ-677). All study participants gave written, informed consent to participation.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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