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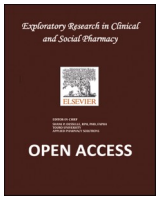

Development of a medication review intervention by seconding a hospital pharmacist to primary care

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ABSTRACT

Background: Medication reviews (MRs) are a well-described initiative that improves health outcomes for polypharmacy patients. However, there is limited knowledge about the performance of medication reviews carried out in general practice especially under the leadership of hospital clinical pharmacists. When developing complex interventions, such as MRs, it is essential to describe the development process to ensure transparency and avoid research waste.
Objective: Thus, this study aimed to describe the steps of developing a new MR intervention targeting general practice to ensure transparency and transferability.
Methods: A stepwise approach inspired by the Medical Research Council framework was utilised in the process, covering two of the phases, i.e., development and feasibility, divided into four steps: 1) intervention drafting by a literature search, 2) expert opinion, 3) pilot testing in general practice clinics, and 4) evaluation of quantitative MR data.
Results: Based on the results from the first three steps, four main themes which influenced the success of the MR intervention were identified: general practitioner resources, patient involvement, implementation difficulties and interdisciplinarity. These themes guided the pilot evaluation in step four.
Conclusion: A new feasible, complex MR intervention utilising clinical pharmacists in general practice involving hospital clinical pharmacists in a real-life setting was developed.

1. Background

An increasing number of people today are treated regularly with numerous drugs. More than half of the population of 75 or above is categorised as polypharmacy patients, i.e., treatment with five or more different concurrent prescription drugs daily.[1] Polypharmacy is associated with an increased risk of drug-related problems such as side effects,[2] drug interactions,[3] falls,[4] hospitalisations[5] and mortality.[6]

It has previously been shown that medication review (MR) reduces the number of drug-related hospitalisations and other drug-related problems.[7–10] This can lead to increased quality in drug treatment[11,12] and financial savings.[13,14] A new update of a Cochrane Review regarding the effects of MR interventions in hospitalised adult patients found that MR is likely to reduce hospital readmissions and may reduce emergency department contacts.[15]

However, performing MRs are a comprehensive and time-consuming process that can be difficult to manage in a busy clinical practice. A Danish national survey performed by the General Practitioners' Organisation (PLO) in 2019 showed that almost half of the general practitioners (GPs) felt moderately to severely burned out.[16] Another study by the PLO investigated burnout in relation to their patients' degree of multimorbidity, and here, the results indicated a positive correlation.[17] The proportion of elderly polypharmacy patients is increasing, and based on the PLO's study, it can be expected that the pressure on GPs will only increase in the future. Therefore, there is an increasing need to investigate efforts that can support general practice - especially by easing the workload regarding multimorbid patients with polypharmacy, e.g., shift of tasks to other healthcare disciplines.[18,19]

There is limited knowledge about the performance of medication reviews carried out in general practice and especially under the

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leadership of hospital clinical pharmacists. In previous studies, it has been shown that MR interventions targeting polypharmacy patients in primary care can be coordinated by a hospital clinical pharmacist (CP).[20–22] The MR interventions utilised a CP to coordinate the MR intervention in order to provide pharmacologic support, reduce the GP's workload, and secure a coherent treatment for the individual patient.[20–22] The MR interventions had an average degree of implementation of medicine changes accepted by the GP of approximately 45 %, which is undesirably low.[20–22] Therefore, there is a continuous need to further refine MR interventions in the primary healthcare sector, including general practice. Furthermore, it has not previously been shown how a CP from a hospital department of clinical pharmacology experienced in MR and with access to pharmacology and toxicology experts (i.e., clinical pharmacologists) could optimize MR interventions by being posted for a longer period in a general practice clinic and thus become part of both the clinic and patient base.

