tOwards a Patient centred mulTIMorbidity Approach FOR chronic disease MAnagement in primary care (OPTIMA FORMA) PHASE 3:

Cluster Randomized Controlled Evaluation Study

(V1, July 2022)

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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)**
CA	**Competent Authority**
CCMO	**Central Committee on Research Involving Human Subjects; in Dutch: Centrale Commissie Mensgebonden Onderzoek**
COPD	**Chronic Obstructive Pulmonary Disease**
CVD	**Cardiovascular Diseases**
CV	**Curriculum Vitae**
DM2	**Diabetes Mellitus type 2**
EU	**European Union**
GCP	**Good Clinical Practice**
GDM	**Generic Disease Management**
GDPR	**General Data Protection Regulation; in Dutch: Algemene Verordening Gegevensbescherming (AVG)**
IC	**Informed Consent**
NHG	**Dutch College of General Practitioners**
METC	**Medical research ethics committee (MREC); in Dutch: medisch-ethische toetsingscommissie (METC)**
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.**
P3CEQ	**Person Centred Coordinated Care Experiences Questionnaire**
PROMIS GLOBAL10	**Patient-Reported Outcomes Measurement Information System GLOBAL - 10**
SDM	**Single Disease Management**
WMO	**Medical Research Involving Human Subjects Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen**

SUMMARY

Rationale: Chronic diseases and multimorbidity are increasingly prevalent. However, over the last decades, attempts at improving primary care for chronic diseases have been focussed on the management of individual chronic diseases and single disease management (SDM) programs have been implemented in Dutch primary care. This causes multiple problems for patients with one or more chronic diseases, such as negative interaction between treatment of single diseases, high treatment burden, negative patient experiences, lack of attention for problems in other domains of life that may interact with the chronic disease, and difficulties in shared decision making by the use of strict protocols in SDM programs. A person-centred and holistic approach is widely recognized as the solution to the problems observed in chronic disease care. Therefore, we guided three large Dutch primary care cooperatives, who have been organizing SDM programmes on diabetes mellitus type 2 (DM2), COPD, and cardiovascular diseases (CVD) in primary care for the last decades, with the development of a new generic disease management (GDM) programme including a person-centered and holistic approach (CMO 2019-5756). The three primary care cooperatives have recently conducted a pilot study in which we evaluated the feasibility of the programme (CMO 2021-8106) to further optimise its content and procedures. In the coming years, all three primary care cooperatives will gradually implement the optimised programme in all general practices in their regions.

Objective: In the current study, our aim is to evaluate the effectiveness of the GDM programme on Quadruple Aim outcomes, i.e. patient experiences, population health, health care provider experiences, and cost effectiveness.

Study design: we will conduct a cluster randomized controlled trial in the three primary care cooperatives with a follow-up of 12 months. Fifteen practices will be randomised to either care as usual according to the current SDM programmes, or to the GDM programme including a person-centered and holistic care approach. Approximately 40 patients per practice with DM2, COPD and/or CVD will be recruited.

Study population: all patients with DM2, COPD and/or CVD who currently receive SDM according to the SDM programmes of the participating primary care cooperatives are eligible to participate.

Intervention: a GDM programme including person-centered and holistic care. This programme will replace the SDM programmes for DM2, COPD and CVD that are currently used in the participating primary care cooperatives.

Main study parameters/endpoints: effectiveness will be evaluated by Quadruple Aim outcomes at baseline, at 6 months, and at 12 months follow-up by comparing changes in the intervention group with the comparator group. Patient experiences will be measured with the P3CEQ questionnaire. Population health will be measured with the PROMIS Global-10 questionnaire. Self-management will be measured with the Patient Activation Measure (PAM) score. Healthcare professional experiences will be measured with the MASGZ and the COPILOT questionnaire. Data for calculating costs and conducting a cost-effectiveness analyses will be measured by the Medical Consumption questionnaire and the EQ-5D questionnaire and by process outcomes such as the number and type of consultations and referrals, and duration of consultations from the Electronical Medical Files. At 12 months, a purposive sample of patients and professionals will participate in focus group interviews to collect information on experiences and facilitators and barriers for further implementation. Also, the competences needed by the healthcare professionals to provide personalised and integrated chronic care will be explored.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

- The intervention has been developed by the three primary care cooperatives in close collaboration with their healthcare professionals and their patient panels and with the guidance of our research group. Also, input from the Dutch College of General Practitioners (NHG) and from InEen, the branch organisation for primary care cooperatives, has been obtained to ensure that the intervention will suit their vision and future plans for reorganising Dutch primary care chronic disease management. The intervention is also in line with current movements in healthcare, such as the Positive Health concept.
- All three primary care cooperatives are intending to gradually implement the intervention throughout their regions in the upcoming years. Thus, the GDM programme will be implemented and will replace current SDM, even without the current cluster RCT as proposed in this study protocol.
- The burden and risks associated with the intervention are negligible and comparable with the usual care, i.e. the current SDM programmes.

