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Effectiveness of an adaptive, multifaceted intervention to enhance care for patients with complex multimorbidity in general practice: protocol for a pragmatic cluster randomised controlled trial (the MM600 trial)

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ABSTRACT

Introduction Patients with complex multimorbidity face a high treatment burden and frequently have low quality of life. General practice is the key organisational setting in terms of offering people with complex multimorbidity integrated, longitudinal, patient-centred care. This protocol describes a pragmatic cluster randomised controlled trial to evaluate the effectiveness of an adaptive, multifaceted intervention in general practice for patients with complex multimorbidity.

Methods and analysis In this study, 250 recruited general practices will be randomly assigned 1:1 to either the intervention or control group. The eligible population are adult patients with two or more chronic conditions, at least one contact with secondary care within the last year, taking at least five repeat prescription drugs, living independently, who experience significant problems with their life and health due to their multimorbidity. During 2023 and 2024, intervention practices are financially incentivised to provide an extended consultation based on a patient-centred framework to eligible patients. Control practices continue care as usual. The primary outcome is need-based quality of life. Outcomes will be evaluated using linear and logistic regression models, with clustering considered. The analysis will be performed as intention to treat. In addition, a process evaluation will be carried out and reported elsewhere.

Ethics and dissemination The trial will be conducted in compliance with the protocol, the Helsinki Declaration in its most recent form and good clinical practice recommendations, as well as the regulation for informed consent. The study was submitted to the Danish Capital Region Ethical Committee (ref: H-22041229). As defined by Section 2 of the Danish Act on Research Ethics in Research Projects, this project does not constitute a health research project but is considered a quality improvement project that does not require formal ethical approval. All results from the study (whether positive, negative or inconclusive) will be published in peer-reviewed journals.

Trial registration number NCT05676541.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is a large trial with a 2-year implementation period ensuring time for implementation, but the follow-up of 2 years may not be long enough to capture the full effect of the intervention.
⇒ The pragmatic nature of the trial improves the external validity to health systems comparable to the Danish but limits the capacity to ensure full adherence to the intervention elements.
⇒ We will not have data on the patient-reported baseline and outcome data on all eligible patients, but we will have data on register-based outcomes on all patients allowing us to weigh our patient-reported outcomes to represent the entire population.
⇒ We have planned to measure a number of patient-reported and register-based outcomes but have not yet planned a formal economic evaluation.

INTRODUCTION

Multimorbidity, which refers to patients having more than one chronic condition, is prevalent and associated with multiple negative health outcomes.[1 2] The prevalence of multimorbidity is increasing over time, ranging from 12.9% to 95.1%, depending on definitions and study population, and

increases with age and patients with low socioeconomic status.[3–5] Multimorbidity is linked to lower quality of life, functional decline, polypharmacy and higher healthcare utilisation.[6–9] Frequently, patients with multimorbidity must attend multiple appointments, often at various locations, and comply with complicated or even contradictory advice and drug regimens.[10 11] Multimorbidity becomes more complex for the patient as the number of conditions, drugs and healthcare contacts increases and can be exacerbated by psychosocial and contextual factors.[12–14] In recent years, the concept of complex multimorbidity is used more often, as an attempt to identify the patients who have the most contacts in the healthcare system, have the highest mortality and experience the most problems in everyday life due to their multidisease, but there is still a lack of consensus and a clear definition.[15 16]

In Denmark, general practice is the key organisational environment for providing integrated, longitudinal, patient-centred care to persons with (complex) multimorbidity. Chronic care in general practice is currently organised around specific conditions.[15 16] This model is suitable neither for patients nor general practitioners (GPs).[17] Patient-centred care has been promoted through decades as a way to design healthcare systems to meet the patient's needs and as a way to approach the patient in individual consultations.[18 19] In this protocol, we use the term patient-centeredness to describe a communicative and structural approach in individual consultations in which the doctor seeks to understand the patient's perspective and develop the care plan in collaboration with the patient.

Several interventions have been attempted in primary care to improve outcomes for patients with multimorbidity, with no evident effect on clinical results, some effect on mental health outcomes and mixed effects on other patient-reported outcomes, such as health-related quality of life.[20–23] In Danish general practice, a feasibility trial including patients with complex multimorbidity and a pilot trial including patients with severe mental illness and somatic comorbidity have laid the foundation for this trial.[24–27] In the evaluation of these studies, the GPs reported that more time in individual consultation increased the GP's opportunity to involve patients in problem prioritising; to incorporate clinical, social and personal factors and resources in the treatment burden analysis; and to improve cross-sectoral collaboration. All of these elements, extended consultation time, patient involvement, overview, prioritisation and coordination, have previously been identified as key elements in improving care for patients with complex multimorbidity.[28–33] The intervention has been developed through experiences from these previous trials rather than through a formal development process and is currently under evaluation in a pilot trial in 14 general practices in two Danish regions.