An intervention involving different healthcare professions collaboration across sectors can be characterised as a complex intervention due to the content of several interacting components.[23] When developing complex interventions, it is essential to describe the process of the different developing steps to ensure transparency and avoid research waste from interventions that never impact healthcare in a real-life setting.[24,25] The development phase of a study is vital to increase the success rate of the future implementation of a new complex intervention. A thorough development phase increases the chances of identifying factors promoting or inhibiting a new practice and will likely enhance the understanding of the intervention development process.[26–28]

To optimize use of MRs in primary care by designing a MR intervention collaboration model for the benefit of general practice with the involvement of hospital-based CPs, the UK Medical Research Council (MRC) framework for developing complex interventions was used.[23,29] Thus, this study aimed to develop an interdisciplinary, collaborative and clinically feasible MR intervention model between primary and secondary healthcare in Denmark. In addition, the present study aimed to describe the steps of developing and tailoring an MR intervention targeting general practice and polypharmacy patients to ensure transparency and transferability to allow the same type of delevelopments in other settings internationally.

2. Methods

The CP who introduced the MR intervention model in general practice possed competencies in rational pharmacotherapy and clinical pharmacology and was responsible for the following tasks:

- Structure the organisation of MRs of polypharmacy patients in general practice
- Conduct medication reviews in collaboration with GPs, clinic staff and patients
- Enhance patient involvement by shared decision-making
- Improve implementation of medication changes and treatment consistency by adding additional resources to the clinic

A stepwise approach inspired by the MRC framework for developing complex interventions was utilised.[23,29]

The MRC framework is divided into four phases: development, implementation, evaluation, and feasibility.[29] These phases are not restricted to a specific order and can be repeated several times if uncertainties remain unresolved. Each phase has a standard set of core elements – considering context, developing, engaging stakeholders, identifying key uncertainties, refining the intervention and economic consideration.[29] The present study used the MRC framework phases *development* and *feasibility*. The core elements consisted of: context consideration; stakeholder engagement; key uncertainties identification; and intervention refinement.[29]

The phases *development* and *feasibility* included four steps: 1) intervention drafting, 2) expert opinion, 3) pilot testing and 4) pilot evaluation (Fig. 1). In each developing step, the MR intervention was adjusted based on the findings from the previous step.

2.1. Development phase

2.1.1. Step 1: intervention drafting

In step 1, the intervention context was considered by reviewing MR interventions from the authors' previous experiences as well as relevant literature. The literature was analysed to inspire the first draft of the MR intervention.

Literature was found by searching literature databases for original research on MR intervention studies in a primary care setting, including the utilisation of CPs and a focus on patient involvement.

2.1.2. Step 2: feedback from expert opinion panel

In step 2, the first draft of the intervention was reviewed by an expert opinion panel consisting of specialists in clinical pharmacology and clinical toxicology, CPs from the Department of Clinical Pharmacology at Copenhagen University Hospital Bispebjerg (DCPC) experienced in MR, and consultants affiliated with the organisation 'Quality in General Practice in the Capital Region' (KAP—H), which is a collaboration between PLO, and the Capital Region of Denmark promoting quality in general practice. The expert opinion panel was presented with the first draft of the MR intervention and asked to provide feedback on clinical feasibility, resource- and responsibility distribution between different healthcare professions in the clinic, the sequence and content of the subelements in the MR intervention, method optimisations and improvement proposals. The intervention draft was adjusted accordingly.

2.2. Feasibility phase

2.2.1. Step 3: pilot testing

In step 3, the intervention was tested in two general practice clinics. The MR intervention was open for adjustments if the clinic found it necessary at any time during the testing phase. Adjustments could be made if the GP clinic staff or the patients verbally expressed concerns or wishes for alternative procedures. Therefore, the GP clinic staff had a high degree of influence. Any adjustments to the MR intervention was recorded to analyze the types of change.

2.2.2. Step 4: pilot evaluation

In step 4, the pilot test of the MR intervention was evaluated based on an analysis of quantitative MR data such as characteristics of enrolled patients, medication change suggestions from the CP, and the degree of acceptance and implementation rates of these by the GP.