- Patients in the control group will continue with their care as usual, i.e. single chronic disease management according to the protocols of the SMD programmes that have been used in the participating cooperatives since the last decade.
- The additional burden or risk associated with participation in this study is negligible. After written informed consent, patients in both groups will fill in a digital or paper questionnaire at baseline, 6 months, and 12 months. Estimated time to fill in the questionnaire is 20 minutes. A purposive sample of approximately 15 patients will participate in focus-groups interviews at the end of follow-up.

1. INTRODUCTION AND RATIONALE

Multimorbidity is increasingly prevalent. In 2016, 52% of the Dutch population had at least one chronic disease; 37% of Dutch population had two or more chronic diseases.[1] This increasing prevalence results in several problems. Multimorbidity is associated with poorer quality of life, functional health status and physical functioning, and higher mortality compared to patients with zero or one chronic condition.[2, 3] In addition, patients with multimorbidity have higher health care utilization than patients with one or no chronic disease; multimorbid patients had more contacts with general practice, more medication prescriptions, and more referrals to specialized care.[4, 5] Because of the impact of chronic diseases and the increasing number of patients with multimorbidity, costs of primary health care in the Netherlands are quickly rising. For instance, over the course of 2013 to 2016, the costs of primary care increased from 2.7 to 3.1 billion euros. This can largely be attributed to the increase in cost of care for people with chronic conditions.[6]

Over the last decade, attempts at improving primary care for chronic diseases have been focussed on the management of individual chronic diseases, with the implementation of single disease management (SDM) programs internationally. In the Netherlands, SDM programs have been widely implemented for diabetes mellitus type 2 (DM2), chronic obstructive pulmonary disease (COPD) and cardiovascular disease (CVD). The disease specificity of these programs causes 3 distinct problems for people with multimorbidity. First, the treatment of one disease according to a disease-specific guideline can interact negatively with the treatment or natural course of a co-existing disease.[7] The second problem is that the combination of various disease-specific guidelines leads to polypharmacy and increased treatment burden.[8] Last, because of the disease-specific fragmentation of primary care, people with multimorbidity are more likely to experience problems with coordination of care and lower quality of care.[9]

A patient centred and integrated care (PC-IC) approach is widely recognized as the solution to the problems in multimorbidity care.[7, 10, 11] Therefore, we guided three large Dutch primary care cooperatives, who have been organizing SDM programmes on DM2, COPD, and CVD in primary care for the last decades, with the development of a new generic disease management (GDM) programme including a person-centered, integrated, and holistic approach (CMO 2019-5756). The three primary care cooperatives have recently conducted a pilot study in which we evaluated the feasibility of the programme (CMO 2021-8106) to further optimise its content and procedures. In the coming years, all three primary care cooperatives will gradually implement the optimised programme in all general practices in their regions.

OBJECTIVES

In the current study, our aim is to evaluate the effectiveness of the GDM programme on Quadruple Aim outcomes, i.e. patient experiences, population health, health care provider experiences, and cost effectiveness.

2. STUDY DESIGN

We will perform a cluster randomized controlled trial with a follow-up time of 12 months.

The three participating primary care cooperatives, i.e. Nijmegen, Arnhem, and Doetinchem, will recruit 15 general practices (clusters) who will be randomized using a 2:1 ratio in two study groups:

1. The intervention group: the GDM programme including a person-centered, integrated, and holistic approach
2. The control group: care as usual according the current SDM programmes

All practices will receive instructions from the research team on the procedures of the evaluation study. Participating practices will then start recruiting patients from a random sample of eligible patients, i.e. patients with DM2, COPD, or CVD who are currently receiving SDM. After written informed consent, information will be collected through questionnaires at baseline, 6 months and 12 months, and by interviews and data collection from electronic medical records. Information will also be collected from the participating healthcare providers through questionnaires and interviews.