This protocol describes a study with the objective to evaluate the effectiveness of a multifaceted intervention targeted at those patients with multimorbidity believed to be most burdened by their conditions, in the following referred to as 'complex multimorbidity' on need-based quality of life, as well as other patient-reported outcomes, health-related outcomes and the use of healthcare services. The intervention consists of access to reimbursement for an extended consultation in general practice, aiming to increase patient-centeredness, obtain an overview of the patient's treatments, prioritise treatment and coordinate care.

METHODS AND ANALYSIS

This study is reported following the Standard Protocol Items: Recommendations for Interventional Trials reporting guidelines (https://www.spirit-statement.org/). See online supplemental material 1

Trial setup and design

Design

This study is a pragmatic, adaptive, cluster-randomised, non-blinded, parallel-group controlled trial run in general practice. The trial is adaptive in the sense that elements of the intervention will be developed based on early trial findings and implemented subsequently during the trial period. The pragmatic nature of the trial indicates that there is no continuous data collection in participating practices, and all outcomes will be obtained from routine registry data and questionnaires. We have chosen this design to ensure high external validity and ease of implementation. However, this design poses a number of complexities, to identify the population for follow-up, to ensure sufficient adherence to the intervention and to collect data on patient-reported outcomes from a sufficient number of patients to identify the effects of the intervention. In addition, a process evaluation will be carried out. Methods and results from this will be reported elsewhere.

Setting

The Danish Regions and the General Practitioners' Organization have negotiated a contract outlining the content, terms, framework requirements and quality measures for this project. According to the contract, the project must be carried out as a scientific study, which is described in this article. A fee-for-service benefit will be implemented to compensate for the time spent by participating GPs for the described focused and interdisciplinary efforts. Participation is voluntary for the GPs.

In Denmark, basic healthcare is free, and all patients are assigned a GP. General practice is organised with the GPs as owners of the practice. In 2022, Denmark had 3488 GPs and 1675 practices, with 41% of these being solo practices with only one GP capacity associated.[34] All patients in primary care who are suffering from a chronic condition may be offered an annual condition-specific check-up in general practice for each chronic condition. Frail elderly and other patients living in assisted facilities can receive an annual extended home visit with, among

others, a medication review. In Denmark, 96% of general practices are affiliated with 1 of 115 quality clusters, each coordinated by a GP. These quality clusters aim to support data-driven quality improvement in general practice.

Identification, eligibility assessment and recruitment

Recruitment and eligibility of quality clusters and general practices

Practices were invited to join by the coordinators of their respective quality clusters. The practices included in the cluster that wished to participate were registered. All general practices with permanent staff in Denmark could participate. We excluded general practices without permanent staff or clinics managed by private firms due to lack of continuity of care, which we considered was a critical underlying component of the intervention's hypothesised effect.

The research team contacted all quality cluster coordinators by email in June 2022 to inform them about the trial and to invite them to join in September 2022.

Patient population

To identify those patients who have the most contacts in the healthcare system, have the highest mortality and experience the most problems in everyday life due to their multidisease (complex multimorbidity), we used a slightly adapted version of the definition of multimorbidity used in the feasibility trial since it includes at least two aspects of the treatment burden concept (medicine and medical appointments), and it was deemed acceptable to identify the majority of patients, whom the GPs thought could benefit from an extended consultation.[14 24] Frail elderly and other patients living in assisted facilities already have access to extended home visits and were therefore not eligible for this trial.

Patients eligible for the intervention and follow-up should be adult (18 years or older) patients listed at participating GPs and:

1. Have two or more chronic conditions (any condition)
2. Have had at least one contact with secondary care in the previous year (inpatient or outpatient)
3. Take at least five prescription medications (repeat prescriptions)
4. Live independently in their own home with or without help from the municipalities

Identification of the patients to receive the consultation

GPs are encouraged to offer extended consultation to patients who meet all the inclusion criteria and, based on their clinical understanding, experience major challenges with their life and health (see box 1). This definition in box 1 was put to the test while recruiting focus groups for a previous study.[35] We included this criterion because we assume the population (30–100 patients per GP capacity; see sample size) to be larger than the number of consultations possible to deliver per GP per year, and we want to provide the consultation to patients who are most burdened by their multimorbidity. We estimated based on clinical experience and the current strain on general practice that most practices would be able to implement a maximum of 15 consultations per GP capacity per year.

Box 1 Qualitative definition of complex multimorbidity for when general practitioners identify those patients most burdened by their multimorbidity

Adult patients with complex multimorbidity can be defined as patients 18 years or older who have at least two chronic diseases, as well as experience major challenges with their life and health as a result of their multimorbidity.

The challenge associated with the coexistence of the two chronic diseases may be biomedical; multiple chronic diseases from separate organ systems or one or more of the diseases are recently diagnosed or poorly regulated. Problems can also be psychosocial; the patient has a limited social network, gets anxious or insecure or feels limited physically and socially confined by his illnesses. Finally, the issues can be seen in the patient's relationship with the healthcare system; the patient has difficulties keeping appointments or feels let down by the healthcare system.

