Effective deprescribing in primary care without deterioration of health-related outcomes

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January 31, 2023

Abstract

Medication reviews focusing on deprescribing can reduce potentially inappropriate medication; however, evidence regarding the effects on health-related outcomes is scares. In a real-life, quality improvement project, we aimed to investigate how a general practitioner-led medication review intervention with focus on deprescribing affected health-related outcomes. We performed a before-after intervention study including care home residents and community-dwelling patients affiliated with a large Danish general practice. The primary outcomes were changes in self-reported health status, general condition, and functional level from baseline to 3-4 months follow-up. Of 105 included patients, 87 completed follow-up. From baseline to follow-up, 255 medication changes were made, of which 83% were deprescribing. Mean self-reported health status increased from 7.3 to 7.9 (0.6 [95% CI: 0.2 to 0.9]); the proportion of patients with general condition rated as "average or above" was stable (74.7% to 80.5% (5.7% [95% CI: -3.4 to 14.9]); and the proportion of patients with functional level "without any disability" was stable (58.6% to 54.0% (-4.6% [95% CI: -10.1 to 1.0]). In conclusion, this general practitioner-led medication review intervention led to deprescribing and increased self-reported health status without deterioration of general condition or functional level in real-life primary care patients.

Introduction

The growing population of older people with multiple chronic conditions and polypharmacy challenges healthcare systems worldwide[1,2]. The term polypharmacy have no single agreed definition, but the most reported is the daily use of five or more medications[3]. Polypharmacy can provide significant health benefits to patients; however, it also increases the risk of medication-related harm[3]. Therefore, increasing focus is being placed on differentiating between appropriate and inappropriate medication rather than the number of medications alone[4].

In general, older people and people with chronic diseases are at greater risk of experiencing polypharmacy and inappropriate medication. These patient groups often require treatment for multiple chronic conditions and are more prone to experiencing adverse drug events e.g., due to drug-drug interactions and age-related alterations in pharmacokinetics and pharmacodynamics[5]. Adverse effects can have serious implications for patient in terms of reduced quality of life, hospital admission, and premature death[6]. Additionally, adverse effects can be misinterpreted as newly emerged symptoms or conditions, which can lead to further prescribing, a phenomenon referred to as "the prescribing cascade"[6].

Polypharmacy interventions as e.g. medication reviews are considered valuable to reduce potentially inappropriate medications through deprescribing recommendations[7]. Deprescribing is defined as the planned and supervised process of dose reduction or stopping of medications that might be causing harm, or which may no longer have a benefit[8]. During a medication review, the patient's complete medication list is systematically and critically reviewed in relation to indications, effects, side effects, interactions, and adherence based on leading evidence and knowledge about the patient, including individual needs and preferences[9].

In the last decade, numerous medication review intervention studies have been conducted with the aim to reduce the number of medications and improve the overall appropriateness of prescribing for patients[10]. A recent review of reviews on polypharmacy interventions in the primary care setting found that, overall, these interventions were associated with reductions in potentially inappropriate prescribing and improved medication adherence[10]. However, in medication review and deprescribing studies, outcomes are frequently medication-related (e.g., number of medications) or resource-related (e.g., cost, general practice visits, or hospitalization)[8,9]. There is limited evidence of the effectiveness of the interventions on clinical outcomes of importance to patients[10].

Therefore, in a primary care settled quality improvement project aiming to deprescribe medication through a medication review intervention, we investigated how the implemented medication changes affected health-related outcomes in real-life patients.

Methods

Setting

Danish healthcare is mainly tax-financed and includes free-of-charge access to services[11]. General practices are typically independent, physician-owned clinics, and nearly all Danes are listed with a specific general practice clinic. General practitioners (GPs) are remunerated through a mix of capitation and fee-for-services based on a national agreement between the Danish Regions and the Organisation of GPs. In Denmark, GPs are responsible for most prescriptions and chronic care management[12].

The current study was a part of a larger quality improvement project focusing on polypharmacy and communication inspired by the World Health Organisations global initiative "Medication without harm"[13]. The project was conducted in a close collaboration between the Centre for Health and Care in the Municipality of Frederikshavn, Denmark, and a large GP clinic in Frederikshavn (hereafter GPF).

The GPF is a large clinic with a strategic focus on older patients and patients with chronic diseases. The GPF has a close collaboration with the municipal and regional health services. The GPF has an affiliated population of approximately 8,900 patients, of which more than 2,300 citizens are older than 65 years. The GPF employs eight GPs, ten nurses, ten medical students, or GP trainees, a social and health assistant, a pharmaconomist, and a physiotherapist.