In the two months prior to the start of the intervention, all practices in the intervention group will be trained in providing GDM by their own primary care cooperative. During follow-up two to three intervision meetings will take place including peer coaching and case study discussions.

Practices who are allocated to the usual care group will not receive any training, but will continue with their SDM programmes.

STUDY POPULATION

2.1 Population

All patients who are currently enrolled in any of the SDM programmes for DM2, COPD, asthma or CVD are eligible for participation.

2.2 Inclusion criteria

- Currently enrolled in any of the SDM programmes for DM2, COPD, asthma or CVD.

2.3 Exclusion criteria

- Limited life expectancy (less than 3 months)
- Unable to speak or read the Dutch language

2.4 Sample size calculation

Due to the complexity of our intervention we will use two primary outcomes, i.e. health-related quality of life and patient experience of care. These outcomes are in line with the 2 patient-related aims of the Quadruple Aims concept. Patient-reported health-related quality of life will be measured using the 'PROMIS Global 10' questionnaire and the patient experience of care will be measured using the 'P3CEQ'. These questionnaires have been chosen after piloting several questionnaires in the preceding Phase2 of OPTIMA FORMA. Patients experienced these questionnaires as easy to complete and to understand.

The 'PROMIS global 10' assesses a person's health-related quality of life and consists of 10 questions. Two dimensions representing physical and mental health underlie the global health items in PROMIS. These global health scales, Global Physical Health (GPH) and Global Mental Health (GMH), can be used to efficiently summarize physical and mental health in patient-reported outcome studies.[12] The 10 global health items include ratings of the five core PROMIS domains with a response scale ranging from 1 to 5.The PROMIS global 10 is publicly available and has been widely used as outcome measure for quality of life in studies on different diseases.

The Person-Centred Coordinated Care Experience Questionnaire (P3CEQ) is a brief questionnaire that meets the requirements for a PREM that could assess the quality of care and guide quality improvement for people with (multiple) chronic conditions. It has been specifically designed to assess the experience of person-centred coordinated care, informed by a theoretical model that was developed to consider the relationship between care coordination, continuity and person-centred care. The P3CEQ was originally developed in the United Kingdom for persons with chronic conditions using primary care services.[13] Recently is has been translated and validated for the Dutch population.[14] It contains 14 items and the response scale ranges from 'never' (0), 'sometimes' (1), 'often' (2) and 'always' (3).

Because we value each aim (population health and patient experience) as equally important, we are using a composite primary outcome, which consist of the percentage of patients who have a clinically relevant improvement of at least the minimal clinically important difference (MCID), defined as 0.5 x SD of the baseline mean, in either the PROMIS GMH score _OR_ the PROMIS GPH score _OR_ the P3CEQ-score _AND_ who experience no decrease of at least the MCID in either the PROMIS GMH score _OR_ the PROMIS GPH score _OR_ the P3CEQ-score.

In our recent pilot study [unpublished] we followed 98 patients who received our intervention for six months. Of the 79 patients who completed all questionnaires, we found that in 30.4% of the patients the requirements for a positive score on the composite primary outcome were met. Loss to follow-up was 20%. Based on these results and the longer duration of intervention in the evaluation study (12 months vs 6 months), we hypothesised that in the evaluation study 35% of the intervention patients compared to 20% of the usual care patients will improve more than 0.5 x the expected SD of baseline mean on one of the scores at 12 months, and show no decrease of the MCID on the other scores. We estimate that we need a total sample size of 680 patients (17 practices with an average of 40 patients per practice) to detect a difference of 15% between the control and intervention group, taken into account an alpha level of 5%, a power of 80%, an intra-class correlation coefficient (ICC) of 0.03 [15], and a loss to follow-up of 20%.

3. TREATMENT OF SUBJECTS

3.1 OPTIMA FORMA intervention

The core of GDM programme including person-centered and holistic approach is a cyclical process described in Figure 1. The practice nurse in the general practice will act as case manager. She/he can consult the general practitioner or other health providers when necessary. The first step in the intervention is assessing the integral health status of the patient (health across multiple domains, including physiological measurements and symptoms of disease), using a (preferably digital) questionnaire at home and physical measurements. The second step is an appointment in which the results are discussed with the patient in a semi-structured way. The case manager discusses if the results are recognizable, if there are other issues which haven't come up, and the priorities of the patient. Personal goals are formulated in the third step, which can range from purely medical goals to social goals. In the fourth step, the healthcare professional and patient will choose through shared-decision making the most appropriate interventions and support to achieve these goals. The goals and interventions are documented in a personal healthcare plan, which is preferably digitally available for all relevant healthcare professionals and the patient. Next, referrals are made if necessary and the treatment is started. An evaluation is planned and carried out, if necessary multiple times. If a treatment goal is reached or another treatment goal is more urgent, the cycle can be repeated.