Identification of the population for follow-up

Since this concerns a pragmatic trial, there will be no continuous data collection in the practices. Follow-up will occur through the Danish registries and additional data sets collected at baseline by GPs and patients (see the section on data collection). Every Danish citizen is assigned a unique identity number that allows linkage between public registers and other data sources. The Danish health registries contain all diagnoses registered at inpatient and outpatient clinics and emergency wards in Denmark from 1977, though they do not contain diagnoses from GPs. Criteria 2–4 can easily be identified in the Danish registries. Criterion 1 (the number of conditions) is challenged by the fact that some diagnoses are only registered in general practice and thus not available in the registries. To identify patients fulfilling criterion 1, we will use a combination of the Danish registries, data provided by the GPs at baseline and data provided from the patients responding the trial questionnaire. Criterion 1 is fulfilled if (1) the patients have reported that they have at least two chronic conditions in the questionnaire, (2) if the patients were identified by the GP with complex multimorbidity at baseline or (3) they have at least two chronic conditions in the registries. The three data sources are described in the data collection section.

The intervention

The intervention consists of financial support to offer an extended overview consultation aiming to

1. Increase patient-centeredness (listen to the patients story and everyday problems, let the patient take an active part in the treatment plan and provide prioritisation)
2. Obtain an overview of the patient's treatments (in cooperation with the patient)
3. Prioritise treatment (by giving some problems more attention than others and possibly defer from guidelines to minimise treatment burden)

4. Coordinate care (in cooperation with the patient)

In the first phase (2023), the GPs are provided with written structural support to implement the consultation (reimbursement, inclusion criteria and suggestions for implementation; see online supplemental files 2–4), and in the second phase (2024), we aim to provide the GPs with additional tools to support elements identified in 2023 as difficult to master. All the details mentioned below are suggestions for the participating GPs. The main element in the intervention is the structural setup with reimbursement to allocate time to perform these tasks. The consultation takes place on a single day and always with the patient's regular doctor since we presume that relational continuity is a key element of our intervention.

The consultation is based on a guideline from the Danish College of General Practitioners,[36] which was adapted for the trial in cooperation with the original authors of the guideline. In the ideal version, the full consultation consists of three phases. All parts are taken care of by the GP and the patient without any delegation to staff.

1. The preparation of the consultation
2. The consultation
3. The follow-up on the consultation

During the preparation phase, patients are encouraged to think about which health problems they experience as well as what concerns or worries them in their daily lives. The only formal tool to support this preparation is a proposal for an email the GP can send to eligible patients. The doctor prepares for the consultation by creating a summary of diagnosis, medication and health system contacts in the electronic health record. This phase is supported by a proposed 'phrase' for the electronic health record. Since follow-up happens at population level, the patients do not have to consent to anything beyond participating in the consultation. GPs are not told whether or not the patients have completed the baseline questionnaire when offering the intervention.

The consultation involves the patient, potentially a relative to the patient and the patient's regular physician. The consultation is structured into three sections: the patient's part, the physician's part and the shared part. Since the 1990s, this way of promoting a communicative approach and structure to consultations to promote patient-centeredness has been taught and practised in Denmark and is quite well known and established among Danish GPs.[37–39] Although it has been developed for acute encounters, it is also suitable for a holistic follow-up visit for chronic disease, and it is also mentioned in the existing guideline from the Danish College of General Practitioners.[36] We decided to use this well-known framework rather than developing a new one to ease implementation. On the patient's part, the doctor seeks a common understanding of the agenda for the consultation and uses open-ended questions to explore how the patient experiences symptoms, worries, problems with processes in the healthcare system and problems with medication. We propose two specific headlines for this part (online supplemental file 4): (1) seek a common understanding for the consultation agenda and (2) ask about symptoms, worries, problems with care pathways in the healthcare system and medication. On the physician's part, the doctor can present their own overview of diagnosis and medication from the preparation phase and ask the patient to fill in the gaps. On the shared part, the physician and the patient combine the preceding two parts and agree on a prioritised care plan that takes both the physician's and the patient's perspectives into account. The structure of the consultation is supported by a quick guide with a visual overview of the three phases in the consultation (online supplemental file 4). The importance of the patient's part is stressed in all information meetings (see implementation support section below).

In the follow-up phase after the consultation, the doctor writes the prioritised care plan in the electronic patient files. The plan can be seen by the entire team in practice and can be electronically shared with the healthcare centre in the municipality and the outpatient clinics relevant to the patient. The possibility to share information electronically is an integrated part of the Danish healthcare system's electronic infrastructure. The only new thing is the allocated time to make an integrated care plan and share it. If considered relevant, the GP might organise a reimbursed multidisciplinary video conference with hospital specialists. The intervention is visualised in figure 1.