In the Municipality of Frederikshavn, the Centre for Health and Care runs 12 care homes, of which eleven are covered by a specific GP practice. The GPF is affiliated "care home doctor" for four of the care homes in the municipality.

Ethics

The project was approved by the Management in the Municipality of Frederikshavn. According to Danish legislation, no formal permission from the national or regional Committee on Health Research Ethics was required for this type of study, as patients were not treated inferior to usual care and no biological material was collected. It was conducted as a quality improvement project and informed consent was not required for the specific data collected. The study was conducted in accordance with the Basic & Clinical Pharmacology & Toxicology policy for experimental and clinical studies[14]. The study is in compliance with the General

Data Protection Regulation[15] and a part of North Denmark Region's record of processing activities (K2023-008). The study is registered in ClinicalTrials.gov (registered January 31, 2023, awaiting ClinicalTrials.gov ID).

Study design and population

The study was conducted in the 2-years period from the January 2020 to December 2021 using an uncontrolled before-and-after design. The study included care home residents living in selected care homes, in which the GPF was associated "care home doctors", and community-dwelling patients with chronic disease listed with the GPF.

The Chronic Care Model

In Denmark, chronic care consultations are provided to patients with one or more chronic conditions. The organisation of these consultations varies across GP clinics, depending on e.g. the size of the clinic and the competencies in the staff group[16]. In connection with this project, a new, local Chronic Care Model was drawn up for patients with one or more chronic conditions such as diabetes, chronic obstructive pulmonary disease, hypertension, heart failure, or atrial fibrillation. The overall aim of the model was to obtain sufficient depth and breadth in the chronic care consultations over a one-year period.

The new Chronic Care Model is illustrated in figure 1.

In addition to the Chronic Care Model, a new cross-sectoral communication model was established. This included regular contact between the care home nurses and the GPF (weekly by telephone, e-mail, visit, and/or online conference); support opportunity from a pharmacist employed in Frederikshavn Municipality; and support opportunity from a specialized geriatric department at the hospital every second week.

figure 1 near here

Care home residents

The four care homes affiliated with the GPF accommodate 190 residents. Of these, 128 were patients in the GPF (the remaining residents kept their family doctor when moving into the care home) (figure 2). In the period from March 24, 2020, to June 16, 2021, the intervention was offered to new residents and residents that had not yet attended a consultation focusing on pharmacological treatment in The Chronic Care Model.

Community-dwelling patients with chronic disease

The GPF had 1,800 community-dwelling patients with chronic diseases listed in the period 2020-2021 (figure 2). From June 3, 2020, to November 16, 2021, patients were invited for the consultation focusing on pharmacological treatment in the month of their birthday and, thereby, included randomly and consecutively throughout the study period.

figure 2 near here

Intervention

In this study, the focus was placed on the annual consultation focusing on pharmacological treatment in the Chronic Care Model. This specific consultation constituted the "intervention". It included a structured review of the patient's health state, in addition to a structured medication review with a focus on appropriate medication and deprescribing. Medication changes were registered as deprescribing (dose reduction or stopping/pausing of medications), new prescription, and other medication changes (e.g., dose increase or change in dosing interval). Additionally, issues such as treatment plans for addictive drugs, dose dispensing, resuscitation, life-prolonging treatment, and terminal care were discussed when relevant. A selected group

of providers (two doctors and three nurses) from GPF were responsible for conduction of the intervention in the present study. The GPs performed the medication reviews. In care home residents, the GPs also carried out the related consultation. In community-dwelling patients, the nurses were responsible for the consultations with the GPs as close support.

Data collection and outcomes

Before and 3-4 months after the consultation focusing on pharmacological treatment, information regarding medication changes and health-related outcomes were collected during consultations.

Health-related outcomes were collected by a nurse or the patient's contact person together with the patient and, if possible, also relatives. The primary outcome was changes from baseline to 3-4 months follow-up in 1) self-reported health status (on a scale from 1 to 10). Secondary outcomes were 2) general condition (rated on a 5-point Likert Scale as "much below average", "below average", "average", "above average" and "much above average"); and 3) functional level (rated on a 5-point Likert Scale as "independent", "frail", "mild disability", "disability" and "severe disability"). General condition and functional level were determined by clinical evaluation. The outcomes were developed with inspiration from Garfinkel[17].