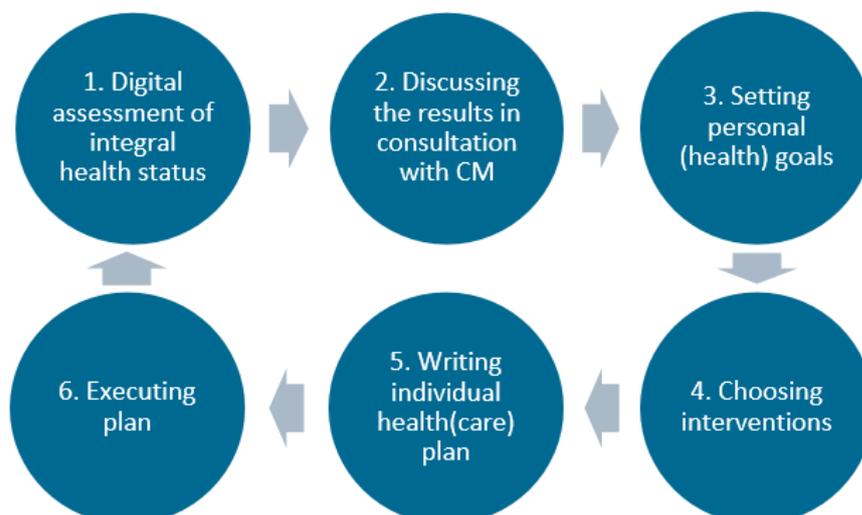Figure 1. Presentation of the cyclic process of the GDM programme

In order to provide the OPTIMA FORMA intervention to participating patients all healthcare professionals involved will be trained by their primary care cooperative on the concept of Positive Health, communication skills, use of materials and ICT, and interprofessional collaboration prior to the start of the intervention. During follow-up, the

practices will receive additional support from the primary care cooperative through intervision meetings and case report discussions.

3.2 Usual care

Practices in the control group provide care as usual, which consists of the SDM programmes according to the national care standards and General Practice guidelines (NHG) for DM2, COPD and CVD. According to these protocolised programmes, patients with COPD, CVD or DM2 visit their general practice at a standard frequency per year (1 – 4 times) and standard monitoring measurements and topics are discussed.

The practices that are randomised to the control group will not receive any additional training related to this study.

4. METHODS

4.1 Study parameters/endpoints

Outcome measurement will be based on the quadruple aim framework.[16] To measure population health we will assess quality of life, self-management, and disease-specific physiological factors. Our composite primary outcome will be health-related quality of life _and_ patient experience, measured with the PROMIS Global 10 and P3CEQ, as described in paragraph 2.4. Secondary outcomes will be: self-management, measured with the Dutch short version of the patient activation measure (PAM-13).[17] Measurement of disease-specific physiological factors will take place as part of routine care in both study groups and include blood pressure, body mass index (BMI), cholesterol, blood glucose levels and lung function parameters, if applicable. All outcomes will be measured at baseline, 6 months, and 12 months follow-up. Physiological factors will be recorded in the electronic medical records as part of routine care and will be extracted from 3 months before baseline until 12 months follow-up. Also, healthcare utilisation and prescription data will be extracted from the electronic medical records at the end of follow-up. Health care provider experiences will be measured with an appropriate self-reported experience measure.

4.1.1 Main study parameter/endpoint

Our primary outcome will be patient-reported health-related quality of life _and_ patient experience of care, in line with the 2 patient-related aims of the Quadruple Aims. Patient-reported health-related quality of life will be measured using the PROMIS global 10 questionnaire and the patient experience of care will be measured using the P3CEQ questionnaire. These questionnaires have been chosen after piloting several questionnaires

in the preceding phase. Patients experienced these questionnaires as easy to fill in and to understand and both questionnaires match well with the concepts we want to measure.