Implementation support in the first phase (2023)

At baseline, practices receive an 'implementation start kit' with a quick introduction to implementation (see online supplemental files 2-4). All practices can sign up for online information meetings, which are held monthly from the beginning of implementation and as long as needed. Additional tools to support the intervention are made available on the project's website.[40]

Implementation support in the second phase (2024)

Based on the findings during the first year after implementation, we plan to develop additional intervention support elements aiming to support one or more of the elements: (1) how to promote patient-centeredness, (2) how to prioritise treatments, (3) how to make shared decisions and (4) how to coordinate across sectors. These elements will be deployed in early 2024.

The control group

Practices allocated to control will continue to provide care as usual, as described under 'setting', meaning each chronical condition can be attended to in an annual consultation, but there is no reimbursement for an extended consultation. Elements of the intervention may also take place in the control group, merely without any formal reimbursements.

Concomitant care

24 months after randomisation, any new interventions or initiatives undertaken by local health authorities,

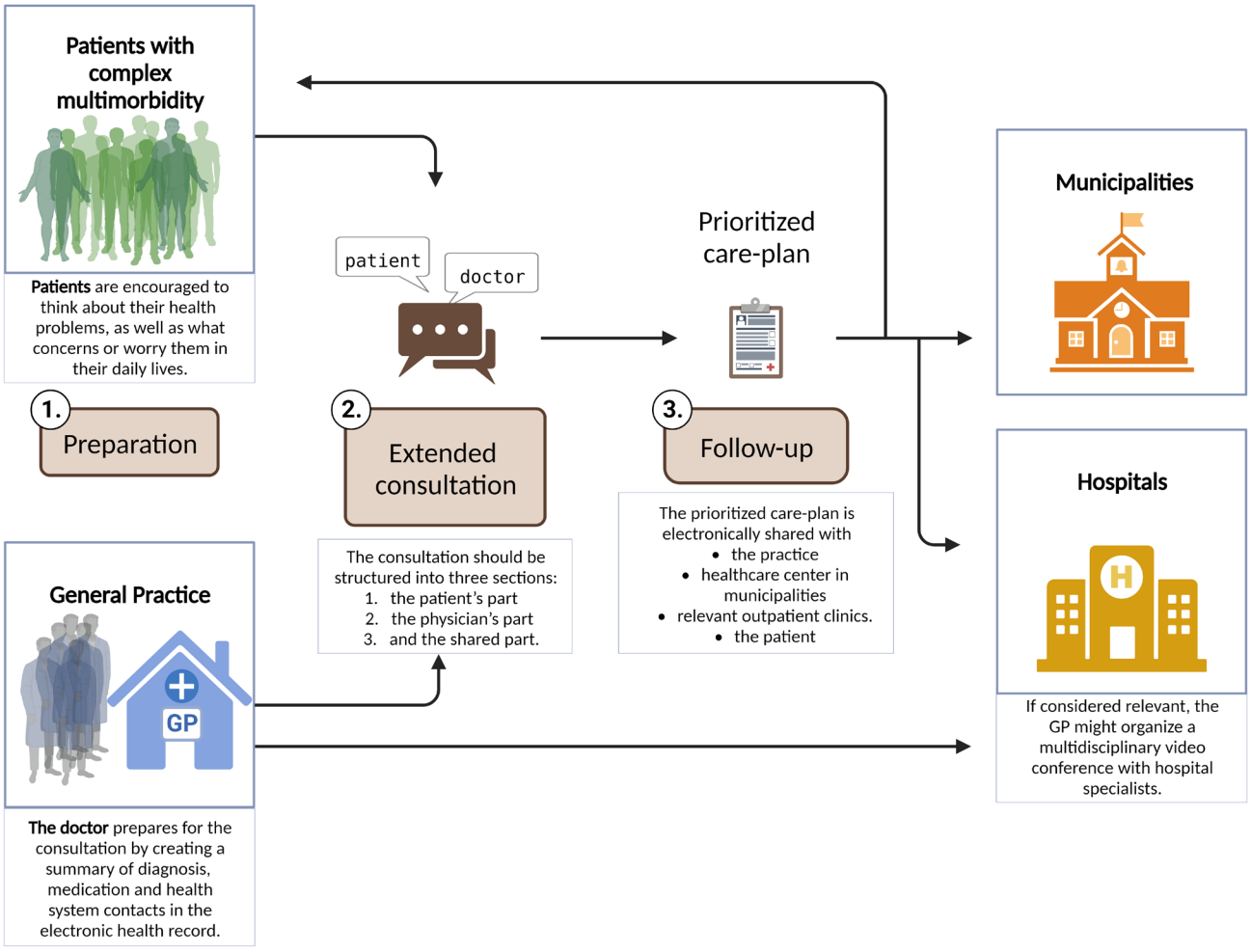

Figure 1 Elements in the multifaceted intervention. Created with BioRender.

municipalities, researchers and health organisations focusing on healthcare for people with multimorbidity will be recorded.

Outcomes and data sources

Table 1 shows the outcomes of the trial. The primary outcome is need-based quality of life measured with the MultiMorbidity Questionnaire 1 (MMQ1).[41 42] The sources are described in more detail in the 'data sources' section. All questionnaire-based outcomes will be measured by the end of 2024 or in early 2025. The registries will not be updated before mid-2025, and data will be collected retrospectively at that point. We hope to perform a long-term follow-up after 3–5 years along with an economic evaluation.