Statistical analysis

Descriptive and non-parametric data were summarized and displayed by medians [inter quartile range (IQR)] for continuous data and as proportions (percentages) for categorical data. Parametric data was displayed by means and standard deviation (SD). Paired t-test was used to compare means of self-reported health status at baseline and follow-up. McNemars test was used when comparing paired proportions for categorical variables. General condition and functional level were dichotomised and analysed as proportion of patients with general condition rated as "average or above" (defined as: "average", "above average" or "much above average"). The proportion of patients with functional level rated as "without any disability" was defined as the categories: "independent" or "frail". Statistical analyses were performed in STATA 17. Statistical significance was indicated by a two-tailed p value of 0.05.

Results

Figure 2 provides an overview of the flow of the participants in the study. In total, 105 patients were included, of which 87 completed follow-up. The study population was composed of two sub-groups: care home residents (31%) and community-dwelling patients with chronic diseases (69%). During the intervention period, 18 patients were lost to follow-up for various reasons.

Eight care home residents were lost to follow-up. Four of them died before follow-up. By clinical evaluation, it was concluded that none of the deaths were directly related to the medication review intervention (e.g., one of the residents died from/with COVID-19). Other four patients were unable to collaborate on follow-up questionnaires. None of the included patients were admitted to the hospital between inclusion and follow-up.

Ten community-dwelling patients were lost to follow-up; five did not show up for the consultation and for five other patients, the follow-up questionnaire data was not collected for unspecified reasons. Four of the 60 included patients were admitted to the hospital during the intervention period. By clinical evaluation, it was concluded that none of the admissions were directly related to the medication review intervention.

Baseline characteristics of the total study population and the two sub-groups are provided in Table 1.

Table 1 near here

Medication changes

Total population

From baseline to follow-up, 255 medication changes were effectuated, of which 83% (n=212) were deprescribing, 15% (n=38) were new prescriptions, and 2% (n=5) involved other medication changes (i.e., dose increase or change in dosing interval). The median ([IQR]) medication changes per patient was 2 [2-4]. Medication changes were maintained for 88.5% (n=77) of patients at follow-up and partly maintained for 10.3% (n=9) (e.g., if several changes were made for one patient, but only some of these changes were maintained). For one patient, the suggested medication changes were not implemented for unknown reasons.

Care home residents

In the care home residents, 93 medication changes were made, including 83% deprescribing (n=77), 15% new prescriptions (n=14), and 2% other medication changes (n=2) (dose increase). Medication changes were maintained for 92.5% (n=25) of patients at follow-up and partly maintained for 7.5% (n=2). For one care home resident, treatment with an antidepressant was stopped as part of the intervention. However, as this resulted in reduced functional level, the antidepressant was re-prescribed, and the patient returned to a stable functional level.

Community-dwelling patients with chronic disease

In the community-dwelling patients, 162 medication changes were made, hereof 83% deprescribing (n=135), 15% new prescription (n=24), and 2% other medication changes (n=3) (dose increase or change in dosing interval). Medication changes were maintained for 87% (n=52) of patients at follow-up and partly maintained for 12% (n=7). For one patient, the changes were not executed for unknown reasons.

Health-related outcomes

Health-related outcomes for the total study population and the two sub-groups are presented in Table 2. In the total study population, mean self-reported health status significantly increased, while the proportions of patients with general condition rated as “average or above” and with functional level rated as “without any disability” remained stable. Overall, the subgroup analyses showed similar trends in self-reported health status and functional level, although statistical significance was only reached for self-reported health status in community-dwelling patients due to the small sample size of the sub-groups. Noteworthy, among care home residents, the proportion of patients with general condition rated as ”average or above” increase non-significantly with 18.5 percentage points, in contrast to no difference among community-dwelling patients.

Table 2 near here

Discussion

Main findings

In this study, the medication review intervention with focus on deprescribing was feasible as part of the developed Chronic Care Model in real-life primary care. The intervention led to 255 medication changes, of which more than 80% were deprescribing. The medication changes were maintained during the 3-4 months follow-up period for nearly all patients. At follow-up, we found that patients’ self-reported health status had increased, while general condition and functional level remained stable. Generally, similar trends were observed in the sub-group analyses for both medication-related and health-related measures.