The PROMIS global 10 assesses a person's health-related quality of life. Two dimensions representing physical and mental health underlie the global health items in PROMIS. These global health scales can be used to efficiently summarize physical and mental health in patient-reported outcome studies, Global Physical Health (GPH; 4 items on overall physical health, physical function, pain, and fatigue) and Global Mental Health (GMH; 4 items on quality of life, mental health, satisfaction with social activities, and emotional problems).[12] The 10 global health items include ratings of the five core PROMIS domains with a response scale ranging from 1 to 5, the labels of those scores different per question, but a higher scoring is always indicating a better health-related quality of life. The PROMIS global 10 is publicly available and has been widely used as outcome measure for quality of life in studies on different diseases.

The Person-Centred Coordinated Care Experience Questionnaire (P3CEQ) is a brief questionnaire that meets the requirements for a PREM that could assess the quality of care and guide quality improvement for people with (multiple) chronic conditions. It has been specifically designed to assess the experience of person-centred coordinated care, informed by a theoretical model that was developed to consider the relationship between care coordination, continuity and person-centred care. The P3CEQ was originally developed in the United Kingdom for persons with chronic conditions using primary care services.[13] Recently is has been translated and validated for the Dutch population.[14] It contains 14 items and the response scale ranges from 'never' (0), 'sometimes' (1), 'often' (2) and 'always' (3).

Because we value each aim (population health and patient experience) as equally important, we are using a composite primary outcome, which consist of the percentage of patients who have a clinically relevant improvement of at least the minimal clinically important difference (MCID), defined as 0.5 x SD of the baseline mean, in either the PROMIS GMH score _OR_ the PROMIS GPH score _OR_ the P3CEQ-score _AND_ who experience no decrease of at least the MCID in either the PROMIS GMH score _OR_ the PROMIS GPH score _OR_ the P3CEQ-score.

4.1.2 Secondary study parameters/endpoints (if applicable)

- PROMIS dimension GPH score
- PROMIS dimension GPM score
- P3CEQ-score

- Patient Activation Measure (PAM)
- EQ-5D-5L
- Health care use according to Medical Consumption Questionnaire
- Health care use according to general practice data
- Body weight, BMI, smoking status, HbA1c, glucose, cholesterol levels and blood pressure from general practice data (registered for normal care).
- Experience of healthcare providers on COPILOT and MAS-GZ questionnaire

4.2 Randomisation, blinding and treatment allocation

The unit of randomisation will be the general practice (cluster). Practices will be randomised to intervention group (10 clusters) or comparator (5 clusters) in a 2:1 ratio. Five additional clusters will be randomised to the control group by a 2:1 ratio randomisation procedure in the parallel cluster RCT named EMBOSS in which the GDM programme will be adjusted to the needs of patients with low socioeconomic status (SES). In the EMBOSS cluster RCT the adjusted intervention will be provided to patients with low SES and at 12 months follow-up the effects will be compared to patients with low SES who have received care as usual. Figure 2 illustrates the combined randomisation procedure of both the OPTIMA FORMA and the EMBOSS cluster RCT.
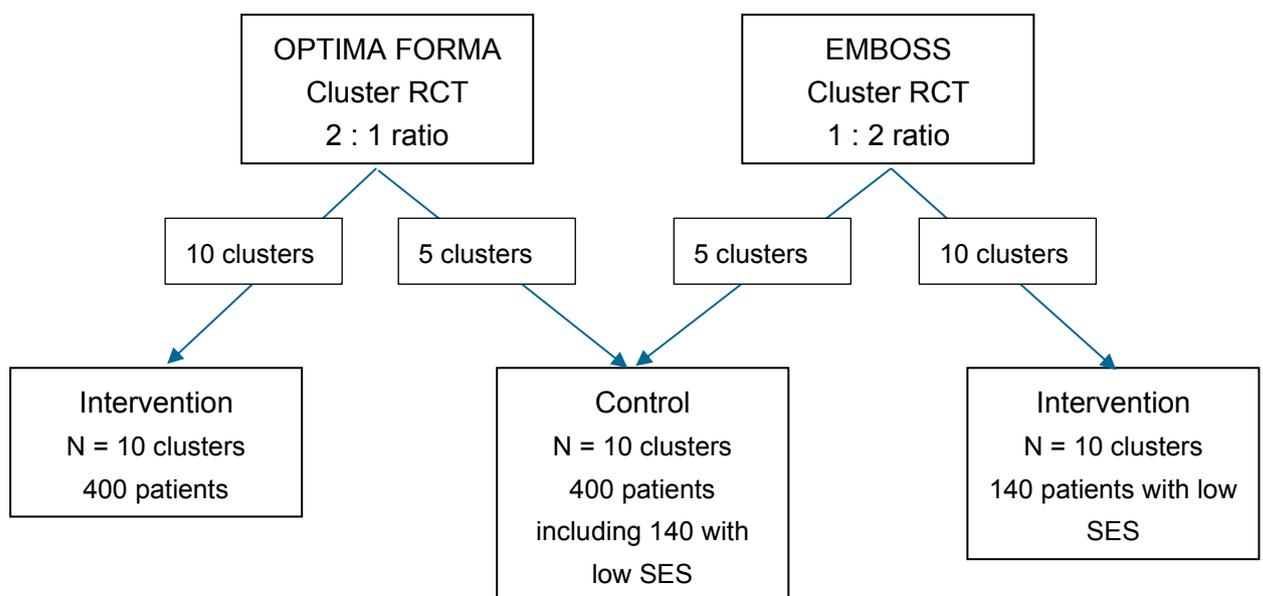
Figure 2. Randomisation procedures in the OPTIMA FORMA and EMBOSS cluster RCTs