Timeframe

We plan to evaluate all outcomes in the first quarter of 2025. In September 2022, quality clusters were recruited. Practices were contacted and included from October to December 2022. The randomisation took place on 10 January 2023. Clusters were assigned to intervention or control as they completed data collecting from January through March 2023. Baseline data collection from practices ended on 19 February 2023, and the allocation for the remaining practices was disclosed on 1 March 2023. The baseline patient questionnaire was also distributed on 1 March 2023. The first consultations could begin in February 2023. The intervention phase will end in December 2024, and data collection from patients will be completed in mid-2025. The timeframe for the study is depicted in figure 2.

Data sources

GP questionnaire

During the first data collection, participating GPs are asked to report data on practice organisation and structure, as well as whether anyone in practice has recently received multimorbidity training or initiatives. They are also asked to provide data on 5–10 patients with complex multimorbidity from their patient population and whom they recognise 'off the top of their heads' based on the definition in box 1. Each participating GP is also asked to answer six questions about the challenges of working with patients with multimorbidity addressing the following

Table 1 Outcomes for the trial, how and when data will be collected

Outcome	Measure	Source	Variables	Timeframe for the final follow-up
Primary outcome				
Need-based quality of life (MMQ1)	Difference in change from baseline to follow-up between randomisation groups	Patient questionnaire	Domains: physical ability, worries, limitations in everyday life, my social life, self-image,and personal finances	Early 2025
Secondary outcomes				
Treatment burden (MMQ1-TB)	Difference in change from baseline to follow-up between randomisation groups	Patient questionnaire	Domains: information, medicine, health system challenges, self-monitoring and health advice	Early 2025
Patient-perceived patient-centredness of consultations (PCC-GP)	Difference in change from baseline to follow-up between randomisation groups	Patient questionnaire	Domains: relation between the doctor and the patient, participation in the consultation, taking responsibility, communication and information, involvement in the treatment plan, attention to relatives and network, attention to everyday life and coordination	Early 2025
Mortality	Difference in incidence in 2024 between randomisation groups	Registries	The Danish Civil Registration System and Statistics Denmark's registers: date and time of death	Mid-2025
Nursing home placement	Difference in incidence in 2024 between randomisation groups	Registries	AEPB: date of nursing home placement	Mid-2025
Hospitalisations	Difference in incidence in 2024 between randomisation groups	Registries	Register, the Danish National Patient Register (NPR, NPR-PSYK): hospital admittances	Mid-2025
Number of prescription medicines	End of study (2024)	Registries	The Danish National Prescription Register: redeemed repeat prescriptions	Mid-2025
Use of unplanned hospital services, emergency room contacts and out-of-hours services	Difference in incidence in 2024 between randomisation groups	Registries	Register, the Danish National Patient Register (NPR, NPR-PSYK): emergency care contacts	Mid-2025
Use of standard chronic care services in general practice	Difference in incidence in 2024 between randomisation groups	Registries	The National Health Insurance Service Register (SSR/Yderregisteret (YDR)): date and type of chronic care consultation	Mid-2025
Use of standard consultation forms in general practice	Difference in incidence in 2024 between randomisation groups	Registries	The National Health Insurance Service Register (SSR/Yderregisteret (YDR)): date and type of other consultations (telephone/email/office/home visit)	Mid-2025
Use of other primary care health services (such as private specialists)	Difference in incidence in 2024 between randomisation groups	Registries	The National Health Insurance Service Register (SSR/Yderregisteret (YDR)): date of consultation, type of specialist	Mid-2025
Use of outpatient and other planned health services in secondary care	Difference in incidence in 2024 between randomisation groups	Registries	The Danish National Patient Register (NPR, NPR-PSYK): outpatient contacts	Mid-2025
Use of health services provided by the municipalities	Difference in incidence in 2024 between randomisation groups	Registries	Date of home nurse visit (AEHJSP), preventive home visit (AEFB), minutes of home visit per week (AELH)	Mid-2025
Cross-sectoral continuity of care (continuity of care index)	Difference in index score between randomisation groups in 2024	Registries	The National Health Insurance Service Register (SSR/Yderregisteret (YDR)) and the Danish National Patient Register (NPR, NPR-PSYK)	Mid-2025

Continued

Table 1 Continued

Outcome	Measure	Source	Variables	Timeframe for the final follow-up
GP work challenges related to care for patients with multimorbidity	Difference in change from baseline to follow-up between randomisation groups	GP questionnaire	Six questions regarding challenges with overview, time, help from other specialists, medication reviews, prioritisation and patient involvement	Late 2024

GP, general practitioner; MMQ1, MultiMorbidity Questionnaire 1.

topics: overview, time constraints, seeking assistance from other doctors, priority, medication reviews and patient involvement. The questions for the GPs about their experiences and potential challenges when consulting with patients with multimorbidity were developed based on a qualitative literature review.[43] Data collection from practices takes place in late 2022, late 2023 and late 2024.