3. Results

3.1. Developmentp

3.1.1. Step 1: intervention drafting

The CPs from the DCPC had previous experience conducting MRs in the primary healthcare sector (i.e., general practice and nursing homes).[20–22] These studies involved an MR intervention for polypharmacy patients led by a CP in close collaboration with a GP or an interdisciplinary team of different healthcare professionals. In the studies, five main factors that influenced a successful MR implementation were identified, which inspired the new MR intervention drafting[20–22]: (1) CP process coordination, (2) limited GP resources, (3) utilisation of different healthcare professions, (4) challenging patient involvement and (5) sufficient project introduction.

The identified five main factors influencing successful MR implementation were used as topics in a literature search. Twelve articles covering medication review intervention studies in a primary care context, including the utilisation of a CP or a focus on patient

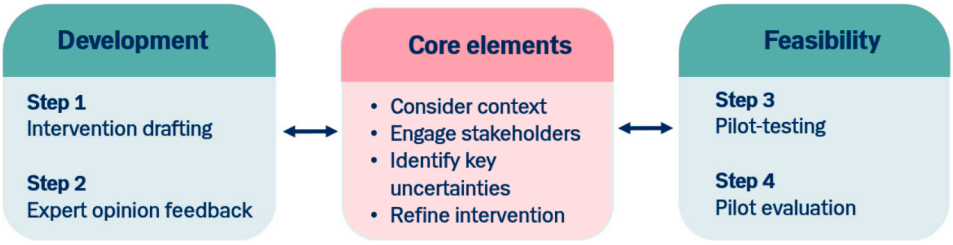

Fig. 1. The developing process inspired by the MRC framework.[23,29]

involvement, were identified. Here, especially the utilisation of CPs to account for limitations in GP resources[30–35] and suggestions for improved patient involvement[32,36–41] were recurring themes.

In the UK, CPs have worked with GPs for over two decades to free GP time and capacity.[30,33–35] A more recent English study from 2022 anchoring CPs in general practice showed that CPs could save GP time.[31] In 2020, the Region of Northern Jutland in Denmark initiated a project in the primary healthcare sector with an interdisciplinary effort between GPs, nurses, CPs, and patients.[32] The results showed that CPs collaborating with the GPs could enhance medication quality and reduce inappropriate medication.[32]

The study from the Region of Northern Jutland in Denmark also showed that approximately 30 % of the proposed changes consisted of corrections due to discrepancies between the medical journal and the patient-informed current medication.[32] The MR intervention was therefore planned to contain a medication reconciliation sub-element to ensure a correct and up-to-date medication list.

Several studies suggest that involving patients in joint decision-making regarding their medication should be a mandatory part of an MR, as patients may achieve an increased quality of life and show increased compliance.[36–39] Increasing patient participation in medical consultations can improve patient recall of information, adherence to recommendations and improved clinical outcomes.[40,41]

Altogether, the lessons learned from the authors' previous medication review experience and the literature search inspired the first draft of a hospital-based CP-led MR intervention (Table 1 and Fig. 1) to contain extra focus on four main themes:

1. Including medicine reconciliation
2. Accounting for limited GP resources
3. Prioritising patient involvement
4. Securing productive interdisciplinary communication and collaboration

3.1.2. *Step 2: feedback from expert opinion panel*

The MR intervention drafted in step 1 (Table 1) was presented to an expert opinion panel in step 2.

The expert opinion panel added three exclusion criteria for participating patients: patients with active malignant disease, known dementia and patients found unsuitable for participation in the intervention by the clinic. They argued that patients with active malignant disease and dementia often are more disabled by their disease compared to other polypharmacy patients, which may influence their capacity to participate in an MR intervention. In addition, the experts argued that the GP clinics should be able to exclude patients they found unsuited to participate based on their unique knowledge of the patient's personality, history, and personal life.