Comparison with existing literature

In recent years, several systematic reviews have synthesised the evidence on the effectiveness of deprescribing interventions. These reviews have focused on older people in general[18] or in different settings such as hospitals[19], nursing homes[20,21], or primary care[22,23]. Overall, the existing evidence suggests that deprescribing is feasible, safe, and ,generally, effective in reducing the number of inappropriate prescriptions[22,24]. A systematic review of deprescribing trials in primary care showed that the proportion of patients who successfully stopped their medication varied from 20% to 100%[22]. In 19 of the 27 included studies, more than half of the participants had successfully stopped medications. In our study, the majority of the medication changes were deprescribing. Comparable to our findings, studies of deprescribing trials have shown average discontinuations per patient between 2.8 and 4.4[25–28]. Additionally, we found that medication changes were maintained for nine of ten patients at 3-4 months follow-up indicating successful deprescribing.

It is well-known that deprescribing can also lead to patient-harm in terms of adverse drug withdrawal events or return of symptoms (e.g., increased pain levels or mood changes), for which the medication was originally prescribed. Importantly, the majority of these harms can be minimized or even prevented by using a patient-centred deprescribing process with planning, tapering, and close monitoring during and after medication withdrawal[29]. This was possible in our study where a patient-centred deprescribing process was undertaken as part of routine chronic care management in general practice in close collaboration with the Centre for Health and Care in the Municipality of Frederikshavn. We found that the intervention led to an increase in self-reported health status from baseline to follow-up. Additionally, general condition and functional level remained stable. In the subgroup analyses, similar trends were seen in health-related outcomes among care home residents and community-dwelling patient.

However, an interesting finding was the considerable, non-significant increase in general condition among care home residents. Although non-significant results should be interpreted with caution, this signals that it may be possible to improve general condition through medication reviews with focus on deprescribing in this vulnerable patient group. Oppositely, no signal of change in general condition was observed among community-dwelling patients, which may partly be explained by the high proportion (80%) rated as "average or above" at baseline, which left limited room for improvement.

Few studies have been able to demonstrate an effect of medication review interventions on health-related outcomes of importance to patients. A recent example is the DREAMeR study, in which community-dwelling older persons with polypharmacy were offered patient-centred medication reviews versus usual care[30]. This study showed improved quality of life measured by the EQ-Visual Analogue Scale and reduced health problems with a moderate to severe impact on daily life. However, no effect was seen on quality of life measured by the EQ-5D-5L or on total number of health problems. This highlights the complexity of measuring improvement in the wellbeing of older and multimorbid patients.

In a recent review by Ibrahim et al., the current evidence for deprescribing among older people living with frailty was reported[24]. Of six included studies, three reported a positive impact on clinical outcomes such as depression, mental health status, function, and frailty. However, results were mixed on falls and cognition, and no significant impact was demonstrated on quality of life[24]. The latter echoes previous findings across a range of studies conducted in primary care using various quality-of-life measures[10,31–33]. These mixed results call for consideration regarding whether we are using the right measures to capture potential benefits of interventions at a patient-level. Moreover, they call for consideration regarding whether a lack of statistically significant improvements in health-related outcomes should be viewed more positively, as deprescribing without deterioration of patient health may also be a desirable outcome.

Primary care as a setting for deprescribing

In many countries, GPs are responsible for chronic care management in primary care and the relational and managerial continuity in this setting provide an optimal basis for deprescribing[34]. In this real-life quality improvement project, the GPs in the GPF decided to construct a new Chronic Care Model, including the

person-centred medication review intervention, to systematize the care of patients with chronic diseases. It has been advocated to integrate clinical practice guidelines more systematically into existing care models to minimise the burden on health systems and primary care providers[35]. Thus, the developed Chronic Care Model employed in this study may have been an important enabler for intervention implementation.

It was originally planned that a pharmacist employed by the municipality would perform an initial medication review and present the findings for the GP, who would then implement clinically relevant medication changes. However, it soon became clear that the GPs performed the medication reviews themselves and took ownership of the process in close collaboration with the pharmacist, the nurses, and frontline staff at the care homes. Ownership, flexibility, and autonomy of the primary care providers have been identified as important enablers for implementation of clinical practice guidelines[35]. Additional enablers reported include a well-organised practice and clarification about the role of primary care providers in disease management. Importantly, multidisciplinary collaborations between different care levels should also be considered to support the primary care providers' recognition of their role and responsibility for clinical practice guidelines implementation[35]. In our study, this was attempted through the cross-sectoral communication model that was established alongside the Chronic Care Model.