Data collection from patients

For questionnaire follow-up, we will use a cohort identified through the Danish Health Data Authority. In Denmark, all citizens have a civil registration number (CPR), which enables researchers to contact them based on predefined criteria. The cohort includes all adults (18 years or older) who had attended at least one annual chronic disease consultation in general practice in 2022 and who were listed by participating GPs on 1 January 2023 (based on GP reimbursement data). We used this broader definition to make sure we captured patients not registered with two chronic conditions in the Danish registries. Patients in this cohort will be contacted via secure electronic email and asked to complete an electronic questionnaire. The questionnaire comprises three patient-reported outcome measures (PROMs) plus a basic questionnaire on their health and chronic conditions. The first PROM, the MMQ1, measures need-based quality of life and is described thoroughly in the validation studies.[41 42] It

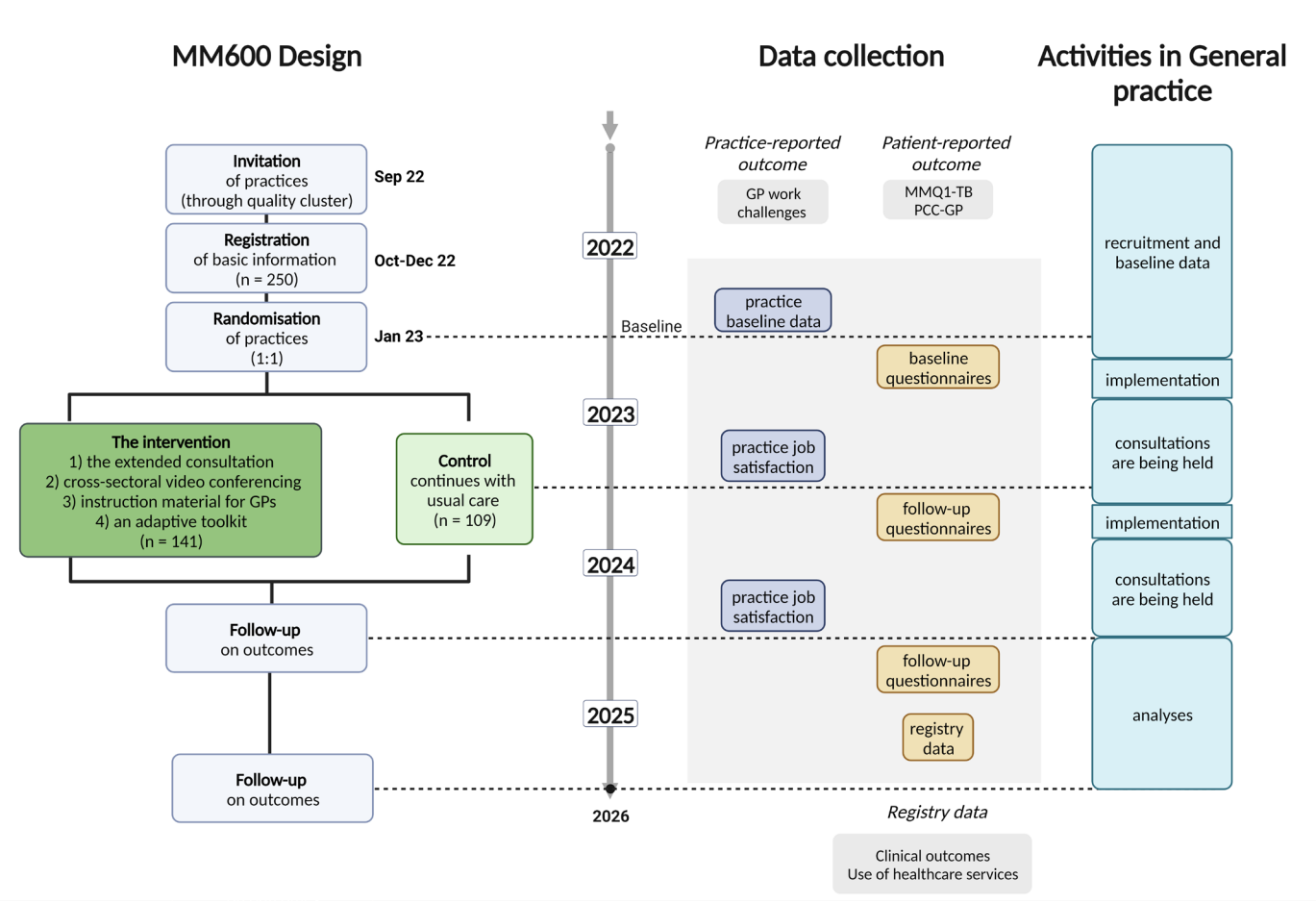

Figure 2 Timeline for the trial. Created with BioRender. GPs, general practitioners; MMQ1-TB, MultiMorbidity Questionnaire 1-treatment burden; PCC-GP, patient-centredness of consultation-general practitioner.

consists of six unidimensional scales: physical ability (6 items), worries (6 items), limitations in everyday life (10 items), my social life (6 items), self-image (6 items) and personal finances (3 items).