After practices have been recruited, the practices will be randomised to the intervention or the usual care group. To avoid an imbalance between the randomised groups stratification will take place according to (i) the primary care cooperative, and (ii) the socioeconomic status of the practice population. Because of the nature of the intervention, it will not be possible to mask intervention allocation from the GPs or the patients. The research nurses who will collect the outcome data and the researchers who will perform the analyses will be blinded to treatment allocation.

4.3 Study procedures

Population health

Category	Measurement instrument	Time
Health related quality of life	EQ-5D-5L	Baseline, 6, 12 months
Self-management	Patient Activation Measure (PAM)	Baseline, 6, 12 months
Health related quality of life	PROMIS GLOBAL-10	Baseline, 6, 12 months
Unscheduled healthcare	Data from medical records	12 months
Physiological paramenters	Data from medical records	12 months

Patient experience

Category	Measurement instrument	Time
Person-centredness of care	Person Centred Coordinated Care Experiences Questionnaire (P3CEQ)	Baseline, 6, 12 months
Experiences	Focus-group interviews	12 months

Healthcare provider experience

Category	Measurement instrument	Time
Positive affect	CO-PILOT questionnaire MAS-GZ questionnaire	Baseline, 6, 12 months
Experiences	Focus-group interviews	12 months
Competences	Focus-group interviews Appropriate questionnaire	12 months At baseline and 12 months

Cost-effectiveness

Category	Measurement instrument	Time
Medication	Data from medical records	12 months

Scheduled and unscheduled healthcare utilisation	Data from medical records	12 months
Referrals	Data from medical records	12 months
Costs	Data from medical records	12 months
	Medical consumption questionnaire	Baseline, 3, 6, 9, 12 months
	EQ-5D-5L	Baseline, 6, 12 months

4.4 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences.

4.5 Replacement of individual subjects after withdrawal

Subjects will not be replaced after withdrawal

4.6 Follow-up of subjects withdrawn from treatment

For intention-to-treat analyses all available data from patients will be used. Patients who withdraw will be asked to fill the questionnaire for the measurement of the primary outcomes at 12 months.

4.7 Premature termination of the study

The study will be terminated in its current design as recruitment of the necessary number of cluster fails.

5. SAFETY REPORTING

As all patients will at least receive care similar to usual care, we do not expect any safety issues for participants.

6. STATISTICAL ANALYSIS

Data analysis will be performed according to the intention-to-treat principle. Data from patients who discontinued follow-up will be included in the analysis up to the point of dropout. Descriptive analyses will be performed to describe the patient characteristics. Mean and standard deviation (std) or median and interquartile range for continuous characteristics and number and percentages for categorical characteristics will be determined. The relationship between treatment and outcome measures measured at 6 and 12 month follow up will be analysed with mixed three level linear or logistic regression, taking into account that the times of measurement (after 6 and 12 months) are clustered within patients, and patients within general practices. We will perform a

model with a random intercept and all other variables fixed. To test the effect of the intervention a model with time, group (intervention or control) and the interaction between time and group will be performed. Covariates included in the analyses will be age, sex, smoking status, education level, and social support. A value of $p < 0.05$ will be considered statistically significant for all analyses, based on two-sided testing. Analyses will be performed using the Statistical Package for Social Sciences (SPSS, IBM Corp., Armonk, NY) version 25.