The expert opinion panel wanted the medication reconciliation to include the patient's explanation of the reason for taking the medication, so an extra focus on this was added to the medication reconciliation.

The expert opinion panel did not want the MR to be conducted at the patient's yearly check-up consultations, as they assessed it would make the intervention too rigid and less flexible. The MR was therefore nor restricted to the yearly check-up consultation, but planned whenever the clinic or the patient had a need.

Table 1
Overview of the medication review intervention sub-elements at step 1 intervention drafting. General practitioner (GP). Clinical pharmacist (CP).

Intervention sub-element	Who	Why	How
Kick-off meeting	GP, nurse, and CP	To align resource and time consumption expectations and clearly define the purpose and responsibilities.	Meeting in the GP clinic.
Introductory meeting	Entire GP clinic and CP	To make the clinic employees and the CP more familiar.	Meeting in the GP clinic.
Patient selection and inclusion	Nurse and CP	To ensure that the most relevant patients were selected.	*Inclusion criteria:* Polypharmacy patient (≥ 5 prescription drugs daily) *Exclusion criteria:* Lives in long-term care facility Terminal
Patient invitation	Clinic staff or CP	To emphasise collaboration between CP and clinic.	Telephone contact.
Medication reconciliation	CP and patient	To update the patient's medication list including prescription medications, over-the-counter medications, herbal remedies, vitamins, and nutritional supplements.	By a conversation at a physical meeting in the GP clinic.
Medication review	CP	To optimize the pharmacological treatment.	The CP wrote suggested medication changes in the patient record.
Conference	GP and CP	To align the suggested and accepted medication changes between GP and CP.	The CP presented medication changes to the GP, and discussed final recommendations.
Consultation	GP, CP, and patient	To involve the patient in decisions about their pharmacological treatment to enhance their acceptance of suggested medication changes.	By a conversation at a physical meeting in the GP clinic.
Medication conversation	CP and patient	To remove some of the burden from the GP and increase patient adherence.	By a conversation at a physical meeting in the GP clinic.
Phone follow-up	CP and patient	To ensure continued patient adherence and tolerability to medication changes.	Telephone contact.

It was also pointed out by the expert opinion panel that the consultation and medication conversation should be timely connected, so that the patient did not have to appear unnecessarily in the GP clinic. The MR intervention was adjusted accordingly.

3.2. Feasibility phase

3.2.1. Step 3: pilot testing

In step 3, the MR intervention was tested in two GP clinics, who were encouraged to give feedback during all sub-elements of the MR intervention. The participating patients were also asked to give feedback at a final telephone follow-up. However, no patients gave feedback that initiated adjustments to the MR intervention, as the feedback was an affirming sort that encouraged continuation of the planned intervention. The participants' feedback was divided based on whether they facilitated passive or active refinements (Table 2). Passive refinements were defined as parts of a natural workflow without any active decisions to change, whereas active refinements were based on a thought-out and premeditated decision to change.

3.2.1.1. Passive change. Only the GP and the clinic nurse were invited to "The kick-off meeting". However, in both clinics, all clinic employees were present anyway. This happened in one of the clinics since it only consisted of one GP and one nurse. In the other clinic, all clinic employees showed up, possibly due to a miscommunication or the fact that "The kick-off meeting" was held in the lunch room directly after the lunch break.

After the CP prepared the MR as planned in step 2, the CP should write suggestions for medication changes directly into the electronic patient record system by adding a "pharmacist's note". However, this was unnecessary, as the GP recorded changes themeselves anyway in the system during the CP and GP conference. This was advantageous, as the GP would formulate the treatment changes and plans themselves in their own words.