The approach taken in our study might be inspirational to other Danish municipalities as well as other countries with a similar organization of primary care. However, our results might not be directly transferable, as primary care medication management constitutes a complex health care system. It encompasses different types of healthcare organization (e.g., home care, care homes, general practices) and health care providers (e.g., nurses, pharmacists, GPs)[36]. Furthermore, both private and public stakeholders exist in most countries and may be highly dissimilar in their organization and available resources. Thus, the specific context, in which the intervention is to be implemented, should be fully considered, as adaptions may be needed to achieve success and sustainability[35].

Strengths and limitations

A major strength of this study was the real-world primary care setting, in which the study was conducted. The recruitment and retention of elderly patients in clinical trials provide many challenges[37]. Thus, in contrast to the highly selected patient groups often included in randomized controlled trials, our study population more likely represent an unselected, real-world patient population, which strengthen the generalizability of our results. Further, it represents real-world implementation of a complex intervention, which suggests that our intervention is feasible and realistic in similar contexts. Even though the study was conducted during the COVID-19 pandemic and the associated restrictions, it was possible to implement the Chronic Care Model and include both care home residents and home-dwelling patients in the intervention.

A major limitation of the study is that no control group was included to compare results against usual care in similar GP clinics. Thus, no causal links can be made between the intervention and our results. Another limitation was the follow-up period of 3-4 months. As medical conditions in older patients are unstable[37], more medication changes, incl. potential restarts as well as additional deprescribing, would have been captured if we had used a longer follow-up period. However, we expect that most potential harms of the implemented medication changes would have been manifested during the 3-4 months period. Four care home residents died before follow-up. However, by clinical evaluation it was concluded that none of these deaths were directly related to the intervention. Furthermore, the incidence of deaths was not higher than expected in care home residents in general [38].

Conclusion

In this real-world quality improvement study settled in primary care, we found that a systematic GP-led medication review intervention led to deprescribing and increased self-reported health status without deterioration of general condition or functional level among care home residents and community-dwelling patients with chronic disease. These results add new aspect to the existing literature and show that it may

be possible to improve patients´ self-perceived health status through medication review interventions with a focus on deprescribing.

Acknowledgements

No funding was received.

Conflict of Interest Statement

None declared.

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Figure legends

Figure 1. The annual consultation flow in the Chronic Care Model.

The new Chronic Care Model consists of three consultations conducted with four-months intervals focusing on 1) pharmacological treatment, 2) external loads, and 3) lifestyle issues, respectively. Additionally, a fourth ad hoc consultation, "Taboo", was introduced to cover typical taboo subjects (e.g., impotence, incontinence, and psychological issues) when needed.

Figure 2. Study inclusion flow-chart.

An overview of the study inclusion divided into the two sub-groups: Care home residents and community-dwelling patients with chronic diseases.

Tables

Table 1. Baseline characteristics of the study population.

	Total population (n=87)	Care home residents (n=27)	Community-dwelling pat
Age, median [IQR]	81 [72-87]	88 [82-92]	76 [71-83]
Gender (females), n (%)	53 (61)	17 (63)	36 (60)
Number of medications, median [IQR]	9 [6-12]	11 [9-13]	8 [6-11]

IQR: inter quartile range

Table 2. Changes from baseline to follow-up in health-related outcomes.

	Total population (n=87)	Total population (n=87)	Total population (n=87)	Care home residents (n=27)	Care home residents (n=27)	Care home residents (n=27)	Community-dwelling patients (n=60)	Community-dwelling patients (n=60)	Co dw pa- tie (n=
	BL	**FU**	**Difference (95% CI)**	**BL**	**FU**	**Difference (95% CI)**	**BL**	**FU**	**Di (9 CI**
Self-reported health, mean (SD)[a]	7.3 (±2.0)	7.9 (±1.7)	0.6 (0.2 to 0.9) *	6.4 (±2.4)	7.1 (±2.0)	0.7 (-0.2 to 1.7)	7.7 (±1.6)	8.2 (±1.4)	0.5 (0.
General condition rated as "average or above", %	74.7	80.5	5.7 (-3.4 to 14.9)	63.0	81.5	18.5 (-3.1 to 40.1)	80.0	80.0	0.0 (-9 9.7
Functional level rated as "without any disability", %	58.6	54.0	-4.6 (-10.1 to 1.0)	14.8	7.4	-7.4 (-21.0 to 6.2)	78.3	75.0	-3. (-9 2.9

[a] n=24 for care home residents and n=84 for total population, as self-reported health status was unavailable for three patients. * indicates significant difference (p<0,05). BL: Baseline, FU: follow-up, CI: Confidence interval, SD: Standard deviation.