6.1 Primary study parameter(s)

Our primary outcome is a dichotomous composite score (yes / no MCID improvement in health-related quality of life or quality of healthcare), which is based on the scores of PROMIS dimensions (GPH, GPM) and the P3CEQ-score.

To test the effect of the intervention over time, we use a three level multilevel logistic model. A model with time , group (intervention or control) and the interaction between time and group will be performed. With this model we can test the effect of the intervention during the entire study period and the intervention effects at 6 months and at 12 months.

In a mixed model both fixed and random effects can be analyzed. We perform a model with random effect for practice and patients. All other variables will be held fixed. Covariates included in the analyses will be age, sex, smoking status, education level, and social support.

6.2 Secondary study parameter(s)

The relationship between treatment and secondary outcome measures measured at 6 and 12 month follow up will be analysed with mixed three level linear or logistic regression, taking into account that the times of measurement (after 6 and 12 months) are clustered within patients, and patients within general practices. A model with time, group (intervention or control) and the interaction between time and group will be performed. Covariates included in the analyses will be age, sex, smoking status, education level, and social support

6.3 Cost analysis

We will perform two different approaches for cost analysis. First, we will assess total costs per capita per month (triple aim measure). Total costs will be calculated from a healthcare and a societal perspective. The healthcare perspective includes all costs covered by the healthcare budget, i.e. medication prescriptions, contact with care providers (GP, medical specialist, nurse, physiotherapist, dietician, podiatrist, occupational therapist), home care, hospital admissions, emergency department visits and rehabilitation. The costs from the

societal perspective include travel costs and costs of productivity loss due to absence from paid work. Total costs will be calculated per group and then divided by the number of patients per group and the length of follow-up to assess the total costs per capita per month. Data on healthcare utilization and medication prescriptions will be extracted from the electronic medical records of the participating general practices. Additional data on healthcare utilization as well as data on travel costs and absence from paid work will be retrieved from patients by questionnaire at 6 and 12 months. In addition, we will conduct a cost-effectiveness analysis in which cost-effectiveness will be assessed in terms of costs per quality-adjusted life years (QALY). QALYs will be based on the EuroQol-5D (EQ-5D) utility values using the Dutch value set.

7. ETHICAL CONSIDERATIONS

7.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki and the privacy law (AVG).

7.2 Recruitment and consent

Eligible patients will be invited by telephone or by e-mail by the practice nurse and will be asked for oral permission to approach him/her for participation in the study. If the patient is interested in participating, a patient infolder folder is shared and personal details (name, e-mail address and telephone number, and preference for information by e-mail or on paper) will be sent to the research team via a secure mail connection. After five days the patient is contacted by the research team to obtain informed consent. The research worker creates a study ID, records the data in the Access logistic database in the folder H:sleutelbestanden and in CASTOR. The study ID consists of the practice number plus a serial number and cannot be traced back to an individual. The researcher sends the CASTOR questionnaire for baseline measurement to the participant. A notification is set up in CASTOR so that a message is sent to the to the mailbox if a questionnaire has been completed. After receiving the notification, the research team informs the practice via secure mail that the participant can start with the new method of care.

7.3 Benefits and risks assessment, group relatedness

- The intervention has been developed by the three primary care cooperatives in close collaboration with their healthcare professionals and their patient panels and with the guidance of our research group. Also, input from the Dutch College of General Practitioners (NHG) and from InEen, the branch organisation for primary care

cooperatives, has been obtained to ensure that the intervention will suit their vision and future plans for reorganising Dutch primary care chronic disease management. The intervention is also in line with current movements in healthcare, such as the Positive Health concept.

- All three primary care cooperatives are intending to gradually implement the intervention throughout their regions in the upcoming years. Thus, the GDM programme will be implemented and will replace current SDM, even without the current cluster RCT as proposed in this study protocol.

- The burden and risks associated with the intervention are negligible and comparable with the usual care, i.e. the current SDM programmes.

- Patients in the control group will continue with their care as usual, i.e. single chronic disease management according to the protocols of the SMD programmes that have been used in the participating cooperatives since the last decade.