It was intended that after "The consultation" between GP, patient and CP, the CP should take the patient into an adjacent room and have a "Medication conversation" with a practical explanation of the medication changes. However, when the CP took action to leave "The consultation" with the patient to start "The medication conversation", the GPs suggested continuing the conversation together. As a result, the GP's time spent on the patient was extended, and "The medication conversation" was hurried. "The medication conversation" was thus merged with "The consultation" and held as a direct extension of the consultation, where the GP remained in the room.

At the end of the MR intervention, it was the idea that "The telephone follow-up" could be repeated several times if the medication change would require longer follow-up, such as a tapering process. However, only one follow-up phone call for the included patients was deemed necessary, as no changes to medication requiring tapering, such as addiction-causing medications, were made, and only one telephone called was thus made.

3.2.1.2. Active change. According to the expert opinions (step 2), it was intended that the CP, in collaboration with the clinic, should select and prioritise relevant polypharmacy patients based on the (in-)appropriateness of their drug treatment. However, this became a practical challenge in terms of coordinating the attendance of the CP and clinic staff. Therefore, it was decided that the clinics should select the patients themselves, as they could better assess which patients could benefit most from an MR intervention.

The clinics wanted to exclude immobile patients, patients who had dose-dispensed medicine or were not Danish-speaking. These criteria were based on the notion that recruiting patients should be as easy as possible due to the short timeframe of the project. Hence, providing transportation aid, translator assistance, and manually changing automatised dose-dispensed medication was assessed to make the inclusion process more difficult.

As all clinic employees were informed about the pilot testing at "The kick-off meeting", it was suggested by the CP to change the focus of "The introductory meeting" to include training of the CP in the clinic's IT medical record system which was therefore done. However, one could have considered a model where CP training in the medical record system occurred outside the clinic (e.g., directly at the IT system provider).

Figure 2 indicates which MR intervention sub-elements were refined and who the sub-element was planned to involve.

Table 2
Overview of types of changes to the medication review intervention.

Passive	Active
Clinic staff at the kick-off meeting	Introductory meeting converted to IT training
Medication review record-keeping	Clinic staff making the patient selection
Merging of consultation and medication conversation	The patient inclusion
Number of phone follow-ups	

3.2.2. Step 4: pilot evaluation

In step 4, the pilot test of the MR intervention was evaluated based on an analysis of quantitative MR data. From the two participating GP clinics, 26 polypharmacy patients were included – 12 and 14 patients, respectively. Of the 26 included patients, four dropped out due to worsening illness, lack of mobility or non-attendance. MRs were thus carried out and completed for 22 polypharmacy patients.

An overview of the included patient characteristics, their prescribed drugs and type of medication change suggestions are presented in Table 3. The GPs' acceptance rate of suggested medication changes was high i.e., 87.5 %. However, not all medication changes were accepted by the patients (acceptance rate 78.9 %) at the medication consultation (due to, e.g. objections to deprescribing painkillers, sleeping medications, or stomach acid-related medications). Patient involvement was an essential factor in this study, so medication changes were not implemented without the patients' acceptance.

Altogether, nine refinements were made to the MR intervention from the development and feasibility phases. Two of the types of refinements concerned more than one intervention sub-element (i.e. "timely connected" and "merged") (Fig. 2).

4. Discussion

The pilot-testing step 3 resulted in most refinements of the new developed and feasibility tested MR model ($n = 6$). This was not surprising, as pilot testing is a fundamental method for establishing background for future studies, and feasibility explorations are crucial for assessing optimal content and delivery.[24,42] In the following, the more fundamental changes are discussed.