The second measure, the MMQ1-treatment burden (MMQ1-TB), is a newly developed and yet unpublished PROM for measuring the workload and exacerbating factors of the treatment burden concept.[14] The MMQ1-TB was developed to supplement the MMQ1 without having redundant questions. It consists of domains regarding information, medicine, health system challenges (including medical appointments and challenges with contacts to the health system), self-monitoring and health behaviour. The third PROM, the patient-centredness of consultation-general practitioner, is also new and unpublished, and it assesses patient-perceived patient-centeredness of the overview consultation or the most recent chronic disease consultation based on the framework by Langberg *et al*.[19] It encompasses items regarding the relation between the doctor and the patient, participation in the consultation, taking responsibility, communication and information, involvement in the treatment plan, attention to relatives and network, attention to everyday life and coordination of care. We decided to use a new measure for quality of life since previous measures have been shown to be quite insensitive to change, and a recently published systematic review failed to identify suitable PROMs for our purpose.[21 44] The patient questionnaires will be distributed in the first quarters of 2023, 2024 and 2025, respectively. We expect a response rate of 20%–40%.[45 46] The translated consent form can be seen in online supplemental file 5.

Data collection from registries

The Danish Civil Registration System (CRS) and Statistics Denmark's registers will provide patient-level information on age, sex, civil status, degree of urbanisation, income, assets, work status, highest completed education, immigration, emigration, nursing home residing and deaths to the study. The CRS holds information on all (live) born children in Denmark as well as all immigrants through an assigned unique identity number that allows linkage between public registers. The register is thought to have high validity because it is used for administrative purposes, registration is required by Danish law and weekly upgrades and corrections are made.[47] The Danish National Patient Register (NPR, NPR-PSYK) provides the study with information on hospital admittances, outpatient care contacts, emergency care contacts, examinations and procedures performed in secondary care, both at public and private hospitals. NPR is considered complete after the year 2000 when diagnosis reporting became the basis for reimbursements for Danish hospitals.[48 49] The Danish National Prescription Register delivers information on redeemed prescription medications since 1995. Data on primary care activity, including contacts to GPs and private practice specialists, will be retrieved from the National Health Insurance Service Register. Information on providers will be obtained from Yderregisteret. Finally, the Patient Database contains information about patients listed in each practice.

Allocation, sequence generation and concealment

The study is a randomised controlled trial using quality clusters as the unit of randomisation to ensure quality clusters can collaborate on the implementation of the intervention. The quality clusters were randomised using a computer algorithm that used a 1:1 allocation stratified by geographical region (five in Denmark) and the number of participating practices per cluster. The allocation (which of the groups was the intervention group) was selected by a University of Copenhagen employee who was not involved with the trial and worked in a different section. The allocation of a cluster was concealed from the researchers until all general practices in a cluster had completed data collection. The randomisation took place in January 2023.

Sample size and power calculation

The politically negotiated agreement specified a sample size of 5–600 GPs, and the collective agreement funding covered 10 000 consultations every year for 2 years. We were encouraged to go as close to this figure as feasible. In Denmark, there are 115 quality clusters, each with an average of 14 practices and 28 GPs attached.

250 practices with about 700 GPs (400 in the intervention group) affiliated divided into 42 quality clusters were enrolled in the trial.

Our inclusion criteria would be met by about 2%–7% of the adult Danish population, and a GP capacity has around 1400 adult patients listed.[4] As a result, per GP capacity, 30–100 patients are eligible for this trial. Thus, the total population would consist of 21 000–70 000 patients out of which 6000–12 000 could potentially receive a consultation if all intervention GPs deliver 15 consultations per year depending on whether the GPs choose the same patients or new ones each year. If GPs turn out to be able to deliver more than 15 consultations per year, the funding allows 10 000–20 000 patients to receive the intervention. However, we are measuring the whole-practice effect in the intention-to-treat analysis and not just those who have received the intervention.

In our primary outcome measure, the cumulative score in each domain is determined by the number of items in the domain: physical ability (0–18, SD: 4.47), worries (0–18, SD: 4.83), limitations in everyday life (0–30, SD: 6.83), my social life (0–18, SD: 4.60), self-image (0–18, SD: 4.74) and personal finances (0–9, SD: 3.05).[41] We expect a response rate on the primary outcome of 20%–40%.

Thus, in the most conservative estimate, 250 practices would have a population of 84 patients each out of which 17 would deliver data to the primary outcome (response rate, 20%). We will be able to detect the following differences with a power of 0.80 at the 0.05 significance level using the conservatively predicted sample size, taking clustering into account, and an intraclass correlation

of 0.1: physical ability, 0.96 points; worries, 1.03 points; limitations in everyday life, 1.46 points; my social life, 0.98 points; self-image, 1.01 points; and personal finances, 0.65 points.