- The additional burden or risk associated with participation in this study is negligible. After written informed consent, patients in both groups will fill in a digital or paper questionnaire at baseline, 6 months, and 12 months. Estimated time to fill in the questionnaire is 20 minutes. A purposive sample of approximately 15 patients will participate in focus-groups interviews at the end of follow-up.

ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

7.4 Handling and storage of data and documents

7.4.1 Qualitative data

Personal data (i.e. name, home address, e-mail address, telephone number) are needed to identify subjects when contact is needed. The personal data is stored in an Access database (key table) and linked to a personal identification number (pseudonym). Only some researchers and the research assistant have access to this database. The database is stored in a separate, secure folder on the Radboudumc drive (H:sleutelbetanden/CL-Ketenzorg Ontketend). The pseudonym is used in ATLAS.ti to identify a test subject. We make audio recordings of the focus groups. These will be transcribed in Word and stored on These transcripts will not contain the names of the study subjects, only the pseudonyms (if necessary). The Word documents are permanently saved as PDF and imported into ATLAS.ti. The pseudonymised data are stored for 15 years.

7.4.2 Quantitative data

If the subject has indicated a preference for a paper version of the questionnaires, they will be sent by regular mail (including a reply envelope) and the data will be entered into Castor

EDC by the study employee. The papers are kept in a locked cabinet in room 3.20 (technical room number M245.03.350) for the duration of the project. Traceable data will be stored separately from the questionnaires for the duration of the pilot, i.e. in a different another locked cabinet, but in the same room. Afterwards, research data will be entered into the ELG archive (technical room number M245.-02.053). Identification Log and Informed Consent forms are stored in a closed cabinet in the ELG archive, thus separate from the data. In Castor no personal data is stored. The data is exported to SPSS for analysis. The pseudonymised data is stored for 15 years.

7.5 Public disclosure and publication policy

Science: The findings of the project will be published in international health-related scientific peer-reviewed journals, and will serve as the basis for the thesis of the GP trainee / PhD candidate on the project. Apart from the international papers, a summary paper with the main findings will be prepared for Dutch medical journal (Huisarts & Wetenschap, Nederlands Tijdschrift voor Geneeskunde). The results will also be presented at at least two international conferences on primary care or integrated care. On the national level, the results will be presented at the Dutch GP science day (NHG Wetenschapsdag) and the conferences of the GPs with special interest groups for respiratory care (CAHAG), diabetes care (DIHAG) and cardiovascular disease care (HartVaatHAG), and at least one national conference on integrated care.

Clinical practice: During the final phase of the project, when the trial has been finished, the data have been analysed and the final results are available, a 1-day national symposium will be organized to present and discuss the findings and their implications. All relevant stakeholders will be invited for this symposium, i.e. representatives of all integrated general practice care groups ('zorggroepen') in the country, health policy makers (ministry of health (VWS), Zorginstituut Nederland, InEen, others), the professional organisations of GPs (LHV, NHG), practice nurses (V&VN Praktijkverpleegkundigen & Praktijkondersteuners), physiotherapists (KNGF), medical specialists (especially chest physicians/NVALT and internal medicine specialists/NIV), health insurance companies, relevant charities (Lung Foundation, Diabetes Foundation, Heart Foundation) and funding bodies (ZonMw, NutsOhra Fund), and patient organisations (NPCF) will be invited. The results will also be brought to the attention of the bodies responsible for the national clinical practice guidelines (NHG, Federation of Medical Specialists, others).

Education: If the GDM approach for patients with chronic diseases in primary care turns out to be effective, the training for practice nurses and GPs that is developed for the project will be made available to all (primary) care organisations that want to switch to this new approach. The best way to organize broad access to the training will be explored during the final year of the project. The preferred approach will probably be to use existing channels for postgraduate training of primary care professionals, for instance through the NHG (or its special interest groups) and V&VN. In the exploration we will also consider the best way to facilitate uptake of (parts of) the training in the vocational training programs for practice nurses

Society: Together with the PR/communication department of Radboudumc we will develop a strategy to disseminate the findings to the national press, to other popular media and directly to organisations that have an interest in the findings (e.g., health insurance companies, chronic care groups etc.). The investigators will be prepared to present and discuss the findings at non-scientific meetings (e.g., for health policy makers, regional care organisations etc., available time allowing) in the year after the project has finished.

The trial will be registered at clinicaltrials.gov

All data will be made available from the principal investigator, upon reasonable request

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