4.1. Merging 'The Consultation' with 'The medication conversation'

Even though refinements were expected in the pilot-testing step, it was surprising how many passive changes occurred, especially the merging of the consultation and the medication conversation. The division of 'The consultation' and 'The medication conversation' sub-elements was planned to remove some of the burden from the GP, by letting the CP handle any discussions of practical medication changes at 'The medication conversation'. The reason why the division of the two sub-elements did not work as intended in the two participating clinics was unsure. Still, some possible explanations could be that the GP did not understand the purpose of dividing the meetings, the GP did not have a need for handing over the assignment, a reluctance from the GP to pass on control to the CP or a lack of trust from the GP to the CP. The

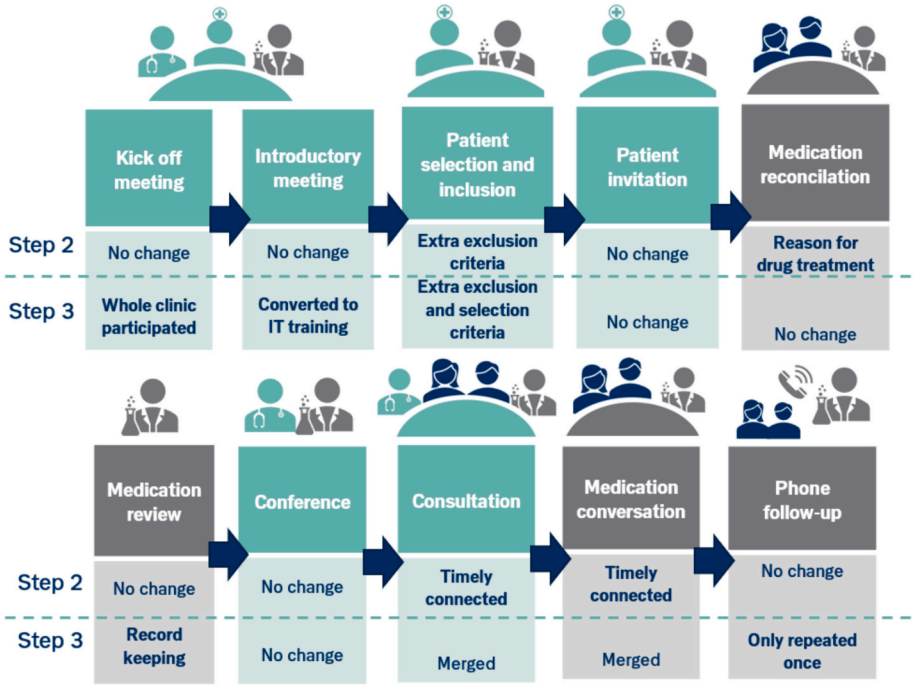

Fig. 2. Overview of the sub-elements in the MR intervention and implemented refinements after step 2 "feedback from expert opinion panel" and step 3 "pilot testing". Participants are assigned, where the clinic staff is green, the clinical pharmacist is grey, and the patient and relatives are blue. Refinements are highlighted in bold. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3
Characteristics of patients ($n = 22$) and medication changes.

Patient characteristics	**Numbers**
Age	44–91 (70 average)
Female sex	15 (68 %)
Male sex	7 (32 %)
Medication changes	**Numbers**
Total number of prescribed drugs	233 (10.6 pr. patient, average)
Clinical Pharmacist medication change proposals	152 (6,9 pr. patient, average)
Accepted medication changes by GP	133 (87.5 %)
Accepted medication changes by GP and patient	120 (78.9 %)
Implemented medication changes*	87 (72.5 %)

* The implemented medication changes were calculated based on the number of accepted medication changes by GP and patient ($n = 120$).

pilot-testing phase took place over a restricted period, which could have contributed to a low degree of trust, as the CP and the GP may not have had sufficient time to evolve a trustful relationship. A previous study by Lee et al. (2019) emphasised that information sharing, professional understanding, and trust between healthcare professionals are essential elements of safe and effective medication.[42] In the future, refinement of the MR intervention should include even more focus on establishing trustworthy working relationships between all participants.