Blinding (masking)

Before reporting baseline data, GPs were blinded to their allocation. Due to the nature of the intervention, blinding participants, care providers or other members of the research team after the allocation will be impossible. The statistician and data manager are unaware of the allocation until after the primary outcome is analysed.

Statistical analyses

Continuous outcomes will be analysed using linear regression models, while logistic regression models will be used to analyse binary outcomes. The generalised estimating equation (GEE) method will be used to account for repeated measurements and patient clustering in practices and quality clusters. The intention-to-treat principle will be used in the primary analysis of all outcomes. To adjust for possible differential attrition, inverse probability weighting will be applied.[50] We also intend to do two per-protocol analyses. We will divide the population into three groups in the first per-protocol analysis: (1) patients in the intervention group who received the consultation, (2) patients in the intervention group who did not receive the consultation and (3) patients in the control group. In the second per-protocol analysis, we will divide the intervention group practices into three groups based on the number of overview consultations completed during the intervention period and compare these three groups to the control group. The following four groups will be (1) patients listed in a 'high-implementing' practice (upper third), (2) patients listed in a 'medium-implementing' practice (middle third), (3) patients listed in a 'low-implementing' practice (lower third) and (4) patients listed in a control practice.

Predefined subgroups for follow-up

1. Diagnoses from different organ systems[4]: one, two, three, four or five or more.
2. Patients with complex multimorbidity identified by GPs versus those who were not identified

Patient and public involvement

Patients will be invited to comment on and guide various aspects of the research process, such as research materials to improve clarity and readability. Furthermore, patients will be interviewed about the intervention, how it works for them and how it can be adapted to their needs. Reporting of patient involvement in this study will be done according to the 'Guidance for Reporting Involvement of Patients and the Public checklist'.[51]

ETHICS AND DISSEMINATION

Data management and confidentiality

The study will strictly adhere to Danish law concerning human medical research and the protection of any personal information. The General Data Protection Regulation is upheld, and data are stored and handled in accordance. All personally identifiable information will be encrypted and securely kept on password-protected servers with transaction logging. Trial data are stored in accordance with the University of Copenhagen's data policy. Data are kept for 10 years after collection before being anonymised or deleted. Prior research has shown that capturing the long-term impact of diverse interventions takes 10 years.[52] The principal investigators will have access to the data sets. Project data sets will be stored on a secure server hosted by the University of Copenhagen. To guarantee confidentiality, project team members' access to data will be blinded to any identifiable participant information.

Ethics approval

The trial will be conducted in accordance with the protocol and the Helsinki Declaration in its most recent form. Good clinical practice guidelines will be followed as will the rules for informed consent. No substantial deviations from the protocol will be implemented without the regulatory authorities' prior review and approval. According to Section 2 of the Danish Act on Research Ethics of Research Projects, this project does not constitute a health research project but is rather considered a quality improvement project. The study was presented to Denmark's Capital Region's Ethical Committee for confirmation (ref: H-22041229). According to Danish legislation, passing on patient information in quality projects does not require informed consent from individual patients. According to the Danish Health Act Section 42d (paragraph 2, no 2), obtaining and sharing patient data for quality improvement projects requires approval from the leader of the treatment site, in this case the general practice. In this project, we wanted data collection to be as straightforward as possible for the participating GPs in this research so that GPs in deprived areas with a high workload might participate. We informed the GPs that informed consent from patients was not required by law, but we urged them to collect it if they believed that not informing the patient would jeopardise the doctor-patient relationship. All patients were informed about the trial when they received the first questionnaire.

Protocol amendments

Any changes to the protocol that may have an impact on the study's conduct, such as changes in study objectives, sample size or major administrative changes, will demand a formal amendment to the protocol. Such amendment will be agreed on by the steering committee and the primary funder.

Dissemination policy

All results from the study (whether good, negative or inconclusive) will be published in peer-reviewed journals. The final list and order of authors will reflect each researcher's contribution and will comply with the Vancouver recommendations as well as the requirements of the Danish Committees on Scientific Dishonesty.

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Contributors AH, ABL, MR, SFB, A-KLC, JK, JSA, FBW, VS, JBB and SR took part in the weekly meetings in which the design of the study was decided and data collection was planned. TGW and AP specifically planned the collection and evaluation of the register-based outcomes. VS planned the statistical methods. AH and ABL have conducted the trial and facilitated the data collection with help from TGW and AP regarding the registry-based data. AH wrote the first draft of the article with input from SR, MR and FBW and later ABL, SFB, A-KLC, JK, JSA, VS, JBB, TGW and AP. All authors made significant contributions to the manuscript and approved the final version.

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Competing interests FBW declares having had received funding for research from the Novo Nordisk Foundation and the Velux Foundation. SR declares being a member of the steering committee for the Steno Diabetes Center in Region Zealand on behalf of the institute, without receiving any financial compensation. All other authors declare that they do not have any conflicts of interest.

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