4.2. Reduction of phone follow-ups

Another surprising passive change identified in step 3 was the number of phone follow-ups. The MR intervention was planned to include several phone follow-ups with the participating polypharmacy patients to ensure patient adherence and tolerability to medication changes over time. However, only one follow-up phone call was deemed necessary for the included patients, as no changes to medication requiring longer tapering, such as addiction-causing medications, were made. The exact reason for this was difficult to determine. As the pilot-testing step ran over a limited period, the clinics excluded patients having unstable disease courses. This might have led to a selection bias. The patient selection process should be refined in the future to include patients with the highest needs. Furthermore, an MR intervention should extend over longer time to secure adequate time to follow up on medication tapering procedures.

4.3. Acceptance rate

The study completion rate, degree of acceptance and implementation degree indicated that the new MR intervention was feasible in clinical practice. The GPs implemented many medication changes directly in the electronic medicine record system during the medicine conversation consultation. This was assessed as a positive approach to ensure high implementation, as the GP could obtain the patient's verbal consent to the proposed amendments and professional advice from the CP. Surprisingly, the patient acceptance rate was lower compared to the acceptance rate of the GPs'as in the literature, it has previously been found that patients prefer deprescribing when it is recommended by their GP.[43–45] In the future, time should be set aside to investigate the lower acceptance rate for patients compared to GPs, as the non-accepted medication changes seemed essential to implement to increase the appropriateness of the patient's medications.

4.4. Future perspectives

After carrying out a stepwise approach to develop a complex MR intervention inspired by the MRC framework, it could be suggested that the patients should have been involved in the intervention development already from step 1 instead of only in steps 3–4. It cannot be ruled out that early patient involvement would have meant more refinements, resulting in a more sustainable MR intervention (e.g. with inclusion criteria that better fit the frail, polypharmacy patients' needs and an increased patient acceptance of medication changes). Furthermore, it should be emphasised that only two of the four phases from the MRC framework for developing complex interventions[29] were utilised in the present study. However, according to theory, the framework can be initiated and finalised at any phase and is intended to be used

continuously.[29] Therefore, it is intended to further refine the present MR intervention in future feasibility evaluation and implementation studies.

5. Conclusions

This study described the steps in developing and tailoring an intervention targeting general practice to enhance interdisciplinary collaboration with CPs, provide professional support and reduce workload concerning MRs for polypharmacy patients in Denmark.

The results from the present study complement the increasing amount of research on how to develop a complex intervention with a particular focus on MRs targeting general practice and polypharmacy patients. It is evident from this study that a comprehensive developing phase gave relevant inputs for intervention refinements. These refinements guided the tailoring process, resulting in a patient-centered MR intervention with an increased focus on collaboration between GPs and CPs and patient involvement in decision-making. This is believed to entail greater patient satisfaction and adherence. The transparency and transferability in the development of this intervention is hoped to inspire others to transfer these findings to other settings concerning complex MR intervention development.

Ethics approval and consent to participate

The study was conducted in compliance with the Helsinki Declaration in its latest form, good clinical practice guidelines, and followed the rules for informed consent. According to Danish legislation and defined in "Danish Act on Research Ethics Review of Health Research Projects, Sect. 2" this trial constitutes a qualitative improvement study and does not directly interfere with patients concerning novel treatments, which does not require external monitoring nor ethical approval according to the Committee Act, Sect. 1, subsection 4. The Regional Ethical Committee was informed about the trial and waivered ethical approval (Journal no: F-22069951). Written informed consent was obtained from all patients involved in the study as well as all participating clinic staff and general practitioners, ensuring confidentiality of data and anonymity of participants. It was stated that participants could withdraw from the study at any time.

Consent for publication

Not applicable.

Availability of data and materials

The dataset supporting the conclusions of this article is included within the article.

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CRediT authorship contribution statement

Sara Sommer Holst: Writing – original draft, Validation, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Johanne Mølby Hansen:** Writing – review & editing, Methodology. **Susanne Kaae:** Writing – review & editing, Methodology. **Charlotte Vermehren:** Writing – review & editing, Supervision, Resources, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no competing interests.

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